VERBATIM PROCEEDINGS

CONNECTICUT STEM CELL RESEARCH ADVISORY COMMITTEE

COMMISSIONER JEWEL MULLEN, CHAIRPERSON

JUNE 11, 2012

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. . .Verbatim Proceedings of a meeting of the Connecticut Stem Cell Research Advisory Committee held on June 11, 2012 at 8:39 a.m. at the Farmington Marriott, 15 Farm Springs Road, Farmington, Connecticut. . .

CHAIRPERSON JEWEL MULLEN: Thank you for being here. I already have a different feeling than a year ago because my recollection is last year it took us a while to get the technology going and we are already. I'm Dr. Jewel Mullen, DPH Commissioner. And I think -- well, thank you Diane for introducing yourself. I know there are some other folks here who I don't know that you all might not have had much of a chance to introduce yourselves to one another, even though you've been working and collaborating. So why don't we go around?

MS. MARIANNE HORN: I'm Marianne Horn from the Department of Public Health.

MS. DIANE KRAUSE: I'm Diane Krause from Yale University.

DR. DAVID GOLDHAMER: David Goldhamer, UConn, Storrs.

DR. ANNE HISKES: Anne Hiskes, UConn,

Storrs.

DR. MYRON GENEL: Mike Genel, Yale University.

DR. RICHARD DEES: Richard Dees, University of Rochester.

MR. PAUL PESCATELLO: Paul Pescatello, CURE Connecticut United for Research Excellence.

COURT REPORTER: I'm Tynan Cooney, the Court Reporter.

MR. RICK STRAUSS: I'm Rick Strauss, Connecticut Academy.

MS. TERRI CLARK: I'm Terri Clark, Connecticut Academy.

MS. SARA DONOFRIO: Sara Donofrio --

DR. ANNE KIESSLING: Anne Kiessling, Bedford Stem Cell Foundation.

DR. RON HART: Ron Hart, Rutgers University.

DR. GERRY FISHBONE: Gerry Fishbone --

DR. MILTON WALLACK: Milt Wallack.

DR. TREENA ARINZEH: Treena Arinzeh, New Jersey Institute of Technology.

DR. PESCATELLO: We're going to really need you to use the mic.

A MALE VOICE: Okay.

MS. MULLEN: Did you say use the mics.?

A MALE VOICE: Yeah.

COURT REPORTER: The mics. don't actually amplify.

DR. DEES: They only record?

COURT REPORTER: Yeah.

DR. DEES: Okay. Then we'll just have to shout.

A FEMALE VOICE: We have to talk more loudly because the air is so loud.

MS. HORN: I just had them turn up the air conditioning since it was already warm in here and we've got the door closed now, so hopefully it won't run this loudly all day, but we will have to speak up. We don't have anybody on the phone, we are all present and accounted for. So thank you all for your efforts and for coming in, some of you last night, and I'm sure many of you spent much of the beautiful weekend looking at grants. So we'll get started.

We have one item to deal with before we get into the grant reviews, but perhaps we ought to go over some of the ground rules first. Last year we did the grants, we started with established grants, and then we

went to group and core and then we did -- I'm sorry, and then we did seed and core. And I'm interested in having some discussion, since we didn't nail this down, about where you would like to start giving the configuration of grants this year. My recommendation might be to start with the group and core grants and then go wherever the Committee would please to go from there. So discussion on that?

DR. WALLACK: We'll go through established after that.

DR. KIESSLING: Was there a discussion on which grants we're going to actually discuss? Because at one of the meetings when I was on the phone there was some discussion about where you were going to cut off the load, which we would not discuss. Has been established?

MS. HORN: Yes. We have done a cut here in terms of the peer review scores and the amount of money that that would take into account and a percentage of the grants. So the chart that's being shown, the established from peer review 1 to 1.5 is 17.2 percent of that proposal, so I put 3.75 million. 1.5 to 2.5 would give us 41.4 percent of the established to review and take us to 8.997 million. Seeds 1 to 2 would be 13 percent at 1.4 million, the blue 2 to 2.5 33.3 percent 3.6 million and up

to 3.5 would 53.7 percent. We have 9.8 million again this year to allocate.

MS. DONOFRIO: And what about the cores and the groups?

A MALE VOICE: (Indiscernible)

MS. HORN: The cores are easy. There are two cores and they are requesting 500,000 each, so it's $1,000,000 there if we review both. There's one group proposal at 1.5 million and two disease directed, one for 2,000,000 and one for just under 2,000,000.

DR. HART: Could we go back one more time to cut off (indiscernible).

DR. DEES: But your question was at what scores should we have an individual grant discussion as opposed to ones where we should just say, does anybody want to (indiscernible).

DR. KIESSLING: Well, the nasty NIH term is triage.

DR. DEES: Yes.

MS. HORN: Yes. And remember, last year we also had a way where if a reviewer, an advisory committee reviewer, had an issue with thinking that a grant really deserved to be reviewed in more detail they can certainly make that recommendation and bring a higher scoring grant

into the discussion. And I think we agree to do that again this year as well, because we have Connecticut specific priorities and may evaluate the grants a little different than the peer review did.

DR. GOLDHAMER: I missed Richard -- Richard, could you please state what you said, I missed your comment.

DR. DEES: Well, I think Anne's question was, did we figure out where we were going to start talking about the grants individually as opposed to bringing them up if somebody wanted to. I take it that was your question?

DR. KIESSLING: Right. I mean, I think last year we decided that the cutoff was four and that anybody who wanted to talk about something that scored higher than four to bring it forward, but that unless somebody really disagreed with the peer review scores --

A FEMALE VOICE: I think that makes more sense than the cutoffs established here.

DR. KIESSLING: Yeah, well, I think this is a lot of money, I mean, but I think the ones that scored a three we would probably most likely to see if they (indiscernible).

DR. GOLDHAMER: Yeah, I think you're right

Anne. Last year, I think it was a four. This year if all grants are reviewed that are 3.5 or better, I think it was something like $24,000,000 cost. In my view, there's really not much of a difference between a grant that's .5 different in score --

DR. KIESSLING: Yeah.

DR. GOLDHAMER: -- maybe even more than that, but at least .5 conservatively. So I had thought that going through 3.5 with this provision of a nominated grant that scored more than that seemed like a reasonable -- and certainly went far enough down the list to capture the top grants for the 9.8.

DR. KISEELING: So you propose a 3.5 cut off?

DR. GOLDHAMER: Yeah. And not -- across the board, not -- any grant, regardless of category that scored 3.5 or better.

DR. GENEL: For the established?

DR. GOLDHAMER: For all grants.

DR. GENEL: Well, that's going to take us down to about 25 seeds or something like that. At 2.5 you're already down to almost 29 --

DR. GOLDHAMER: But we're basing this mostly on -- I don't know why subdividing by category

really matters.

MR. STRAUSS: Let me explain what we did here. At your last Advisory Committee meeting you had discussed looking at the top 40 percent, so we didn't -- this whole thing is just for your taking a look at based on that guidance that you discussed in your last meeting. And then when we looked at the scores they kind of fell into these two ranges, so that's why we just separated it by color. In the seed, there's a jump from 2.5 to 3.5, there's nothing -- there are no 3's. So that's why we added in that to get you to overlook 40 percent. But that's really the intent of, you know, what you're seeing here. That's all.

DR. GOLDHAMER: So you did it by 40 percent in each category?

MR. STRAUSS: For seed and established, based on your discussion that that was the guidance you were thinking about at the last meeting, as compared to, you know, going to a peer-review score.

MS. HORN: Paul?

DR. PESCATELLO: We might want to just circle back to this discussion, especially on the established and seed, because depending on what we do on the group and the core, I mean, we may or may not have a

lot of money. And we might have a lot less money and then we might want to just go with anything new or below. But I think we should do that first and then have this discussion.

DR. KIESSLING: And then some of the reviewers were conflicted among themselves and very conflicted with my thoughts.

(Laughter)

MS. MULLEN: I think we're going end up getting to that. I'm a little bit reluctant to establish this year's cut offs based on what we did last year without knowing that the distributions were identical because last year we decided a cut off based on the distribution and what we thought was going to be likely to be funded below a certain level. And we also early on tasked ourselves with a realistic number of proposals that we could review and do justice to.

DR. GOLDHAMER: I agree with that and I think this year, I don't remember the distribution from last year, but this year one of the issues I think is that the grant scores are compressed towards that lower better score end, especially for the established. And if you agree with the premise that there's little difference between a grant that scores a half a point different from

each other, then even though 40 percent only gets you to 2.5 in the established, I'm, you know, I'm not sure it makes sense to stop at 2.5 for any of the grants.

DR. HART: There's only two additional grants if we go 2.5 to 3 in the established category.

MS. HORN: So that seems to make some sense. So I'm hearing that we would like to start with the group and core and deal with those first and then perhaps circle back?

DR. HART: I'm sorry, I just read the chart so it's more than that.

MS. HORN: And circle back to this decision once we're warmed up.

DR. WALLACK: So do you want a motion before we do that on out of our packet request to change the P.I.?

MS. HORN: No.

DR. WALLACK: No. Okay. I'm sorry.

MS. HORN: Okay. I don't think there are any other preliminary matters. Yes?

MR. WILSON: Do you want me to just briefly talk about the peer review process and how the scores were finalized, or not? Does everybody need it?

MS. HORN: Is the committee interested -- I

think the committee is pretty --

MR. WILSON: Okay.

MS. HORN: -- okay? No, I think we're all set on that. I'm just reminding everybody that if you have a conflict that you've identified, I think the Yale and UConn ones are pretty clear, and I believe one other investigator recused himself from a grant with which he had a conflict. So we'll just keep those in mind, and only vote on those -- and only engage in the discussion and vote on those which you do not have a conflict. So do we have a motion to proceed this way?

DR. KIESSLING: How are we proceeding?

MS. HORN: Sorry. That was a little vague. We're going to proceed with reviewing the group grants and the core in no particular order, we could do the core first and then the group grants, and then we will come back to look at the established and seed grants and determine what the cutoff point is at that point.

DR. KIESSLING: Well, I'm never comfortable doing it that way. But that's just me. So if everybody else wants to do it that way. My enthusiasm for the core funding is always based on what other grants, you know, what are our trade-offs? So I like to go with the established investigator grants or the seed grants first

so we know how much money we have left for these bigger budget items. If that's a minority opinion, then -- and you want to review the cores first.

DR. KRAUSE: When I've been an observer in the past, the decisions about, oh, we have like 20, you know, there's only $9.8 million, but we've said yes to 20,000,000, then there is some paring down, but that kind of yes, no, maybe part can happen without keeping track of where exactly you are in the 9.8. So I would say it's fine to go ahead and start with the small category and have the discussion and then realize we might have to revisit once there are too many to fund.

MS. HORN: Okay. Further discussion?

DR. WALLACK: I'm not sure Diane. So you would want to do seeds first?

DR. KRAUSE: No. I would like to just go ahead and start with the cores and the groups because you have to start somewhere and that's the place to start.

DR. WALLACK: Oh, yeah, I agree with you. That was what the motion was that I think that I would totally agree with you.

MS. HORN: Okay. So Milt, you're moving that we start with the core and the group and return and revisit the established and seed once we have dealt with

those two in a preliminary way. Do I have a second?

DR. KRAUSE: Second.

MS. HORN: Diane second, okay. All in favor?

VOICES: Aye.

MS. HORN: Okay.

DR. PESCATELLO: Any opposed?

A FEMALE VOICE: Yeah.

MS. HORN: Okay. And again, with the caveat that anything that the Committee would like to bring forward to discuss that isn't -- doesn't fall within those parameters can be brought forward. So let's go now then to the first item on the agenda with a change of P.I. And Sara would you present this please?

MS. DONOFRIO: This is a request for a change of P.I. This is for stem cell grant number 10-SCA-16 from Dr. (indiscernible), he's the current P.I. and would like to request a change --

MS. HORN: I believe there's a C.V. that is attached with the budget revision.

MS. DONOFRIO: -- and the name change would be to P.I. Erik Shapiro. I believe that was it, just the P.I. being changed.

MR. STRAUSS: Do you need to see more?

MS. HORN: So I think you all had an opportunity to review this. Were there any concerns with this replacement of P.I.?

DR. WALLACK: Move it's acceptance.

MS. HORN: Second?

A FEMALE VOICE: Second.

MS. HORN: Any discussion? All in favor?

VOICES: Aye.

MS. HORN: Okay. Then I guess we're ready to move into the review. So starting with the core proposals. So what would you like to do? We have one at 1.5 and one at 3. Would you like to start with the 1.5?

DR. GOLDHAMER: Should we start with the Yale core?

MS. HORN: Yes. So we'll start with the Yale core, 12-SCD-YALE-01. The reviewers are David Goldhamer and Anne Hiskes.

DR. GOLDHAMER: Alright. So this is a request for one year funding for $500,000 from the Yale core facility. I'll just say a few things. Most of you know some of these details, but I'll just remind you that Haifan Lin is the director, Diane Krause is the associate director and Paula Wilson is the administrator for the core. Their plans are to continue the five more

facilities that have been in operation for now a number of years.

They ask primarily for salary support. This was a recommendation for what the Advisory Committee wanted to see last time was for most of the funding to go to salaries so most of the support goes to salaries for technical support, technical directors of several of the cores. There's also support for other technical staffing of cores. So except for I believe $70,000 that is for service contracts the rest of it is for the salaries.

As in last year's application it is well written, it extensively details the successes of the core, it notes that I think 67 investigators at Yale have used the core and it's clear that the core is essential for the stem cell programs and the number of labs at Yale. So all in all I thought that they've listened to the Committee in terms of how the money should be spent, that they justified the continued operation of the core with Connecticut -- reduced Connecticut funds and I was strongly in support of funding it for $500,000.

DR. HISKES: So I'm the second reviewer. This is Anne Hiskes speaking. I regard this as a very strong application. The Yale core has indeed been very productive over the past five years or so. The future

plans are well articulated. For example, they're going to go further investigating genetic manipulation of stem cell lines, which is where the program is at this point. I think it's very well written.

The integration of the core, the central core, would define other cores. It's praised by the reviewers, and I concur with them and so I also recommend funding.

DR. GOLDHAMER: And I'll add one more thing. We had also asked that the goal be that in the future that the cores work toward independence from Connecticut money and this grant has a nice section that describes the efforts being made, and the successes so far, in generate or in finding sources of funds outside of the state funds that includes philanthropy, cost recovery, and also there is a plan, it was unspecified, but it had gotten -- the stem cell center and the cores are strong enough to competitively apply for NIH monies for core facilities. My understanding from the reading of the application is that such higher fees are not available at this moment, but they are ready to write such grants when they become available (indiscernible).

MS. HORN: Any discussion from the rest of the committee? Do we have a motion?

DR. WALLACK: I'll second Anne's motion. I think I heard her say that she would recommend funding.

MS. HORN: So we have fund, maybe, and no, it really is preliminarily fund, preliminarily maybe, and preliminarily no. So, just as long as we understand that, that all of this can be changed. All in favor?

VOICES: Aye.

MS. HORN: Okay. I think it's the next one down

MS. HORN: Okay. 12-SCD-UCHC-01, Dr. Genel and Dr. Krause.

DR. GENEL: Well, this is the second -- this is the second core, it's the UConn/Wesleyan core. The peer review reports were not quite as glowing. I think the telling comment is at the end of the first reviewer's comments. It says, "I don't think his potential has been realized to his full capacity." One interesting aspect of this in the proposal is the mention that the Jackson Laboratory for genomic medicine will be getting going soon and the expectation is that the core will actually also serve the Jackson Laboratory, which I suspect I would guess, offers an opportunity for additional funding as well.

But my view is that the cores are essential

to the operations of the rest of the grant and I would support continued funding. We could perhaps discuss whether or not it should be at 500,000 or not, but I would support -- I would support the application.

DR. KRAUSE: I think this is an excellent application and there was -- there was a discrepancy in the scores with one of the reviewers giving it a one, and the other initially giving it a five, and then improving their score to a three. But on reading both the grant and the comments of the reviewers, I think that the reviewer who gave it a worse score really didn't understand the true purpose of these cores and I think that this core is excellent. They're providing core services. They're making IPS for people at a really, really good cost. They're state-of-the-art technology and they're a beautiful core. I highly recommend funding it.

And then I'll put in a little bit of a comment that's going to be relevant to a lot of these reviews, which is that the reviewer who didn't like it mentioned that they should use zinc finger technology and I think this same reviewer, I don't know who reviewed which grant, seems to have said that in every single one of their reviews. And zinc finger technology, just for those of you who don't know anything about it, is

extremely expensive. So, for example, if they say a seed grant should use zinc finger technology, it costs about $30,000 just to use it and, you know, you only have $80,000 for your whole grant. So again, this person seems to have a chip on their shoulder about zinc fingers, and is wondering why the core isn't using them.

So, I think it's a great core, and it deserves to be funded.

DR. DEES: Diane and Mike? So the comment that it wasn't reaching its full potential, did you get the sense that it was improving over time?

DR. KRAUSE: Absolutely. I think that the core has continued to develop as technology develops. I mean, IPS didn't exist a few years ago and now they're routinely making IPS lines for investigators both at UConn, also at Yale, people who are in Boston, people from Harvard, they're really serving a core function. Not only for making IPS, but they're continuing to do training, etcetera.

DR. DEES: Do we get a sense from the UConn people -- they had mentioned that the Yale grant specifically mentioned why they're trying to generate funding from external sources among Connecticut paid sources? Do we get some of that in this grant as well?

DR. KRAUSE: They certainly --

DR. GENEL: The only thing --

DR. KRAUSE: -- I'm sorry. Go ahead.

DR. GENEL: -- no, no, go ahead.

DR. KRAUSE: They're certainly trying for cost recovery, so they bill for their services and determine their charges based on cost recovery.

DR. GENEL: The only thing I saw that is not specifically tied to funding is the coming of the Jackson Laboratory, but I think it's obvious that it's a potential source of support for the core. I think that's implicit.

DR. KIESSLING: What was it, that the Jackson Labs would use their core facilities?

DR. GENEL: That's the expectation. And the a lot of purpose of the Jackson Labs is genomic research. So I think there's certainly a synergy there that is patently obvious.

DR. HART: Is there anything in the grant saying what the arrangement would be with Jackson Labs? I mean, we're not funding support for the Jackson Labs through this grant, are we?

DR. HISKES: We're not allowed (indiscernible).

DR. HART: We're not allowed.

(Laughter)

DR. HART: So consistent with what Diane was saying, I think the first reviewer indicated that it's a strong proposal by an outstanding group of researchers, and I would move then to fund it at the $500,000 level.

MS. HORN: Do we have a second?

A FEMALE VOICE: Second.

MS. HORN: Any further discussion? All in favor?

VOICES: Aye.

MS. HORN: And if there is anybody who's recusing themselves or abstaining, please let me know, otherwise I will not call those out as categories. So we'll move this into the preliminarily funded category. We have two categories within the group proposal. Should we just take the group proposal as identified as a group proposal next? It's 12-SCC-WESL-01, again, Dr. Genel.

DR. GENEL: Well, there's some interesting aspects of this. This is essentially a continuation of work that we have funded since the inception of the stem cell program, which is the use of stem cells for treatment of temporal lobe epilepsy using a mouse model that was developed at Wesleyan. And this is now a continuation of

this model with the expectation of using cells generated from human stem cells as replacement therapy in the mouse model.

Now, I did not have -- I meant to ask for copies of the current grant and I'm sorry I didn't have a chance to look that up. But we are funding a grant that's now in its last year that as the reviewer points out calls for some of the same -- some of the same studies. The progress report -- the progress as reflected in the grant application suggests that they have not yet gotten to the point of using human cells for implantation in their model. But there is overlap with an established investigator grant that is currently in place that has another year to go and I think that's a consideration that we have to take into account.

The one criticism that I think is unfounded from the reviewers is concern about how three established groups will collaborate with each other and I think they misunderstand the setting that this research, which is clearly pointed out in the grant, these are three independent investigators, who are all housed on the same floor in the same laboratory at Wesleyan. So I think that to me is a non-issue. But I think I do have concerns that there's clear overlap with an established investigator

grant that's now in its last year.

DR. WALLACK: So I agree with what Mike has just led us through and I think that the issue of overlap -- I think the issue of perhaps not leading to new insights and the issue having to do with the continued added value to this kind of research, I'm not sure if it's here. And I also have a hesitancy about moving ahead positively with this grant, unfortunately. I say that, unfortunately, because this is a research team that I think has from the beginning been doing very notable work and I wish there were more money available to us to be able to fund many more projects. This grant, to me at least, is on the cusp of needing to be funded, but because of some of the limitations that Mike first outlined, and I agree with, I can't yet move in that direction.

DR. GENEL: I agree.

DR. KRAUSE: May I ask a question? Did the P.I. address potential overlap? That's sometimes done in the bio-sketch, at the end of the bio-sketch there's funded grants and they usually address overlap there. I'm trying to download it, and it's a little slow here.

DR. WALLACK: I have it here Diane and I didn't -- I've read the grant and I may have missed that part but I don't recall having read that.

DR. KIESSLING: Do we have any other applications from Wesleyan?

DR. GENEL: This is the only one.

DR. KIESSLING: This is the only one?

DR. WALLACK: And Anne, that's exactly why my comments were truly hedged with concern about maybe not being able to move at this time on the grant. And especially because of the research team that's presenting the grant. They have a very notable record.

DR. KIESSLING: How many years are they asking for?

DR. WALLACK: Four.

DR. GENEL: Four. It's a group.

DR. HART: Is there any sign of productivity in terms of publications?

DR. WALLACK: I'm sorry Ron?

DR. HART: Is there any sign of productivity on the current grant in publications listed from the current grant?

DR. GENEL: Yeah, there's good product.

DR. WALLACK: But to Ron's question also, Marianne especially, we've talked at previous meetings about the issue of documented productivity and I know it's not directly relevant, but I know we also take notes to

come back to separate from this, and that might be a very key question that Ron asks relative to making sure, and I know we've talked about this summer trying to do an analysis of the productivity at all of the institutions, and maybe that underscores the need to document that and not forget about doing that this summer.

MS. HORN: We did indicate that we got to try to find an intern.

DR. WALLACK: Right.

MS. HORN: Dr. Krause had volunteered to look at what had been produced, where various grants were, the status of patents, and so on. So I think we need to take that forward.

DR. GENEL: This is a painful discussion. Diane, the title -- the title of the currently funded grant is, Brain Grafts of GABAergic Neuron Precursors Derived from Human and Mouse ES Sells for Treating Temporal Lobe Epilepsy. So, you know, but I did not get any sense of the progress and the background that they had yet moved to actually doing a human -- the human embryonic stem cells. I think that's part of a lot of -- a lot of material here about utilizing human embryonic stem cells.

DR. KRAUSE: And when does the existing, established investigator grant end and when would this

grant begin?

DR. GENEL: 2013. This one would begin in 2012. There would be, well, I wouldn't say a year overlap, but it would probably be something -- given the timeframe in which grants -- the money actually gets there, but probably six to nine months of overlap is what I would think.

DR. KRAUSE: So in my opinion the overlap is probably something that could be dealt with quite easily once we looked at the details. The bigger concerns are, you know, concerns of the primary reviewer's adhered with the merits of the grant and less so with the overlap, because it's a short time and if any established investigator grant -- they'll just be getting started on this is the funding kicks over for the new grant, it would just be a continuation of ongoing productive work.

DR. HART: Would there be more enthusiasm for a reduced budget or a reduced time scale?

DR. GENEL: I think we ought to keep it on the table.

DR. KIESSLING: I didn't get to read this. So Mike, are they going to run out of money? If this is not funded are these investigators going to be without funds?

DR. GENEL: I think the answer to that is, yes. Because I don't think they have -- I don't recall seeing alternative sources of funding.

DR. KIESSLING: Because this is a really unique project that they're doing. They're uniquely designed to do.

DR. GENEL: I agree.

DR. WALLACK: So, Ron's point, idea about how to maybe manage this I think resonates with me at least Ron. I mean, how would you then do it? Would you do it on a two-year basis?

DR. HART: It's up to you, you're the reviewer.

A MALE VOICE: Have you looked at the budget? I didn't, that's why I said that.

DR. HART: Right.

DR. KIESSLING: I mean, there are a few people, there aren't a lot of people injecting stem cells into brains. So this group has gotten really good at this. I didn't read it.

DR. DEES: But there's some overlap here though, right? So what would happen if we said, try again next year?

DR. KIESSLING: They'll run out of money.

DR. DEES: They'll run out of money before next year?

DR. KIESSLING: That's devastating.

DR. GENEL: Yeah, this is -- among the three investigators this is the only -- this is the only source of funding that is available through 2013.

DR. ARINZEH: Do you want me to make a recommendation maybe and then revisit -- revisit, maybe revisit and adjust the budget if need be?

DR. WALLACK: Treena, can we do a maybe as a placeholder specifically identifying the reduced number of years, and reduced budget? Mike, would you be willing to do that?

DR. GENEL: I didn't hear you.

DR. WALLACK: Would you consider wanting to do a reduced number of years at a reduced budget and put it in as a maybe as a placeholder?

DR. GENEL: Well, I made a calculation here. They're 1.5 million. That's the same as two established if you look at it from that perspective.

DR. WALLACK: Right.

DR. GENEL: And they're asking for four years, so yes, I think that's a very -- I think that's a very reasonable idea. A very reasonable idea. I would

support that.

DR. WALLACK: So I would move to do it as a maybe on that basis.

DR. KIESSLING: Are the P.I.'s going to get their reviews?

MS. HORN: The peer reviews? They already have. So the motion is to move it into the maybe category with reduced funding of perhaps two years and we'll revisit it on our second round. Do I have a second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: That goes into the two. Moving on to disease directed collaboration group proposals. 01-SCDIS -- I need my glasses fixed, YALE-01, reviewers David Goldhamer and Anne Hiskes.

DR. GOLDHAMER: Okay. So this is a -- this grant is from Eugene Redmond is the P.I. It scored very well. Both reviewers gave the grant a score of -- it says right there, 2. The title of the grant is, Are Dopaminergic Neurons Derived from Human Embryonic Stem Cells or from Fibroblasts, the Best Candidates for Treatment of Parkinson's Disease as Studied in the Best Primate Model?

So Gene Redmond has a current grant from the state and this is -- that's ending soon, it's ending this year, and this is a follow-up to that grant. So I'll give you a little bit of -- he's asking for a lot of money, so I'd like to give you just some details of what they propose to do. Let me first say that this is a collaboration between a number of co-PI's at Yale who are asking for some effort on the grant and various consultants from different universities who are not putting effort and are not asking for salaries. Gene Redmond is putting 20 percent effort on this grant.

So basically -- and this is excerpted from their one sentence description. What they really want to do is to test critical questions regarding the selection and development of the most effective replacement cell to reverse the dopamine deficiency model in Parkinson's Disease in monkeys. And so they are looking for the best cell for these kinds of experiments with an eye to looking at side effects, toxicity, inappropriate migration of cells, immune rejection, and their goal is to move forward for its translation of this therapy in a clinical setting. And they put together, I thought a very comprehensive extensively documented and thought out grant.

So I'll tell you what the three aims are.

In the first aim they would like to determine the efficacy of transplanting dopamine neurons derived from monkey IPS cells and comparing the engraftment efficiency when those cells go back into the same monkey, so there's no immunological rejection, and into different monkeys where there may be immunological issues. Now, the brain is immunologically protected to some extent, but it's not clear in other studies that have been done by this group and others, and this has been done a lot in rats, in mice, some in monkeys, engraftment efficiency tends not to be that great. And there is considerable disagreement as to the role that immunological factors play in this less than great engraftment of neurons -- dopamine producing neurons in the brain. So they want to do that comparison in their first aim.

Now, they have not worked with monkey IPS cells, but IPS cells from monkeys have -- different types of monkeys have been made by a number of groups and they have the technical expertise at Yale to do this and he's enlisted the appropriate collaborators to do that. And aim two, what they want to do is compare the effectiveness and safety -- so in aim two what they want to do is they're using here -- now they're switching to human ES cells and this is because their past grant and all their

experience to date has been with human ES cells. And what they would like to do is compare the engraftment efficiency and functional recovery of dopamine neurons produced from human IPS cells and compare that efficacy to progenitor cells or to neural stem cells produced from the same IPS cells.

So the question is, is functional recovery greatest when you use the differentiated endpoint, the dopamine producing neurons, or is there benefit to using more primitive cell type that may respond to the environment in advantageous ways and engraft to a higher degree and form better, you know, and more neural connections. So I think this is an important question and a relevant question in many areas of stem cell research is, what is the appropriate cell type to engraft? The most differentiated form or a progenitor that may be more plastic and better able to engraft.

And then in the third aim they're going to use both IPS cells, monkey IPS cells, as well as human ES cells. And what they want to do here is similar to studies that they've already conducted where they have seen some success, success, but what they want to do now is extend their studies out to a much longer time point and they (interruption on tape) experiments which have

ranged from six weeks, I believe, to about six month, have not been sufficiently long to really evaluate in terms of getting ready now for the folks in the FDA for clinical trials. They feel like they haven't taken these points to a long enough endpoint to really see if there are possible long-term rejection effects, loss of grafted cells, either because of immunological issues or some other issues, cell overgrowth, inappropriate migration, all of these things that they studied on shorter timeframe they want to now study on a longer timeframe.

All right. So that's basically the three aims again. It was -- it was really beautifully written and almost too much detail, but it was very nice. And let me just read I think three or four sentences from the reviews just to give you a flavor for how the reviewers thought of this grant. They said, "This is a well-written elegant proposal describing a comprehensive effort to continue evaluation of human ES cells an IPS cell therapy approaches to Parkinson's disease. The rationale is well presented, supported by strong preliminary data and previous experience." They described it as comprehensive. They describe the investigators as superb. So there is really no -- they had minor weaknesses that didn't affect their enthusiasm so the science I thought was great, it

wasn't necessarily too innovative, but they're necessary studies to move to the next step. And he has about a two-page presentation of, you know, when, you know, how -- after they evaluate the data how they're going to approach the FDA, what kinds of data will warrant, you know, opening up dialogue with the FDA and so forth.

It was just very well, and not oversold, you know, went through all of the possible caveats and problems. I do want to spend now a little time with the budget because this is a sticking point. This was a sticking point in the last funding of their first grant. So the monkey research is done on St. Kitts, okay? So outside of the United States. And they make, I thought, as strong an argument that they could make for why this is an essential thing to do. They do acknowledge, under evidence of commitment they say, we are aware of the position of the Connecticut Stem Cell Initiative money should be spent entirely within the state, but we believe that this project should be an exception for the use of primate resources, which are not available in sufficient quantity in Connecticut or anywhere in the United States. And they go on and elaborate more.

They did a cost analysis, how much this research would cost if they use St. Kitts, versus if they

use a U.S. facility or try to do these experiments at Yale. And there's about a four to eight-fold or six-fold higher cost. So, I was convinced that if we want the research done, that the animal research should be done at St. Kitts. Now, if there is statutory -- if there's reasons why it's impossible to fund -- to provide money outside the United States, that's one thing, but otherwise I think they could not have justified that any better than they did.

I think that's all I really need to tell you. So Anne?

DR. HISKES: I was very impressed with the logic of the experiments and the logic of the proposal. The investigators are really asking themselves, what do we need to know before we could approach the FDA? What do we need to know about safety? What do we need to know about efficacy? So very careful comparative studies of allograft versus iso grafts, you know, IP cells versus hES cells, what stage of development might be the most efficacious. Looking at migration of cells, you know, toxicity of cells. So really a very carefully crafted proposal with the end goal of approaching the FDA and actually bringing this to clinical trials.

I think the group of researchers has a very

impressive track record. They're well positioned to bring this to fruition. And I guess it will be -- the primary question is about the three St. Kitts monkeys with which they have a lot of expertise and which are cost effective. I don't know what happened last year, did we not fund that part?

DR. GOLDHAMER: Well, it was a 2008 grant and I believe that was not.

DR. HISKES: So we eliminated the monkey business.

(Laughter)

DR. HISKES: Okay. So I would recommend funding, and if legally possible and politically possible, the St. Kitts part as well. If that part isn't possible, I recommend funding as much of it as we can.

DR. GOLDHAMER: Let me add one more thing before there's questions or comments. So the St. Kitts' facility is operated and fully controlled by the Connecticut nonprofit organization, Axion Research Foundation and they estimated that $338,000 would go towards the Axion Research Foundation and about half of that would go to St. Kitts, something like $169,000 total out of 2,000,000 would be going to St. Kitts.

A FEMALE VOICE: What's that?

DR. GOLDHAMER: 169,261.

A FEMALE VOICE: This is over four years?

DR. GOLDHAMER: Over four years.

DR. HART: Let me just comment first, I mean, I thought David, you did a wonderful job kind of going over the details of this. I didn't read the grant, obviously, but I love the way you covered it. In particular, because of the history of fetal cell transplants in this field, and it seems as though every point you made hit on some of the criticism and some of the failures of fetal cell transplants 10 to 20 years ago. And in that light, I think it's really important to consider how much we've learned from those mistakes in a project like this and how the state of Connecticut certainly does not want to set up a primate research facility in the state.

DR. WALLACK: So I totally agreed with the reviewers and Ron's comments. I'm enthusiastic about having this project go on. I'm trying to restructure my mind on how we handled this the last time and I think that we did reduce it substantially, by a few hundred thousand dollars. And it seemed to me that as I recall, that Gene Redmond was able to acquire the funding, which he obviously did, in order to have the project move ahead

with the St. Kitt portion of it. I'm not sure if he's done this collaboration with this work, I believe he has, but I know he was working on trying to establish a collaboration in California.

DR. HART: There is a California Institute listed here, but no funds, but as a collaborator.

DR. WALLACK: So I'm only moving in this direction if I think -- because I know how tight the dollars are and I know the project was not prevented from going on in the past with a reduced amount of funding, but I don't recall how much we reduced it last time. I think it was by a few hundred thousand dollars. It was a significant amount. And I remember he was very grateful for that degree of funding and he was able to find funding for the remaining portion that we didn't fund. So maybe, at least from my perspective, that might be something to consider on this round also. Not taking away from the validity of the overall need for this, I totally support all of this, but also I think maybe we can do it in a slightly different manner than funding the $2,000,000.

MS. HORN: So do we have a recommendation?

DR. GOLDHAMER: Well, I'm wondering, are there -- is this a legal matter?

MS. HORN: The way the stem cell

legislation has been interpreted does allow a tiny -- for extraordinary circumstances for research to be funded outside of the state. I think this is consistent with what California has been doing as well. I think in terms of extraordinary circumstances the thinking had been if there was a piece of equipment that would be utilized for a short period of time during research, it didn't make sense for the state to invest in that and that that portion of the research could be funded with Connecticut funding. This seems rather large expansion of that, but it's up to you guys.

DR. GOLDHAMER: He does make a very strong argument that this research cannot -- I know it's a little different than what you're saying, and he obviously found ways to do the research without those funds last time, he probably reduced effort on personnel or who knows what, or found other sources of money, but it's very clear that this research can not be done in the United States, either because the facilities don't have the capacity, or for instance, the New England Primate Facility would cost -- the same work would cost eight or 900,000 in 2007 numbers, which was his comparison, compared to 160,000. So in terms of bang for the buck, and just, you know, it's clearly, this is the way to go.

Now, one possibility, you know, when it's all said and done when we try to find and free up money for -- to fund more grants and we sometimes cut grants because of that, you know, so that we can include a grant or two that we don't have money for but want to fund, if it happens that we decide to cut some of the larger grants by some amount and this particular grant we could perhaps specify that that cut is targeted, whereas we haven't done that for other grants. I mean, personally I prefer to fund it at the full amount and allow the funds to be used in St. Kitts. But if there is funding reduction for reasons of freeing up money for other grants, that's one potential way to do it.

DR. HISKES: Well, given the logic of the argument that he's laid out, Marianne, a big piece of equipment are not cost effective to buy one here, it seems to me the monkeys -- they're not pets, they're not in a zoo, they are medical equipment and they have a unique colony of organisms at St. Kitts and so it would not be cost-effective to move that colony here, you know, so much research -- or to start a new colony, so much research has been done on that particular population, it's a known population, controlled population. So I would say that, you know, thinking of the monkeys as a research tool, a

piece of organic equipment, that the rationale for the exception would apply here.

DR. PESCATELLO: A couple of points. We want this kind of translational research, we've talked about that a lot. We want this disease related research. This is what this is. The primate, I mean it's absolutely true, I mean, it's prohibitive to do primate research certainly in Connecticut, it really doesn't exist. I would say, as a practical matter, remember that the dollars are flowing through a Connecticut entity, it's not going directly to St. Kitts.

And also, if we truly want translational research, it's got to go -- eventually it's going to go through primates. There's just no way. And so I think we should send a signal that we don't have a problem with that.

DR. KIESSLING: Well, the last time that this came up the Commissioner I think got some information from somewhere. Marianne, do you remember that? The last time this came up about how much money could go to St. Kitts I think the Commissioner got a reading from someone, could Connecticut money do this? Do you remember that? You talked to somebody about it.

MS. HORN: Yes. I don't recall whether it

was a hard and fast rule. I think it was just a general sense that that was not funding the travel, the Connecticut dollars flowing out of the state were concerns and not just for a one time use of a piece of equipment, but for an extended period of four years' worth of research. And I think the appearance of flights to St. Kitts and so on, was something that just tipped the balance in terms of keeping the money in Connecticut and encouraging him to find the funding for that portion of the research from some other source, while we funded the rest of the research that was Connecticut-based.

DR. KIESSLING: Okay. So there wasn't actually any opinion that came from anybody about how to use that. I thought we had gotten an opinion from, I don't know, the Governor's office.

MS. HORN: I think we probably had discussions with -- I think Henry Salton was at the table when that decision was made and that's why I'm hesitating to bless a much broader exchange on that narrow exception to Connecticut money going somewhere else.

MS. MULLEN: Just going back to the framework for review, just reading from the framework asking for a description of the organization, plans for research, proposed arrangements concerning financial

benefits to the state as a result of any patent royalties, etcetera. It's pretty much talks about advancing research in Connecticut and I think there's on top of that the interest of having this discussion on the day of the groundbreaking with Jackson Lab and it just means there's a lot going on in the scientific world. But that we -- given the source of these funds and what the intent of this project was, probably want to acknowledge the folly of the proposal, and think a little bit more about whether or not it's fundable in the overall context. And some of that is just perhaps, opinion, but the rest might be that we have to figure out whether or not you can make the leap from, you know, hardware to monkeys as being equipment.

DR. WALLACK: David or Anne, how much of the project would involve St. Kitt? I totally agree, by the way, that the research as Ron indicated, and I agree with what Ron said, should be done. I'm not disputing that at all. But to pick up on the tone of this conversation, how much of the money, of the 2,000,000 is involved with St. Kitt?

DR. GOLDHAMER: So the value was 169,000 was for St. Kitt and that's for all of the in vivo experiments, all of the postmortem analysis is done back here, so all of the live monkey work which -- and so forth

is done there, and the total cost from my read of the budget and the narrative is about $169,000. And it's over four years. Over four years. And that's a fixed -- he made a point that this is a fixed rate. That when it's done in other places there's up charges for various things, unforeseen veterinary care requirements can jack up the price, they have a fixed rate agreement with St. Kitts, so these are solid numbers that won't increase.

MS. HORN: So, the only additional funding related to the research in St. Kitts would be the travel of the researchers down there and the accommodations being paid for.

DR. GOLDHAMER: I believe that amounted to $4,000 a year for two investigators to go twice a year I believe, which is quite reasonable. The per diem's are something like 35 percent of the hours.

DR. ARINZEH: And that in vivo work is substantial in terms of over the course of those four years, they are analyzing that data continually, so it's really significant.

DR. GOLDHAMER: Yes. It's significant, and it's -- the first three years, the costs are about evenly distributed, about 109 in the first year through 121 in the third year, 121,000, and then in the fourth year it

gets down to 15,000 presumably because they are now analyzing the data from the in vivo work that had been done in the first three years.

DR. WALLACK: So David, would you guys be comfortable in voting to fund this at 1.8 million and let him, as he did in the past, which he was successful in doing, being able to find funding for a portion pertaining to St. Kitt? I mean, totally agree with the idea that it has to be done?

DR. GOLDHAMER: But if we really think the experiment is important and worth doing, then to up front give them this liability of trying to find this $200,000 or in reducing effort -- and I will say that I think the effort that they -- the salary support that they're asking for is not at all unreasonable. It's not -- I don't see much fat to trim from that. You know, if translational research is a priority for Connecticut for us to fund, which it is, and he is the person -- one of the few people in the country that can do this, I just feel uncomfortable tying a hand behind his back and then hoping that the funds become available or that he can reduce other aspects of the grant to make up that deficit.

DR. KIESSLING: This guy is a world resource for Connecticut.

DR. WALLACK: No, I'm not -- trust me, I'm not disagreeing with any of that, I think, you know that.

DR. HART: The idea here is that we asked for this kind of grant. We asked for this kind of (multiple voices).

A MALE VOICE: This is what we're begging for.

DR. HART: We don't have the budget to support this kind of work done any other way. I think it would be just handcuffing our own goals to say cut out the St. Kitts' funding.

DR. PESCATELLO: And this history of this fund has been to fund difficult research. I mean, it started off when the federal -- when it was harder to get the federal dollars in this kind of research. And to the extent it's hard to get funding for primate research, I mean, we shouldn't be shy about something that really is just a P.R., to some sense an image problem more than there's any kind of science -- there's nothing that's been raised that it's a scientific issue. So we shouldn't encourage that kind of anxiety here.

DR. HART: Let me just finish my previous comment. Obviously, if we go with this program, we're going to make many post-docs and probably several

professors very unhappy by cutting many other programs. But again, this is exactly what we were asking for, especially late in the term of the original charge of this Committee.

DR. DEES: So I move we fully fund it.

DR. HART: Second.

MS. HORN: Further discussion?

(Discussion off the record)

MS. HORN: We can take that as a recommendation -- I'm sorry, yes?

DR. FISHBONE: I just have some concerns about your political implication as we had four years ago, I mean, and, you know, I'm wondering if we were to reduce the size of the grant. I'm sure, you know, say you could do it up to 100,000 up to 2,000,000 --

A MALE VOICE: I'm sorry Gerry. Could you speak up?

DR. FISHBONE: Yeah. I'm just wondering if we should make a little consideration for the political implications for funding research outside of the state. And my own feeling, not being a researcher, is that when you ask for $2,000,000, because that's what we're offering, there is a certain amount in there that is fungible. If you said 3,000,000 they would have come in

for 3,000,000. I'm wondering if you take a few hundred thousand out of there would that prevent the work from being done? Would it allow us the ability to stay in there if we were very comfortable at funding --

A MALE VOICE: This is fine, but I don't know if you were giving him 2,000,000.

A FEMALE VOICE: Yeah. I was going to say, it's a bargain already.

DR. GOLDHAMER: I mean, this is a very stiff -- by NIH standards, very small grant. This is a RO-1 and maybe a quarter or a half worth of funding, so it's really not -- 1.6 million in direct costs, so there's really not much room here to trim out.

DR. HISKES: Well, it seems to me that, you know, testing in primates is the next stage of this kind of research on the way to therapy. If the FDA approves it for clinical, is that going to be research done out of the state of Connecticut? Will it be restricted to Connecticut patients or will it be open to patients around the country? And so I think this is -- that we're at the stage where we need to think about what it takes to bring this kind of research to fruition. The whole point was that eventually we're going to have therapy, so you know, primate research is part of it, the next stage is going to

be clinical human patients. Is that going to be restricted to people in the state of Connecticut?

MS. HORN: I think the line is the research has to be conducted in this state, so not restricted to people in the state. So, should we put this in the funding and come back and revisit the funding amount at the end of the day? Do I have a motion for that?

DR. HART: I prefer not to revisit it. There is a motion on the floor.

MS. HORN: Okay. There was a motion on the floor. Okay. We moved it to the funding and we will explore further whether this is possible to fund it. All in favor?

VOICES: Aye.

A MALE VOICE: Is that -- what did you decide here are you looking at funding at the requested amount?

MS. HORN: Yes. We're just going to make sure that we're solid in terms of whether this is actually allowable. I do have a call in to California to find out how they have handled it but I've not heard back then if the ISSCR had handled it.

(Discussion off the record)

MS. HORN: Okay. So moving onto the next

disease-directed grant, this is 12-SCDIS-UCHC-01 and the reviewers are Dr. Genel and Diane Krause.

DR. GENEL: Well, this is another disease-directed grant per our solicitation from the group at UConn that I think received their first group grant, I think this was the first group grant that we gave in the program. It's an interestingly written grant. I mean, I think the -- it reads very well. The reviewers point out a couple of major issues, and I'll just highlight two.

Basically the whole premise is based on developing osteoblastic cells from induced pluriponic -- pluripotent stem cells and using a -- using an osteoblast reporter. And then, the first reviewer points out that a major weaknesses is that this has not been shown to be successful by other investigators. So the basic premise of their work has not been -- has not been proven that they can develop mature osteoblastic cells from the induced pluripotent stem cells.

The second -- the second caveat is that the group already has a Department of Defense grant that at least is outlined in the grant. It looks very, very similar to this, which is -- I don't know the level -- I can't see the level of funding, but it's a four P.I. directed project integrated towards building a skeletal

repair strategy based on progenitor cells derived from human sources, with four projects that simply parallel this one. So the reviewers suggest that we could cut the funding in half very easily. I think the real problem is, whatever its merits, I don't see that we have enough room in the 9.8 million to fund it, whatever we might decide are the individual merits.

So I would -- I would suggest that we not fund it.

MS. HORN: Diane?

DR. KRAUSE: So, we're discussing a grant that got a score -- an average score at the end of four and a half. So I'm kind of questioning what our policy was here, given that it's one of the disease directed, I think it falls outside it's beneficial intention. The initial reviewers gave it a three and a seven and then came together with a four and a five, so I'll just give you my opinion. It's an excellent grant, and it's a wonderful collaboration amongst experts, each of whose expertise will contribute to the progress. The weaknesses, as far as I'm concerned, are that they claim that they'll be ready in just a few years for this to go to the clinic, but as you've just discussed, models beyond an NOD SCID mouse are probably necessary before you would

do that. So I think they're a little over ambitious in terms of saying that they're going to get this, you know, ready to be send to the FDA and be thinking about things a little -- they're a little ahead of themselves.

But that said, otherwise it's a very good grant and they -- despite the fact that their data are not beautiful for having pure osteoblast form from pluripotent cells, they have used zinc finger technology to create knock-in mice, I mean, knock-in cells that have a reporter. So if they were to get good osteoblastic rentiation they have a good reporter for that. So I think there are a lot of strengths to the grant, but I will respect the peer review scores that this really is a step below our best grants and probably should not be funded this year with our limited $9.8 million total budget.

DR. KIESSLING: Mike, how is their -- how is their progress? I mean, this group was debated poorly -- how much of they gotten done?

DR. GENEL: Well, I'll defer to Diane on that. I think the major flaw that I saw, not being absolutely conversant with the work, is that there is controversy as to whether or not they can create an osteoblastic cell when they say they can. Now I --

DR. KIESSLING: But we funded them, three,

four years ago?

DR. GENEL: -- well, we funded them, I think from the very beginning. I think it was the first big group grant that got funded in this program.

DR. KIESSLING: So, how much did they get done with that money?

DR. GENEL: Oh, I honestly can't --

DR. KRAUSE: They've done a good job.

DR. GENEL: -- I can't say that --

DR. KRAUSE: They've done a tremendous amount. And in terms of modeling -- coming up with better ways of imaging to prove that you actually have engraftment using both in vitro and in vivo, that is the maxim on what they're following up on them. They've created these reporter human ES lines in order to be able to see this and that's a very expensive and important thing to have achieved. They've published several papers on osteoblastic rentiation all on the mice. So I would say they've made progress, it's just not ready for a disease directed grant.

DR. GENEL: And the other thing one can say is that I think to a large extent, because of funding from this program, they've received a very large grant from the Department of Defense, and I see listed a couple of NIH

grants, as well as the Department of Defense grants, that I think clearly reflect work that was initially supported by this Board.

DR. WALLACK: So, picking up on what Diane said, I think they have made tremendous progress also and I think allowed them, Diane, you know, maybe I'm wrong on this, but I think it's allowed them to build a great team there. I think one of the other grants on the established investigator side that we'll be reviewing by Dr. Kumbar is part of that whole team and as a matter of fact, and there is some overlap on that established investigator grant and David Rowe is the co-P.I. on that grant. So that I think about while they've done a tremendous amount as Diane has indicated, and they may not be ready to move ahead at this point with this grant, but it will not, from my perspective at least, inhibit continuation of the work that is able to be done because of our initial funding the first year in the program.

MS. HORN: I just have a question for the committee. This came in as a disease directed collaboration group proposal. And the way we described that was, arrangements between industries, such as biotechnology and pharmaceutical companies, medical centers and academic institutions. So does this grant

fall within a disease directed, or is it really more of a group grant? I didn't see --

DR. KIESSLING: Do they have any collaborations outside themselves?

DR. KRAUSE: They mentioned a lot of collaborators, but I think they were all -- I'm not 100 percent sure. I only remember seeing the UConn collaborators, but I'd have to go back and take a look. I am looking again at the progress little more specifically. The progress has been in mice and not with human cells, so that remains a weakness, although I don't remember exactly what the goals of the initially funded grant were. But he is well funded to continue this work.

MS. HORN: Okay. Did we have a motion?

DR. GENEL: Remind me, did we actually specify a collaboration with a pharmaceutical company or something like that?

DR. KIESSLING: Evidently.

MS. HORN: We suggested that priority would be given to disease directed collaborative arrangements between industry, such as biotechnology and pharmaceutical, medical centers and academic institutions as distinguishing it from a group grant, which would be a number of different --

A MALE VOICE: I stand corrected.

DR. KIESSLING: I guess we did.

DR. KRAUSE: I think this is more of a group grant.

MS. HORN: Yes. It didn't seem that dissimilar from the first one you put in. Okay. So we have a motion that this not be funded, be moved into the not funded? Second?

DR. KIESSLING: I'll second that.

MS. HORN: Any further discussion? All in favor?

VOICES: Aye.

MS. HORN: Now, a question for the group. It's almost ten o'clock, we are scheduled to take a break at 10:15, is this a time that people would like to take a 10 minute break, or should we get started on the next round and come back?

DR. KIESSLING: 10 minutes.

MS. HORN: 10 minutes. Okay. We'll take a 10 minute break.

(Off the record)

DR. HART: I'd like to make a suggestion now that we've made a few initial decisions about funding. We, by my calculation, have considered roughly 4,000,000

as positive. I think we ought to be very parsimonious in our further deliberations and for the established grants I think it might be a good idea to consider the five top scoring between 1 and 1.5 grants and then have reviewers suggest any other meritorious grants that they have considered. Therefore, we can kind of prioritize things very quickly. Is that acceptable? So we cover the top five in detail and then any of us can pick out our favorites from those not being considered if we think they should be considered?

DR. KRAUSE: It seems a little draconian, but I think it makes sense because if you have the option of bringing up any that you want to have considered then we can do what we want.

DR. HART: Right. And then realistically, there's just not that many that we can consider, considering our current restrictions. That's why I say this.

MS. HORN: Further discussion?

DR. KIESSLING: So we would go deeper than 1.5 if we're going to be --

DR. HART: We would select out those that we have a favorite nominees, let's say, over 1.5.

MS. HORN: Yeah. I think if we get into

the 2.5 you're considering another seven grants.

DR. HART: That's my concern, exactly. I didn't say that, but that's my concern.

DR. GOLDHAMER: If I can make a comment? Yes, so I'm in favor of that. I think looking forward to next year that I think one of the problems we're facing or the problem we are facing, again, is that the review scores are compressed and I'm not sure exactly what the instructions are by the peer review chair to the peer reviewers, but I think a greater effort has to be made to spread out the scale and use more of a one to nine scale. Because this is -- this is the problem that the NIH faced before they went to the one to nine scale.

DR. KRAUSE: And it's a problem they may have had because they went to the one to nine scale. So I think part of it is that we're using the NIH scale, which doesn't work, even at the NIH.

DR. GOLDHAMER: Well, the original NIH scale was one to five and grants tend to be punched at 1.8, 1.9, 2.0, so the intent was good with the NIH scale and they actually describe what each numerical score means from one to nine, but I'm not sure that reviewers -- well, as Diane points out, the reviewers don't really use the full scale. But every effort that can be made to expand

the scores so that we're not here almost it seems arbitrarily deciding this grant with a two gets funded and this grant with a two doesn't, because we're not peer reviewers, we're not, you know, our job is a little bit different.

DR. KIESSLING: But our mission is to make sure -- is to figure out which ones meet the -- our mission, right? So, their job is just to look at the science, our job --

DR. GOLDHAMER: I agreed you, but I'm saying 90 plus percent meet the mission.

DR. KIESSLING: -- no, I don't think --

DR. GOLDHAMER: Well, a large percent. Far more than could be funded potentially.

MS. HORN: All right. We'll certainly take note of that. I think at our next meeting, which will be in August, not July, we can -- Rick is going to do some evaluation in some further discussion on the peer review process this year and I think that's a really good point to add to that list. Okay. So we have a motion then to look at the established grants up to 1.5. Is there a second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Okay. And then of course, anybody who wants to bring a higher -- lower score -- higher score, lower ranked grant --

DR. KIESSLING: Wait, what was the question?

MS. HORN: -- if you want to bring in another grant to be reviewed we can certainly have that once we finish with this review.

DR. KRAUSE: To do the top five and then add in?

DR. GOLDHAMER: Yes.

DR. KRAUSE: Okay.

DR. WALLACK: Then there's the rest of the process.

MS. HORN: Okay. So the first grant is 12-SCB-YALE-10. The reviewers are Milt Wallack and Paul Pescatello.

DR. WALLACK: So, I thought that this was an excellent proposal and it has the potential to enhance cell maintenance and differentiation of critical steps for new and innovative approaches to treatment of a variety of diseases. It's written in a very clear and concise manner, very important objectives, and has the potential

to significantly advance stem cell therapy, as one of the peer reviewers noted, and it might've been the same one who used this term before, he called it simple and elegant. Somebody else use the word elegant. I would definitely -- I was excited, actually when I read it by its potential and the way that it was presented. I would definitely recommend funding.

DR. PESCATELLO: Yeah, I agree completely. Again, I think this is great basic research and Milt mentioned all of the accolades that went along with it from the peer reviewers. And I think also one of the things that was pointed out was that a very -- a researcher with a, you know, very significant track record is going to put one third of her time into this project. So, yes, I would wholeheartedly support funding it.

DR. KIESSLING: How many years of asking for?

DR. WALLACK: Four.

MS. HORN: Okay. Do we have a motion?

DR. PESCATELLO: Yes. So moved.

MS. HORN: And --

A MALE VOICE: Move acceptance.

MS. HORN: -- moved into the preliminarily funded. Second. Any -- all in favor?

VOICES: Aye.

MS. HORN: I would just mention that we should remember to have a backup fund as well, backup grants, reserve grants in the established and seed categories in case any of the grants fail. Okay. The next grant is 1.5 peer-reviewed, 12-SCB-UCON-02, Anne Kiessling and Milt Wallack.

DR. WALLACK: Anne, do you want to start?

DR. KIESSLING: Yeah. So this is also a wonderful grant. This is a very interesting project where they're going to try to deal with the potential stem cell rejection by organizing the (indiscernible) to recognize the stem cells as self. The peer reviewers were excited about this. This is actually definitely on our mission. Although it's focusing on mouse, they're going to propose some human stem cell work in here too. And they're also asking for four years of funding. They're asking for four years.

So I thought this was, you know, a very nice grant. I thought some of these grants this year, some of the scores were clustered so closely together because the quality of the applications is improving so much. This was an excellent application, and I recommend it gets funded.

DR. WALLACK: I totally agree. Unless I misread it, my understanding also, and this is a very positive, is that it's the merging of immunology with cell biology and from my personal perspective, whatever it's worth, I think that's a very, very important coming together, merging of activities, and one that from things I've read is not being done enough. So not only was it a very, very fine proposal, but as one of the peer reviewers noted, very novel, well-designed, and feels strongly that there's a real chance for this to succeed. So for all of those reasons, I'm very enthusiastic in definitely funding this and move for funding.

MS. HORN: Anne, will you second?

DR. KIESSLING: Yes.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Moved to the preliminarily funded. The next grant, 12-SCB-YALE-01, this is Dr. Arinzeh and Dr. Dees.

DR. DEES: This is a study that's designed to generate skin cells from human embryonic stem cells, I mean, generate skin cells from human embryonic stem cells in large numbers with the hope that they will be able to use them in large grafts for therapies, including not only

the skin, but also other elements of the skin, like the follicles. So this is described as a -- this project is a imperative to bringing skin engineering significantly nearer. So it's not -- it's clearly on a clear path that they're, I mean, so it's a well-written grant. The reviewers are pretty enthusiastic, thought it was sound, very highly polished and I would recommend funding.

DR. ARINZEH: Yeah, I agree. I think the reviewers were very favorable. You know, they mention some minor weaknesses, but the score is reflective of that. It also comes from an assistant professor who is actually very productive and is publishing and doing very well in this area, so I recommend it.

DR. GOLDHAMER: One question. In your comments, one of the reviewers gave this a three, which according to the number of the good grants we have on it's own would be outside of the funding line. Were there comments about that -- from that reviewer that would suggest some concerns?

DR. ARINZEH: So the only thing that the reviewer was saying was that -- that the way she's got her aims structured, it's more of an opinion, the reviewer thought that the first aim may be too time-consuming and suggested doing aim two first. And then what they

identify in aim one is these transcription factors, maybe do that in aim two instead. So it was just a restructuring of the aims. So, I don't see that as being something major. I don't think the score of three --

DR. DEES: And in the reconciliation it may be the same.

MALE VOICE: Yeah, I agreed that that wasn't a good reason to give a score.

COURT REPORTER: Hold on one second. (Tape Change)

MS. HORN: Do I have a motion?

DR. KIESSLING: How many years are they asking for?

DR. DEES: Four. I move it to the yes category.

DR. ARINZEH: Yes. I second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Moved to the fund -- preliminarily fund category. The next grant is 12-SCB-YALE-05, Dr. Dees and Paul Pescatello.

DR. DEES: This is a study to examine the remyelination of neurons to show that human embryonic cells, dry cells are doing the work of remyelination in

monkey studies. Using the Geron cells that the FDA approved, they've already been used in now abandoned clinical study so the therapy contingents are very high. So maybe somebody can explain to me why now that they already have been -- now that they've been FDA approved, why we need to do a monkey study, but the reviewers were very enthusiastic about it. They think the preliminary data shows this proposal to be really quite promising. One worried about some intellectual property rights, but was satisfied that the issue was scratched by the way the state of Connecticut already has this handled. So I would recommend funding.

DR. PESCATELLO: I agree. I mean, I think this is exactly what we've been asking for its therapy directed to MS and a spinal cord injury. I guess, I'm not sure, I thought there was a little bit more of an issue about the Geron, intellectual property rights to Geron. I think that's a very minor issue. We said we want connections to industry. This is some relationship to a very important player, one of the few in the industry with stem cells. So I think --

A MALE VOICE: (indiscernible)

DR. PESCATELLO: -- maybe more. Anyway, so I concur.

DR. GOLDHAMER: Same question as before. Why the three?

DR. DEES: He was worried about the embryonic property rights.

DR. KIESSLING: So how many years are they asking for?

DR. PESCATELLO: Four.

DR. WALLACK: So in regard to this subject, but slightly different. Kocsis, Jeff Kocsis was going to get his cells from Geron?

DR. DEES: Yes.

DR. WALLACK: He was going to get them from Geron?

DR. DEES: Yes.

DR. WALLACK: Geron is no longer doing this kind of work, so are they still going to -- is he still going to be able to get his cells from Geron?

DR. DEES: Yeah. In fact, they explicitly address this, they have some cells from them, but they have plans to --

DR. WALLACK: Okay. Okay.

DR. PESCATELLO: I mean, the issue is that if something comes from the research, there's profit, but that some of that profit would go back to Geron because

they're supplying the cells.

DR. WALLACK: But the question -- all right. So the first question is, yes, he'll get the same cells, right? Okay. The second question was, and that was going to be addressed by our legal team, how do we handle the intellectual property situation when Geron is involved with this at this point? Is there any sense of this? Is this important discussion or not?

MS. HORN: I don't think it's a huge issue. Although they specify in the grant what they will provide to the state of Connecticut, they have five percent.

DR. PESCATELLO: Right.

MS. HORN: So I don't think it impacts the return to the state.

DR. WALLACK: Okay.

DR. DEES: And that was basically what they -- the second reviewer was worried about, the state of Connecticut specified in this contract that, you know, the state gets five percent, and that was the issue that was specified in the grant that that's they would provide.

DR. WALLACK: So do we need -- so obviously, this is a wonderful grant by a wonderful researcher, who I would be totally 110 percent in favor of funding. Do we need a sign letter at all addressing this

subject? Or are we perfectly happy that no sign letter is required?

MS. HORN: I can take a second look at that. I think we've had this kind of situation come up before and we've not done anything. The contract and the royalty agreement that they have to sign spells out pretty clearly what they have to report to us, and what they have to pay to us and who gets shorted on that isn't our concern as long as the state comes out with five percent, at least five percent. Some specify more. But I will certainly take another look at that.

DR. PESCATELLO: I would move to fund.

MS. HORN: Okay. So we have a motion to fund.

A MALE VOICE: Second.

MS. HORN: Second. Any further discussion? All in favor?

VOICES: Aye.

MS. HORN: Okay. We'll move this to the preliminarily funded category. And the next grant is 12-SCB-YALE-11, Dr. Arinzeh and Dr. Fishbone.

DR. ARINZEH: So this proposal addresses Rett Syndrome, which is one of the most common causes of mental retardation in females and so this P.I. has created

IPS cell with this genetic mutation and plans to conduct work -- he's looking at transcription factors really going through the whole genetic kind of screening and understanding of how they play a role in the development of -- in neurons with these mutations. So this was a well-written proposal and reviewers were very favorable, actually they mentioned no flaws whatsoever. So their scores, you know, reflect that, I think. So, I recommend that we fund.

DR. KIESSLING: But what's the EF cell component? They made IPS cells?

DR. ARINZEH: It's IPS.

DR. KIESSLING: And how many years are they asking for funding?

DR. ARINZEH: Four years.

DR. FISHBONE: I have little to add to that.

MS. HORN: Do we have a motion?

DR. KIESSLING: So do they have any other funds?

DR. FISHBONE: -- continuing on in work --

DR. ARINZEH: Yeah. He has -- he's an assistant professor, he has some pilot grants, but nothing of his own. It looks like he's -- well, something that's

ending in June, but it looks like a foundation grant.

DR. FISHBONE: He's funded?

DR. ARINZEH: It's on his C.V.

DR. FISHBONE: I'm trying to find it.

DR. ARINZEH: Page 25. He says he's a co-P.I. on an IH grant that goes through 2016.

DR. FISHBONE: -- some reference that his co-P.I. with Weissman at Yale. I don't believe he has a lot of funding. (Indiscernible)

MS. HORN: You have to speak up a little bit, we're not picking it up on the Court Reporter.

DR. FISHBONE: Yes, I'm sorry. He's sort of a leader in his field and he just came to Yale a year ago and is enrolled in a lot of other things, indirect. He doesn't seem to have a lot of grants in his name though.

DR. HART: One of the reviewers was very positive in that he said that the P.I. had solid funding from other sources. Is that matching what you --

DR. ARINZEH: He's got this one program project it looks like.

A MALE VOICE: Is he the P.I.?

DR. KIESSLING: No, he's a co-P.I. with Weissman.

DR. ARINZEH: No, he's a co-P.I. on Weissman, that's it.

DR. KIESSLING: And the other funding was -- is this the guy that was at George Daley's lab?

DR. ARINZEH: Yeah, he's published with him, yes. Yes. Same person.

DR. HART: There's been a real flurry of published work on Rett Syndrome lately. How does this stand out?

DR. ARINZEH: Good question. Let's see. I think it's because they've created -- they've created IPS cell line that has the genetic mutation. So they have those models.

DR. HART: There are about four or five groups that have done that.

DR. ARINZEH: Have they? Okay. The reviewers have not seemed to pick that up as being an issue. And there's -- I guess it also expressed some variations on the mutation, so I think that there's a uniqueness there in the model.

DR. HART: And one of the unique things about Rett Syndrome is since it explains -- it's been shown -- it's been used to show that you can reactivate x-inactivation and make both well-type and new cells for the

same individual.

DR. ARINZEH: And he mentions that.

DR. FISHBONE: He was a research fellow at Harvard before he came to Yale.

DR. KIESSLING: Yeah, George Daley.

DR. FISHBONE: Yeah.

DR. KIESSLING: Which is not a --

DR. ARINEZH: So they plan to map the goal of each domain of that -- of that mutation, that protein in neurons from those IPS. Yeah, it's not quite clear.

DR. KIESSLING: Okay.

DR. ARINEZH: They certainly -- I don't think they did comparisons to, or substantial comparisons to other people's work.

DR. FISHBONE: I was impressed by the reviewers, they gave it one and two, they thought he was terrific. This is very important work and they're characterizing -- using the unique set of isogenic IPSC lines expressing this -- having the key methodologies worked out, leading position in the field with a P.I. in the field of IPSC, number of publications in high visibility journals. It sounded like they liked him and what he was planning to do. So what can we tell you? I have to admit, I didn't understand a lot of what he was

trying to do but the reviewers thought he was very good. They liked the project.

DR. HART: The only thing I'm bringing up is that there's -- I just was checking my sources here, there's about four to five publications in the last year on this topic from various labs.

DR. FISHBONE: Yeah. Would that make you less keen on funding it?

DR. HART: I just hope the reviewers would have caught it, that's all.

DR. FISHBONE: Yeah.

MS. HORN: Do we have a motion?

DR. KIESSLING: We can't think of a reason not to fund it.

(Laughter)

DR. KIESSLING: Unless somebody has a project that we think is more on target?

DR. WALLACK: I would move funding.

MS. HORN: Is there a second?

DR. ARINZEH: I second.

MS. HORN: All in favor?

VOICES: Aye.

DR. HART: Now by my calculation, we're up to 7.75 million committed if we follow our own advice,

just so everybody knows where we are. We've got room now for about 10 seeds if we stop here.

DR. GENEL: 10 seeds?

DR. KIESSLING: Well, if we want to fund everybody full speed.

DR. HART: Yes. That's right, that's without any further discussion, right.

MS. HORN: So at this point in the established grants are there any that reviewers would like to bring forward that they feel are particularly meritorious and deserve a view by the full review?

DR. KRAUSE: Yes. The one that I was assigned, 12-SCB-UCON-01.

DR. HART: What number is that?

DR. KRAUSE: What number is that? I don't know what you mean by what number is it.

DR. HISKES: Who's the P.I.?

MS. HORN: Goldhamer.

DR. GOLDHAMER: I think the process is best served if I step out. I would feel more comfortable if I step out.

DR. KRAUSE: I'd feel more comfortable if you stepped out too.

DR. HART: I feel even uncomfortable asking

you to do that.

DR. GOLDHAMER: Don't forget I'm out here.

A FEMALE VOICE: We can't leave him out there until lunch.

MS. HORN: I don't think we require a second in terms of bringing the grants forward. Is there anybody else who has a grant that they would like to have heard?

DR. HART: Yeah. I'd like to bring up 12-SCD-YALE-06.

MS. KRAUSE: Q-Y-A-N-G.

A MALE VOICE: What's the score?

DR. HART: It was 2.5.

DR. KRAUSE: Can we just discuss the one that I recommended, only because David's not here and he might want to bring up some of his or whatever.

MS. HORN: Okay. Very good.

DR. HART: I was primary on that, so do you want me to just start then?

DR. KRAUSE: Please.

DR. HART: So the proposal was to use mouse models to understand how muscle satellites become programmed for myogenesis and whether alterations in that programming are implicated, infiltration of adipose

fiberoptic tissues and muscle degenerative diseases of aging. So it's a really nice application. The P.I. has a great deal of experience in myogenesis studies and has obtained all of the necessary animals -- genetic variants of animals for this work, driver animals and so on. The strategies are carefully described. It's a very well written grant. The approaches are largely feasible and the reviewers show the -- find that the information will likely shed light on how myogenetic transcription factors regulate the developed function of these important satellite cells during the developing generation.

The P.I. has been a professor since 2011 and is director at The Center for Regenerative Biology up at UConn, Storrs. Quite productive, established in his field. He hold and IHR-1, a Muscular Dystrophy Award, a DOD project. There is a note in the grant that aims two and three have some overlap, partial overlap with the DOD -- I'm sorry, the MD grant.

My evaluation of reading the reviews and the scores is that, yes, this is very good work. The reviewers sounded lukewarm. I think that's the nice way to say it.

DR. GENEL: What was that?

DR. HART: I felt like the reviewers

sounded very lukewarm in their description. Their scoring kind of reflected that. I open to be contradicted.

DR. KRAUSE: So here's my opinion. This was a really, really good grant. He has preliminary data, he has all the models, and the part where I particularly felt strongly about it is we're talking about stem cells and it's great to do immunology and see how things are effected when you play with the immune system. But stem cells are about, how does the cell self-renew and how does it differentiate? And that's exactly what he's working on. And the -- so basically how do muscle stem cells self-renew and how do they differentiate and this is what he focuses on and he's been very productive.

I did not interpret the reviews the same way.

DR. HART: Okay.

DR. KRAUSE: So the reviewers as far as I could tell found absolutely no fault with the grant except he isn't using human cells. And that's basically all they say in terms of weaknesses. It would be ideal to address similar questions in human myogenic cell lines. And that was it for weaknesses. It would be a benefit, you know, human. So I understand that concern and it ends up that the P.I. directly addressed this right at the beginning of

the grant as to why he chose mouse models instead of human models and it's a beautifully written paragraph that basically says he wants to treat human disorders, but his mouse models are what's going to get him there because if he puts a human cell into an immunodeficient mouse you're not going to get the same data as how these cells are regulated, you know, within the endogenous muscle of the mouse.

So he says, you know, in aim three, utilization of mouse stem cells provides the greatest versatility and precision in manipulating gene expression and a use of allogeneic cells would effect the outcome, you know, using the z-genig egg (phonetic). So I just -- so many of these grants, even at the top, got an occasional three for reasons that were somewhat weak, you know, questioning something about, you know, do they have the appropriate agreements in place with Geron and I felt like the concerns of the two reviewers here, he just happened to have gotten two that gave him a three, were both really the human aspect. And I just think that it's so much more responsive to be doing stem cell related research as in self-renewal versus differentiation that I think it's entirely responsive to the kinds of things we're trying to fund.

DR. HART: Let me take advantage of the opportunity here to say something about the reviewers in general. I find, especially concerned to my service on NIH reviews and what I've seen from scoring of my grants as well that there's a real lack of text describing justification for the numeric scores. A very, very serious lack. So it makes us here second-guess the intent of what the score meant to these reviewers. And I feel like this is a real problem that needs to be fixed.

DR. KRAUSE: Yeah, I agree. There's room for interpretation one way or the other. I interpreted it as strong, and you said lukewarm and you really --

DR. HART: Right. The problem is that you sometimes see this kind of language when people are trying to criticize with praise and that's the way I read it. But I'm happy to be contradicted.

DR. KIESSLING: So do we have any other, I mean, the uncomfortable part of this, of course, is that Dr. Goldhamer serves on the committee and we've kind of talked him out of a three category. Are there any others in the three category that are human related that got a similar kind of review?

MS. KRAUSE: Well, I wasn't assigned to Stormy Chamberlain's, but I thought that her one and seven

was quite a disparate score on (multiple voices). And I felt that seven seemed a little bit undeserved. So, if we were pulling up others with a similar score, if I were one of the two people who had been assigned that and read it in detail, I might have brought it up. But that wasn't one to which I was assigned.

DR. DEES: Yeah. The Laurencin grant that's up above, I mean, there's a similar kind of problem and what they were worried about was this is a grant where they're using -- developing protocols to construct bone from mesenchymal cells and the complaint, the big complaint was that the researcher was only -- the P.I. was only putting in five percent of his time. That was the complaint. I mean, there were no other real weaknesses in the grant.

DR. KIESSLING: Is it a mouse grant?

DR. KRAUSE: I'm not sure.

DR. DEES: No, it's not a mouse grant.

DR. KRAUSE: Are you concerned that it's a mouse grant?

DR. KIESSLING: Well, I mean, our mission has been to promote work that is human embryonic stem cell rated as much as possible and it's kind of branched into IPS and the goal is to get to translation. So your

point's well taken, if a mouse model is the best way to get there, that's fine. I mean, there's a beautiful application in here that is, you know, a wonderful grant that's looking at follicle development, one of the ones I reviewed, it's beautiful. She's made hair follicles, you know, act like c. elegans, but it doesn't really -- it's beautiful work, it doesn't relate to our mission. I mean, it's much -- it's a mouse grant, it's a, you know, it's a model, it's great.

DR. HART: This is -- I'm sorry, I have to look at the grant, but I mean, they were going to model in rabbits. I don't remember what cells they were using.

MS. HORN: I mean, you can spread this money, you know, as broadly --

DR. KRAUSE: You know, I completely, completely agree. The mission of the Connecticut Stem Cell funding has expanded beyond just funding things the federal grants won't fund.

DR. KIESSLING: I didn't see anything in any of these grants that the Feds. wouldn't fund.

DR. KRAUSE: Right. So we've moved beyond that to, you know, enhancing stem cell research in Connecticut and you wanted to have some human potential for treating human disease. I think we're looking for

things that are directly applicable to human disease. And I feel that, you know, his focus on understanding muscle and muscle repair is entirely within that focus.

MS. HORN: What we've said is, animal models will be considered, but after it has been demonstrated direct relevance to human cell biology and it's therapeutic implications.

DR. HART: I think that he remain at this project. That's not the question.

DR. KRAUSE: I understand the concerns. So, you know, it does end up -- you know, you have to bend things sometime, you know, why is this fly model appropriate? But I think here it's pretty direct, but Anne, I completely respect that opinion.

DR. FISHBONE: He's got wonderful reviews except that he should be ashamed that he's only spending .6 month's commitment.

DR. KRAUSE: Joe, was that him?

DR. DEES: No, no, that's the other, that's the Laurencin.

DR. FISHBONE: Laurencin? Oh.

DR. KRAUSE: We'll get to that one maybe today.

(Indiscernible, multiple voices.)

DR. WALLACK: So picking up on what Ron was saying, when I read the review, the narrative, the impression I got relative to the score, that the score was actually lower -- I'm sorry, it was not as good as it should've been. The narrative read very, very well and frankly, I was surprised to see that the score was only three. I would have anticipated two or something like that, or whatever it was, but certainly not three. So from that perspective I understand why Diane, you're picking that particular proposal up as something that we should be reconsidering, especially -- I mean, Anne's right. I mean, he's part of this team, but aside from that, he's a very fine researcher, he's produced extremely well, and he wrote a very impressive well organized proposal so that I wouldn't have any problem perhaps for the time being putting him into the maybe category. But not to say that we're definitely going to fund him at this particular time, but at least keep him in the running for now.

DR. GENEL: How does that address Anne's question?

DR. KIESSLING: Yeah. I mean, there's a grant that we could discuss that has a better score, that's more to our mission. I mean, I'm concerned --

DR. HART: We're saying that the score doesn't reflect the reviews, it's part of the problem.

DR. DEES: Right. But it goes back to your other problem Ron, which is, we're left second-guessing again. If we go down that path we're actually -- we're lost because we don't really have -- especially those of us who our time is -- had no way to make these cuts or evaluations.

DR. HART: You're absolutely right.

DR. KRAUSE: But one of the points that was brought up was, you know, is a .5 difference in score a big difference? I mean, you're talking about a three and a three, versus two and a three, versus a one and a four.

DR. DEES: Yeah. I think you had a .5. We're talking about, you know --

DR. KIESSLING: 1.5.

DR. KRAUSE: Well, I'm blaming it -- no, we were talking about, does anybody have a grant? Now, if you look at my assigned grants, I'm not assigned anything in the 2.5 category. So of the grants that I reviewed, the ones that I would question whether they should be brought up, this is the one I would bring up, that's all.

DR. DEES: -- fair enough.

DR. KRAUSE: And everybody else in the room

can bring up theirs.

DR. PESCATELLO: I guess the question is, from what we've heard about David's grant versus the first five that we -- having now heard about it, do you want to move putting that into -- making it six that we are considering, or is it nevertheless not of the same quality as the first five?

DR. KRAUSE: My judgment is that it was the same quality.

DR. PESCATELLO: Because we have enough money spent -- we have, I think -- what do we have left? It's like 2,000,000 for those seed grants if we were to fund those five?

DR. KIESSLING: If we fully fund them.

DR. PESCATELLO: If we fully fund everything.

DR. KIESSLING: Right.

DR. HART: I mean, from a point of view, let's put it this way, the five that we've already looked at are like -- to me, the numerical scores were too good, you know, we are taught not to give out that many one's, it's just not allowed. This grant, if you take the comment that the problem is, he's not working in human cells, and just discount that it becomes in the same

range, there's no question about it.

A MALE VOICE: I guess I'm speaking in support of the motion for a maybe.

DR. PESCATELLO: Can I just ask another question? Just the procedure. So it keeps coming up that if we fully fund, and so, as a nonscientist I'm just -- what is the generally accepted practice, especially with the NIH, I mean, so that when somebody submits a proposal it's for a certain amount of money for a certain research, you know -- is it easy to scale it back? I mean, are you then asking for a different -- are you asking them --

DR. KIESSLING: There's lots of ways to do that. But one of the things to note is, for instance, if you look at the Horsley grant, the 1.5, this is a well-funded lab, so whereas some of the other projects are going to go away, I mean, I think part of our mission is to make sure that none of these projects that are really good and ongoing dry up because then all the people leave. I mean, I think that's a consideration that we need. The Horsley lab, which it got a great score, because it's a really good application, also already has a lot of money.

DR. KRAUSE: So Paul, to address your question, in terms of the NIH, the only considerations that can be made for cutting funding are within that grant

itself. If you feel that they could do the work proposed with less funding, then you can say, and it depends on the budget, but if it's within the ones that are done called modular budgets, you can say, I propose that they fund it without one of the modules. Now that doesn't mean it's what's going to happen, but that's what you, as a reviewer, can recommend and say, I think they're asking for too much for what they're proposing, therefore I propose they cut one module. But you don't do it based on, you know, their other funding, etcetera.

DR. PESCATELLO: Because you identify something in the budget, and you say --

DR. KIESSLING: Right.

DR. KRAUSE: So you don't just cut it -- it used to be they'd say, oh well, let's just get rid of aim three and give them, you know, two thirds of the money. But that's not kosher anymore.

DR. HART: But realize that almost no NIH grants are fully funded at this point right now because of the federal budget. The administrator just take a percentage off the top and that's it.

DR. KIESSLING: Right.

DR. KRAUSE: You can't afford to do the work.

DR. HART: Do it or don't do it, here's the money we're able to give you.

DR. PESCATELLO: So I guess in our case if we were to do that, to say we'll fund it, but for a lesser amount than the researcher is I guess free to say, well, sorry I won't do it under those circumstances. And that's why we have -- we always choose a couple of more.

MS. HORN: You know, they are required to come back with a budget demonstrating how they will do the work for the money given. But we've taken it off the top. We've also suggested that they do it for a short period of time, that we fund for two years instead of three, or that they not do one of the projects. So there's been a variety of ways that we've handled that.

DR. KRAUSE: So why don't we move ahead now with the maybe and maybe with a slightly decreased budget to be determined when we get back to the maybes?

DR. HART: I agree.

MS. HORN: Was that a motion?

DR. KRAUSE: That's a motion.

MS. HORN: All right. Do we have a second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

DR. KRAUSE: And obviously, we can bring up other grants as well.

MS. HORN: So were there any other grants that a committee member would like to bring forward for discussion?

DR. HART: I wanted to nominate Yibing Qyang, which was 12-SCB-YALE-06. His score was 2.5.

MS. HORN: Do people want to bring the other ones forward? I know we did David's because he needed to be out of the room. Do we have a sense of the scope of what we're dealing with? Are there other grants that people would like to bring forward?

DR. GENEL: We're thinking.

MS. HORN: You're thinking.

DR. FISHBONE: Well, did somebody mention Laurencin?

A MALE VOICE: Do you want to bring that up?

A FEMALE VOICE: Would you like to?

DR. FISHBONE: Well, at the time (indiscernible).

DR. WALLACK: So just a comment on Laurencin, I'm not sure, but isn't he also a co-P.I. on the Kumbar grant?

DR. ARINZEH: He is.

DR. WALLACK: I was right?

DR. ARINZEH: Yes.

DR. WALLACK: Right. Which is very similar to this grant.

DR. ARINZEH: I didn't read that one.

DR. WALLACK: So I guess what I'm asking, if you want to bring up Laurencin don't we have to bring up Kumbar and have a comparative kind of consideration there?

MS. HORN: Sure. I don't think that necessarily follows, but --

DR. KRAUSE: Well, one uses MSC? I don't think they both use MSC. I think they're actually pretty different. I mean, they both work on --

DR. ARINZEH: Well, the Kumbar uses MSC. Is that the one you're talking about?

DR. KRAUSE: Right.

DR. ARINZEH: Yeah.

DR. KRAUSE: But what does Laurencin use?

A MALE VOICE: (Indiscernible)

DR. KRAUSE: Oh, they both use them?

DR. ARINZEH: But if there's -- Kumbar one is a human -- they're using human cells --

MS. KRAUSE: Given that they're both from the same lab, I think we only need to discuss one anyway. Is that the same lab or is it a separate lab?

DR. WALLACK: It's the same lab. As a matter of fact, Kumbar is in Laurencin's lab I think.

DR. ARINZEH: They share the same space.

DR. WALLACK: Right.

DR. ARINZEH: He's a former post-doc.

DR. WALLACK: Kumbar is a young researcher and so forth.

MS. MULLEN: Are we making these determinations based on personnel or on the applications?

DR. WALLACK: Well, both. Right. And I guess what I'm also saying here is that the peer review marks -- scores for Kumbar with that -- I think the main concern about Kumbar is the scores may have been higher except for the fact that they questioned his publication record. But he's also a young researcher, so perhaps the fact that he hasn't had an opportunity yet to publish as much as the reviewers may have expected to see. So I guess I'm not making my point and I apologize. But if we're going to consider Laurencin, I would recommend that we also consider Kumbar and see if we want to differentiate one from the other.

DR. KIESSLING: In order to just keep that lab funded is what you're saying?

DR. WALLACK: Right, right.

DR. FISHBONE: The problem with Laurencin is he is asking for -- he must have a very large salary because he's asking for $40,000 a year for .6 months.

DR. DEES: The problem is he's a surgeon and makes a ton of money so five percent of his time is $40,000.

DR. FISHBONE: Yeah.

DR. KIESSLING: So let's fund Kumbar.

(Laughter)

DR. FISHBONE: Laurencin is getting -- asking for $40,800 a year and Kumbar --

MS. HORN: I think we just need to look at the particular grant and decide whether it is somehow meritorious and fits better into Connecticut's proposal and not worry so much about where the individuals --

DR. WALLACK: Then I'll recommend -- if it has to be individually-based also discussing Kumbar.

MS. MULLEN: That sounds like a reasonable recommendation that keeps us in our appropriate plane.

MS. HORN: -- okay. Anybody else? Okay. Hearing none, let's move then to --

A FEMALE VOICE: So we're going to discuss three, Kumbar, Qyang and Laurencin, is that correct?

MS. HORN: -- that's what we have.

A FEMALE VOICE: Okay.

MS. HORN: Okay. So, 12-SCB-UCHC-05, that is Dr. Arinzeh and Paul Pescatello. Just the Kumbar.

DR. ARINZEH: Okay.

DR. PESCATELLO: Yeah.

A MALE VOICE: Just Kumbar?

DR. ARINZEH: Okay. So this proposal is about tissue engineered tendon for rotator cuff tears. So, you know, they're going to be using the human MSCs derived from the bone marrow and combine those with a scaffold and they're going to be testing that in a new rat model to look at long-term function. And so the reviewers overall were favorable on this, but there were some -- I think the scores reflect it, because the primary reviewer said that they thought that there was a bit of a fishing expedition looking at different factors in the design of the device. I think they have different -- they have different types of scaffolding materials, different adhesion proteins that they were looking at and then insulin release. And then reviewer two also thought that the new rat model may be problematic. I don't know, that

didn't seem much of an issue to me anyway. I don't know how else you would test function of a tendon without going to a slightly larger animal model. The mouse I can't imagine. They recommended using a mouse, but I just can't feasibly see how they can do such small tissues there, but maybe it's something they could do.

So, you know, and like I said, Kumbar is a former post-doc and they also were worried about his ability to be independent maybe from Laurencin. That was also a reviewer comment, or something like that, similar to that along those lines, independence from his former mentor was mentioned just because they appear to share the same laboratory space.

DR. PESCATELLO: And I think there was some design experiment or design issues in terms of certain things didn't happen and lack other components of the proposal. So I would just say that I would agree with the description and I guess from what I've heard about the other six so far that we're looking at I would not recommend putting this on and going forward with anymore discussion about this given that the other six I think have greater merit. I don't know if you --

DR. ARINZEH: I mean, you know, they are testing human cells and looking at efficacy and they did -

- they are -- they actually showed preliminary in vivo data showing that it could work. So they are moving at least towards, you know, translation and getting this to really work functionally. So I did really like that aspect. So I'm leaning toward the maybes.

MS. HORN: It sounds like you're leaning more toward a maybe?

DR. ARINZEH: Yes.

MS. HORN: Would you accept that?

DR. ARINZEH: The scores are not too bad.

DR. KRAUSE: Well, one of the things that the reviewers say is to consider potential overlap with Laurencin and if there is overlap, and I haven't read these two grants, then maybe the discussion of the next grant will help to determine what we do with this one?

DR. GENEL: I agree. I agree.

MS. HORN: So put it in the maybe for now?

DR. KRAUSE: And then maybe after discussing Laurencin decide whether it moves from the maybe.

MS. HORN: Okay. We have a motion.

MS. MULLEN: Sounds like a weak maybe. That's my observation.

MS. HORN: We have a weak maybe.

DR. KRAUSE: Well, I would be leaning towards no, but we'll see.

MS. MULLEN: You just made it weaker.

(Laughter)

DR. PESCATELLO: This may be an unfair comment generally about, you know, all of the grants, but we've put an emphasis on translational so there definitely seems to be a component of highlighting the translational aspects of it. Because you could always say, oh, this is going to -- you know, and I have always on this committee been a proponent of basic research. You can't just -- I haven't seen it ever in my life where you can jump start and go -- you've got to do the basic research and I think you should be very proud of the basic research we have funded and the value of it. And since the other six that I've seen so far to the extent they're -- they're more basic and less translational I have no problem -- because of my roots I have no problem with that.

MS. HORN: Okay. So where are we on this one?

DR. PESCATELLO: We were agreeing to do maybe.

MS. HORN: We're agreed to do maybe? Alright. We have a second. All in favor of maybe?

VOICES: Aye.

MS. HORN: Okay. So then we will move to the Laurencin grant. Okay. This is 12-SCB-UCHC-06 and the reviewers are Richard Dees and Gerry Fishbone.

DR. KIESSLING: Who are we talking about?

DR. DEES: This is a proposal about material structures and the protocols to construct bone in primal healing different kinds of stem cells and they needed them to repair bone injuries in I think rabbits. So it has a clear, sort of clinical outcome. The reviewers were really impressed with this grant and it's structure and how it's laid out and they pretty much said we're disappointed that the P.I. was going to spend so little time on it. And the problem is that if he's spending any more time on it he can't stay under budget. So it's sort of a funny position to be in, I mean, they're right, he's not spending much time. Actually Dr. Kumbar is spending five percent of his time on this grant as well.

DR. FISHBONE: Which sounds like Kumbar is going to do the work.

DR. DEES: Well, no. He's only spending five percent. I mean, the work is going to be done by, you know, other people in the lab, a post-doc is going to

do most of the work. It's going to be fully 100%.

DR. KIESSLING: And this is a rotator cuff grant too?

DR. FISHBONE: No. It's bone repair. He's developing a three-dimensional model. The objective of this is to develop smart osteo-inductive biomaterials, therefore inducing osteogenic differentiation of human -- using primal stem cells. It's a different project, but I mean, it can certainly --

DR. DEES: Yeah. They were going to do stuff in like all (indiscernible), rabbits -- repair.

DR. KIESSLING: He'd be better off to devote more time and ask for no salary, right?

DR. FISHBONE: Yeah. I mean, the salary was very disturbing for the amount of time he's giving, more than a post-grad would get for doing 100 percent of the time. He's asking for 40,000 a year but he's been (indiscernible). I wasn't very thrilled with -- and he's apparently a very important person with many, many projects going on. He's a professor and chairman of the department.

COURT REPORTER: Hold on one second (tape change).

DR. DEES: I had no idea what to think of

that. I mean, they were really enthusiastic about the grant, but I think we have to talk to him -- he doesn't have time for this because he makes too much money.

DR. FISHBONE: Yes.

DR. DEES: Yeah.

DR. FISHBONE: Yeah.

DR. KRAUSE: I understand what you're saying. I think it gets back to the fact that the reviewers didn't say very much. But I wouldn't say they were very enthusiastic, they basically said almost nothing, it's like almost an empty review. They're saying, yes, it's shameful that it's a low percentage, but otherwise they're not even saying -- they're saying, oh, it's good. There's like no -- I don't know, content to what they're saying. And if I'm comparing it with Laurencin, the other grant, Kumbar, I don't see that either one is a super strong grant in terms of an independent investigator because the Laurencin grant is just a low percent effort and Kumbar is the co-P.I. I don't know. I guess -- I'm not convinced by what the four people here have said and by reading these reviews that these are great. But I didn't read the grants.

DR. HART: If you completely discount the comments on P.I. effort, co-P.I. effort, and everything

else, what's the science? Is the science worthwhile on either project?

DR. KRAUSE: That's the question I'm trying to figure out and I can't.

DR. FISHBONE: Yeah. It sounds like it is, but there's a lot of things about it --

DR. DEES: Yeah. I mean, we're not giving it a whole lot. I mean, there are some strange -- no weaknesses or a listing for those weaknesses, so it's hard to say, okay, well, what's the problem here?

DR. HART: And you can't give without list the weaknesses.

DR. KIESSLING: Have these people been funded by us before, either one of them?

A MALE VOICE: No.

DR. KIESSLING: No? This is new?

DR. KRAUSE: So if you look at Laurencin funding page he's got a bunch of projects that are running out of money. When did he come to UConn?

DR. GENEL: He's the former Dean. He's the former Vice President and Dean of the Health Center. He stepped down last year.

MR. WILSON: 2007 I believe.

DR. WALLACK: He got a better job. I have

just an observation, not a scientific reading of this. But my observation is that we are going to be, to pick up on Ron's narrative, your arithmetic narrative, we're going to be running out of money very soon. And the best that I'm hearing that we can do for this, these two grants, is a maybe. But at some point we're going to have to make a decision, so it seems to me that we should make that decision now because I don't hear compelling arguments in favor of keeping it on the table. And maybe we should say, no funding, to both of these grants.

DR. PESCATELLO: In relation to the other six, I haven't heard anything that makes me say, this puts them in the same category of those six.

DR. WALLACK: So if you need motion I would move to not fund these two grants.

DR. KRAUSE: I'll second that.

MS. MULLEN: So the question, it turns out that nobody can go to St. Kitts? I have to have some goal here.

DR. WALLACK: Yeah, yeah.

MS. MULLEN: No, seriously though, if it turns out that nobody can go to St. Kitts, then there's 1.994 million dollars out there that if we vote, you're going to get 1.9 million, not really, but no seriously, is

there a backup list where there will be some other considerations?

DR. KIESSLING: But the only part of going to St. Kitts was $160,000.

DR. HART: That's one seed grant.

MS. MULLEN: Well --

MS. HORN: Over four years.

DR. HART: But that's at best one seed grant.

MS. MULLEN: -- but something happened and the entire grant didn't get funded. And we don't know, we don't know.

DR. WALLACK: So to address that subject, which is a real incentive, my sense is that if we award that grant at 2,000,000 and we can't fund that, he's been able to before find the funding for the St. Kitt portion and my sense is that he's not going to turn down the award of the grant because he has to find separate funding. And maybe what we should do is -- maybe what we should do is have a side letter in that proposal that if Connecticut money cannot be used for St. Kitt that money has to be returned to us and he has to find funding on his own for that portion of it, that $170,000.

MS. MULLEN: We don't know that.

DR. WALLACK: I know.

MS. MULLEN: We don't know. So I only raise the point to say, we could be going through these determinations in a very finite way so that by the time we go through all of the seed grants everything adds up to 9.8 million, or throughout these considerations we've generated a fund lists of fall back so that we are not just trying to create one later without getting back into the specifics of that specific application. So that being said, I wonder whether or not we want to scrap these maybes, or remember that they could start to generate a list of secondary considerations, that's all.

DR. WALLACK: I would endorse the recommendation to keep the maybes for secondary consideration.

DR. HART: The next question is, are these two grants part of the maybes?

DR. GENEL: Of the two, though I would put only one of the two on the backup list.

DR. WALLACK: I would move at this point that while we have the backup list Commissioner, that these two perhaps from my perspective should not be on that backup list.

DR. KIESSLING: I'll second that.

MS. HORN: So we are voting for maybe at this point on these two or --

DR. DEES: The motion is for now.

MS. MULLEN: -- okay. And then the other question I have -- so Dr. Laurencin is no longer dean and vice president, or whatever his specific title was, but not back to what he is. So just -- and my understanding is that those jobs actually usually come with relatively higher salaries than the average university's salary, which makes me wonder whether or not arithmetically what goes into a budget to reflect the percent effort on the grant realistically reflects the amount of thinking and input the individual will actually devote because, you know, I think we would balk if someone said, he's putting 25 percent effort, or 20 percent effort, and then looking at how much of the 750,000 is going to salary support for an individual.

So I just hope science is one consideration, but if we're worried about the numbers in the context of salary that's, you know, if they're a standard deviation out or something, and that's a different --

DR. KRAUSE: Yeah. And that's a really interesting point, because we don't do it in Connecticut,

but at the NIH there's ceiling, there's a maximum salary, so if somebody makes $1,000,000 a year their maximum salary, rounding up is 200K, and therefore the percent effort, you know, 47,000 would be, you know, almost 25 percent effort, even though that person makes much, much more money. So the NIH got around that by defining a ceiling above which they wouldn't go. Just as an FYI.

So one of my concerns -- it sounds like we're going to vote no and maybe we're done, but just -- these are engineers. Did they really address the biology and did -- we just don't know, because the peer reviewers didn't talk about it.

DR. KIESSLING: If you look at what they've been doing, they've probably addressed the biology. But Kumbar is addressing rotator cuff tears and I don't know that that's a huge health issue. The other one is more basic, they're looking at overall tissue engineering, which is a big health issue.

DR. ARINZEH: I didn't read the Laurencin proposal, but the Kumbar, I mean, yeah, they're engineers. I'm an engineer, so --

DR. KIESSLING: So you understand.

DR. ARINZEH: -- I know exactly his stuff, his scaffolding and everything. But Kumbar, I mean, they

do -- they're looking at differentiation and the markers and things where the cells turn in genocide's I guess and so there's enough there. You know, in an animal model it's showing function, so -- which is, you know, mechanical. Function is the way people can.

DR. KRAUSE: Thank you. I appreciate that. So I would second the motion on no for both of these just given limited funding.

MS. HORN: Okay. All in favor?

VOICES: Aye.

MS. HORN: So that is -- yes?

DR. HISKES: I'm just concerned about these seven 2.5's. We have seven possibles that rate at 2.5 and I just -- I wasn't assigned to them, so I didn't read them, but I'm concerned that they get a fair hearing and none of them then should be discussed.

DR. KIESSLING: Well, I was the primary reviewer on one of these, on the Greco grant, which is the Yale -- 12-SCD-YALE-04, and it's an absolutely outstanding grant, it's wonderful. This person has turned watching hair follicles develop into hair to the level of C. elegans. But it doesn't really speak to our mission, okay? So, I mean, that's why I haven't brought it forward. It's a wonderful skin development grant. This

could be funded by any agency whatsoever, and probably will be. It's a good -- it's a good young investigator, already has some funding, so that's why I didn't bring it forward. It's just -- it does not speak to our mission, like the others do.

And one of the other 2.5's I was secondary reviewer on, the primary reviewer is a lot less enthusiastic than the reviewers were. So this is the Dr. Maye's grant --

DR. HART: That would be me.

DR. KIESSLING: -- yeah, which is also an interesting proposal that's using human embryonic stem cells. It does kind of wander around in space, so even though it speaks more to our mission, I'm not too sure exactly what's going to get accomplished. And this is -- these are -- some of these I think should have been seed grants.

DR. HART: Yes. That one I can say is a very good example, it would have been a good seed grant.

DR. KIESSLING: It would have been a great seed grant.

DR. HART: It doesn't have the preliminary to propose such a big project.

DR. HISKES: Which one?

DR. KIESSLING: Maye, one of the other 2.5's. Yeah. We're speaking to two of the 2.5's that we're concerned about.

DR. HART: That was -- I specifically selected the one that I thought deserved to have been scored higher than 2.5 on the list for that reason.

DR. KIESSLING: And we still have another one too.

DR. HART: Yep.

DR. KIESSLING: So at this point, even though those are nice applications, I would not bring them forward.

MS. HORN: We do have another one that was nominated, 12-SCB-YALE-06, Dr. Arinzeh and --

DR. HART: Qyang.

DR. ARINZEH: Qyang, is that it?

DR. HART: It's what we decided over here.

DR. ARINZEH: Okay. I was saying Q-yang, but that can't be right.

DR. HART: Yeah. It must be Qyang.

DR. ARINZEH: Okay.

DR. HART: So do you want to go first?

DR. ARINZEH: You go.

DR. HART: Okay. Because no one has the

opinion about this one.

DR. ARINZEH: Yeah. I mean, I'm actually very in favor of this one.

DR. HART: Oh, okay. This was on tissue engineered blood vessels using induced pluripotent stem cells. The reviewers gave it a two and a three. And a summary of the science very quickly is that the goal is just to characterize smooth muscle cells derived from both embryonic and induced cells to investigate therapeutic potential by developing tissue engineered blood vessels and then implanting them as aortic interposition grafts in mice. So again, they've got a disease relevance, they've got a kind of engineering basis, and they've got an animal application for it.

One of the comments from the reviewers, for example was, excellent proposal from talented young investigator building on innovative idea and a large body of preliminary results. That sounds like a lot better score than was given. Strengths include a high significance of unmet needs and the demonstration of function in in vivo model. That sounds a lot better than the score that was given. Dr. Qyang has been assistant professor since 2010, but already has six publications in high profile journals and has relatively robust funding,

American Heart, an internal award, an NIHK-02 training grant for his own salary, and several portions of Connecticut Stem Cell awards from other people as well.

In my mind, again, it was a solid two as a rational score. It's a high-quality proposal from a productive young scientist. So at worst, I would put it on the list for the backup grants. I think we ought to consider it better than that, actually.

DR. ARINZEH: I agree. I reviewed it and I looked at -- the reviewers really didn't have anything negative to say. I guess one minor weakness of that generation of integration free IPS they thought it was not necessary, but I don't know why --

DR. HART: That's ridiculous.

DR. ARINZEH: -- yeah, so a ridiculous weakness. So, I mean, based on the way they reviewed this I would see them scoring a one and a two, you know, or something like that, along those lines. I'm in favor of maybe a backup, same thing, backup list.

DR. KIESSLING: But would you like to see --

DR. HART: No, actually, I said at worst a backup list. I actually move in favor of putting it on the real list.

DR. ARINZEH: Okay.

MS. HORN: You have the prerogative, you can make that recommendation.

DR. ARINZEH: Okay. So real list.

DR. GOLDHAMER: I just wanted to point out that the same investigator has a seed grant that we'll be discussing.

DR. HART: Yes. Yes. So we should consider that.

DR. GOLDHAMER: Which also got a very good score so the question is --

DR. KIESSLING: And a couple of people that are post-docs in this lab -- in this lab have seed grants too.

DR. HART: Absolutely.

MS. HORN: Okay. So I here we have a motion to fund? Put it in the preliminary funding category. Do I have a second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. MULLEN: Well, is there a -- do I hear a call for anything below two and half or three or are we set with the established?

DR. WALLACK: So question? Was there a point made, I think by Diane, on the Chamberlain grant, the one and a seven? That grant was not one of my grants, but the --

DR. KRAUSE: It wasn't one of mine, either. I was just looking at really disparate scores and then reading the comments. But I didn't read it in depth. I think very highly of her work, so it's possible if I read the grant I would like it, but I didn't.

DR. HART: Who's the reviewers?

DR. PESCATELLO: I was one of them.

DR. HART: How do you feel about it?

DR. PESCATELLO: From the others that we're considering I wouldn't put it in that category. I know there was a big difference between the reviewers, the peer reviewers.

DR. KIESSLING: Why did the one give it a seven? Why did one reviewer give it a seven?

DR. WALLACK: I was on the grant and it wasn't for any scientific reasons.

DR. PESCATELLO: Overly ambitious.

DR. WALLACK: And I'm just trying to find that right now.

DR. KIESSLING: She's a post-doc, right?

DR. KRAUSE: Now she's back in -- and she's independent, there was a question about independence, but she's independent from Mark Larlard (phonetic).

DR. PESCATELLO: With no consideration given to the number of cells required to do all of the assays proposed.

DR. KRAUSE: But then they went back and decided that it wasn't too many cells.

DR. KIESSLING: I'm a big fan of CTCL's.

MS. MULLEN: So is this a request to discuss it, or are we just talking about it?

DR. KRAUSE: That's a very good question.

DR. WALLACK: So let me answer Anne's question. Somebody said ridiculous about some of the comments. On the one hand, the P.I. has been productive. The reviewer who gave it a seven goes on to say, but the P.I.'s track to independence does not appear to be well planned out since the P.I. is still in a laboratory of previous mentor. Now, this investigator, I believe, is in fact an independent investigator, so the assertion and the rationale for giving this investigator a seven, to me at least, I couldn't understand it. And this same reviewer doesn't have real issues with the rest of the work. And then it's offset by the fact that the first reviewer --

DR. HART: I wouldn't say that. I mean, these are things that they're saying about us.

DR. FISHBONE: Highly ambitious.

DR. WALLACK: I happen to like highly ambitious, if that's okay?

DR. FISHBONE: I think maybe he's over.

DR. WALLACK: Well, it's not -- so let me just finish. So, the first reviewer says, and I think that Anne, to your point, that overall this is one of the best proposals reviewed this year.

DR. KIESSLING: From the first reviewer?

DR. WALLACK: Yes. One of the best proposals reviewed this year.

DR. FISHBONE: And he gave her seven?

DR. WALLACK: No, no, no, no. This one gave her a one.

DR. KIESSLING: Gave her a one.

DR. WALLACK: No, no, no, no, no. The original grade, the score, I'm sorry, was one. And reconciliation that reviewer went up to three. Went up to three. So with the second reviewer, who is the real problem from the standpoint of the investigator here, and the rationale for the seven, which I don't understand, and then when the second reviewer is able to say one of the

best proposals of the year, I feel that it can't be eliminated. Again, that would be my recommendation, not to eliminate it at this time. And at minimum to put it in the maybe column.

MS. MULLEN: Based on what?

DR. WALLACK: Based upon the fact that it's a continuation of work that the researcher's already have shown the ability to have good results from, publications from, and that the researchers acknowledge that the -- a talented researcher.

DR. PESCATELLO: You know, I was the other reviewer and I would say that there seem to be -- so as a nonscientist that there did seem to be some problems with the underlying science as well as being overly ambitious. There is a process, and the processes did end up, even with a reconciliation, he did end up with a three. And as a nonscientist, looking at the seven that we've now identified in my opinion, my vote would be that it doesn't fall within that category of the seven. I guess I would ask some of our colleagues, who are scientists, if you could take a look at it now? Because I think it was one of the more densely scientific in terms of having to make an assessment of it.

DR. HART: Can I act then as a tertiary

scientific reviewer and kind of rebut some of these comments? I've heard Dr. Chamberlain speak and I thought it was very clear from her speaking with her and her presentation that she's independent of Dr. Woolard (phonetic). The criticisms in the seven reviewers' major points include things like, how many cells are required for one step. The number that is used in the review is 1000 times more than we use in my lap, it's 100 times more than is commonly used in the field. Either the reviewer doesn't know what they're talking about, or there was a typo in the application. I don't know which, because I didn't read the application, but there's no way that you need that many cells to do what she's doing.

The comment about not clarifying what she means by (indiscernible) state I think is probably undeserved, again, I have not read the grant, based on her publications, and what she presents, because she is very clear and how she presents what she means by that term when she talks about science. So again, I really think that that primary reviewer is misguided in scoring a seven, based on these criticisms.

DR. PESCATELLO: And syndrome disease is -- it's focused on Angelman Syndrome and Prader-Willi Syndrome and so how do those compare to the other seven

we're looking at how important are those --

DR. HART: These are very rare diseases --

DR. PESCATELLO: -- very rare.

DR. HART: -- but they tell a very important story that relates directly to autism. And it's not going to be a one-to-one connection, but I think what is learned in these diseases about some of the imprinting that goes on is absolutely going to be essential in how we understand autism as a much larger disease.

DR. PESCATELLO: I just -- one rebut I would say, to the extent I understood it, and the connection to autism, and this is just my own antidotal sense of autism funding, there's a ton of autism funding going on in the world right now and whether we need to add to that, I don't --

DR. HART: Yeah, but that's part of the problem is that this is such a small disease and so much can be learned from it that it's going to get lost in the shuffle from autism funding. That's my count, but --

DR. PESCATELLO: -- yeah.

DR. KRAUSE: Having looked at that, do you think that there would be overlap between that and an RO-1 she has on regulation of UVE-3A genomic imprinting by tissue specific alternative splicing?

DR. KIESSLING: And that's her only -- that's their only -- her only source of funding right now, right?

DR. KRAUSE: No. That is not her only source of funding. She has -- it's the only one on which she's P.I. but she has four other grants on which she -- from which she gets some funding.

DR. KIESSLING: And when does that one run out?

DR. GENEL: 16th, June 16th.

DR. KRAUSE: 2016.

DR. KIESSLING: Oh, 2016.

DR. DEES: Can I ask you a question on the scoring here? Because when they did the reconciliation on this grant they reconciled at three, but if you look at what the -- it says in the comment, the secondary reviewer heard the primary reviewer and wanted to stick with the one. And then the secondary reviewer, I mean, the primary reviewer said, okay, I'll move it to three. And so it got resolved at three and that strikes me as odd.

DR. KIESSLING: Because it should have been a two.

DR. DEES: It sounds like it should have been a two.

DR. KRAUSE: There is a third person who's weighing in on these scores, so that could --

MR. WILSON: No.

DR. KRAUSE: -- no, there isn't? It's just between the two of them?

MR. WILSON: It only goes to the co-chair if there's more than a one point difference.

DR. KRAUSE: But it was, it was a one and a seven.

MR. WILSON: No. The secondary and the primary reviewer had a discussion, and they agreed to each rank the proposal as three. The proposal --

A MALE VOICE: But that's not what it says in the statement.

MR. WILSON: -- well, no, you're right, would like to, but that's not what they did.

(Laughter)

MR. WILSON: The secondary reviewer concluded that there was an agreement and that person said, okay, I'll revise my score to be a three. So there was really only a one point difference in the second -- in the reconciliation review by the primary and secondary reviewer, it would have gone to the co-chair for consideration. In this case, that didn't happen, so it

didn't go past the reconciliation.

A MALE VOICE: Thank you.

DR. WALLACK: I would move that it be placed for the time being in the maybe category.

DR. KRAUSE: I second the motion.

MS. HORN: All in favor?

VOICES: Aye.

DR. FISHBONE: Do we know what's in that category?

DR. KIESSLING: As a general thought, would it be useful for us to discuss the grants in which there was this huge disparity in the scientific reviewers? You don't think so?

DR. KRAUSE: Well, I think that -- I think that because that happened then they went to secondary review and then there are two of us who were assigned, so I think theoretically that happened.

DR. KIESSLING: This is the worst peer review comments we've had since I've been on this committee.

DR. GENEL: But we have -- we have them from the very beginning Anne, where before what we had was basically the summary statement. In point of fact, we have much more peer review available to us than we ever

had.

DR. KIESSLING: Yeah, but they didn't -- I mean, I don't know.

DR. GENEL: It's a messy process.

DR. KIESSLING: I thought these were really cryptic and not useful.

MS. HORN: We certainly get that feedback.

(Laughter)

MS. MULLEN: Well, I mean, I guess the other reality is that this is part of a continuous colleague improvement project because some people said the same thing last year and now we'll have to figure out the next series of improvements that we need to see. But Marianne reminded me that last year probably was the worst.

MS. HORN: And I think part of this really is that the peer reviews are not in the same room as they would be at NIH, and it's just a difficulty, we have to deal with.

DR. KIESSLING: Well, the NSF they're not in the same room either. They did it different.

MS. HORN: We would welcome all input into how we can make the process better and certainly have a case on board was helpful.

MS. MULLEN: Any other proposed established grants that people want to surface for discussion?

DR. ARINZEH: Shall we look at Zhong, is that it? Zhong? Because he got a score of 1.5 and a 4? But I didn't review that one, so I don't know.

DR. HART: YALE-03?

DR. ARINZEH: Yeah, YALE-03.

(Discussion off the record)

MS. MULLEN: So you answered your own question?

DR. ARINZEH: Yeah. That's fine. If it's worse than what it is, that's fine.

DR. HART: In the idea of fairness here to give as much consideration when there's disparity as possible, I don't object to talking about it. I can be fairly clear about my opinion.

MS. HORN: Okay. So 12-SCB-YALE-03, is that the grant we're on?

DR. HART: Okay. The title of this was Mechanisms for Balancing Stem Cells Self-renewal in the Differentiation During (indiscernible) Neurogenesis. The initial reviews were a 4 and a 1.5 and they reconciled at 3 and 2.5. Scientifically it's a very exciting topic. The P.I. studies molecules involved in specifications of

daughter cells. When stem cells undergo cell division they normally produce a cell that's headed toward neurogenesis and one that continues to be proliferative as a precursor. Two of the key molecules in that process are NUM and NUM-L and they're segregated and the cytoplasm of the precursor cell prior to division, which helps to specify the product.

The P.I. argues in the introduction that if we knew more about this process, the problem of adult stem cells not being capable of replenishing a population after a neural injury might be solved by this mechanism alone just by rebalancing that neuronal and precursor division on self-division of adult precursors. The -- let's see, the reviews on this plan was, it's limited and that further information on the proposal would have been helpful. There's no clear plan to establish a number of candidate genes that can practically be tested after initial screening. A large portion of the project was to do a very open-ended fishing style screening expedition here.

What kind of phenotypic analyses will be performed? Some of the proposed sections are vague and/or unrealistic were comments from reviewers. The P.I. is an associate professor since 2004 with no accepted peer-

reviewed publications since 2007. He's had two NIHR-01's although one is in no cost extension. Several private awards. He inherited a portion of a Connecticut Stem Cell group or core award, I don't know which, given to Michael Snyder (phonetic). There's no evidence of publications from that previous Connecticut Stem Cell award.

So combining the reviewer's criticism with the lack of recent productivity I'd be concerned about scoring this proposal as high as it was scored by the reviewers. It's unfocused, it's high on concept which is important, but low on detail and in a sense, this becomes a large fishing expedition with no clear impact and no clear detail on how that fishing would be followed up. I would have scored in the range of three and a half to four. So I think that provides a little fairness here.

DR. HISKES: I was the other reviewer. Not being a scientist, you know, I had difficulty contravening the analysis of the reviewers and so again, you know, the primary theme of the reviewer was not enough details, too vague, they don't -- they can't really evaluate the possible potential success of the proposal.

DR. HART: Right.

DR. HISKES: And given the track record, you can't go on that as evidence of success either.

DR. HART: So I would recommend a no.

DR. HISKES: And I would agree.

A FEMALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: So this will be placed in the no category. So, we noticed another grant where the score was a 1 and a 4. Kim, perhaps in the interest of fairness we ought to look at that one as well? 12-SCB-YALE-02, Fishbone and David Goldhamer.

DR. FISHBONE: If I can find it.

DR. GOLDHAMER: Do you want me to start Gerry?

DR. FISHBONE: Yeah, because I got things a little mixed up here.

DR. GOLDHAMER: All right. So this got scored at 2.5. The grant title is, heterochromatin (indiscernible) by OCT4. As we know, OCT4 is a key pluripotency gene and it’s critical for reprogramming cells and maintaining potency of embryonic stem cells. So this investigator discovered an activity of OCT4 that remodels heterochromatin and zoonotic cells and he wants to study the mechanism of action further.

I could tell you all the details, but I

think -- I'll say that it's a strong grant. I think, you know, the score of a 2.5 was deserved. There were some criticisms of the grant. I did nominate it for discussion because given the other grants I didn't think there was anything, you know, about the reviews that warranted reinvestigation and to bringing up again, this grant, but it was -- but it's a quality grant and there's no major criticisms of it. So I have all sorts of details I could show you about what he wants to do and how, and so forth, but it didn't seem to rise to the top, there were a number of grants higher.

DR. HART: The one real criticism that the reviewer who gave the score said -- a four said, was that there was low productivity, is that real?

DR. GOLDHAMER: I looked at that, I don't -- it didn't strike me as being terrible. I think it was okay. I don't think that that alone would warrant the score of a four.

DR. HART: We have nothing else to go on.

DR. GOLDHAMER: Well, I think one thing we're finding about these reviews is that there is typically more detail in the primary review then the secondary and this is a subject for another time, but probably it would be a good idea if the secondary review

was as detailed as the primary with all of the different components included. And I understand why that is not done because of the number of grants to review, but that would help the process.

DR. FISHBONE: Yeah, there was really -- the primary reviewer was very positive and gave it a one and a secondary said nothing, he just described what it was, and so he hasn't written very much and gave it a four. I mean, there's no justification --

DR. GOLDHAMER: Exactly. So we had one -- the first review is very positive as you said Gerry, very positive. The second review a four. So clearly wasn't too enthusiastic about it, but we can't get into the reviewer's head and really understand why that four was given except for the comment that there wasn't great productivity.

DR. FISHBONE: He just described what it was, he didn't say really anything about it.

DR. KIESSLING: So what do we do?

A FEMALE VOICE: It sounds like a no to me.

DR. FISHBONE: (Multiple voices)

DR. GOLDHAMER: I had put it in the no category because, you know, if the reviewer who gave it a four had said some things that I disagreed with, then I

argue, you know, against those, but it's really difficult when there's no details to know how to interpret -- and I purposely, you know, my position is not to do a full peer review of the grant, so it's a little bit of a difficult situation to know how to deal with that situation.

MS. HORN: So what would your recommendation be?

DR. KIESSLING: So he has funding till 2015, or she.

DR. GOLDHAMER: So my recommendation was a no because I didn't nominate it to be discussed.

MS. HORN: Dr. Fishbone, are you in agreement with that recommendation?

DR. FISHBONE: It bothers me because the one reviewer who really reviewed it, gave it a one, and the other one didn't seem to review it at all, he just said what it was. And we have limited funds, so I guess, I mean, I feel uncomfortable about it, but I'd probably have to agree that we don't push the funding, but I feel badly about it.

DR. KIESSLING: Do you want to put it in maybe or backup?

DR. FISHBONE: Well, I mean, I would be comfortable with that, but I don't know if it's going to

be at the top in any event.

MS. HORN: Dr. Goldhamer, was there anything about the grant that would encourage you to put it into the maybe?

DR. GOLDHAMER: I can be -- I mean, I thought it was a very good grant. I would be okay with it being in the maybe. I'd like to kind of make decisions as we go along so we don't have to revisit all of the grants, but I think in terms of -- I think the grant is meritorious.

DR. DEES: I'm hearing that you're comfortable with it as one of the backup grants but not one of the ones we're safe for funding.

DR. FISHBONE: Yeah.

MS. HORN: So for further discussion we'll put it in maybe.

DR. DEES: Well, I'm confused about what we're doing. So if we're thinking about backups that might be a slightly different discussion because there's a grant that I think -- one of our grants, I don't think it's nearly as good as it can be, but I think it would be a fine backup. So that's a slightly different discussion.

DR. WALLACK: So David, it doesn't sound like you're pressing for this grant, to be held onto. So

rather than torture ourselves again later --

DR. GOLDHAMER: Well, my initial recommendation for that reason was a no, but I feel the same discomfort that Jerry does. But having said that, given the two scores and the lack of more information I had decided not to nominate it for discussion, which means I vote no.

DR. WALLACK: -- so isn't that something -- I mean, we're not going to change the discussion later, so why don't we just do what we'll probably be doing later anyway and go with a no at this time? Gerry, how do you feel about that?

DR. FISHBONE: Well, yeah, nothing's going to change. But I hope we can look at who the reviewers were, not us, but maybe Rick could -- if there's one who's giving all of the people sevens then maybe do something about that. But it's just disturbing when it's the right call amongst experts about what somebody's trying to do.

DR. GOLDHAMER: I agree.

DR. ARINZEH: Well, they have that reconciliation statement.

DR. FISHBONE: But it's never brings them into the range, because if one guy is so high they can come down to a three or four and a half, but it'll never

be in the range.

DR. KIESSLING: Yeah, that's right, it's never going to go up above it.

A FEMALE VOICE: Right. Exactly.

MS. HORN: So we're hearing -- are we back to no?

DR. GOLDHAMER: Yes, I think we're back to no.

DR. FISHBONE: Second.

MS. HORN: And Gerry second. All in favor?

VOICES: Aye.

DR. ARINZEH: I guess I'm confused about the backup list. How are we going to make the backup?

MS. HORN: I think when we go back and consider the grants that we have put in the maybe that we may decide to fund some of those, we may decide to have some of those in the backups.

DR. ARINZEH: Okay. We only have one of each.

DR. DEES: I think you have questions, though, because -- I mean, the ones we passed were, I mean, I think I have a value in my head that I think it's not in this category, but it would be a perfectly good backup, one that should be funded at some point. It would

be nice to fund it, but we don't have the money for, it's not nearly as good as the other grants. And I would put it forward as one to fund because it's not in the same category. So do you want us to put those as -- do you want us to put those forward now as possible backups or do you want to revisit that question later?

DR. KIESSLING: If you have an application you're excited about and want to --

DR. DEES: I'm not excited about it, that's the point.

(Laughter)

MS. MULLEN: May I suggest that we pause, as we are, and see where we are? Let's see where we are, reconsider what we've been thinking about, backups versus maybes, because it may be that it's possible that those two categories have meant different things to different people, before we go on to think about seed grants. Now that we have considered ourselves perhaps committing to certain things, why don't we go back through all three, core, group, and established, see where we are, see whether or not any of you -- given the way the discussion has gone thus far, wants to bring anything else up? And then, perhaps even talk for a moment about backup versus maybe so that for anything that we particularly put in

those categories, we're clear about what they mean to us. Is that okay?

A MALE VOICE: Yeah.

DR. PESCATELLO: I would just add this is probably a good time too for any of us who have reviewed and looked at the budget to say if there's something about the budget that could clearly be reduced. Or we could take that off, that whole issue of the budget off the table.

DR. KRAUSE: That's a good idea because people are doing the math along the way and thinking about how much we may have already committed and it's hard to -- to force ourselves to think we only have a certain amount of money left.

DR. KRAUSE: I've been thinking about this as we go along. If we fund the two fours and the one disease grant and then we funded the five established investigators plus two of the additionally discussed grants, and I don't know whether it will be a maybe or yes, but whatever, that we have seven established investigators then we would still have funding for eight seeds. So this is just where we are. And that's a possibility. And then my opinion in terms of backups would be that you'd fund -- you'd put at least one seed in

the backup category and at least one established investigator in the backup category and that would be it depending on what happens. If it's an established investigator who doesn't get their funding --

DR. GENEL: You're not including the Wesleyan grant --

MS. MULLEN: So if we want to fund the cores -- so that's an approach that we can take.

DR. KRAUSE: You're right, I have not included the Wesleyan grant.

MS. MULLEN: Excuse me.

DR. GENEL: You had not included (indiscernible) grant.

DR. WALLACK: Yeah, that's right.

MS. MULLEN: Right. So that's an approach we could take. It is. Before we get to approaches, let's take a look at where we are in a bigger way.

DR. WALLACK: Okay.

MS. MULLEN: Okay?

DR. WALLACK: Do you want to run it through on each grant?

MS. MULLEN: Yes. So we'll go back --

MR. WILSON: You've got in the yes category for established you've got four and a half million

dollars. And then --

MS. MULLEN: Can you slow down for a second?

MR. WILSON: -- I'm sorry?

MS. MULLEN: I just want people to have a moment to go beyond the money to think about applications, think about the discussions we've had, think about different considerations around merit and move this beyond how we're going to spend $9.8 million to giving everybody a chance to reconsider even what they thought were the merits the first time around.

DR. PESCATELLO: This is just the established or are we going to go back to the beginning?

MS. MULLEN: Well, we want to go -- I think we should go all the way back to the beginning. Because otherwise we can say to ourselves, all right, we figured some things out, now we'll work with what we can do for seeds.

DR. PESCATELLO: So the (indiscernible) discussion isn't really four with 500,000 each to the core. I support that.

MS. MULLEN: Okay.

DR. PESCATELLO: I think we can get that off the table if people agree, right?

DR. WALLACK: So with that in mind, I'm on -- so I would recommend that we view that grant as an established investigator grant and reduce the amount of funding in half to $750,000 and keep it over a -- and Mike, I know you may have a slightly different approach to it, but I would recommend keeping it over a four-year period, 750,000 over a four-year period.

DR. PESCATELLO: You're talking about the group proposal?

DR. WALLACK: Well, Mike has a different viewpoint on the time, so maybe that'll answer you.

DR. GENEL: Well, I mean, I think this is -- if you really look at the grant it's an established investigator grant, it's really not any different than any of the other established investigator grants. I think they erred strategically in putting this in as a group proposal, but be that as it may, I think that I would fund it as an established investigator grant, whether we call it that or not, I would fund it at the same level for 750,000 and I think I would give them a three-year, which is what we're giving the established investigators.

DR. WALLACK: I thought we were giving them four?

A FEMALE VOICE: Four years.

DR. GENEL: Four years, that's what I --

A FEMALE VOICE: It's the same amount of money, you can spend over three or four.

DR. GENEL: -- are we giving them four? Okay. That I would fund it at four years.

DR. WALLACK: Okay. So we're the same thing. Okay.

DR. GENEL: The same, exactly the same.

DR. KRAUSE: And Milt, I have a question then. I hear what you're saying. First of all, there's three P.I.'s, so that would be at least at some point the equivalent of three established investigator grants. So to fund just one of them would be telling the three people, okay, do the work of just one of those projects. Secondly, it doesn't matter if it's three or four years, it has to do with the total amount that we allow for the grant and especially if you're cutting it, it might be spent in less time.

DR. WALLACK: So to your point Diane, I understand what you're saying. I think we have to go back to the investigators, and indicate to them what we're recommending and we have to find out if that's going to be acceptable. But that doesn't mean that I can't make a recommendation along those lines. If it works out that

the investigator finds it unacceptable, then we'll have to reconfigure what we're doing.

DR. GENEL: I think they'll figure it out very easily.

DR. WALLACK: I do too.

DR. GENEL: It's not substantially different. The collaboration is not any different than the established investigator grant that Megley(phonetic) now holds. It was the same two investigators as co-investigators on that. I think it's a matter of semantics. If we want to fund it then as a group grant at 750 then we can let them figure out how they want to use it.

DR. PESCATELLO: But my sense was that -- if I understood Diane's comment earlier, that the issue was to identify something in the budget that could be carved out, it could be clearly carved out. I think we shouldn't get into, you know, we don't want to get into a negotiation with the investigators, and I think just making a percentage cut doesn't sound like that is the common practice. Unless we can identify something that can be carved out we have to take it as it was proposed.

DR. GENEL: So before we've arbitrarily cut the amount that we've awarded. I mean, I don't find any

problem -- I have no problem with that.

DR. WALLACK: I mean, I would rather go back to the investigator, and indicate to them, we're willing to fund this at $750,000 over four years, you have the prerogative of rejecting that grant. My sense is though that somehow or other they're going to be able to reconfigure the grant. They are not going to throw away the $750,000. And I feel good about doing this because more than -- more important to me about this is that it allows them a continuation of some very fine work that they have initiated a number of years ago. And I think there's value in doing that. And I also think that there's value in keeping the funding for Wesleyan. It's the only funding that we are going to be able to provide for them. So I have no concern at all about going that route. I could not go for 1.5, but I can go for this.

DR. KIESSLING: So how much can you go for Milt?

DR. WALLACK: $750,000 over four years.

DR. FISHBONE: Do we think that they put it in the wrong category?

DR. GENEL: Well, I mean -- I think it's irrelevant. I mean, I think the point is, and I quite agree with Milt. I think -- I feel that first of all,

they do have no other source of funding that I can identify from their grant. This is research that we have supported from the very beginning. It is relatively unique, they have a very good track record in terms of publications and so forth, I think we ought to maintain support. But I don't think we can afford to support them at the level they've requested, and I think this is what I feel is a reasonable way of accomplishing those goals within the constraints that we have in the budget.

DR. KIESSLING: And you would go with the 750,000?

DR. GENEL: That would be what I would -- yeah.

DR. KIESSLING: Instead of the million?

DR. FISHBONE: Why not -- yeah, why not go 1,000,000 if you've got three P.I.'s? from what Diane is saying, you know, that's --

DR. GENEL: Well, I really don't think it's any different than the previous -- the way they've work before. It's arbitrary as to whether or not they're co-P.I.'s or whether or not there's a P.I. and collaborators. I mean, it's Chen and Moore are the two PI's. They're the ones with the history and so forth.

DR. HISKES: Can you refresh my memory

again of the discussion about the scores? So we're not distinguishing between threes, or seeds versus threes, or established versus threes for groups. This proposal though is a 3.25, and so are we just not seeing those scores in this case? And if so, why?

DR. PESCATELLO: I mean, Diane was arguing we shouldn't.

DR. HISKES: No, I'm detaching -- I'm in the process of detaching myself from (indiscernible). So from an outsider's point of view, okay, we really like these people. We've had a long-term relationship with them. We feel really, really badly if we don't fund them. But those aren't good arguments.

DR. HART: So look, as best we can --

DR. GENEL: Well, that isn't the point of what I said.

DR. HISKES: No, I know, but that's how I -- I mean, I -- we really admire these people.

DR. GENEL: No, no, no, what I said was that they've been productive, this is unique research, it's well received and is relatively -- it's relatively unique. That's the role of an advisory committee, we're not a second peer review committee, we have to make -- we have to make these types of decisions.

DR. HISKES: Well, then what about the threes?

DR. WALLACK: So -- so we've discussed before in at least two or three different proposals, the interpretation of the score, relative to the narrative. And if we want to go back to the peer reviewer I won't read the whole thing, I'll go to the last sentence. Overall, the project is well written, clear aims with identifiable pitfalls, which are duly addressed. It seems as though this reviewer feels that it's a doable project by established investigators, who have been working in this field now for a number of years, much of which is being funded by us.

DR. GENEL: And I would point out that one of the concerns raised by the reviewer number one was, how three independent laboratories could collaborate together when they're not -- when they're are really three separate laboratories on the same floor in the same building and they've been collaborating for the last 10 years.

DR. HISKES: At a small liberal arts college.

DR. GENEL: At a -- well, university.

DR. PESCATELLO: But I think the answer --

DR. HISKES: Well, (indiscernible) has

accepted the Wesleyan so I know what size it is and I know --

DR. WALLACK: The other point, I don't know -- is that we're talking about two or three investigators. It's basically the Naegele grant and the Grabel grant. Grabel has somebody else in her lab now that is also working with her. Forgive me, I'm not familiar with (indiscernible). But it seems to me that it's no different than the approach that they've had before. So I'm comfortable with the $750,000, whereas, I couldn't vote for the 1.5 million. And I want this -- I want her to continue her work -- their work. And I'm willing to have them come back, as I said before, and tell us why, unfortunately guys, we can't accept your grant, we'll have to look elsewhere for the money. I don't think they're going to do that. And I'll be happy if they don't do that because I think they deserve to go on with their work.

MS. HORN: Paul?

DR. PESCATELLO: I think Anne's point though was that, you know, unfortunately the stark fact is the score is what it is, and in relation to the others I would hate to see cutting that in half and then what do we do about the next one, the disease-related, the Parkinson's one which seemed so, you know, so unique and

so superior, frankly? I don't know where we're going to find the money to do all of the things that we -- and the first five or six of the established that we've looked at are so good, and we still need money for the seeds.

DR. GOLDHAMER: I think it's very difficult to divorce the grant from the funding request. The grant as written that got good, but not great, scores was written with the idea that they need $1.5 million to accomplish that grant. If you now cut their granted half the grant may not be able to be accomplished as written. In fact, that's a huge cut. We've talked about smaller cuts in the past, but this is 50 percent. So I don't know that it's -- I'm sure they'd take the money if offered, but the grant is not going to be the same grant if it has to be done with half the money. So I don't think we can just, you know, separate the science from the budget that's asked for to do the science.

DR. PESCATELLO: You're absolutely right. The one counter though to that is that if this group has no other support and will lose talented people, it'll keep them going another year to come back with a better grant if they can. That's the only argument.

DR. GOLDHAMER: So let me ask -- so I haven't looked at this. Grabel got an established grant

last year and it was a different question, but the same model I believe.

DR. WALLACK: Did she get one? I don't think she did.

MS. HORN: She did. She got a grant last year.

DR. GOLDHAMER: Last year.

DR. WALLACK: Did we grant her last year?

DR. GOLDHAMER: It was an established grant last year.

MS. HORN: Angiogenesis of embryonic stem cell arrived to (indiscernible), it scored 750.

DR. KRAUSE: And Naegele has one that ends in 2013. Right? Just based on the comments of the reviewers that I was just looking at.

DR. HART: So if that's the case, they're not going to all fall apart tomorrow.

DR. HISKES: I'm worried about fairness. You know, we're struggling to rewrite the grant for these people, to reinterpret what they should've done, you know, they applied for a new grant, unfortunately they couldn't apply for an established investigator. Maybe some of these established investigators should have really applied for seed grants and then they would've had a better -- a

stronger proposal if they had been more limited in scope, not overly ambitious. Maybe they would have been more detailed. I'm just not comfortable with second-guessing what people should have written and what they should've done. You know, if you do it for one, then you have to do it for everybody. So this is the schoolteacher in me. How to have, you know, fair standards that are applied equitably across the board.

DR. KIESSLING: So we're struggling with whether to fund this or not at all, is that the struggle? Because both of the reviewers were very close.

DR. DEES: Yeah, I mean, part of the problem is we are second-guessing the reviewers. If we took the reviewers score we should just say no and leave it at that. So what we're doing is we're starting to second-guess the reviewers by saying they don't understand something important here, which may be fair, right? They don't understand -- so one of the criticisms, they don't understand how the three labs can work together and we think we know better.

DR. KIESSLING: We do know better than that.

DR. DEES: Yeah. Okay, then we do know better.

DR. WALLACK: I think it's only two labs. Aaron (phonetic), he's independent, Glossar Aaron (phonetic) is independent.

DR. GOLDHAMER: So Aaron's not working together with Grabel?

DR. WALLACK: While, they're working together, but not in the same lab. He's an independent.

DR. PESCATELLO: But if we fund this, what are we going to do about the next one, the Parkinson's one? Because I can't see from what I know about that budget, I mean, maybe -- and correct me if I'm wrong, we can't cut that one and half or it doesn't seem like there's anything that --

DR. DEES: No, we don't want to do that.

DR. PESCATELLO: -- well, then, we're using up a lot of money.

DR. DEES: And part of what I am also hearing here is, now how much of this is right from what I'm hearing? Is that we think it's important to find somebody at Wesleyan.

DR. WALLACK: Yeah.

DR. KIESSLING: Well, we think it's important to use Connecticut's money in more than just two institutions.

DR. DEES: Yeah.

DR. KIESSLING: I mean, I think that -- I think that's important.

DR. DEES: (Multiple Voices)

A FEMALE VOICE: I think another core.

DR. KIESSLING: It doesn't have to be Wesleyan. It doesn't have to be Wesleyan.

DR. DEES: Yeah it doesn't have to be Wesleyan, but the point is is that --

DR. KIESSLING: You know, each year we hope it's some other institution that's going to come up and try to --

DR. DEES: -- so one of the reasons that I'm offering for why I don't want to support this grant is we want to support stem cell research at Wesleyan or at another institution, in this case we happen to pick Wesleyan, and I think that's a perfectly legitimate goal for us to have, right? But that should be explicit, that's why we're doing it.

DR. WALLACK: So the answer to Anne's fairness question is, yeah, we're bumping this up because we have a larger goal, and the larger goal is to support stem cell research throughout the state and not just at Yale and UConn. That's the answer to Anne's fairness

question.

DR. KIESSLING: I mean, this is the only non-Yale and UConn application at this time, right?

DR. KRAUSE: That's right. Can I make a comment? And I think this is separate from the merits of this grant. There are different numbers of stem cell researchers at these various institutions and from what we've seen at Wesleyan there are two with one new one who recently developed. People who are P.I.'s. So the chances of one in three of them getting a grant every time is going to be a little different. UConn really is two institutions, there's UConn Storrs and there's the Health Center. And Yale is really two different places, there's the main campus, which is like Weimin Zhong and then there's the med. school. And each of them has different numbers of people who apply. Storrs doesn't have as many as the med. school at UConn and Yale is the same way. So it depends on how you count, but just to say we fund Wesleyan because we like Wesleyan, and we do like Wesleyan, that's not the reason to fund it. So just, you know, point in fact.

DR. WALLACK: So I think we have to bring this to a conclusion. And in order to do it up or down I will move that we fund this proposal, four years,

$750,000.

MS. HORN: Is anyone willing to second?

A MALE VOICE: I'll second.

MS. HORN: Further discussion? Okay. We're going to have to take a roll call here. Milt?

DR. WALLACK: Yes.

MS. HORN: Yes?

DR. FISHBONE: No.

MS. HORN: Dr. Hart?

DR. HART: No.

MS. HORN: Dr. Kiessling?

DR. KIESSLING: No.

MS. HORN: Paul?

DR. PESCATELLO: No.

MS. HORN: Dr. Dees?

DR. DEES: Yes.

MS. HORN: Dr. Genel, yes?

DR. GENEL: Yes.

DR. HISKES: No.

A FEMALE VOICE: I'm giving you time. No.

MS. HORN: Okay. So the motion is defeated. Do we have another suggestion?

DR. KRAUSE: I motion we put it in the maybe category.

DR. GENEL: That's where we had it.

MS. HORN: That's where it is.

DR. KRAUSE: Oh, okay, never mind then. I don't have a motion.

DR. WALLACK: No, no, no, Diane, Diane. You said something that I think is interesting.

DR. KRAUSE: I wasn't ready to say yes.

DR. WALLACK: No, I understand. But from what the Commissioner was saying we're going to have a discussion about -- in the bullpen I would sense some of those might be the maybes, so that may not be a bad consideration in a reconfigured approach to it.

A FEMALE VOICE: That's where it is anyway, so there's no change.

DR. WALLACK? What's that?

DR. PESCATELLO: That's what it is already.

MS. HORN: I would really like to see if we can't move toward a decision at this point, but if we can't, then we can leave it in the maybes. We're moving into our lunch hour here and I don't want to push people too far beyond that.

DR. HISKES: Well, what was the total tally?

MS. HORN: Seven to three.

DR. HISKES: Seven to three, okay.

DR. PESCATELLO: Don't we need to create another category, which is potential -- a category where somebody declines the grant?

MS. HORN: Reserved, the reserved grant?

DR. PESCATELLO: Yeah. I mean, we could move it to that category and consider for that list -- we usually rank those.

MS. HORN: Yeah. We've typically done it once we voted to fund and then we realize we just didn't have enough funding and so we had to make the difficult decision of moving somebody out of the funding into the reserved grant. But there's no hard and fast rules.

DR. PESCATELLO: I think this should just go into that bucket to consider at that time.

MS. HORN: So do we have a motion to leave it in the maybes for now?

DR. HART: It's in the maybes. Let's hear a motion to move it out.

(Laughter)

MS. HORN: Do you have a motion to move it out?

DR. KIESSLING: Well, I'm just looking at their other funding. And they do, they have funds for --

they could bring this back to us next year without a big impact, I think.

DR. FISHBONE: Well, what would we recommend they do differently?

DR. KIESSLING: Well, that's up to them. But, so the P.I. has another year of funding, not exactly this, but similar. And the co-P.I., Grabel, her funding last until 2015, because we funded her last year. I don't know. I mean, I think, all things considered, I think it might be best to not fund this this year.

MS. HORN: Is that a motion?

DR. HART: No. I mean, the motion's in, we're not changing it.

(Laughter)

DR. KIESSLING: It's still a maybe, right?

DR. HART: Right.

DR. KIESSLING: Except we could make a decision.

DR. PESCATELLO: You could say no.

DR. DEES: Yeah. We could change it to no if you wish.

DR. PESCATELLO: Do you want to move it to say no? That's the question.

MS. HORN: We can either leave it in maybe,

or we need a motion to move it to the no's.

DR. HART: Well, essentially at this point if for any reason the Redmond proposal were not be funded in completion this would serve as a backup, is that palatable?

MS. HORN: Why don't we move then to the Redmond? Because I do have some information on that.

DR. HART: Okay. But if that were to happen would people be happy about that? Is my first question I was asking.

DR. KRAUSE: No, I'd rather it went to whoever is next in line.

DR. HART: Okay.

DR. KIESSLING: Whoever's next in line from any other category?

DR. KRAUSE: Yeah.

DR. KIESSLING: Okay.

MS. HORN: Okay. So we're going to leave it in the maybes for now and move on to discuss the Redmond. Do people have the energy to do that before lunch?

DR. HART: Sure.

MS. HORN: And we can wrap this up? Okay. So I did some further thinking and consulting on this and

I think the wording in the statute and the intention to fund research that is performed in Connecticut, the suggestion that we fund research that's going to be continually performed down in St. Kitts really drives a much too big of a hole through that extraordinary exception. So I think that we're going to have to find a way to choose to fund some of that grant, but not the funding that would go to the research being performed in St. Kitts.

DR. KIESSLING: That's the $163,000?

MS. HORN: Per year.

DR. WALLACK: No, for four years.

A FEMALE VOICE: Oh, you're doing it four years now?

DR. KRAUSE: No, they're saying that the -- he said that to round up, that the 200 K was the total over the length of the grant.

DR. HART: Four years.

DR. GOLDHAMER: Right. There was 300 and something that went to the Axion Foundation, half of that is for work on St. Kitts, so, $169,000 for work outside of the United States.

DR. DEES: Over four years.

DR. GOLDHAMER: Over four -- a total of 169

over four years.

A MALE VOICE: So it's a hole for one thing.

DR. KRAUSE: Yeah. It's not that big a hole.

MS. HORN: No. I think it's just that when we had talked about perhaps a piece of equipment that somebody would go into a discrete piece of research out-of-state on that piece of equipment and then come back into the state. This is really a much --

DR. KRAUSE: So Marianne, this is really important, and I completely trust your opinion on this as a legal matter. So the question would be, can they do the research, can they find that $170,000 to do the St. Kitts work from another source and still basically do the brunt of what they've proposed on the remaining funds? My guess is yes, but I don't know the answer. I mean, we talked about that.

A MALE VOICE: Right. Right.

DR. KRAUSE: If we take a part of their funding can they still do -- so that's going to be something where you might need to ask the P.I.

MS. HORN: Well, what we've done in the past is we've presented them with the reduced funding and

asked them to come back with their budget demonstrating what they would need to cut or how they would perform or what would they be able to perform given that funding.

DR. KRAUSE: Well, they basically have to do the same experiments because we're funding them to analyze those animals for those proposed experiments, the analysis taking place in Connecticut. So they wouldn't be proposing less experiments because the money basically just can't go to St. Kitts.

DR. KIESSLING: This is exactly the same thing that happened last time, right?

DR. KRAUSE: Yeah.

DR. KIESSLING: It's precisely what happened to them before.

MS. HORN: They managed to come up with the funding.

DR. KIESSLING: Yeah.

DR. WALLACK: So Diane, rather than you argue this point --

DR. KRAUSE: I'm not arguing.

DR. WALLACK: -- just your --

DR. KRAUSE: Oh, that's a good point. I was just thinking about the legal issue.

DR. PESCATELLO: Our grant would be

contingent -- we would grant everything contingent on their finding $169,000 from some other source, who are the primates.

DR. KIESSLING: I think we should just find their money minus the hundred $169,000.

DR. DEES: Except -- we can't quite do that because if what Marianne is saying is right then they can't rebudget and send some of the money to St. Kitts.

DR. PESCATELLO: Right. We have to be specific that they can do that.

A FEMALE VOICE: Yeah, yeah, yeah, they can't do work --

DR. WALLACK: Yeah. So in the past -- when we did this in the past, they were able to obtain the other money. So what we would do, I think, is fund it for $170,000 less with the instructions that they have to -- they have to find the other funding because we want the project to go on the same basis as is being presented. So I would move that we fund the project, minus $170,000, with a side letter indicating that because of regulatory restrictions, they have to find the funding for the other $170,000 for the St. Kitts portion.

DR. HART: I think you're being a little too specific.

DR. WALLACK: Okay.

DR. HART: I think you can fund whatever you choose to fund, but just say, none of these funds may be used for St. Kitts.

DR. WALLACK: Okay. Okay.

MS. HORN: I think that's what we did last time.

DR. WALLACK: Okay. That's fine. That's fine. Okay. So I make that motion.

DR. HART: Do whatever you have to do, but none of these dollars can do it.

DR. WALLACK: Right.

DR. FISHBONE: Was there some mention about travel to and from St. Kitts?

MS. HORN: Maybe at the break we can take a look and get a more accurate number of what we think --

DR. PESCATELLO: But since we know why we're doing it, why not be clear? Because sometimes we don't, and I think this is a perfect example of finding one budget item and carving it out rather than taking a percentage. So we might as well be clear, that's why we're -- and I'd also just want to go on the record as saying we're asking them to reduce it by 170 for the primate research because Connecticut law does not allow

money to be spent outside of Connecticut, not because we're against primate research.

A MALE VOICE: Right. Absolutely. Right.

DR. FISHBONE: And I guess if you buy the tickets in Connecticut --

DR. GOLDHAMER: And this is not something that we, as a committee, can say we're comfortable with this and we don't think it's significant enough --

DR. KIESSLING: Yeah. We should fix this problem.

MS. HORN: I think it would require a fix -- I think the language does say it.

DR. DEES: There's not enough give in the law for us to say, we think this is a small enough portion central to the research --

DR. KIESSLING: How about, we think this is a bargain?

DR. DEES: -- we think it's a bargain, yes. We think doing it in Connecticut would be --

DR. HISKES: But it's essential to the aim of the --

DR. DEES: -- and it's essential to the broader range of what -- of our charge, right? Which is to come up with disease directed --

MS. HORN: It is. I think the other charge is to develop stem cell research in the state, and that's what the language of the statute says, so I am comfortable that we've given a little leeway in terms of being very practical and not wanting to buy some unique kind of thing, if that's what's needed, but not to establish a precedent for research being performed outside of the country for, you know --

DR. DEES: But sometimes it's like -- it's like a big piece of equipment. I mean, it's not a big piece of equipment, but it's like that essentially. We don't want to buy this big piece of equipment, we want to buy the lab, the primate facility for Connecticut is essentially what we're saying. But that's fine if you think that's the way to word it, that's fine.

DR. WALLACK: Can I ask you a question? So we just cut the 170, that 170, does it include the dollars of travel allowance also, or not?

DR. GOLDHAMER: I don't think it included -- no, that was a fixed rate for the housing and the support of the animals.

DR. WALLACK: Okay. Alright.

DR. GOLDHAMER: But that travel was low.

DR. WALLACK: So, wouldn't we be safer that

we eliminate that portion also? So I would recommend -- I think I heard you say that there was an additional 4,000? So I would -- frankly, I would be more comfortable about making that $1,800,000 period.

MS. HORN: Well, what I would recommend is we take --

DR. WALLACK: No, no, 820,000. I'm sorry.

MS. HORN: -- if we take a break and Dr. Goldhamer, if you could figure out exactly what it is that we would be removing from the budget over the lunch break and then come back and have an exact amount?

DR. PESCATELLO: But then would we be saying that anytime a grantee travels anywhere outside of Connecticut that we're not going to fund it?

DR. KIESSLING: Yeah. That's hard.

MS. HORN: No, no, no, it becomes a certain budget amount, a travel allowance for conferences and so on, so that is not -- I think they're fairly specific in the grant about two trips each and how much a trip cost and the accommodation expense.

DR. GOLDHAMER: And the fact that the center is kind of owned or functions through a Connecticut entity doesn't enter into the equation?

MS. HORN: Correct.

DR. WALLACK: So Marianne, we've discussed this a lot. I don't think anything will change. So I would be happy to form the question on that number at this point if you're okay with that?

DR. DEES: Is it 4,000 a year, or 4,000 --

DR. GOLDHAMER: I'll have to look it up.

DR. WALLACK: Okay. You know what then? So we have to wait.

DR. GOLDHAMER: I think, is 4,000 a year.

MS. HORN: Okay. So I would recommend that we take a break at this point, come back and firm up that number and make emotion on that, and then decide whether we want to go back to the Grabel grant -- or the Naegele grant rather.

DR. GOLDHAMER: Okay.

MS. HORN: Okay. Lunch is down the hall. We have half an hour budgeted.

(Whereupon, a 30-minute lunch break was taken.)

MS. HORN: So I think during the break Rick Strauss did some figuring and Dr. Goldhamer, and so did you narrow down the amount that we would need to reduce this grant?

DR. GOLDHAMER: Well, according to what I

saw in the budget they're asking for $4,000 per year for travel, so 16,000 total, and in the best that I could figure was the number that I gave before, that 338,000 plus is going to Axion Research Foundation and half of that is for St. Kitts, approximately. So that would be about 169,261. So those are the only costs I saw. Rick, was there anything else that I --

MR. STRAUSS: That's what we found too.

DR. GOLDHAMER: -- but it is an approximation, so I don't know, do we need to -- do we need to ask for a re-budget removing all of the expenses related to St. Kitts and see what that number comes in at? It will be about one, whatever, 170, plus 16.

A MALE VOICE: He's got it up there.

MR. STRAUSS: 1,808,847.

MS. HORN: We can put it out there as a grant of 1,808,847 and ask for a re-budgeting, removing all of the items and then we can make an adjustment after the fact. But I'd kind of like to end the day with a hard number on each one of these.

DR. WALLACK: I would move that.

A FEMALE VOICE: Can I just ask for a clarification of what that overhead is?

DR. WALLACK: Indirect.

A FEMALE VOICE: Indirect? That's what I had.

DR. WALLACK: Because it's now 1808, do you want to lower the percentage piece?

A FEMALE VOICE: Usually they'll take that into consideration.

A MALE VOICE: The 185 plus 10 percent.

MS. MULLEN: I think it's a reasonable consideration. Thanks for bringing -- I'm almost tempted to say, I'll pay the rest myself.

(Laughter)

MS. MULLEN: I think is a reasonable consideration. I said almost ready.

DR. WALLACK: How do you address the question? Do we reduce that 1808 or not?

A MALE VOICE: You basically just reduce the direct cost budget and just take -- is it 10 percent here?

DR. HISKES: 25.

A MALE VOICE: 25 percent.

A FEMALE VOICE: 20 percent.

MS. MULLEN: Mathematically 20 percent of the total ends up being 25 percent overhead.

MS. HORN: Okay. So we need a figure.

DR. WALLACK: So Rick, can you refigure that taking off the indirect?

MR. STRAUSS: That's off of the 185? We're saying --

DR. WALLACK: 1808.

DR. STRAUSS: -- no, but it's off of the 185,261? It's 20 percent of that number is what you're saying?

A FEMALE VOICE: Right.

A MALE VOICE: Yeah.

A MALE VOICE: They have a subcontract for that work. How (indiscernible, laughter). Because maybe there's no indirects on that amount, or a portion of the subcontract.

(Discussion off the record)

MS. MULLEN: Can we just let it -- we're talking about a few thousand dollars.

MS. HORN: Right. I think if we fund it at this level and then if there's any further adjusting we need to make we can do that.

MR. STRAUSS: So you want to leave it at this time?

MS. HORN: Uh-hmm.

MR. STRAUSS: Okay.

MS. HORN: Okay. So then we have a motion to fund this 01-SCDIS-YALE-01 for $1,808,847.

A FEMALE VOICE: I move.

DR. FISHBONE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Okay. So that is there. So we were then going to go back and revisit the grant above that, no?

DR. HART: I should've commented on that. I actually abstain from that vote because I object to taking the funds out for the St. Kitts' work. I think that that's well within the mission of this Commission and if that's in error in the way the law is written or interpreted I think that ought to be addressed.

MS. MULLEN: Do you want to oppose? I mean, I'm asking whether or not you'd rather oppose than abstain? It's just in terms of making a statement. I'm just -- I'm not trying to vote for you.

DR. HART: I'd be happy to oppose.

MS. HORN: Yeah. Abstain really means you don't have enough information to make the --

DR. HART: Then in that case I oppose. I oppose the motion.

MS. HORN: -- it sounds like you have enough -- okay.

DR. HART: I would be in favor of fully funding.

COURT REPORTER: Would you identify yourself, please?

DR. HART: Dr. Hart.

COURT REPORTER: Thank you.

(Discussion off the record)

MS. HORN: Okay. So then we're going to move back to the grant above that and make a decision here in light of what we've done on the Yale grant.

DR. KIESSLING: Make a decision about what?

MS. HORN: The Wesleyan grant.

DR. KIESSLING: About whether or not to cut it in half?

MS. HORN: Yes. We have it in the maybe. When you were out of the room we voted a number of different amendments and none of them worked, so we left it in the maybe, revisited the Yale grant and decided to cut that.

DR. KIESSLING: Before we consider seeds?

MS. HORN: Yes.

DR. WALLACK: So Marianne, was the sense of

the group that you wanted to hold that one as one of the reserve grants at 750,000 over four years?

MS. HORN: I think that was part of the larger discussion we needed to have about what a reserve grant really was and what being in the maybe category meant.

A MALE VOICE: The problem with that argument is that there's many other better scoring grants in the established grants.

MS. MULLEN: I think what we came to was that there is funding to keep this project going for another two or three years. To me, that was key. So, because the scores so much lower than others in a meritorious --

A MALE VOICE: And if we fund at 750 then you're not really funding this grant really, your funding some fraction of the grant and in an unspecified way it'll change and maybe wouldn't have gotten a 3.25.

A MALE VOICE: It sounds like the consensus is that we're not going to fund it?

DR. PESCATELLO: Yeah. So why don't we all move and put it in the no category?

MS. HORN: Okay. Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Opposed? Abstain? Recused? Good. 12-SBC-WESL-01 is moved to no. Okay. I think that's it then for the core and group proposals.

A MALE VOICE: Are we going back to established or are you moving onto --

MS. HORN: At this point, why don't we -- why don't we decide -- we have a series of established proposals ranked in various different ways, and so we really need to figure out what we need -- what we mean by a reserved grant and how we are going to determine that and what we are going to do with the other grants here that are in the maybe category.

A MALE VOICE: So can we begin the process of establishing reserved by taking the maybes and putting them possibly in the reserve area?

DR. KRAUSE: How many do we have of each? Do we have five yes's and then what?

DR. WALLACK: We have six --

MS. MULLEN: Are we clear what we mean when we say reserved versus maybe?

DR. KRAUSE: We haven't determined reserved yet. Reserved we think is going to be the ones that if

there were more money that would be the next one in line. So it's probably going to be one of the maybes, unless we picked some of the yes's and get rid of them.

MS. MULLEN: Well, or in case somebody can't accept their grant. I mean, that's happened.

DR. WALLACK: I think we have to prioritize them, one, two, three, four.

DR. KRAUSE: So how many yes's do we have?

DR. WALLACK: Six.

A MALE VOICE: Six for 4.59.

DR. KRAUSE: Okay. And my calculation -- and we don't all have to agree on this, but from my calculation we could do seven and how many maybes do we have?

A MALE VOICE: Right now, two.

DR. KRAUSE: How many seeds?

DR. GENEL: Why do we have to decide is now? Why don't we go to the seed grants, and then see where we are when we've gone to the seed grants?

DR. KIESSLING: Yeah, that's what I think.

DR. GENEL: I mean, we may decide to fund a little more seed or we might decide to fund a little more established. But let's see where we are.

DR. PESCATELLO: Well, no, you've got it.

I'm sorry. I'm sorry, you've got it. I'm sorry, you've got it.

MS. HORN: So just for my clarification, because I tend to blend the maybe and the reserved, are we looking at those differently?

DR. HART: Those are all maybes right now.

A FEMALE VOICE: Who's maybes?

DR. HART: All the threes on that list. No, the twos, I'm sorry, the twos.

DR. PESCATELLO: Twos are, yeah. Okay.

DR. KIESSLING: This is the second page of established, right?

DR. PESCATELLO: Well, it's reordered though.

DR. KIESSLING: So we have the first page, yeah.

MR. STRAUSS: We have these five funded, plus this one, which is from yellow, six. That's six for a total of four and a half million. You have two in the maybe or reserve area, and then the other ones noted are the ones you reviewed, but said no, as compared to others that have not been, which are those that you did not review. And that takes you through the whole table.

MS. MULLEN: So maybes could end up being

reserves is what you just said? Is that right?

MR. STRAUSS: It's possible.

MS. MULLEN: Could, right, could. Is it also possible that the yes's could be reserves depending on where we land them?

DR. PESCATELLO: Yes.

A FEMALE VOICE: Yeah. You had too many yes's.

MS. MULLEN: Yes. Okay. So I just want to keep that in the back of people's minds. All right.

MS. HORN: So moving on to the seeds. So we had divided these into percentages. Was there any interest in starting with any particular score and working down?

DR. WALLACK: Marianne, did you entertain the thought that we concentrate on those that are a 2.5 or better score?

MS. HORN: It's up to the Committee, but that sounds -- that's a third of the grants.

DR. KRAUSE: That might end up being the fairest way because when we started pulling certain ones out in the previous, you know, in the established, well, why did you pull that one and not the other ones? And so we discussed a whole lot more. So we could say yes to all

18 and make them brief. If you're not in favor then that should go pretty quickly.

DR. KIESSLING: Well, any that got a score higher than that get to be discussed though, if you want, right?

DR. KRAUSE: Yes, if you want, definitely.

MS. HORN: Okay. Does that sound like a reasonable approach to people?

DR. KIESSLING: And the ones with highly disparate initial -- highly disparate peer review scores. These all seem to be more uniform.

MS. HORN: So starting with --

A MALE VOICE: 2.5, right?

MS. HORN: -- do you want to go backwards or do you want to start at the bottom?

(Indiscernible, multiple voices.)

MS. HORN: That's what I was thinking.

A MALE VOICE: You want to start with the best one?

MS. HORN: Start at one. Okay. 12-SCA-YALE-02.

DR. KIESSLING: This is the first year we've gotten any ones.

MS. HORN: Dr. Arinzeh, Dr. Goldhamer.

DR. ARINZEH: Do you want me to go? Okay. So this P.I. proposes to look at RNA molecules that are bound to LIN28, a protein in human embryonic stem cells. So, this investigator has generated a lot of interesting preliminary data using their approach, which is called Cliff technology, and established a solid set of data in C. elegans and would like to translate that then into embryonic stem cell work. So they're looking at validating individual genes critical for LIN28 stemness functions in human embryonic stem cells and also in IPS.

It will greatly improve understanding of stemness and help generations of these IPS cells. So this was reviewed very highly by the scores. The P.I. has substantial experience with this technology so the reviewers thought this was a particularly interesting person to go about doing this because of the background. So very favorable, I would recommend funding.

DR. GOLDHAMER: I was also in support of this. There were some minor, relatively minor problems. For instance, there's no prioritization of which RNAs are studied of the potentially hundreds of the binding LIN28 (indiscernible) instead. But clearly, reviewers were favorable, LIN28 is an important factor. LIN28 is also expressed in some tumors and trying to figure out what

role it plays in pluripotency versus tumorigenesis is important, and some of that will be teased out. So I was also in favor of the grant.

MS. MULLEN: Okay. So --

DR. WALLACK: I have a question.

MS. MULLEN: -- yes?

DR. WALLACK: So clearly it's a very, very good grant. I may be wrong about this, but I believe that this is an established investigator who is not new to this field. Now, I'm not sure how we want to handle this because if we go back to the -- yeah, go ahead --

DR. GOLDHAMER: Well, let me just say one thing. He's primarily a C. elegans investigator, so he works in mean code and he's applying some of the technologies and information he's gained from that work to this field. So he is new to this.

DR. ARINZEH: So he's new -- yeah, he's new to stem cells.

DR. GOLDHAMER: He's new to stem cells. The technology development has happened prior with his other work, so it seemed like a nice blend of adapting and applying the technology from other systems to the sense of well -- now, it is known that LIN28 is important in stem cell biology, so that's what's important and has been

shown by others. So I don't think they need to worry about that --

DR. WALLACK: So that's a good clarification on this particular grant, but in other grants, and we've run into this in the past, I mean, do we want to ignore that at this point? In other words, if in fact, it's an established investigator who's not new to the field, I mean, and just do it on the merits of the grant and ignore the fact that it's somebody hopefully new to the field one way or another?

DR. GOLDHAMER: Only if he's an established investigator who's branching out into a new -- to new areas within the field should be considered --

DR. WALLACK: I get that. I understand that. But I'm specifically asking the question, if it's the established investigator who is not new to the field?

DR. GOLDHAMER: -- well, let's say -- okay, it's semantics. Let's say it's the same overall general area of stem cell research they've been studying for years, but they have a new project, they want to gather preliminary data for their next NIH grant or wanted to branch out into a distinct but related project. So, you know, not brand-new to the lab, but a new project. I would think that this investigator should apply to receive

funding. It won't be competitive for NIH funding without the preliminary data and if it's meritorious than I think so.

MS. MULLEN: And so it's a seed grant for the research and not, say, a new investigator?

DR. WALLACK: Well, that's a slightly different interpretation, I think.

MS. MULLEN: Well, I'm sure that is the differentiation.

MS. HORN: It's in our -- what we say in our RFP is established investigators knew to stem cell research or developing new research directions may apply for seed grants and these awards are intended to support the early stages of projects not yet ready for larger scale funding. So I think we should just discuss it in the context of a particular grant when it comes up and then we have a better idea of whether it's across one line or the other.

MS. MULLEN: Okay. So recommendations to fund from both reviewers. Does that constitute a motion and a second?

MS. HORN: May we have a motion -- are you picking up the motions and seconds? Okay. All in favor?

VOICES: Aye.

MS. HORN: Okay. That takes us to 12-SCA-YALE-26, David Goldhamer and Ron Hart.

DR. GOLDHAMER: So this grant by Jing Zhou is a direct differentiation of human IPS seeds facilitated by mechanical force. So the investigator is an associate research scientist in Gloria Nichelson's (phonetic) lab. And the investigator is essentially an engineer. So this is a bioengineering project and the goal of this project is to develop lung epithelial cells from pluripotent cells -- from pluripotent cells. So, the background is that it has not been easy to drive pluripotent cells to epithelial lineage and so what they would like to do is to use a higher group approach in order to combine some of their bioengineering and cell biology expertise to try to define the complex mixture and proportions of growth factors that are optimal to driving cells to the one epithelial lineage.

And then, the added twist, and which makes it more attractive is they have appreciation that the bio-mechanical forces applied to cells can effect their differentiation behavior. So they have this microfluidic system where they can apply different stripped forces to the cells combined with their optimized growth factor optimum and very low parameters to try to get the most

efficient differentiation that they can. The reviewers both listed many strengths with no real weaknesses, no significant weaknesses. And I thought it was a strong grant from a good lab and I am recommending funding.

DR. HART: I agree.

MS. HORN: Any further discussion? Motion?

DR. GOLDHAMER: The motion is to fund it.

DR. HART: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: 12-SCA-UCHC-06, Dr. Kiessling and Diane Krause.

DR. KIESSLING: So this is an application from a young assistant professor I think he is, and it's excellent. So they're going to take advantage of a genetic predisposition to multiple sclerosis and they're going to derive induced pluripotent stem cells from patients with that genetic predisposition and they're going to compare that with matched family members to see if they can show -- or come up with these specific defect that prevents mono-lineation by the affected IPS cells. That's aim one.

And then in aim two they're going to use those cells in a mouse model to see if they can figure out

which ones will or will not incorporate into the central nervous system. It's an excellent, really well focused, it's just an excellent project. It probably could even be bigger than a seed grant. I really recommend it. I move that we fund this project.

DR. KRAUSE: I have no additional comments. That was good for me.

MS. HORN: Is that a second?

DR. KRAUSE: Sure.

MS. HORN: Okay. Any further discussion? All in favor of funding this project?

VOICES: Aye.

MS. HORN: 12-SCA-UCHC-12, Dr. Fishbone and --

DR. FISHBONE: This is Dr. Wang, who is an MVPHD, outstanding investigator and he wants to -- let's see what he wants to do. He wants to use human embryonic stem cells to produce mesenchymal stem cells for therapeutic use in patients with MS and would benefit from immune suppression or immune modulation. And has a number of aims in the plan to characterize the optimal bio-activity of a radiated human embryonic stem cell derived mesenchymal stem cells. He also wants to obtain highly immune suppressive radiated human embryonic stem cell

derived using mesenchymal stem cells and then he wants to find out if they can induce long-term immune tolerance.

He's had a couple of grants, I think, from us. I'm getting a little confused with him and somebody else -- one moment. But the reviewers liked the grant, thought it was a very good grant and that the, you know, the enthusiasm for a proposal is high. They're concerned that he has a lack of a career track for a P.I. He's been a post-doc since 2008.

DR. GENEL: We've seen a lot of post-docs with career paths since 2008 and earlier actually on some of these.

DR. FISHBONE: A lot of what? Post-docs who haven't made it to the next level, or what?

DR. GENEL: I've seen some post-docs in these applications who have been there longer as post-docs.

DR. FISHBONE: Yeah. Yeah. And that --

DR. KIESSLING: There's only so many jobs.

DR. GENEL: Yeah. We all have.

DR. FISHBONE: -- his mentor is Ren He Xu and Dr. Crocker is working with him. And the only real criticism is that he's been a post-doc for a long time and he should get a faculty position. I'm sure he feels the

same way. So basically he's looking for using irradiated immune suppressive mesenchymal stem cells working in Muscular Sclerosis. I would recommend that we fund him.

DR. HART: I just have a few details. This is kind of interesting because there's been work on using bone-derived stem cells for this sort of application and the P.I. very nicely argues why that isn't sufficient on a kind of industrial scale, that it's going to be hard to get a large number of them, there's issues about immune tolerance, there's issues about uniformity of production and so forth. And so the idea is to take human embryonic stem cells, possibly, you know, not autologous of course, but -- and to develop them into mesenchymal stem cells and then irradiate them to prevent any form of tumor genesis upon injection. So it's a kind of a nice idea knowing that these cells do not permanently graft, they merely promote a temporary immune tolerance for some period of time and the question is, how long?

So from a project point of view it's actually very interesting. And it's based upon your acceptance of that idea that the bone marrow stem cells are not sufficient, and some of the reviewers were not totally convinced by that. I just want to make sure that's clear. From a development point of view, yes,

she's been a post-doc since 2008. She previously was awarded a seed grant in 2010 from us and I don't see any publications on that topic in the record. There's relatively few publications actually, there's on the order of -- well, I didn't write down how many, but it was a modest publication record in this time.

So I'm a little concerned about awarding a second consecutive seed to a long-term post-doc that hasn't shown productivity from a previous seed. And, you know, the criticism that there's no clear path to career development is even worse when you put it in that context.

DR. KIESSLING: Is this a new area of research?

DR. HART: Well, it's still stem cells. Before the topic was stem cell regulation of Caspase activity. This is now mesenchymal stem cells. She previously had studied MS, I guess in a previous -- if this is the right person, I think she had a previous record of MS in her previous training. So I'm a little mixed.

DR. KRAUSE: I have a thought about this. Having read the Crocker grant I also looked at this because they're both related to MS and in fact, Crocker is one of the mentors on this grant. I can't exactly tell

whose post-doc this person is. They've published with Ren-He Xu (indiscernible) they claim Crocker. I think that seed for a post-doc is different than seed for a P.I.

DR. HART: Oh, yes.

DR. KRAUSE: A seed for a P.I. is a new direction or new to stem cells, for a post-doc it's, this is my post-doc project, as post-docs are generally starting, you know, something that they hope to build on. But not knowing who's the P.I. it's a little tough to know whose new thing this is because the post-doc doesn't generally --

DR. HART: And this thing is her second.

DR. KRAUSE: -- and it's her second one. The other thing I guess they are starting with human ES, but the immunosuppressant qualities of MSC, and I must admit, that's something I've read a lot about so I'm a little bit on the fence about it, I don't consider that a stem cell issue. I consider that an immunology issue. So while they're making the MSC from human ES the questions they really need to address are how are MSC immunosuppressant? I mean, you can even compare human ES derive to bone marrow derive MSC. But I don't exactly see this as fitting into the theme -- the core focus of the Connecticut Stem Cell funding.

DR. KIESSLING: Can you make -- can you make the, I mean, can you make functional MSC's from ES?

DR. KRAUSE: That's a really good question. So what is function? So if you think -- so MSC stands for two different things. It stands for -- it stands for a bunch of different things, but we'll say mesenchymal stem cells and also mesenchymal stromal cells. When you're referring to them as stem cells then the point is that they can self-renew and they can differentiate. That's not what they're concerned about here. Here whether they're stem cells or stromal cells they're immunosuppressant when you put them in temporarily. And a lot of people have worked on this for many years. And how they're immunosuppressant is interesting and not yet fully worked out, but I'd say there are 200 publications on it.

So this person is jumping into something where it's human ES derived MSC, I'm sure others are looking at this as well, I just don't see that they're going to make a significant splash in this long existing field. A post-doc with whom? Is it somebody who's already done this? Who has some expertise on it?

DR. HART: I'm glad you spoke up, that was useful.

DR. KRAUSE: It's also just an interesting

comparison of the Crocker grant. Crocker's claiming that in primary progressive multiple sclerosis it's not an autoimmune phenomenon, and therefore, we're going to study how they have messed up all the adendro site formation and then this person is coming in and saying, well, MS is immune expressive, I mean, immuno -- autoimmune and there are obviously different types of MS so they're coming at it from different directions.

DR. KIESSLING: But the reviewers like this one. Do they like it or do they just give it a two?

DR. HART: Both.

DR. GENEL: There are a lot of caveats in their review for a two.

DR. HART: Yes. There were -- oh, they had some very detailed criticisms, which really are technically false. They were worried about the etopic (indiscernible) eliciting an immune response which was ridiculous. They were only partly convinced of the need for the project in the first place, whether we need to make ES into MSC for this project.

DR. FISHBONE: And how long it would last.

DR. HART: Yeah, and how long it would last. That's right. That's right.

DR. WALLACK: So this sounds like this is a

maybe.

DR. HART: I think that's about fair.

DR. FISHBONE: Yeah.

DR. HART: I was trying to go back to whether we should say no, but, yeah, maybe we better turn --

DR. FISHBONE: Well, they're saying this extra (indiscernible) immunosuppression MSC's is an important step, but not essential, if there is significant immunosuppression. In other words, they are not sure that this is necessary.

DR. HART: Yeah. That's it.

MS. HORN: So we have a motion for maybe Dr. Hart?

DR. HART: Yes.

MS. HORN: In second by Dr. Fishbone?

DR. FISHBONE: Yes.

MS. HORN: Okay. All in favor?

VOICES: Aye.

MS. HORN: This grant is put in the maybe category. 12-SCA-YALE-15, Dr. Kiessling and Dr. Pescatello.

DR. PESCATELLO: So this has been an important area, cardiomyopathy, and the reviewers were all

very positive. Very few weaknesses, other than it doesn't involve human stem cells, so I would be very much in favor of this.

DR. KIESSLING: Yeah. This is an IPS grant, it's a really nice grant. The thing to note about this is Randy is a post-doc in Qyang's lab. Somebody else that we're -- so this is one of the post-docs. We decided that we're going to pronounce Q-Y-A-N-G, Chung, right? Chang? Chang. In Dr. Qyang's lab who is the young investigator, we've already talked about in this grant. I can't remember what we decided about his grant.

So this is a, I mean, it's a project very similar to the MS project in that they're going to take advantage of a genetic defect that, you know, predisposes people to this disease and they're going to differentiate IPS cells, study the defect. They're not putting anything back into mice, this is all going to be in vitro work. They're going to try to understand the pathway. It evidently takes two aberrant genes to give you this genetic predisposition. And it is nice project, it's nicely designed, they've got some preliminary data. And now I think we just need to consider this in the context of the rest of the funding for that lab.

MS. HORN: We did decide to fund that Yale

Qyang grant.

DR. KIESSLING: So that is an established investigator grant, right?

DR. PESCATELLO: Yes. Yes.

DR. KIESSLING: So do they -- does it have -- it have, since I didn't read it, does it have overlap with this?

MS. HORN: That was reviewed by Dr. Arinzeh and Dr. Hart.

DR. KIESSLING: Okay. So this is cardio -- okay. So they are going to get skin biopsies from people with genetically predisposed to cardiomyopathy. They're going to differentiate them into IPS cells --

DR. PESCATELLO: No. Nothing like that.

DR. KIESSLING: -- nothing like that. So is Dr. Qyang and appropriate mentor for this project? Did they do anything apart? What's he working on?

DR. PESCATELLO: This one is engineering smooth muscle cells.

DR. KIESSLING: Oh, okay.

DR. PESCATELLO: Vascular smooth muscle cells.

DR. KIESSLING: They are into muscle.

DR. PESCATELLO: So it's for blood

vessels.

DR. HART: So Dr. Qyang is targeting with cardiovascular system training intense level -- genes -- definitely in Connecticut.

DR. KIESSLING: Okay. So this comes down to, you know, kind of -- if we want to spread the funds around how much money do we want to give one lab? You know, the work is really good. I mean, this was an excellent application from a young investigator, so it's right in there with what seed money should do. Do you want to make it a maybe just to see?

DR. PESCATELLO: It's a classic seed grant. I would say yes.

DR. GOLDHAMER: I would say maybe for the fact that there's another Qyang grant coming up as well that's a seed.

DR. KIESSLING: Yeah. Another post-doc.

DR. GOLDHAMER: So then we could --

DR. KIESSLING: So they put in two seeds and one established investigator this time, which is noteworthy. I mean, it's not -- that's the way to do it.

MS. HORN: So Dr. Kiessling, you're moving to put into the maybes?

DR. KIESSLING: I'd like to make it a maybe

till we get everything that's going to this lab sort of organized.

DR. PESCATELLO: I'll second.

MS. HORN: Paul second. Okay. All in favor?

VOICES: Aye.

MS. HORN: This is into the maybe. 12-SCA-YALE-18, David Goldhamer and Anne Hiskes.

DR. GOLDHAMER: I'll start off. So this is a young investigator who's a post-doc in Andrew Johnson -- and so the major -- so they are interested in a condition known as William Syndrome and, a factor that is responsible for at least some of the aspects of William Syndrome and the factor is WSTF. WSTF is a modeling factor. And so, they studied WSTF in other contexts, in particular a cellular response to DNA damage and they want to now look at the role of the WSTF in human ES cell pluripotency, okay? So they have two aims, one is to characterize and identify the WSTF enriched genomic sites in human ES cells. They want to know where WSTF binds, okay? And they're using appropriate technologies to do that.

And they also want to investigate the function of WSTF in human cell differentiation into neural

crest cells. Neural crest cells arise during the formation of the brain and the spinal cord and they give rise to many tissues in the body, including a lot of the bones of the face. And William Syndrome patients have dysmorphias of the face and it's some kind of a -- it's a neural crest defect that hasn't been -- the mechanism hasn't been elucidated. But WSTF is involved in some way.

So their second aim then is to look to see what WSTF -- what its role is in driving human ES cells to the neural crest lineage, okay? So I'll say a little bit about that in a moment. So both reviewers liked the proposal and they point to the relevance to human disease. Both reviewers had some concerns and one of the primary concerns was that too much was proposed. One reviewer thought that this was approximately two $1,000,000 grants worth of work, okay? So you can forgive a new post-doc a little bit for being a little over ambitious, but I think that's significant, because if there really is that much work then what will they really accomplish? What aspects of this will they be able to get done in two years? Likely not all of it. I don't put a tremendous amount of weight on that. If it's really quality science, something good will come out of it and I don't care necessarily that everything's going to be accomplished. So that was one

thing.

But I actually had a couple of other concerns. I didn't think that their rationale for looking at WSTF in human ES cells was that great. The only thing they know about it in human ES cells -- the only thing they know about the factor is that it remodels chromatin so they say, well, chromatin dynamics is important to make human pluripotent is so maybe WSTF plays some role in human ES cells, so let's look. It may reveal some interesting findings and probably will, but I didn't think the rationale was great, why WSTF?

The second thing is, the facial dysmorphia is a neural -- in Williams patients is probably due to neural crest defects after their generation in their migration, their survival, something else. So the rationale for studying the role of WSTF to go from a pluripotent cell to the neural crest cell, again, I did not think was a very strong rationale. So like, you know, so I thought it was a pretty good grant. I thought that a two was a little bit too good of a score for and I wasn't terribly enthusiastic. I had given it a maybe, not knowing what the other grants would look like. But I didn't think it was -- certainly I didn't think it was a sure yes. So I had voted or I recommended maybe at this

point. A weakish maybe.

DR. HISKES: And I'm the second reviewer for it, so and again, not being a scientist, I would defer to David's expert opinion about the rationale for WSTF. I thought the virtues of the proposal are both reviewers thought it was very excellent. The major criticism was that it really would take millions of dollars to do what was proposed and I don't know, maybe it's a very fast person and very efficient person, or they've done a lot of the work already, you know? Who knows.

But I, again, would not, you know -- I would not second-guess the author of the proposal. If they think they can do it, I would go with that. To me it sounds like a very important disease to study. The neural crest defects are relevant not just to this particular disease, but to many, many other diseases and so I see it as along the lines of our focus on practical applications, potential therapies down the line. Whether there's a good reason for studying WSTF I'm simply not qualified to judge.

So but my own -- based on what I had felt, I thought I would give it a yes.

DR. GOLDHAMER: I'll add one more thing. So I think it was a good grant, I just didn't think it was

a great grant. It's interesting, in their preliminary data they show some very nice data in a mouse model. They have a conditional knockout of WSTF and it has the same facial features as humans with the disorder. To me, they can propose more elegant and more relevant studies in their mouse model and they're probably writing to other agencies for that work.

DR. KIESSLING: What do you mean the same facial characteristics?

DR. HISKES: Well, it's funny you should ask. They have photographs.

DR. GOLDHAMER: The mouse and human look identical.

(Laughter)

DR. HISKES: But there's also light pigment -- it associated with pigmentation issues as well, so they have arrows pointing to white spots on the mouse's tummy.

DR. GOLDHAMER: Well, there's --

DR. KIESSLING: Do they not have a nose?

DR. GOLDHAMER: -- they have -- they have nasal frontal problems, underdeveloped nasal structures and other things that are definitely, you know, neural crest, you know, it is -- so, no, they are not, you know, one is hairier than the other. But I mean so there are

differences.

DR. HISKES: And smaller.

DR. GOLDHAMER: But it is -- but it looks like a nice phenol copy of like a nice model for the (multiple voices).

DR. HISKES: With analogies.

DR. FISHBONE: We have a number of grants that we've sort of approved or are considering approving that are very rare and unusual diseases. The one on Angelman Syndrome we felt had real benefit because it might be, if I remember correctly, lead us toward autism and information about that. Is this anything for us generally other than tell us about William Syndrome?

DR. GOLDHAMER: So I'll answer -- I'll give a similar answer to what Ron did. I mean, first of all, I don't know the prevalence of Williams Syndrome, I'm not familiar, specifically with that (interruption on tape) but there are many, many neural crest disorders, innervation problems with the G.I. tract that leads to something called megacolon, there's Waardenburg Syndrome. There's many neural crest diseases, excess of alcohol cause neural crest problems, vitamin A excess, so the neural crest are really essential and diverse cell type. So, you know, studying the neural crest, or studying a

gene that causes -- causes in part William Syndrome will reveal information about neural crest biology. So I would say I don't really care if Williams is rare and not of a kind of important or, you know, health-related issue in terms of the broader population, but it will reveal interesting information.

I just have problems with the rationale. If there's neural crest defects I don't think they articulated what you will learn by studying this factor and its role in going from the pluripotency to the neural crest. What's happening in William Syndrome, from what I can tell, is downstream of that. So I just -- I just don't think the rationale is there.

DR. FISHBONE: I just have a concern that we fund a list of grants that taxpayers in the state look at that list and say, what the heck are we doing, you know, we are funding all of these bizarre kinds of things rather than things that would relate to me.

DR. GENEL: But for the rationale Gerry is that you can use these as models to understand the underlying biology. I mean, that's the whole rationale of study of very rare genetic disorders.

DR. KIESSLING: Neural crest -- yeah, neural crest cells play a role in lots and lots of things

but we don't understand them very well.

DR. HART: The prevalence of this particular disorders is something like one in 7,500 births, so it's not that rare.

DR. PESCATELLO: I was going to say, that's pretty common.

MS. MULLEN: I read one in 20,000. I guess we should be paying attention.

(Laughter)

DR. KIESSLING: Well, it isn't that, it's that we don't -- neural crest biology is really fundamentally important and we really don't know very much about it.

DR. HISKES: Well, apparently neural crest defects can effect a wide range of things, your head, your stomach, your legs, all kinds of things.

DR. GOLDHAMER: Peripheral nervous system, pigmentation, there's many, many things. But I still -- and so I'm a big neural crest fan. I teach about neural crest, I mean, I think -- you know, it's one of my favorite subjects.

(Laughter)

DR. GOLDHAMER: But I just do think that this particular grant would necessarily be terribly

important in terms of elucidating what they hope to in this grant.

DR. HISKES: So you know a lot about neural crest in other words?

DR. GOLDHAMER: Yes. I tell my class --

DR. HISKES: This is relevant.

DR. GOLDHAMER: -- if they wake up in the morning and look in the mirror and they don't like how they look, well, they can blame it on the neural crest because your looks are entirely --

DR. FISHBONE: Well, I'm just concerned. I've seen this in other, you know, organizations I've been involved in in grants and that is, you know, we funded something for Rett Syndrome. We funded, oh, we're going to fund something for Angelman's. We're going to fund something for William's. And we'll probably end up funding about 10 things and I understand, you know, the importance of what you're saying, but I'm wondering if other people would understand it. Why are we spending all our money on these rare things?

DR. WALLACK: I'm hearing something even more fundamental. And that is that I don't hear you being overwhelmingly impressed with the proposal.

DR. GOLDHAMER: Yes.

DR. WALLACK: So if we're not overwhelmingly impressed by the proposal. Why are we torturing ourselves about the proposal?

A MALE VOICE: That's a good question.

DR. HISKES: So, that's my argument. So David obviously knows a lot about neural crest.

DR. WALLACK: Said David, are you happy with a no on this?

DR. GOLDHAMER: I'm happy with the no. But I had given it a maybe because of its score and I -- but you know, I think -- I think the only reason I said maybe I think, is because there's other grants with good scores and I wanted to hear a little bit more about those, you know, before permanently eliminating this. But having said that, I'm comfortable with the no.

MS. HORN: Is that a motion?

DR. GOLDHAMER: So I'll make a motion to not fund this grant.

MS. HORN: Do we have a second?

MS. MULLEN: Before anybody seconds, I'm just looking at science now. Nature review, one in 7,500 (multiple voices) accounting for six percent of all cases of mental retardation of genetic origin. I mean, because in terms of relevance to the population.

DR. DEES: But even one in 20,000 births is fairly common.

DR. HISKES: Yeah.

DR. DEES: I mean, you know, most neonatal testing is done on stuff that's a lot rarer than that.

MS. HORN: So we have a motion for no, do we have a second?

DR. FISHBONE: I'll second.

MS. HORN: Second. All in favor?

VOICES: Aye.

MS. HORN: Opposed?

DR. HISKES: I'll oppose it.

MS. MULLEN: You want it to be a maybe?

DR. HISKES: I want it to be a maybe so we can come back to it.

MS. MULLEN: It's all about fair.

MS. HORN: 12-SCA-YALE-20, Dr. Fishbone and Dr. Goldhamer.

DR. GOLDHAMER: All right. Gerry, should I start?

DR. FISHBONE: Please do.

DR. GOLDHAMER: Okay. So this is another grant from Qyang and the title of this is, Functional Characterization of Engineered Heart Tissue from Eyelet

One Cardiovascular Progenitor Cells in a Model Myocardial Infarction. So what that means is, what they would like to do in this grant -- okay, so let me just give you the background.

So the investigators want to find cell types that can effectively be used in stem cell therapies to repair infarctive hearts, okay? So they have a model to create ischemic hearts and they want to take cells and they want to see if those cells can repair damaged hearts, okay? So they want to derive cardiovascular progenitor cells from human embryonic stem cells. So this gets back to another issue that we talked about before. Is it best to use the mature cardiac cell for implantation, or is it better to use a progenitor cell for that? And so they are trying -- they want to make progenitor cells that express this particular transcription factor eyelet one, and test them for their ability to repair hearts. Okay. So this grant combined tissue engineering approaches with directed differentiation approaches for their studies in rats. They point out again that direct cellular injection of cells has not worked very well and so they’re making a structure in collaboration with Chris Brewer’s (phonetic) lab, a so-called cell sheath engineering approach where they’re going to make kind of a tissue that incorporates

these cardiac progenitors and see if that more three dimensional structure, this tissue, can when implanted can repair hearts. And so they were going to do this and they are going to evaluate by histology, by electrophysiology, they're going to do echocardiograms and so forth.

So both reviewers were very positive. They pointed to the preliminary data, the clinical relevance, the combined expertise of the P.I. and the team of collaborators. They did have some minor issues, but the issues did not seem to effect their enthusiasm very much. I thought it was a good grant and I did not have any major concerns. So, I had recommended this be funded.

DR. FISHBONE: The only comment I have to add is that they didn't like the choice of the rat and said they should use mice instead. I'm not sure why.

DR. GOLDHAMER: Okay.

MS. HORN: So do we have a recommendation?

DR. WALLACK: Before we do, can I ask a question?

MS. HORN: Certainly.

DR. WALLACK: So --

DR. KIESSLING: This is the third --

DR. WALLACK: -- what?

DR. KIESSLING: -- go ahead.

DR. WALLACK: So we funded Qyang for a established investigator and it may not be specifically the same grant, but certainly there's overlap in the developing tissue engineered blood vessels. In this instance they're implanting them as aortic into position perhaps in new grafts. So I'm not sure if this is not an example of where we shouldn't be funding this is a seed, because we've already funded it as an established, and it's -- well, slightly different, but this is in the same field. So I don't know. I mean, I have some hesitancy, frankly.

DR. GOLDHAMER: And I'll add to that Milt, that he has two active Connecticut grants right now, one as P.I. and one as co-P.I. that deal with the ESL and IPS cell derived cardiomyocytes. I haven't looked back at those to see what the distinction is. One might be that he's working with progenitors now, and the other of course with cardiomyocytes. And so there's I'm sure distinctions there, but I think the overall thrust is at least related. I don't know how similar without looking for more details.

DR. KIESSLING: He also has an NIH grant, that's good until 2015, looking at hearts -- using heart -- deriving heart cells from EGS.

DR. WALLACK: So with the intent of what we're trying to do with these grants and with the observation of what we've already done for this investigator earlier today and in the past I'd be willing to offer a recommendation of not to fund this particular grant. Would there be a second to that recommendation?

DR. HART: Second.

MS. HORN: Okay. Speak up. So Anne, you're seconding?

DR. KIESSLING: No, I was mumbling.

MS. HORN: Oh, you're mumbling?

DR. HART: I'll second.

DR. GOLDHAMER: My question though is, so he has three grants, two -- he has P.I.'s, one as a post-doctoral and --

DR. KIESSLING: And one -- he's got an NIH grant and he's just written a new NIH grant that's going -- that's pending. Although he says there's no overlap with the current Connecticut -- but it's using patient IPS cells to derive for cardiac disease with research.

DR. GOLDHAMER: I mean, so it may not, you know, we have to be a little bit careful if you're not in the field things, you know, can look similar --

DR. KIESSLING: Very similar, yeah.

DR. GOLDHAMER: -- and not really when you get down to it. So I want to be a little bit careful with that that if we're making a decision clearly, you know, we have to, you know, be cognizant and we want to spread out the money. Milt, you had a motion I think to not fund this. The question though is, what are the relative merits of the established grant versus this grant, and I haven't read the established grant. Do you feel more comfortable funding the established grant and not the seed?

DR. KIESSLING: Where did the established grant end up?

DR. WALLACK: It's recommended for funding.

DR. KIESSLING: So it's a 2.5.

DR. PESCATELLO: It was a 2.5 score.

DR. HART: You know, I was the one that argued for pulling the established grant out and considering it, and I think that considering the limitations of this Commission I think we ought to fund the established grant and with all the seed grants at this time, just based on the fact that we have limited resources, and we prefer to fund a larger project from it.

A MALE VOICE: So your argument --

DR. KRAUSE: You'd preferred to fund a

larger project instead of this one?

DR. HART: Instead of this one, which was actually higher-rated, better rated, better scientifically rated. But that's my position based on reading the bigger grant, and you read the smaller grant.

DR. ARINZEH: I mean, the bigger grant -- we thought these scores actually didn't reflect -- because they were very favorable, there were really no weaknesses, but they still gave this kind of lower score, though it was really a good --

DR. GOLDHAMER: And there was no real -- there were no major criticisms of the seed grant either and so your argument is that they're both meritorious, we don't want to give two grants to the same lab, so it makes sense for the bigger grant?

DR. HART: Yeah. You can't really put this in a letter, but the thing I would say if I could was, they were both excellent grants, you know, scientifically approved both, but we chose to fund the larger of the two.

DR. GOLDHAMER: Yeah.

DR. DEES: We assumed that if you were asking us to make the choice you would want to have the bigger one funded.

(Laughter)

DR. HART: Exactly. It's not practical to say, but there are people in the room.

MS. HORN: If you can read the transcript --

DR. HART: Yeah, exactly.

DR. ARINZEH: It seems as though it's distinct from potential overlaps.

DR. GOLDHAMER: Yes, yes.

DR. HART: So did we have a second on the motion?

A MALE VOICE: So Milt's motion was to not fund.

MS. HORN: And we need a second.

DR. HART: I second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: 12-SCA-UCHC-07, Diane Krause and Milt Wallack.

DR. KRAUSE: Shall I go Milt?

DR. WALLACK: Yeah.

DR. KRAUSE: So this is a grant to use drosophila that are deficient in a specific gene called Indy, and these drosophila have increased life span. And they know they have increase life span and decreased

oxidative damage, so that's a -- metabolism in stem cells is really hot, so we are talking about an animal with a longer life span, most likely due to decreased oxidative damage to DNA over time. So the idea is to address synergy metabolism in stem cell behavior. And I didn't read the grant so I don't fully understand why they decided to focus on the gut stem cells. But they're looking at the gut stem cells of the fly in a fly that has a prolonged life span and less oxidative damage.

So the question that the reviewers came up with this also my question, and I don't know the answer to it, which is, what do we do with the drosophila grant in this setting? It's certainly an important question. Using a non-vertebrate system is sometimes the fastest means to an end because you can do a whole lot of genetics very quickly, and a whole lot of assays very quickly. The higher up you go, the slower the research goes. Using human ES is probably, you know, 10 times slower than drosophila, maybe 100.

The clinical relevance is probably a little bit distant, but it's certainly very, very clinically relevant because we're talking about metabolism and life span, which we all care about clearly. So, I am a little on the fence with what I would recommend. It got very

good scores. Clearly this person knows that she's an expert, he or she, I can't remember, is an expert in aging and drosophila, that's what they're bio-sketch is all about.

DR. WALLACK: So I had reservations about the overall grant. I have to defer to the scientists in the room, but I also didn't see any clear trajectory, and it may not be important, to any eventual clinical issues. So with the reservations I have in the overall grant one of the reviewers, the second reviewer actually, had some issues about the overall grant being not cohesive, lack of detail, and so on. I wouldn't be willing to fund, unfortunately.

DR. KRAUSE: You would not?

DR. WALLACK: I would not.

DR. KRAUSE: What was your reasoning?

DR. WALLACK: Based upon the overall approach of the application and the relevancy of the subject and the peer review statements, interpretation about the lack of cohesiveness in the grant request and the lack of some detail and full understanding -- so there were just too many issues for me to want to fund it.

DR. GENEL: Marianne, what does the RFP say about seed grants, the --

MS. HORN: The seed grants?

DR. GENEL: -- yeah.

MS. HORN: Established investigators new to stem cell research or developing new research directions may apply for seed grants.

DR. KRAUSE: This is an established investigator looking at the stem cell is a new direction. Recent publications, Aging Studies in Drosophila Melanogaster, you know, that's a review -- two on Longevity into Drosophila, this is the kind -- I mean, she works on aging in drosophila and this is new that she's working on stem cells.

DR. KIESSLING: But it's got stem cells in the drosophila, right?

DR. KRAUSE: Yeah.

DR. HART: I'm so disappointed you haven't brought up the Monty Python reference yet.

DR. KRAUSE: I missed it.

DR. HART: INDY stands for, I'm Not Dead Yet.

DR. KRAUSE: Oh, very good. Thank you. No, I didn't think of that.

(Laughter)

DR. KRAUSE: That's very good. Thank you

for pointing that out. I'm on the maybe side here.

DR. PESCATELLO: Is there something in the RFP about animal models, right?

MS. HORN: Yes.

DR. PESCATELLO: Maybe that's what you were looking for?

MS. HORN: Oh, I'm sorry. Yes. Animal models. Animal models will be considered, but applicants need to demonstrate a direct relevance to human stem cell biology and its therapeutic implications.

DR. GENEL: That's right. Yes, okay.

DR. ARINZEH: So how does this relate to human disease?

DR. KRAUSE: As we age our stem cells stop working as well. And here they have a model where they're not aging, presumably their stem cells continue to work. But I don't get all the way from A to B because --

DR. ARINZEH: So in the gut they won't age?

DR. KRAUSE: -- in these animals, no, I don't know why they specifically picked GI stem cells in these animals.

DR. ARINZEH: Okay.

DR. KRAUSE: But the --

A MALE VOICE: There's probably a lot of

them.

DR. KRAUSE: -- the link is that stem cells and aging is a very important concern to everybody in this room, and drosophila are an excellent model for studying things. I'm stuck.

MS. MULLEN: So that's more of an inferential link as opposed to something that they fleshed out really well though?

DR. HART: Well, that's the question. Did the grant application justify the direct connection between this model system and a clear disease?

DR. WALLACK: I couldn't find -- I wasn't comfortable with that Ron.

DR. HART: That's a good answer.

DR. FISHBONE: Good answer.

MS. HORN: It sounds like the peer reviewers had a little trouble with that.

DR. WALLACK: Right. I was not comfortable.

DR. KRAUSE: How can our findings be beneficial for humans? The relevance of Indy(phonetic) in mammalian health has already been shown by report that deletion of mammalian Indy has a beneficial effect on energy metabolism. Our study is open to new possibilities

for Indy mutation and preservation of stem cell (indiscernible). So that's where they chose to start their focus.

DR. FISHBONE: I like a two for this one.

MS. HORN: So maybe?

DR. FISHBONE: Yeah.

DR. KRAUSE: I second the motion.

DR. FISHBONE: I like a maybe.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Anybody opposed?

A MALE VOICE: How many things do we have in the maybe column?

A MALE VOICE: Oh, a whole bunch.

MS. HORN: Three.

A MALE VOICE: Three?

A MALE VOICE: Yep, two no's -- two no's and three maybes.

MS. HORN: We have three in the maybe, we have two in the no, and we have three in the yes.

A MALE VOICE: We're looking for three more good grants.

MS. HORN: Okay. 12-SCA-UCHC-09.

DR. KRAUSE: So Johnny or John Lee, I've

seen it both ways, Wang, is a post-doc in Ren He Xu's lab. And the work -- and she wants to look at whether it's IPS making induced pluripotent stem cells whether they would be better if you knock down (indiscernible) or highly repetitive sequences. It's a nice basic science question. It's new work for Ren He's lab and it's certainly new work for this post-doc. She's a new post-doc in the lab, she has very little experience.

The reviewer said that she has extensive -- has a good publication record. I would say she has a fair publication record. She got one low-level paper, I don't mean low-level, but it wasn't in a top-tier journal, from her PhD work and then several middle-authored papers. But one of them was in Cell Stem Cell, which is probably our top journal. So she's a promising post-doc who just started working on a new field, which is knock down of (indiscernible) sequences in generating IPS cells. And one of the reviewers was more enthusiastic than the other, but neither of them articulated their thoughts very well.

DR. PESCATELLO: So I think that's a good description because the one reviewer said it was a bit of a fishing expedition, but good basic science. So I was inclined to put this in the maybe category.

MS. HORN: Are you moving to put in the

maybe?

DR. PESCATELLO: Diane?

DR. KRAUSE: Sure. Maybe.

MS. HORN: All in favor? Further discussion before we have that vote? No? Okay. All in favor of maybe?

VOICES: Aye.

MS. HORN: 12-SCA-UCHC-10, this is Dr. Arinzeh and Dr. Fishbone.

DR. ARINZEH: Okay. So this project proposes to generate mature and naive effector T cells through differentiation IPS. And this again, is eventually for use as an immunotherapy treatment for cancer. I think overall, though the reviewers were, I think, favorable. This is a resubmission by the P.I., who included more preliminary data that demonstrates feasibility.

But there was still some weaknesses and they thought it was significant. They're still unclear about how the P.I. will produce the IPS from primary T cells. So there was still some issues there with the approach of how they go about doing -- generating some of these things. And they also thought there should be an amigo component to evaluate function, which that is an

important part.

DR. FISHBONE: He applied last year and got a 5.5 score and he's modified several things, and I'm not sure what he's modified.

DR. KIESSLING: This is a resubmission?

DR. FISHBONE: Yeah.

DR. ARINZEH: This is a resubmission, so the score has gotten better --

DR. FISHBONE: He wants to -- anti-tumor responses using induced pluripotent stem cells to generate CD-4 and CD-8 T cells and engineer them to express T-cell receptor mark one. Some issues remain with the revised progene. No in vivo component to evaluate the function of the IPS cell derived T cells. Not entirely clear that he will be able to produce IPS cells from primary human T cells. So again, the rating seems better than the words that are used.

DR. ARINZEH: Yeah. I mean, at least that second, I guess it was the second reviewer that the --

DR. FISHBONE: Yeah.

DR. ARINZEH: -- thought there was a lot of other weaknesses there.

DR. FISHBONE: It is not clear if the simple addition of cytokines will result in generation of

TH-1, TH-2 and regulatory T cells, respectively. So they weren't sure that what he wanted to do would in fact be effective.

DR. ARINZEH: He also has a seed grant that's going to end in July.

MS. MULLEN: So he's going to be out of money in July?

DR. ARINZEH: It similar -- it looks similar very similar. So it looks like maybe a continuation of this -- of a seed, of another seed.

DR. FISHBONE: He sent you a letter Dr. Mullen. Do you remember reading it?

MS. MULLEN: That sounds like one of those questions get in court. Do you remember?

(Laughter)

DR. FISHBONE: This says, we've enclosed our revised grant application which scored 5.5 last year. We think the reviewers are finding our proposal study to have a significant goal research and a sound approach and recognizing the concept of generating patient specific anti-tumor T cells from ISP cells is interesting. The reviewers made a number of suggestions, which he says he's taken into consideration.

DR. ARINZEH: You know, the reviewers --

they want more preliminary data and he was able to present some of that just to say that he could actually do some of this. So I would just -- I would vote for a maybe only because --

DR. KRAUSE: You guys really don't sound like a maybe, you both sound very unenthusiastic.

DR. ARINEZH: -- well, I mean --

DR. FISHBONE: Well, you know, he improved it from a 5.5 to a 2.5.

DR. ARINEZH: -- yeah. He addressed the issues. The scores are now --

A MALE VOICE: And that counts why?

DR. ARINEZH: -- the score is okay. You know, I think the driving thing was this one reviewer that felt that he should have an in vivo component to demonstrate function. With this seed grant, I don't even know can he do it? I guess that's enough time to do that part.

DR. FISHBONE: Yeah, it's -- you know, it's really borderline because he obviously has done the things that they asked him to do it last year's review and he's proved it. But it still leaves him sort of --

A FEMALE VOICE: Remind me, what's his -- what does he -- faculty --

DR. ARINEZH: He's assistant professor at --

DR. KIESSLING: In health sciences.

DR. ARINEZH: -- stem cells.

DR. FISHBONE: Yep.

(Discussion off the record)

DR. KIESSLING: And his only other funding is a seed grant? That name's familiar.

(Discussion off the record)

DR. ARINEZH: Yeah. He has a young investigator -- well, no, that's ending, or ended. Yeah. He's just a co-P.I. on an R-1 that ends in 2013.

DR. KIESSLING: So he has some funding for another year.

DR. FISHBONE: Yeah. I mean, if his research works it would be terrific, you know, they just don't seem to feel that it will work. Is that fair to say?

DR. ARINEZH: Yeah. I mean -- yeah. They're asking for him to demonstrate a little more in this two-year window.

DR. KIESSLING: This is really a cancer grant.

DR. WALLACK: So I'm sensing a total lack

of enthusiasm.

A FEMALE VOICE: I know.

DR. ARINEZH: It's not a total lack, it's just that they want him to do more. So that's why --

DR. WALLACK: So he's making progress, that's good. But by the same token, I don't see that he's gotten to a point where he has to be.

DR. KIESSLING: Well, the only stem cell aspect of this is to try to get engineer an anti-tumor agent. So this is really a cancer grant.

DR. FISHBONE: Yeah.

DR. KIESSLING: So the only stem cell piece is --

DR. ARINEZH: Deriving of T cells.

DR. KIESSLING: To derive a T-cell, right.

DR. ARINEZH: It's deriving T cells. We could use them as immuno-therapy.

A FEMALE VOICE: If you had to move right this moment what would you do?

DR. WALLACK: Knowing that you're going to have to discuss it again later.

DR. FISHBONE: Probably not.

A FEMALE VOICE: I heard Gerry say, probably not. So are you proposing no?

DR. PESCATELLO: That was a motion.

DR. FISHBONE: That was a motion. Yeah.

A FEMALE VOICE: Well, you guys are leading this and (multiple voices).

DR. ARINEZH: You know, I'm comfortable, it's fine. I make a motion, based on the other ones I'd say yes.

DR. FISHBONE: I'll second it.

MS. HORN: Dr. Fishbone seconds. All in favor?

VOICES: Aye.

A FEMALE VOICE: Man, that was painful.

A FEMALE VOICE: Good job.

MS. MULLEN: So my observation is there hasn't been much enthusiasm in the room for quite a while now. So don't you two feel conspicuous in any way because maybe it's the post-launch lull, but you know, we've gotten -- I don't know, if you scroll up, we have a few threes and I was thinking that, you know, there's a 2 there that was actually a 2.9.

DR. WALLACK: I'm building towards enthusiasm.

A MALE VOICE: I think we also have to be careful of not judging seed applications with the same

degree of rigor that we may have done earlier this morning with the much more elaborate established investigators. They're different -- they're entirely -- they're different mechanisms.

DR. WALLACK: And I am building enthusiasm. I want you to know.

MS. MULLEN: Well, right. But I just don't want you to kill everybody else's until we get to what you want to be enthusiastic about.

A MALE VOICE: Let's keep going. Keep going.

DR. WALLACK: I did make a motion.

MS. HORN: And there is coffee down the hall if anybody would like it.

MS. MULLEN: And it might be just that, you know, we've moved into this seed round and it's a different series of considerations.

DR. FISHBONE: But also they give everybody the same grade and it's very hard to --

A FEMALE VOICE: Yeah.

MS. MULLEN: Yeah, we need that to spread that out a little bit more.

DR. FISHBONE: We have to pick out the exceptional ones and these don't seem to fit that bill.

MS. MULLEN: Maybe we'd be better off looking at the ones where there's a big difference.

A MALE VOICE: Let's keep going. We've got seven more 2.5's to go. Let's keep going.

MS. HORN: 12-SCA-UCHC-15, and we have Richard Dees and Paul Pescatello.

DR. DEES: All right. So this is a proposal to study the effects of protein secreted from undifferentiated embryonic cells and induced pluripotent cells in humans to understand the regenerative facts of muscle stem cells taken from patients, both young and old patients. The hope is that finding these factors will lead to therapy to counteract aging and various forms of degenerative diseases. He intends to look at the effects of the package on muscle stem cells and see basically what has changed in the muscle stem cells and try to unify what in fact has led to these changes.

This is a assistant professor (indiscernible) is the professor. The reviewer thought the proposal is very sound and innovative. The primary reviewer wondered whether the analysis will actually tell him all he wants it to tell. I actually thought this was kind of an interesting grant and I was actually in favor of it.

DR. PESCATELLO: Yeah, I agree with the description. I think this is the one actually where this -- one of the reviewers said it was a fishing expedition, but otherwise he's a new investigator, he has a promising good publication record, interesting research. I would vote in favor, enthusiastically.

MS. HORN: So we have a motion and a second defined. All in favor?

VOICES: Aye.

MS. HORN: Aye, enthusiastically. Okay.

A MALE VOICE: I forgot how to do this.

MS. HORN: 12-SCA-UCHC-16, that's Dr. Genel and Ron Hart.

DR. GENEL: Well, this is a seed grant application by two established senior investigators who are described in the peer review as experts in RNA trafficking and translation. Essentially what they are doing is studying a interesting rare disease, Fragile X Tremor Ataxia Syndrome, which they have identified with the -- and epigenetic translational error, which leads to expansion of the gene, and suggests that this might be corrected by using a binder, an inhibitor. TMP (indiscernible) T-4, I don't know what that stands for, but whatever, using induced cells pluripotent potential

cells derived from patients with this disorder.

It's well received by the reviewers. I think that I would -- I think it ought to be funded.

DR. KIESSLING: They're both -- are they new -- they're new to stem cell science?

DR. HART: No. Yes.

DR. GENEL: As far as I can tell this is the first time that they've moved into stem cells using induced pluripotent stem cells as a model. So, you can never expect -- I think it qualifies under our definition with applications for seed grants.

DR. HART: So, it's interesting because it's -- actually, there's been a lot done lately on Fragile X it is very exciting what's going on with Fragile X these days and the understanding of how that works. And while this is kind of a rare subtype of the disease, it still involving the basic mechanism of dysregulation of the FMRP protein. They do have relevant mouse strains to complete the aims, but there's really no documented evidence anywhere in the grant, I looked hard, for procurement of the donor cells from the effected patients. They listed two names of potential collaborators, no letters or anything, saying that they were going to be getting the cells from these patients.

So, I'm a little skeptical about the fact that they can get the donor cells, much less -- I mean, of course if they had the cells they could make the IPS cells, I'm sure that, with Ren He Xu's help. The reviewers really liked the single cell tests on DNA repair mechanisms in RNA granular assembly, that's exactly what these people's expertise is. But many of the experimental details, particularly with rating to stem cell methods are really lacking and the rationale for using stem cells other than the grant, you know, the application to the grant program, is really not developed very well at all.

So it sounds to me like a very well designed, well-crafted grant that's been adapted to send us.

DR. KRAUSE: They didn't justify why they're using stem cells?

DR. HART: They didn't do a very good job of justifying. They tried. And it was -- my larger complaint was the fact that they needed those diseased stem cells and they had only had two names.

DR. KRAUSE: And they don't have (indiscernible, talking over each other).

DR. GENEL: My presumption is because it's the disease. It's the disease in the stem cells. The

patient's stem cells do have --

DR. HART: No, but I mean, the problem is they haven't identified people they can get the samples from. They've got two collaborators out of state that say they can get the cells for them, but there's no letter from the collaborator, no human IRB to get it locally.

DR. KIESSLING: Is this a husband-and-wife team?

DR. HART: I don't know. So I was a little less enthusiastic for those reasons.

DR. KIESSLING: They both have funds that run out this summer period.

DR. KRAUSE: They're talking about making IPS from patients with this disease. But they don't actually have access to these patients, and never mentioned.

DR. HART: They mention two names of collaborators at other institutions where they can get cells from, but no documentation of that. From Dr. Steve Warren (phonetic), from Emory, and Phil Schwartz, National Human Neural Stem Cell Resource.

DR. KIESSLING: So if everything works what will we have learned?

DR. HART: That DNA repair pathways mediate

the accumulation of the mutation where you expand the tri-nucleotide repeat.

DR. KRAUSE: In a human cell, because they've already shown it in a mouse.

DR. HART: Yeah, exactly. Exactly.

DR. KIESSLING: Why would you even need stem cells? You could just get primary cells, right?

DR. HART: Good point. Good point. Although you'd really want to do it in neurons where you get the real phenotype. Although, there's not much -- they do talk about making IPS derived neurons, but --

DR. KRAUSE: Do they have collaborators who have worked on human ES to neurons?

DR. HART: -- they only have a letter from the core facility. And, you know, the reality is they can do it.

DR. KRAUSE: No, the core can help them do that, that's a good point.

DR. HART: They can do it.

MS. HORN: So, do we have a recommendation from the reviewers?

DR. KIESSLING: What happened to enthusiasm?

DR. KRAUSE: These grants have big flaws.

DR. KIESSLING: Yeah.

DR. HART: And these are --

DR. KIESSLING: So this is two senior investigators that are trying to find funds to support a pre-doc student basically, or graduate student?

DR. HART: -- yeah.

DR. KIESSLING: And some supplies.

DR. HART: And you know, one of the problems I always have with judging an established investigator applying for a seed grant to go into a new area is. I expect there to be a higher level of quality in the application.

DR. KIESSLING: And you didn't see that?

DR. HART: I saw plenty of quality, it seemed just that it was adapted to stem cells. The basic underlying biochemistry is quite good.

DR. FISHBONE: They knew we give out money for stem cell grants is what you're saying?

DR. HART: Yeah. Yeah, I think they modified.

DR. FISHBONE: I like your enthusiasm.

DR. PESCATELLO: I'm hearing it now.

A FEMALE VOICE: Yeah. It seems like this is a lock.

DR. HART: I was hoping to hear from the primary reviewer, you could convince him.

DR. WALLACK: Somebody's got to make a motion.

MS. HORN: Dr. Genel?

DR. GENEL: Well, I would put this in the maybe category. I think the issue is whether or not they have access to cells or not and you can require a letter from the proposed collaborators that cells are available, and would be made available. If that's -- if that's the only issue. If the issue is you really don't need stem cells in order to do this work, then I'll defer to my colleagues on that.

DR. KRAUSE: I guess now that I'm looking at this grant based on what you were saying. So if I were reading the project grant, I would imagine the first thing is, we get the cells, we give them to the core, they make us IPS, we prove that the IPS are pluripotent and can go down the neural lineage, no. They say, we're going to look at repeat numbers in the individual stem cells and the neurons. Not even the neurons that we derived from them, just the neurons.

DR. HART: That's exactly it.

DR. KRAUSE: So, it seems like it's

skipping something, like important grantsmanship that tells you that they've thought through what they're going to do in this brief time span, which is just two years --

DR. HART: Yeah. I consider that to be a more significant criticism than the lack of documentation of the source cells. But it all ties together in my mind.

DR. DEES: Well, that's sort of basic homework.

DR. KIESSLING: Well, then that's a no.

DR. DEES: Isn't that basic homework?

MS. HORN: Dr. Genel?

DR. DEES: If you're going to get cells from somebody you get them to tell you, yes, I'm going to give you cells?

DR. HART: Yeah.

DR. FISHBONE: And we come down to these imponderable questions today.

DR. HART: And let's not forget the grant that we had so many issues with that had so much trouble getting the disease source cells from other countries.

DR. GENEL: Well, may I suggest that we move this to a different category?

DR. HART: Okay.

MS. HORN: We have a recommendation to

place this in the no category. Do we have a second?

DR. HART: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: 12-SCA-YALE-04, this is Richard Dees and David Goldhamer.

DR. DEES: Do you want to explain the science David, you're better at it than me. Why don't you go first?

DR. GOLDHAMER: Alright. So this is an application from a post-doc --. He's a brand new post-doc, he was trained in the biomatics and he doesn't have any obvious (indiscernible), except maybe in the last few months. So what they would like to do -- the title is, For Every Program Human Fibroblasts for Neurons using Long Nonfloating RNAs. So there's various classes of nonfloating RNAs, long nonfloating RNAs, a relatively new class of molecules in their D of RNAs where there's some evidence that certain linked RNAs can repress differentiation and maintain in everyone's favor. Okay.

So there is some -- this might be an interesting class of molecules. So what they've been doing on the bottom of the screen, they identify 12 long nonfloating RNAs that are present in brains and apparently

not other tissues. And so what they would like to do is test the biology of these linked RNAs specifically whether these RNAs can convert fibroblast to neurons directly. This is another approach for generating differentiated cell types for therapy is not -- IPS first direct conversion from a fibroblast for some other cell types for use on individuals.

Okay. So, they have two aims, one is to validate the 12 link RNAs, identify the database are actually neuron unspecific, they don't officially know that yet in their own work. And then they want to test each of the 12 to see if they can convert human ES cells -- if they can use them to either differentiate between embryonic cells to neurons or I think their major goal is to see whether they can convert fibroblast directly neurons. Both reviewers, you know, judging from the scores and the comments, were favorable. They thought it was innovative and clinically relevant.

Fundamentally I had some issues with this. So the rationale, again, I didn't think was very strong. They identified 12 neuron specific RNAs and with no other evidence they now want to test, a full grant to test whether these 12 RNAs can convert fibroblast to neurons. Very risky. You know, he rationale just isn't there.

There are occasional molecules, I know in the muscle field there's a few molecules that can do this in the genome. The fact that these are neural specific to me is not a good enough justification for devoting a grant to the testing of whether they can convert fibroblast into neurons. There's no reason to think that they can.

And so I just thought it was, you know, it's an interesting project, these linked RNAs are probably going to be interesting, but I just didn't think their background justification -- although, you know, the standard preliminary data is far lower in seed grants and established grants, I just think it's a very, very risky grant and there's no basis to think that any of these will be effective in this, which is a rare feature of, you know, most -- the vast majority of molecules do not have this ability to transform and reprogram cells. So, it got good scores, but it think I just was not very enthusiastic about this expanding (interruption on tape) of this grant.

DR. KIESSLING: Why did the reviewers like it?

DR. GOLDHAMER: They thought they liked the idea. They, you know, the importance of direct reprogramming they thought was therapeutically relevant, no argument there. The reviews were not very informative,

they didn't raise really many weaknesses. And one of the weaknesses that the reviewers mentioned, I didn't agree with. They didn't understand why the main focus was on the direct differentiation of fibroblasts to neurons, and to me that's the most obvious part of the grant, but to me that wasn't a (indiscernible).

DR. DEES: (Indiscernible)

DR. GOLDHAMER: Right. And I'll also say that -- I mean, yes, the grant really just wasn't that well written, rationale wasn't well laid out, the particular approaches were not detailed, patients weren't given. They only used four pages of the five pages for the grant. Only two of those pages were on the research plan. It just wasn't -- it could be interesting, but in it's current state indiscernible better justification (indiscernible).

DR. DEES: Yeah. I don't really have much to add. It would be kind of a cool thing if they could do it. If you can directly reprogram these cells, but that's obviously -- that's (indiscernible)

DR. GOLDHAMER: You can do it.

DR. DEES: If you could do it, it would be cool.

DR. GOLDHAMER: Not with these

(indiscernible), but you could.

DR. DEES: They were very impressed with themselves and thought this was -- if you could do this it was like safer.

COURT REPORTER: Please move that microphone. Thank you.

DR. DEES: Emphasizing that this would be -- if you could do this it would be a lot safer than all these other technologies, and I don't know why, it seems like you have to do the tests first to figure out whether they're safer or not. It's just sort of written off you've already found.

So I was basically -- to say no to this. I would move to say no.

DR. FISHBONE: And the parameter says this won't take two years to do.

DR. KIESSLING: It won't take two years?

DR. FISHBONE: It will not -- does not require the two-year timeline to do -- and then look at 12 cell (indiscernible, coughing) on these.

MS. HORN: So we have a motion for no and a second. All in favor?

VOICES: Aye.

MS. HORN: 12-SCA-YALE-06.

DR. DEES: That is me again.

MS. HORN: Richard Dees and Milt Wallack.

DR. DEES: Okay. So the goal of this project is to investigate the role of the number of related small molecules that might play a role in making the reprogramming of somatic cells into induced pluripotent cells more efficient. The plan seems straightforward and sensible. The chemical uses here are pretty far away, but I would think that these kind of study in developing induced pluripotent cells are going to become important.

This is an assistant professor of pathology since 2009, so that was (indiscernible) researcher. The reviewers thought that additional controls were needed, they felt that a much more efficient method of using these micro-RNAs have already been developed using altogether different techniques. So they felt these methods didn't really compare that well with them.

The secondary reviewer also had some concerns about whether the second aim to understand the function of these molecules didn't really show very much. So my initial reaction was a maybe, probably not, and so I guess at this point I would say no.

DR. WALLACK: I was the other reviewer on

this project and I thought that it was a proposal by an accomplished P.I., his collaborator also, Dr. Park, who we funded for a established investigator grant at another -- so the team is strong, I think. It seemed as though it had potential to provide some interesting information. And I was leaning more towards possibly funding it.

DR. DEES: I have a different idea.

DR. WALLACK: Yeah, I mean, I didn't basically disagree, Richard. I mean, it -- it's not something that just jumped out at me to absolutely fund.

DR. DEES: And I was looking at a number of grants that were all scored at 2.5 and of all those grants this is the one where the reviewer seemed less enthusiastic about it. So I was corresponding with --

DR. FISHBONE: There were a lot of weaknesses expressed by the reviewers.

DR. WALLACK: There were weaknesses expressed by the reviewers. Some of them indicated that it's not particularly novel, wanted them to --

DR. DEES: And thought --

DR. WALLACK: -- but they felt that it was a competent proposal. I probably at this time, and I've argued against this in other instances, you might want to put it in the maybe category. Richard, if you wanted to

put it in the no category --

DR. DEES: -- I move for no.

DR. WALLACK: -- I would not argue with that.

DR. DEES: So I hear a motion over there.

MS. HORN: Okay. We've got a motion for no, do we have a second?

DR. WALLACK: I would second Richard's motion.

MS. HORN: Any further discussion? All in favor?

VOICES: Aye.

MS. HORN: 12-SCA-YALE-09, Ron Hart and Milt Wallack.

DR. WALLACK: So I promised enthusiasm.

DR. DEES: I feel it.

(Laughter)

DR. WALLACK: I feel it. I'm going to start off by saying that I would enthusiastically endorse funding this project. This is a researcher new to this field with excellent credentials in other work that he's been involved with -- this person is been involved with. Interestingly, this individual has good entrepreneurial background as well with patent history and so forth. The

-- I would because of the subject matter -- I would, without reading it, which you all have in front of you, I would -- I would nominate this for funding with enthusiasm.

DR. HART: So this is a little tough because --

DR. WALLACK: Enthusiastically.

DR. HART: -- it's clearly two very, very talented people, the P.I. is a physicist interested in biomaterials with a long track record of success and the co-investigator is an expert in stem cells in skin, Valerie Horsley. So you would expect, and you would be right, that the grant is exceptionally well written as a read. You know, it's lacking some detail, it's fairly high level, very engineering oriented, which is all what you'd expect for a project like this.

The main new idea here is that they're willing to look at how matrix stiffness effects keratinocyte differentiation, and how local mechanical factors are involved as well. The reviewers liked the unique combination of expertise, the clear leadership in material science being brought to the table, the potential for groundbreaking discovery, is all quoting from the reviewers.

They noted, however, that effort of the P.I.'s was low, which of course is by necessity for a small grant with such high paid people. We've had this before. You know, realistically, the only reason why I reserve some enthusiasm for what otherwise is actually a very good project is, I wished they'd had a post-doc who'd applied for this as their post-doc. That's it.

DR. WALLACK: Well, and I would also add that one of the reviewers indicated that this project has exquisite potential. So that in the context of what we are dealing with, that's why I'm enthusiastic about this particular grant, because they are excellent researchers and I think that they have real chance to succeed in this area. And I'm willing to take a bet on this one.

DR. HART: And my last negative comment is that they don't really need this money to do this project. They seem to be well funded for all kinds of things.

DR. FISHBONE: The P.I. will only commit one percent of his time?

DR. HART: Yeah, it's a seed grant. There's not enough money to pay him more.

MS. HORN: So we have a motion to fund.

DR. WALLACK: I'll support.

MS. HORN: And a second.

DR. WALLACK: Unenthusiastically second.

MS. HORN: Unenthusiastically second.

(Laughter)

MS. HORN: Any further discussion.

DR. KIESSLING: This is a yes or a maybe?

DR. HART: Yes.

DR. WALLACK: Yes.

DR. PESCATELLO: They're saying yes.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Okay. That was all in favor.

A MALE VOICE: Was there a question there? Okay.

MS. HORN: 12-SCA-YALE-16 is Anne Hiskes and Milt Wallack.

DR. HISKES: Okay. I'll just start.

DR. WALLACK: Go ahead.

DR. HISKES: The P.I., and excuse me for mispronunciation, is Zheng Wang, a post-doc at Yale. His supervisor will be Dr. Natalia Ivanova, and I believe we've seen a very excellent proposal from her, which we've decided to fund, so he would have an excellent mentor.

The goal of this project is to better understand the role of C120RF-CORE-9, which is a novel

candidate for EF self-renewal. And it will compare the role of this molecule for protein in self-renewal to something that's already known called, TP-53, which is a known regulator of cell proliferation and reprogramming efficiency. So one question that has come up in connection with some other proposals is, why did they choose this molecule rather than some other molecule? And the reviewers praised the reasoning behind selection of this C-12 molecule.

It was discovered through an innovative screen procedure. It took a library of S.H. RNA screening, applied it to a bazillion different things on record and came up with a correlation that this chemical was very closely affiliated -- deletion of this chemical gave rise to a lot of proliferation of stem cells. So that it's thought that this is a regulator to control wild proliferation of stem cells. And therefore, understanding the role that this plays in cell proliferation self-renewal will also provide a key to understanding the rise in cancers.

So, it has several aims. Aim one is to assess the relative effect of this known regulator, TP-53, compared with the C-12 depletion. Their effects on self-renewal, genome stability and developmental potential --

potency of hES's. Aim two is to characterize the TP-53 and the C-12 molecular networks in hES's. And the third aim is to assess the effect of these two regulators on cellular reprogramming.

The reviewers I think were quite enthusiastic. The proposal could have said more I think. The one objection of the secondary reviewer is that the P.I. talked about investigating genomic integrity and it seems that this is not really geared at investigating genomic integrity, but rather cell proliferation, but had no other negative comments. That reviewer gave it a three and they thought it would have widespread implications for setting and understanding carcinogenesis.

Reviewer number two gave it a score of two. Thought that a weakness was that the effects of the C-12 was not described, therefore, it's possible that it is a determinative cell proliferation survival differentiation but not of self renewal in the sense of proliferation was not lost of differentiation potential. Under approach identified multiple strengths and no weaknesses, identified the investigator as having provided solid preliminary data, which is well suited to the proposed studies. He's also first author of an important paper, Impress at Cell Stem Cell, that revises the current view

of the core pluripotency network in ES cells and then cites the expertise of his mentor, Dr. Natalia Ivanova.

So I was favorably impressed, I didn't see any major weaknesses. You know, again, I'm not in a position to say how important understanding this particular molecule is, but it seems to have potential importance in understanding this origin of cancer cells. So, I will turn it over to my co-reviewer.

DR. WALLACK: I thought it was a strong proposal. I think the team is strong. I think that it has potential, as one of the reviewers indicated, to elucidate important information about cancer. And without repeating what Anne, what you've already said, I would endorse this project.

DR. HISKES: So I would recommend a yes.

DR. WALLACK: Right. I would also. I would second that.

DR. HISKES: Okay.

MS. HORN: Any discussion?

DR. KIESSLING: What other funding do they have?

DR. HISKES: Good question.

A MALE VOICE: (Indiscernible, too far from mic.).

DR. KIESSLING: Yeah, we just gave her some money, didn't we?

DR. HISKES: My computer went down. Do you have that information handy, Milt?

DR. KIESSLING: Does she have another application in this group? Don't we have another --

DR. HISKES: Natalia got a -- went to number one established investigator grant.

DR. WALLACK: Yeah. She got a -- she was the top of the established investigator ones.

DR. KIESSLING: Okay. And this is her post-doc?

DR. WALLACK: Yes. Yes.

DR. HISKES: Correct.

DR. KIESSLING: Okay. How much more money do they have?

DR. HISKES: So, let's see.

DR. KIESSLING: Not be personal, but if we're going to give one lab $1,000,000 and they already have $1,000,000 --

DR. WALLACK: Let's spread the wealth.

DR. KIESSLING: -- that's always my argument against funding the cores.

DR. HISKES: I don't have his proposal in

front of me. I'm scrolling down to the funding place.

DR. KIESSLING: Who reviewed the Ivanova grant?

MS. HORN: That was Milt and Paul.

DR. KIESSLING: Okay. Do you remember how much money she has? No?

DR. WALLACK: Ivanova?

DR. PESCATELLO: (Indiscernible, too far from mic.).

A MALE VOICE: That was 750.

DR. KIESSLING: Yeah. We're going to give her 750, so this would be 950. What other money does she have?

A MALE VOICE: She has the grants.

DR. PESCATELLO: I believe she does, but I don't know that.

(Discussion off the record)

DR. HISKES: So the post-doc has no ongoing research support.

DR. KIESSLING: Right.

A MALE VOICE: Of course.

DR. HISKES: And let's see. Dr. Ivanova, ongoing research support, departmental startup grant, Yale 2008 to present, it doesn't say how much. Those were

startups. Co-investigator on an NIH, which runs through May of 2015, but it doesn't say on Dr. Wang's proposal how much Ivanova's NIH is worth. And then she has a bunch of completed grants.

DR. HART: I think we ought to consider this under the same kind of strategy as previously with Dr. Qyang where we fund the larger of the grants, in this case the established investigator, even though it's not exactly on the same topic, and consider withholding --

DR. DEES: Actually, this is a different category because, I mean, the Qyang grant had -- there were three grants --

DR. KIESSLING: There's actually four.

DR. WALLACK: There's one more coming.

DR. DEES: -- oh, there's one more coming? But anyway, there was two grants from the primary person and we were going to give both of those grants, and we said no, we're going to give you the bigger of the two.

DR. WALLACK: That's true.

DR. DEES: The seed grant we were willing to give to the post-doc. At least we have been so far.

DR. HISKES: So I want --

DR. GOLDHAMER: Considered a seed grant for a post-doc separate from funding for the lab, so in a

sense it all goes to the same place, but in terms of development and competitiveness for moving on in the field, having gotten their own funds is a very big deal.

DR. KIESSLING: And so --

DR. HISKES: -- I think that's penalizing somebody for having a good mentor.

DR. KIESSLING: -- no, it's not that. It's just really how far you can spread the money. I mean, it's really all about the money. And it doesn't sound like she has tons of money, she's got -- she's co-investigator on one NIH grant.

DR. HISKES: No. And she has her start up funds.

DR. KIESSLING: So there's no -- there's no overlap between this project and her main project?

DR. HISKES: That would be something to look at.

A MALE VOICE: Anne, I don't think there is.

DR. HISKES: So who reviewed Ivanova's established investigator grant?

MS. HORN: That was Milt Wallack and Hart.

DR. HISKES: Okay.

DR. WALLACK: I don't see the overlap.

DR. PESCATELLO: Yeah, I agree with you. It's like a punishing her for (indiscernible, too far from mic.).

MS. HORN: Okay. So we have a motion to fund. Do we have a second?

DR. WALLACK: I move.

MS. HORN: We have a second. All in favor?

VOICES: Aye.

MS. HORN: 12-SCD-YALE-23. This is David Goldhamer and Anne Kiessling. There is coffee outside of people would like to just grab it on the run.

DR. HART: This is the one that I picked up from David.

MS. HORN: Oh, yes. Right. David recused himself. I'm sorry.

DR. GOLDHAMER: Oh, right. That's near my name.

DR. HART: Yeah, that's right. Okay. And actually, I was glad to get it. It's a really interesting grant and I was very happy to read it.

A FEMALE VOICE: Which one are we on?

DR. HART: Julieann Sosa from Yale.

DR. KIESSLING: You're one of the collaborators.

MS. HORN: Dr. Goldhamer identified a conflict and recused himself, and Dr. Hart kindly picked it up.

DR. HART: So the title is, Stem Cells for Cell Therapy in Hypoparathyroidism. This is a M.D. with clinical experience in medical publications directly related to the post project. She's provided several collaborators with experience in stem cells, including some of our members here.

It was interesting. I had no idea of the prevalence of hyperthyroidism -- hypoparathyroidism, I've got to keep correcting myself, based on all kinds of --

A MALE VOICE: -- searching --

DR. HART: -- yeah, exactly, so that's where it came up. And I had no idea, so I thought this was very interesting for me personally. The current therapy of frequent dosing with, you know, regular drugs is rather inefficient and difficult to follow because you have to do this very frequently, and it's hard to track as well. It's been shown that transplanting a small number of parathyroid tissue cells is sufficient to maintain calcium homeostasis. I'm tripping up late in the day here. And so the P.I. has built a back reporter system in an embryonic stem cell environment for tracking

development of parathyroid markers, and now wishes to develop and optimize protocols for differentiation. She'll also validate function of the derived cells, both in culture and following transplant in mouse and to generate IPS from patients with -- with the condition.

The reviewers noted the novel approach and clearly had high enthusiasm for the project. The primary reviewer originally had a score of one and then in conference came down to two. The secondary reviewer started off at four and went to three. The secondary reviewer complained about a lack of preliminary data, which was not a requirement for this program, basically they're wrong. They criticized the back reporter, instead suggesting a much more difficult tactic of knocking in using zinc fingers. This is silly.

The third aim of making patient specific IPS may be unnecessary and over ambitious, but I'm not going to worry about that right now. If she gets the first two aims done I think we'll be very very happy. So discounting the kind of misguided secondary reviewer, I think this is a solid two at worst, maybe even better than that. It's an excellent opportunity to draw a clinician with direct experience on a direct medical application into this field and to gain the appropriate lab experience

to help develop these therapies firsthand. And so I, with very high enthusiasm, recommend support of this project.

DR. KIESSLING: Yeah. I totally agree with that, actually. My first comment on this was, this was worth a much higher score than 2.5, given the other grants that I'd read. And so, this is a really nice mid-career clinician investigator. And so, I would very much recommend this for funding.

MS. HORN: We have a motion to fund and a second from Dr. Hart. All in favor?

VOICES: Aye.

MS. HORN: 12-SCA-YALE-27, David Goldhamer and Anne Hiskes.

DR. GOLDHAMER: All right. This is a grant from Kumar. It scored a 2.5, a one and a four, and then I think it's in the range of a two and a three. So this investigator has long-standing interest in the pathogenesis of West Nile virus that's carried by mosquitoes. Currently, there's no therapeutics or vaccines.

The investigator made the comment that in most studies of West Nile virus the eco-studies used non-neural cell lines because it's hard to maintain and propagate and take high (indiscernible) using primary

neurons, so there's a need here to generate neurons from a renewable source. So they want to use human embryonic stem cells and make neurons of different types that are susceptible to infection by West Nile virus. And then they want to try antiviral and anti-apoptotic inhibitors using RNA-I approaches to see if they can rescue cells that have been affected by West Nile virus and keep them alive.

So they're aims are that. They want first, they want to establish protocols to develop neuronal cell types that are effected by West Nile virus. And they mentioned floor brain cells and also motor neurons of the anterior portion of the spinal cord. In aim two they want to identify apoptotic pathways operative in West Nile virus infected cells and figure out what genes are active and why the cells died. And third, they want to try therapeutic approaches, as I said before, targeting pro-apoptotic pathways and the viral RNA to see if they can rescue cells.

So an important problem, an interesting study, the reviewers liked the grant in some ways and had some criticisms in other ways. I think it's encapsulated by what reviewer two said. Reviewer two said this is a novel and proper proposal and it generated human ES drive

neurons. The author seemed well worth the caveats and inefficiencies, and directed the (indiscernible) protocols and are preparing to address these experimentally. But they had concerns. And one of the biggest concerns that I agree with, is a heterogenating of these cultures. So they're going to make neurons. Depending on the type of neuron that they're going to generate the efficiency of making that neuron is -- it's inefficient. So they quoted a number of, I think nine percent for making the motor neurons and the anterior (indiscernible).

So you can imagine you have this mass of cells in the dish, nine percent of them are infectable, and then they want to use biochemical approaches to define hemopoietic pathways to figure out what genes are involved in this process, but they have this background of 90 percent of cells that are not infected. So there's real interpretive limitations and value using mixed cultures like this where some are effected and some are not. So I think that is a big concern.

And then secondly, the same reviewer says, use of RNA-based rays to screen for apoptotic pathways is not rational as a vast majority of apoptotic triggers are a result of post-transcriptional events, or post-translation events. So defining genes that are up and

down regulated will not define the apoptotic pathways involved. And I'm not an expert on apoptosis, I know that an early stage of apoptosis it is post-transcriptional and post-translational. I think though, over longer terms, there are significant changes in gene expression. So I'm going to be quite as hard on that aspect of it, but they were quite critical of that aspect of the grant.

So there's two of the three aims I think had significant technical problems or potential problems. So both agreed clinically relevant, very interesting and relevant proposals, but quite a bit of unknowns in terms of how much valuable data this will -- this would generate. So I really like the grant, I liked how it was written, I gave it a maybe when I was reviewing this. If I had to be a little bit more rigorous because of the limited funds, I would probably reluctantly put it in the no category because of those technical caveats.

DR. KIESSLING: What kind of culture facility do you need to culture West Nile virus?

DR. GOLDHAMER: I didn't check that. I do know that this investigator has been working with West Nile virus for years and years and so I assume that whatever is needed they have, but I did not look to see what type of facilities they have.

DR. KIESSLING: It's got to be right up there with --

A MALE VOICE: Three. It requires PSL-3.

DR. KIESSLING: -- it requires three?

DR. HISKES: So I was the second reviewer and my impression is that, again, it's a really cool idea, you know, a novel idea. I haven't seen much about West Nile virus in stem cell land. But so if it were to work there would be potentially high rewards because this is an area that really needs attention, but it's high risk in its success because of some of the -- because of exactly the problems that David mentioned. It's unlikely that the method of observation of the apoptotic triggers, the RNA-based surveys are able to detect these things and then the, you know, the heterogeneity of the neurons is another problem. So, you know, I think, given the limitations on the funds, the high-risk versus, you know, the possible benefits I think we can't go with high-risk at this point.

DR. KIESSLING: Why is it a stem cell grant?

DR. GOLDHAMER: It's a stem cell grant because there's no other easily available sources of cells to do these studies. They mention the primary neurons are hard to grow and maintain, and there can't be higher group

kinds of analyses with them. So they're not trying to learn anything really specifically about stem cells, but using stem cells as a tool to generate a renewable source of neurons of different sources and types.

DR. HART: Are they making any particular type of neuron that's special for this project, or not?

DR. GOLDHAMER: They're trying to generate two. One can be generated at high frequency and one cannot. So I wouldn't say that -- so for four grain neurons, you know, they can get reasonably high efficiency in conversion. And so there would be less background in the system for that. So there will be data generated, but there's a combined review, the combined technical problems I think is what really gave me pause is that, you know, very interesting but just perhaps a little too risky at this stage of the funding.

MS. HORN: I'm hearing a motion no? All in favor?

DR. KIESSLING: For no?

MS. HORN: For no.

DR. WALLACK: So before you do no, did you discount the reviewers' feel that this is an exciting proposal and that there was some other pretty strong favorable comments about it? I mean --

DR. GOLDHAMER: Well, I tried to mention those. No, the reviewers did think that it was exciting and clinically relevant. Upon reconciliation they both agreed that the (indiscernible) cultures is going to be a problem, so they went from one and four to two and a three and split the difference at two and a half. No, I mean, I was excited by the concept.

DR. HISKES: It looks like you have a high number for possible benefit multiplied by a low probability of success.

DR. WALLACK: Yeah, but isn't that also what a seed grant is possibly about? I mean --

DR. HISKES: Taking risks?

DR. WALLACK: -- and where I see the initial reviewer, one reviewer giving it an enthusiastic one, I don't know. I'm not ready to personally vote no. I mean, if anything I would -- I don't think I'd want to go any lower than a maybe on this one.

MS. HORN: So we have a motion --

MS. MULLEN: You can oppose.

MS. HORN: -- yeah. We can take a vote and you can oppose.

DR. WALLACK: So I'm just making the argument then.

DR. HISKES: It's a good argument.

DR. GOLDHAMER: Yeah. I mean, I will say that I was swayed more by the -- by the technical difficulties raised by reviewer four and reviewer one was influenced by the things that I also found to be very favorable, you know, the clinical relevance, I think the justification for using stem cells was there. At the end of the day I think the second reviewer who gave it a four if their critique, if their criticisms was significant enough that I think that I just worry that the impact of the study will be low.

DR. HISKES: The person who gave a one said nothing other than their little narrative at the beginning. So basically, no comment, no comment, on the sheet. What they said was they -- the track record of the P.I., the simplicity of the approach increases significantly the chances of success. The legality of the P.I. and the availability of the needed tools in his lab are also important and contribute to the high level of enthusiasm of this reviewer. Under strengths it just says, important public health problem that currently has no treatment. Weaknesses, no comment. Approach, the strength is that the tools are in the lab. Weaknesses, no comment. Investigator, strong track record. Innovation,

utilization of tests that makes him a valuable tool to develop new therapy with proposals like this. High impact for the amount of funding requested. So not a rigorous analysis of the logic of the experiment or of the details of the techniques.

DR. KIESSLING: How do you usually study West Nile virus? Do they just infect birds?

DR. GOLDHAMER: They get -- well, I only know what he said and they usually use non-neuronal cells fibroblast. But I don't know -- I don't know the limitations to that approach (indiscernible) are actually looking at it and so I really can't say. I'm just repeating what their argument was for why neurons have been -- it's not easy to do this with neurons and that's the appropriate cell type. (indiscernible)

DR. HART: I mean, realistically if they were ordering their human stem cell derived neurons from Cellular Dynamics, I mean, would we be enthusiastic about this as a project for stem cell study? No. Right? That's essentially what they're doing is they're preparing their own. They could easily go out and buy them, human neurons derived from stem cells. And if that's all they need they'd be better off buying them.

A FEMALE VOICE: Yeah. There's a lot of

companies that sell them.

DR. GOLDHAMER: I don't know if he's specific in, you know, motor neurons in the anterior heart, I mean, I don't know.

DR. HART: That's definitely (indiscernible)

DR. GOLDHAMER: But I think the criticism of the entire second approach when you look at -- he tried to define apoptotic pathways based only on transcriptional changes and then base their entire third aim on the results they get from the second aim when the second aim, the pathways again are (indiscernible) and they might not even see genes up and down regulated during the time frame of this alternate experiment. I think they're just -- it's just there's problems with the approach and I'm not sure, and the investigator didn't mention these things as potential caveats and work arounds. And so I'm just a little -- I wasn't convinced that this was going to generate the impact that I would hope it would.

MS. HORN: Any further discussion? The motion is to vote not to fund. All in favor?

VOICES: Aye.

MS. HORN: Opposed? One opposed. Okay. We've gone through now the 2.5's. I'm going to ask to

turn the air conditioning up a little bit and suggest we maybe take a 10-minute break. There are cookies and drinks down the hall and then I think when we come back if there are any other seed grants that people would like to put forward for discussion that they felt should have been rated higher we can do that and then we need to wrap up.

MR. STRAUSS: We are at 1.4 million so far.

A MALE VOICE: The seeds.

MR. STRAUSS: 1.4 on the seeds and 7.7 on the total.

A MALE VOICE: 7.7?

MS. MULLEN: Is that including seeds?

A MALE VOICE: I've got 8.7 million.

(Off the record)

MS. HORN: Should we go ahead without her? We're all back. This is without maybes, correct?

MR. STRAUSS: Right.

MS. HORN: Okay. So Rick Strauss tells me that we are at $8,708,847 without any maybes.

A MALE VOICE: So we've got another million?

MS. HORN: Yes.

DR. HISKES: Without any maybes, not babies?

MS. HORN: Without any maybes. Okay. So does anybody want to pull a grant -- a seed grant up for review that was not reviewed?

DR. KIESSLING: I have one. I don't have huge enthusiasm for it, but I think it should be discussed. It is, UCHC-13, SCA-UCHC-13. It's a 3.5. It was one of these split scores. It's really -- it's an interesting project and if it worked, it would be awesome. And I just don't know if there -- if there is some work around that has proven it isn't going to work.

So this is a -- let me pull it out here.

DR. HISKES: Which one is it Anne?

DR. KIESSLING: It is UCHC-13.

DR. HISKES: Oh, okay.

DR. KIESSLING: Wait a minute. I can't find it here.

DR. KRAUSE: I could talk about it a little bit. Do you want me to introduce it?

DR. KIESSLING: If you -- I mean, I could introduce it, but I --

DR. KRAUSE: Oh, well then go ahead. I'm sorry.

DR. KIESSLING: -- maybe you can tell me -- yeah, go ahead Diane.

DR. KRAUSE: So this is --

DR. KIESSLING: I'm trying to find it.

DR. KRAUSE: -- so this is by an associate professor of neuroscience, use of human glia for a conceptually novel approach in the therapy of Parkinson's disease and basically the P.I. is proposing to convert glia cells directly into dopaminergic neurons, which are the ones that are killed off in Parkinson's patients in vivo.

Feasibility was the main issue, but the experience of the P.I. gives credence to the notion that this work could succeed. If so, the impact would be high. Reviewer two was less enthusiastic with well-thought-out concerns. His concerns -- or his or her concerns were, no ex vivo studies were proposed to examine adult astrocytes and no in vivo studies were proposed to verify the function of the proposed transcription factor combos in the adult cells of the brain.

The P.I. is not that well-funded and has not been very productive. He was an assistant professor from 042-2010, according to his C.V., and then it wasn't clear what happened after that. I look for a C.V. on the web to see if he'd become an associate, and the only sign is that actually on the front page of the grant, I'm just

seeing it, he wrote that he's an associate professor. So he's now an associate professor, so he has been promoted from assistant to associate.

But, you know, it's a cool idea. The feasibility was really the question and that's why it didn't get great scores.

DR. KIESSLING: I thought there were two things about it when I looked at it that I thought were in it's favor. One is that, yes, this investigator is going to run out of money. He has a small grant now, that I think is ending. This is the kind of project that's exactly our goals. So he's going to take ES cells, differentiate them into glia cells and then directly differentiate the glia cells into dopaminergic neurons.

I know that somebody has reported that that transition from glia to dopaminergic neurons is possible. I don't know if anybody's reported that it's not possible.

DR. HART: You wouldn't report that if it was impossible.

DR. KIESSLING: Well, I mean, maybe somebody -- maybe somebody would. So, I mean, this so fits our goals and the reviewers were so split that I didn't think the lack of in vivo studies was a useful

criticism because this is a seed grant. This is to get the technology going. I don't think you've got time to do the kinds of studies that person wanted to see. So I thought it was worth bringing this up and talking about and seeing if anybody else wanted to talk about it.

DR. KRAUSE: So people have already published in mouse and he can get -- there's no embryonic stem cells here, but he can get glia cells to directly differentiate into dopaminergic neurons. So there you go. It's already been proven that that can happen. But it opens up that you could use this therapeutically in humans. So it would get rid of current problems with (indiscernible).

But the problem was, how was he going to do it? And is it going to be safe? And how is he going to prove it? And why isn't he doing in vivo studies to show that he got it to succeed? So it was more with the actual experimental design than with the concept of reprogramming the glia cells into dopaminergic neurons for this purpose. So it was a good idea, but not so well executed, at least in the way the grant was written.

DR. KIESSLING: So you don't think it's even a seed project? I mean, what he's got to do is design a gliatropic virus and that's I think what's going

to take the most time.

DR. WALLACK: So Anne, to pick up on what you're saying, I would also agree that it's the kind of grant that we look for in a seed.

DR. KIESSLING: Right.

DR. WALLACK: And one of the reviewers who originally gave this proposal at 2.5 indicates that the P.I. is proposing an extremely bold approach.

DR. KIESSLING: Right.

DR. WALLACK: Feasibility is an issue, but the experience of the P.I. gives credence to the notion that this could work. And this to me is a very, very key statement. If so, the impact would be enormous.

DR. KIESSLING: Right.

DR. WALLACK: So from the standpoint of what we're trying to do with seeds, when I can get this kind of response from the reviewer it resonates at least with me.

DR. DEES: So even that reviewer wasn't -- he wasn't really enthusiastic right? I mean, 2.5 is good, but not --

DR. KIESSLING: Well, I mean, I think that they were being cautious because it isn't clear that this

will work.

DR. DEES: Yeah.

DR. KIESSLING: So -- but if it would work, I mean, this is one of those way out there possibilities. And this individual, this particular investigator, is not going to be able to even find out it's going to work if this isn't funded because he's out of money. It isn't like there's a backup that he can get some money.

DR. KRAUSE: I still don't quite get the -- why take human ES and make them into astrospheres and then make those into dopaminergic neurons when you can make dopaminergic neurons directly from human ES, which is what, you know, Redmond is doing, you know, we're talking about funding him to do that.

DR. KIESSLING: Right. But I think -- as I understand it, it's going to give you a purer population. I mean, the problems with all the dopaminergic neurons that are made is that there is a significant percent of undifferentiated cells in those cultures.

DR. KRAUSE: That's how you could purify after it's more usable.

DR. KIESSLING: Yeah. And I think going this route is supposed to give you, you know, a cleaner compilation.

DR. KRAUSE: I don't know. I think that was executed -- if the grant had been written as a seed grant that was highly developed than the reviewers would have given it better scores. I didn't read the entire grant as a peer reviewer myself, it's not my area of expertise.

DR. HART: Yeah but, the other point though in response to the question about why make astrocytes this way is, how else are you going to get human astrocytes so easily?

DR. KIESSLING: Yeah. I mean, you've got --

DR. KRAUSE: But you don't need astrocytes if you can make dopaminergic neurons.

DR. HART: No, no, but his point is to model the astrocyte that he's going to have in vivo and he's going to eventually hit with viruses to turn into dopaminergic cells. So it's not -- the point is not to make cultures of astrocytes in the dish in order to make them dopaminergic neurons and put them in the brain, right?

DR. KRAUSE: I'm not sure. I thought at first that it was just to reprogram astrocytes. But then, when I'm reading it more carefully. The idea is to make

ES into astrocytes, have them frozen away, and then make dopaminergic neurons when you needed them.

DR. KIESSLING: Right.

DR. HART: Oh, okay. I misread it.

DR. KRAUSE: I misspoke before. I introduced it to you incorrectly.

DR. HART: No, I'm skimming this as you're reading it so that's why.

DR. KIESSLING: You're starting with human ES cells -- he's starting with like E-9 or something. I didn't know quite -- remember what he was using.

DR. HART: The point is, that it would be less tumorigenic to start with astrocytes?

DR. KIESSLING: Yes.

DR. HART: Okay.

DR. KIESSLING: It's supposed to be less tumorigenic and faster.

DR. HART: Okay.

DR. KIESSLING: This is just so mission -- it's our mission. This investigator is not going to be able to do this if he doesn't have some funds. It's a high risk --

DR. HART: So then if they're going to -- if they're going to start with cultures of astrocytes why

do they need gliatropic virus?

DR. KIESSLING: -- I don't know.

DR. ARINZEH: That isn't the developmental pathway is it? Astrocytes?

DR. HART: No.

DR. KIESSLING: No. Well, I don't think anybody knows.

DR. ARINZEH: Okay. (indiscernible).

DR. HART: Well, (indiscernible).

DR. ARINZEH: I think we're doing that in other areas. They're trying to really go down the developmental pathway and stop, you know, don't skip over to get pure population or more potent cells or something like that.

DR. KIESSLING: So that -- so the work has done in the mouse, it's been shown. I don't -- this isn't my strong area either. So I'm just bringing this up because I think this was exactly the kind of project we'd like to see and if it would work it would be awesome.

MS. HORN: So are you making the recommendation to fund?

DR. KIESSLING: If it doesn't work. We've lost $200,000.

DR. WALLACK: You've not necessarily -- we

haven't lost 200,000 --

DR. KIESSLING: Yeah.

DR. WALLACK: -- there'll be a paper that will come out of it and you've invested --

DR. KIESSLING: Hopefully. Since it didn't work. Well, I think it's really tough to, you know, I think that's such a really cheap shot when you review a grant, this might not work. Well --

DR. KRAUSE: Well, and also, they're saying it might not work because we don't -- they didn't say they have the clones yet for the things that they're talking about getting, or the viral vectors, the (indiscernible) this vector. I mean, I think what this grant, based on the reviews, was missing was what we call grantsmanship. I mean, where you put in -- you know, we can do -- this is feasible because of this, this, this and this. You know, even though it's a pilot study, a seed study, you have to say it's feasible. And it was missing a lot of that too. So we'd be losing out on $200,000 and not getting anything.

DR. KIESSLING: Maybe.

DR. KRAUSE: It's unclear. And delivering the vectors directly to the brain, is that the long-term goal?

DR. KIESSLING: I think they're trying to get around, you know, the really high death rate --

DR. KRAUSE: Do you want to fund it? We'll put in the yes category.

DR. KIESSLING: -- well, no. I want to talk about it. I mean, I want to fund it if there's a consensus to fund. I just think it's a project that really meets our goals and this investigator doesn't have enough money to do anymore on it. It isn't like this is a second project they're adding. If this doesn't get funding, we're not to find out if this is going to work.

DR. KRAUSE: Are you proposing yes?

DR. ARINEZH: So they don't have any other funding?

DR. KIESSLING: As near as I could tell. I couldn't find -- he's got something and it is dying this summer or just died or something. And maybe, I mean, I always look at that because I think if you don't like the grant, or if there's something about it that they can do it, but if they can't do it --

DR. HART: It ended 4/30.

DR. KIESSLING: -- yeah, it ended in the spring, right?

DR. HART: Then there's a Connecticut Stem

Cell grant ending on September 30th.

DR. KRAUSE: What was the title on that one?

DR. HART: Oh, it's a core facility.

DR. KRAUSE: Oh, okay.

DR. KIESSLING: Do you want to put it in the maybe category? And does anybody else have a grant they want to talk about? We can balance out all the maybes? We still have quite a few maybes to discuss, right?

MS. HORN: We do. We have a motion for maybe.

DR. KIESSLING: I move that we put it in the maybe category so it gets discussed again.

DR. WALLACK: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Okay. Does anybody else have a grant they would like to bring forward for discussion in the seat category?

DR. WALLACK: So Marianne?

MS. HORN: Yes?

DR. WALLACK: Are you asking before -- this kind of consideration if we have disparities like a five

and a one. You've talked about the seven and a one before, because there seems to be --

DR. KIESSLING: There's a couple in here.

DR. WALLACK: -- well, there are. I'm looking at the Nair grant.

DR. KIESSLING: Yeah. We just talked about that among ourselves.

DR. WALLACK: Oh, okay.

DR. KIESSLING: The primary here would have given it a seven.

DR. WALLACK: Oh, it's not a seven. It's not that bad.

DR. PESCATELLO: Can we go over where we are dollar wise? If we fund everything we said yes to?

MS. HORN: So, did we add anything, Rick since you --

MR. STRAUSS: No. You're still at 8,700,000.

MS. HORN: -- $8,708,847.

DR. KRAUSE: And that's how many seeds?

MR. STRAUSS: Seven.

DR. KIESSLING: With how many maybes? How many maybes do we have?

MS. HORN: I have five maybes. Rick, can

we make that a little bit smaller so we can get it on one page?

MR. STRAUSS: This is five there and two is seven.

DR. KIESSLING: We have two established that are maybes?

MR. STRAUSS: And what do we want to get on one page?

MS. HORN: The seeds into one page.

MR. STRAUSS: You mean like the maybes?

DR. KIESSLING: I don't think we'll be able to see it.

MR. STRAUSS: These are all the maybes on one page.

MS. HORN: Okay.

MR. STRAUSS: And these are the ones you've funded. So there's --

DR. KIESSLING: What does the blue and the green mean?

MR. STRAUSS: -- those were the different categories that we started with. So green was in the top level -- oh, here it is.

DR. KIESSLING: Oh, okay.

MR. STRAUSS: So that was related to this,

dealing with getting you to the 40 percent level for discussion.

MS. HORN: So I think at this point if there's anybody who has a grant that they feel is meritorious on the seed grants and would like to bring it forward, we'll make one last call.

DR. KIESSLING: There's one that has this huge disparity, so maybe we don't need to discuss it.

A MALE VOICE: What's the number?

DR. KIESSLING: It is YALE-22. 12-SCA-YALE-22. It's got a one and a five. Milt, you are the primary on that.

A FEMALE VOICE: Who's the first author? Oh, there he is, Yu.

DR. PESCATELLO: This is about dyslexia, right? It's a look at dyslexics and non-dyslexics. (Indiscernible). I had a no on this.

MS. HORN: And Milt, you were the other reviewer.

DR. WALLACK: Just give me a second please?

A MALE VOICE: Which grant are we on? I can't see it.

MS. MULLEN: Well, it's the one that had a one in a five.

A MALE VOICE: YALE-22, okay.

MS. MULLEN: It is YALE-22.

DR. PESCATELLO: I guess the reviewer who had the low score, he thought that it was a very inefficient methodology.

DR. WALLACK: Yeah. When I looked at it. I was not impressed with the -- I thought there was lack of innovation in the approach.

DR. KIESSLING: Why did one reviewer give it a one?

DR. WALLACK: Well, the one who gave it the one felt that it had potential of advancing the field of vascular biology and regenerative medicine in general, didn't highlight very many weaknesses in all.

DR. PESCATELLO: But I mean the way that it's summarized by reconciliation, it says, despite these weaknesses, the proposal does have some novelty, although both reviewers agreed that subjectively the likelihood of identifying a reproducible phenotype in dyslexia patient IBSC derived neurons versus controls seems very low.

DR. KIESSLING: Oh, okay. Okay. So that answers that. Then there's one more, YALE-08.

MS. HORN: So we'll withdraw that grant from consideration. Okay.

DR. KIESSLING: YALE-08, one reviewer gave it a 1.5 and the other one give it an 8.

A MALE VOICE: And what was the total for a final peer-review score?

A FEMALE VOICE: 5.

DR. KIESSLING: I think maybe it's an 8, but this is such a disparate score, and some of these reviews were so off-the-wall.

MR. STRAUSS: Well, it was, and I couldn't reconcile. That's why I went to the co-chair for review and that ended up as a five.

MS. HORN: That was Anne Hiskes and Paul.

DR. PESCATELLO: Yeah. It's under the fives.

DR. KIESSLING: That's also -- it was Paul, you had some winners, didn't you?

DR. PESCATELLO: Right. I think one of the main things here, I meant to look deeper into my notes, but a lot of the work was to be done outside of Connecticut and that is for us, I think that's a big deal. This is a melanoma study. So it was set up to -- it's meant to come up a super faster way to extract melanoma cancer stem cells, but I guess the reviewers were not sure that the existing process was efficient enough. So, given

the score, the low score, and also that so much of the work would be done outside of Connecticut, I gave it a no.

DR. KIESSLING: Okay. That's probably it then.

MS. HORN: Okay. So then we need to go back and consider the maybes. Shall we start back with the -- let's see, what have we got left in the group?

A MALE VOICE: We're done with the group.

MS. HORN: We're done with the group?

A FEMALE VOICE: I think we exhausted that.

DR. KIESSLING: We have established -- we have some maybes in the established investigator, right?

MS. HORN: Okay. Very good. So, just to review, we are funding both cores for 500,000.

DR. KIESSLING: I guess.

MS. HORN: We are not funding the Wesleyan group proposal and we are funding the YALE-01 disease directed for at this point $1,808,847 and that is it. We'll come back at the end and we will adopt all of these by motion.

DR. KIESSLING: Oh, so there are no maybes in that group?

A MALE VOICE: No.

DR. FISHBONE: What's the 4.5, what is it?

DR. KIESSLING: Oh, there's maybes in the established grants.

DR. FISHBONE: One has a rating of 4.5.

MS. HORN: That's a 3 on the -- yeah.

DR. FISHBONE: Oh, okay.

DR. PESCATELLO: I would just throw one comprehensive deal on the table, so to speak. I'm not necessarily endorsing this, I'm kind of going against my earlier comment on Wesleyan. But if we wanted to send a message and we wanted up the score at Wesleyan, essentially just for the value, the Connecticut value of showing support for Wesleyan, this wouldn't be cutting it in half, but to give the balance we have a little bit under 1,000,000 to give. If we said yes to everything that we've said yes to and we took that balance and gave it to fund that Wesleyan, that would be one comprehensive package.

DR. KIESSLING: But I think we determined that they have enough funds to come back to us. It might be to their advantage.

DR. HISKES: I would prefer we look at the maybes.

DR. KRAUSE: Right now we have seven seeds and six established. So we have enough money for another

established investigator --

DR. KIESSLING: And a seed.

DR. KRAUSE: -- and another seed.

DR. KIESSLING: Or all the seeds.

DR. KRAUSE: Well, we have two maybe established, Stormy Chamberlain and David Goldhamer. And I don't know how I would decide between those two, but that could be --

DR. HART: Why don't we have that discussion about those two grants now as long as David's already getting up?

MS. MULLEN: Yeah. I think that's what -- we're trying to move to that place.

DR. HART: I move we discuss the maybes and the established, how's that?

MS. HORN: Okay. Okay. Let's do 12-SCB-UCHC --

A FEMALE VOICE: Which one is that?

MS. HORN: -- that's Chamberlain. I'm sorry, you don't have these memorized? Milt Wallack and Paul Pescatello.

DR. KIESSLING: Can she keep working if she doesn't get this?

DR. WALLACK: I'm sorry?

DR. KIESSLING: We're talking about Chamberlain. Can she keep working if she doesn't get this award?

DR. WALLACK: Yes.

DR. KIESSLING: Does she have enough money to come back to us next year?

DR. WALLACK: I don't know if the -- the thing that I found distressing about this, I'm not reading it now, I'm just giving it to you in narrative form, was that the comment of the second reviewer -- I guess the first reviewer, was clearly unjustified. It was not based upon anything having to do with reality. It had to do with the fact that she was part of Mark LeMond's (phonetic) lap, she wasn't going off on her own and in a career direction and so forth. And those are the things that I think that we, who live in the state, you guys have met these people, have an advantage, frankly. And I think that with that in mind, I paid more attention to the one, which was very, very strong. And I felt, knowing what this researcher has done, her enthusiasm, her successes, her publishing record, and so forth, that I was inclined to consider the funding curve.

DR. KIESSLING: How many years was she asking for?

DR. WALLACK: She was asking for four years and that's a very, you know, I think, a very good question. And let me ask the scientists? So if you take a grant like this and cut it to two years -- I don't know, I'm asking the question, is this still a viable grant application?

DR. KIESSLING: It's hard to know. I mean, that really depends.

DR. WALLACK: So there's no strict yes or no?

DR. KIESSLING: Cutting something to two years is tough. Cutting something to three years is standard NIH time. So if you wanted to fund both of these at a reduced level just to justify their --

DR. HART: Well, actually, before we get to that point, then, to answer the same questions about David's situation, he's got an NIHR-01 through '15 and he's got a muscular dystrophy for another year or until a year from this January, January 14, you could say the same thing about him. It's like, does he need this to keep going? No. But, you know --

DR. KIESSLING: But he will next year.

DR. HART: -- yeah.

DR. PESCATELLO: Just on the Stormy

Chamberlain, I would just ask the scientists among us, I mean, my reading of this was that it was really a call about the basic -- the design -- this is a bet on basic research on imprinting and there seemed to be such a variance among the reviewers, among whether it was a bet worth taking and worthwhile, and it was so scientifically dense, I recall, and we can look it up, you know, I know Stormy Chamberlain's reputation, so based on that I would probably -- and given there was a review of one by one reviewer, I would probably be inclined to say -- look favorably on reevaluating it.

Generally, I'm not in favor on cutting it, I mean, they apply for what they apply for and either to go up or down --

DR. WALLACK: So, let me just go back again and just remind the group that this was viewed by one of the reviewers as one of the best proposals reviewed this year.

DR. KIESSLING: Right.

MS. MULLEN: How many -- which ones did they review?

DR. WALLACK: What's that?

MS. MULLEN: Which ones did they review?

A MALE VOICE: Yeah.

MS. MULLEN: There are a lot that we never talked about today.

A MALE VOICE: Was this (indiscernible) or what?

A FEMALE VOICE: Yeah.

DR. KIESSLING: And we also have to be fair, so would it be fair to fund these at a reduced rate? I mean, would that be fair? What if they got 500,000 instead of 750?

DR. WALLACK: So you're saying 500,000 each?

DR. KIESSLING: Yeah. That would save us 500,000 and we can do three or four seeds.

MS. MULLEN: I'm still trying to balance out the technical and scientific merits on that transcend reputation, but the scientific merit for somebody with good -- with a proposal that there's some questions about, there's some favorability, and then depending on which sound bite you read, you know, I see, you know, overly ambitious, I'm not sure you can -- this is achievable. So, in that context, one, do we want to consider funding it? And then, if it is overly ambitious, and I don't know, is it going to be even harder to accomplish it with less funding? So, but first I'm just trying to reconcile

beyond the numbers what the review is.

DR. KRAUSE: So, I don't have an answer --

MS. MULLEN: Yes.

DR. KRAUSE: -- but I can at least tell you, they're very different grants, they are both good. And I'm not sure -- I don't really like the idea of splitting the difference, but I understand where that's coming from.

DR. KIESSLING: Because otherwise we are not going to be able to fund any more seeds.

DR. KRAUSE: I understand. So just to clarify, and I'm just going to read one sentence from Stormy Chamberlain's. The purpose of this project is to determine the chromatin structure of maternal and paternal, blah, blah, blah, alleles in IPS and IPS derived neurons and to develop and test a reporter Prader-Willi cell life for direct discovery.

Very cool stuff. It's basic science at the imprinting level, how it's different in Prader-Willi Syndrome and then develop some kind of an assay using these cells to blah, blah, blah, blah, blah. And I don't, you know, I didn't read all the grant.

The other one, completely different. Behavior of cells in a transplant system, how do you get

them to self renew? How do you get them to differentiate? And how are they regulated at the transcriptional regulatory level? Both have clinical applicability. One is getting directly to drug testing, one is more mechanistic in cells in a mouse. I could go either way with it. I think they're both good grants. They're just different kinds of grants. So I don't think one is more clinically applicable than the other, they are both really cool.

DR. HART: Yeah. I mean, in favor of Stormy's grant again, the idea of this imprinting -- this is probably the best model where testing is very important, fundamental property of imprinting in cells, and it affects not just Prader-Willi, it affects many, many diseases, but you can't get at them as well as within this disease where you're deleting or duplicating particular regions of genome and then it helps you figure out where the imprinting is.

Cutting a budget from like 750 to 500, if that was the choice, I mean, they could come back and say, well, for that amount of money I can't do aim three, or something like that, and modify the scope of the project. Or they could say, I'd rather make it a two-year grant at that price, or something like that. But I think that

again, the investigator can better tell us how to adjust if we say, here's your limitations and what we're willing to support.

And of course, no one wants to be cut, but if it keeps someone going one or two more years, that's a good thing.

DR. WALLACK: So, to that point Ron, so I can see doing what I think Anne intimated, and that is doing 500,000, but do it over three years, and the differential per year is not that much, it's $17,000. So I have to assume that both of these investigators can get done -- you're giving them a three-year window, they can come back at any time afterwards. And I'd be very comfortable because as Diane said, they're both good science, so we are driving it with science as well as understanding who these people are.

DR. HART: And if they came back to with a new application saying, we weren't able to complete everything under the old grant, we weren't fully funded, we wouldn't argue.

DR. WALLACK: Right. Right.

DR. KRAUSE: And we might have another 50K for each one of them, because if I did the math correctly I'm at 9.7, if you did 500 and 500.

DR. HART: Yeah. Yeah.

DR. KIESSLING: But then we can't do any more seats.

DR. KRAUSE: I know, that's why I'm saying. So if you add 50 and 50 to these two votes then we get --

DR. WALLACK: I would leave a little room for seed and I would move at this point that we do 500,000 for each of the applicants over a three-year period.

DR. KIESSLING: Then we can't do any seeds.

DR. WALLACK: Well, we can do one more seed.

DR. HART: No, there's only 100,000 left.

DR. KIESSLING: There's only 100,000 left.

A MALE VOICE: We're going to give you one year of the seed.

DR. KRAUSE: But you've got seven seeds.

DR. KIESSLING: So maybe -- what?

DR. KRAUSE: You've got seven.

DR. HART: We've got seven so far funded, yes.

DR. KIESSLING: -- so do it -- is anybody going to be really upset if none of the maybes on the seats get funded?

DR. HART: There was so little enthusiasm

during those maybe discussions that I cannot believe anyone can stand up now and say they're enthusiastic now.

DR. KIESSLING: I was enthusiastic about some.

DR. HART: About a maybe?

DR. KIESSLING: Yeah.

DR. HART: Which one?

MS. HORN: Should I have David come back in since we're --

A MALE VOICE: No, we haven't even voted yet.

MS. HORN: Okay. I just asked.

A MALE VOICE: (Indiscernible) totality.

A MALE VOICE: David Goldhamer is just -- who reviewed his?

A FEMALE VOICE: What?

A MALE VOICE: -- who can summarize David's --

DR. KRAUSE: I think I might have, but --

DR. HART: And I did too.

A MALE VOICE: -- so can you just review these?

DR. HART: Yeah, let me get my notes out, because I lose track of details.

DR. KRAUSE: There are two major transcription factors that determine whether a cell is going to be a muscle cell and both of those are expressed by muscle stem cells that are known satellite cells. And he's studying actually how those two transcription factors allow a satellite stem cell to be a satellite stem cell and remain a satellite stem cell and then he's manipulating them and seeing how -- I don't have the details in my head, how the cell renewal differentiation are effected.

DR. HART: He's going to --

DR. KRAUSE: And -- I'm sorry, go ahead.

DR. HART: -- he's going to selectively knock out those two genes only in this one cell type in adults. So after you've knocked out this one important gene, what happens to that satellite cell in terms of forming more muscle?

DR. WALLACK: So at this point, Diane and Ron, and Anne, would anybody have a problem if we made a motion, because I will if you don't have a problem, as I said before, $500,000, three years for each of them?

DR. KIESSLING: But then we can't do any more seeds. I really -- I'm sorry, but I really think we should quickly look at the seed maybes and just remind

ourselves who's not going to get any money.

DR. WALLACK: So, what about if we did this and we looked for another hundred thousand someplace --

MS. HORN: Rick, could you give us an actual total, Rick, of what we have funded without these two grants, please?

DR. HART: If you wanted to split hairs you could fund these two at 450,000 total and have 200,000 left for one more seed.

DR. KIESSLING: There you go.

MR. STRAUSS: Okay. So this is four and a half million --

DR. KIESSLING: Or we could give up the core.

(Laughter)

DR. HART: Yes you could.

MR. STRAUSS: -- so far of the established, 1.4 seed. And I'll pull that up. That's 1.4 in the seed and in group we've got 2,808,847. So that puts you at --

DR. FISHBONE: Can I ask a question while counting up the numbers?

MS. HORN: Sure.

DR. FISHBONE: Does anybody have --

MR. STRAUSS: -- 8.7 on your

(indiscernible) 8,708,847.

MS. HORN: I'm sorry. 708?

MR. STRAUSS: 8,708,847. 8,708,847.

DR. HART: The total budget for this year is 9.8 even?

MS. HORN: Yes.

DR. HART: So it makes sense to help us get a total if we modify this to 1.8 even, it would help our math quite a bit. Otherwise we are going to have to cut a little tiny chunk out of somebody else's grant.

A MALE VOICE: I would move to do that.

DR. FISHBONE: Could I just ask --

A MALE VOICE: Well, let's just get this done.

DR. HART: Because remember, this is the one we were going to figure out indirect costs.

DR. FISHBONE: -- right. I want to ask a question before we get it done.

MS. MULLEN: I am still with you, Diane.

DR. FISHBONE: Could I ask if anybody has a problem with taking two grants that are outside of the range of what we were talking about? One of them is a member of the Stem Cell Advisory Committee, and the other is a favorite researcher that everybody likes.

MS. MULLEN: Well, no, I think --

DR. KRAUSE: Wait, wait, wait.

DR. FISHBONE: I mean, looking at this afterwards.

DR. KRAUSE: What are you talking about? Say that again. Look at it afterwards? After what?

MS. MULLEN: -- are we being impartial is the question. That's always a good question to ask ourselves.

DR. FISHBONE: Spirits of the old boys club, old boys put you on the committee --

DR. KRAUSE: Actually, I wish David were not on this committee because I was assigned grants and, you know, some of them were good and some of them weren't.

DR. FISHBONE: -- then there wouldn't be a problem.

DR. KRAUSE: Then there wouldn't be a problem, exactly.

DR. FISHBONE: Right. But, you know --

DR. KIESSLING: But he's on this committee because he's an expert.

DR. WALLACK: So that's unfair to David though. I mean, why penalize him for that?

DR. KIESSLING: Yeah. I mean, NIH study

grants do this all the time. I mean, they try really hard now to get their grants to go to another study section, but if your grant comes to your study section, you just have to live with it.

DR. FISHBONE: Yeah, but all the people who had the better ranking --

A MALE VOICE: We went through those and we evaluated those very carefully.

DR. FISHBONE: -- I know, I know. I'm just saying, that if you see the list and you --

A MALE VOICE: Gerry, I really don't care about that.

DR. DEES: We want to be sure -- it's an appearance problem here and we need to make sure that we feel comfortable and we think that the science in David's grant is really good and it deserves to be put over all of the grants that are higher score, so we need to be sure that we think that's --

DR. FISHBONE: -- that's what I'm up against.

DR. KIESSLING: Well, what we're really doing is balancing his grant against two seed maybes.

DR. HART: No, but I mean, you're right. That's exactly what we're talking about. We've got to

this list with some rigor, examining the scores that were given to us very critically, and trying our best to combine with the scientific review panel said, what we can read into the grant, what our goals are, and I think after the, you know, it's extensive review we've come back to these two maybe grants with some desire to fund them. I don't think we've done anything to be concerned about.

DR. KIESSLING: The Chamberlain grant had such a split review, I mean, that's weird.

DR. DEES: I have to say, I mean, I have no problems coming back to the Chamberlain grant, precisely because it was weird.

DR. KIESSLING: It was weird.

DR. DEES: David's grant, on the other hand, there wasn't a whole lot of split there.

DR. KIESSLING: That's right.

DR. DEES: Right. So we're not doing that, we're pulling that one out, basically because we think this is -- well, I hope the reason we're doing it is because we think it's good science and that it wasn't really reflected in the scores.

DR. HART: No, you know, the criticisms -- one of the main criticisms was that this was not human stem cells and the argument was made that it's better to

do this in mouse, and it'll be more easily accessible to get it to a human disease model by starting in mouse.

DR. DEES: Yeah. So what we're saying is, we think the scientific score here didn't really reflect the good science that this grant is doing. That's what we're saying.

DR. HART: That's exactly right.

DR. GENEL: Am I correct that this is the only grant that would be funded out of Storrs?

DR. KRAUSE: No, there's another one. L-A-I.

DR. GENEL: There's another one?

DR. KRAUSE: L-A-I.

DR. KIESSLING: I mean, maybe what we should do is decide on the Chamberlain grant, look at the seed maybes, and then come back to the Goldhamer one.

DR. KRAUSE: So I have a comment --

A MALE VOICE: So David can come back in.

DR. KIESSLING: That's right. David's out of the room.

DR. KRAUSE: -- I want to avoid any sense of there being bias and if there is bias, make sure we look it in the eye and say, okay, with that bias we can't do this. So one possibility as we go ahead, fund the

Chamberlain grant, David will come back with a grant next year and he'll put in human cells, even though, in his opinion, that's not the best way to do it, and theoretically, that would get -- if it had the same reviewers and everything was the same, which we all know is not the way reviews go, he'll get a one and a seven and theoretically both of these reviewers would have given it a better score if he put in human, he'll do the grantsmanship thing and put in the human cells and so be it. And we've done our job.

MS. MULLEN: Or, anyone who we might approach to be a part of this process who also thinks that they would want to apply for a grant will say, they can't participate and lend their expertise to this effort because they'll be penalized in the review process. Which is something else to just think about and -- I want to believe. I'm going to grant that everybody came in here doing what you do every month and every year, which is to be as objective as you can in a world where relationships blend and it's hard to be absolutely objective ever, wherever you are.

But I still believe that everybody comes to this with utmost integrity and, you know, I get to sit in this position and go out -- back and forth every day, or

all day long, hoping that everything I said today somebody in the newspaper or anyplace else will believe the Commissioner acts with integrity, because she works for government. So, I mean, there's a certain piece of that that we are never going to get away from and we've had lots of little kinds of conversations, whether or not it's about, you know, if you're too senior and you make too much money, then maybe you also aren't eligible for certain kinds of funding because it looks like your percent effort.

So we do the best we can in all these contexts. And it's really important to stop and ask ourselves these questions, especially when we get to this point, because there's so many gray zones.

DR. DEES: I mean, I have a sense that they'll want to say that we should, you know, shouldn't fund him because he's on the Committee. I just want to, you know, I think fair discretion, all right, we need to look at it and say, okay, are we comfortable with saying that we think the science of this project is good enough, that it's better than the science of other projects?

DR. FISHBONE: Yeah, that's the only question I'm asking.

DR. PESCATELLO: Is David Goldhamer -- are

we saying that David Goldhamer is being penalized. Perhaps because we said in our parameters we set forth of percent effort, wherever possible emphasis on translational research on human health and in some kind of narrow sense, because he wasn't using human stem cells, even though -- are we now saying the benefit of his research to human health might be just as high as Stormy Chamberlain's or others, even though he's not using human embryonic stem cells? That's my hunch.

DR. KIESSLING: It was the reviewer who said that.

DR. PESCATELLO: In fact, having read Stormy's, I would put David's higher than Stormy's in terms of what I personally believe his basic research and the value of that to Connecticut. Although, I would fund both.

DR. KIESSLING: I don't Stormy Chamberlain, so I'm not biased. I thought Stormy Chamberlain was a guy.

DR. WALLACK: So, to Paul's point, and I think Diane, you said it even better than anybody, and that is that David is doing the research this way because he believes that it's the best way to go with this research. And I believe that he really thinks that way.

Marianne, correct me if I'm wrong, when we were sitting with him redoing the RFP, I think didn't he want to put in language in the new RFP that gave credence to research on animals?

MS. HORN: I think it would have expanded a little bit on what we have. I think we have the language in there that covers this kind of research.

DR. WALLACK: Right. So what I'm trying to get at, I'm trying to substantiate, Diane, what you're saying in a sense that I think that to force him to come back next year and do it with human stem cells is contrary to what he really feels he should be doing in this research.

DR. KRAUSE: Yeah, but it's how we write grants all the time. You get reviewers who say, do X, Y, Z, you go, okay, I revised the grant, I've taken the reviewers' very astute suggestions and I'm doing X, Y, Z, and you get your grant the next year if you get the same reviewers. I mean, I --

DR. HART: He rightly says that the first two aims of the grant could not be done human cells.

DR. KIESSLING: All right. So we have to do something.

DR. WALLACK: I would move that we do

500,000, three years for each.

DR. KRAUSEZ: -- oh, let's -- I have a comment about that. David's grant is a three-year grant, Stormy's grant is a four-year grant, so if this gets back to my point about, you know, you get the budget of that grant, you can spend it over two, four -- you can spend it in two years. So, you know, it just depends on how you write your budget, how much work you can get done in a time based on staffing and --

DR. KIESSLING: Can you really spend it in two years? I don't think so.

DR. HART: No, I don't think these you can. I don't think these you can. They only give you --

DR. KRAUSE: -- you only have your option of three or four?

DR. KIESSLING: No, I think you just get so much money a year.

DR. HART: -- is that right? Is that how it's dispersed?

MS. HORN: Oh, that's right. It is budgeted --

DR. KIESSLING: It's like a state contract.

MS. HORN: -- up to four years.

MS. KRAUSE: It says it's for up to four

years.

MS. HORN: Up to four years, and the investigator sends us a four year budget allocating it out over four years.

DR. HART: It is if that's what you ask for.

MS. HORN: So the only -- in the seeds they have to have a budget of 100,000 split over the two years, but otherwise it doesn't specify.

DR. KIESSLING: So they get the whole four year grant up front?

A FEMALE VOICE: I don't know.

DR. DEES: Since the money is allocated it may be all up front, right?

DR. HART: Yell. We're always being asked to reallocate funds.

MS. MULLEN: And occasionally to carry it forward.

DR. HART: Yeah, that's right.

DR. KIESSLING: So where is the money sitting?

MS. HORN: It's out there somewhere.

DR. KRAUSE: It's out there somewhere.

(Indiscernible, multiple voices.)

DR. KRAUSE: I think that we can say 500K per investigator, but we can't say over how much time you spend it.

DR. HART: I agree.

DR. DEES: Oh, I see. Fine, fine.

DR. HART: And let them tell us how long it'll take to finish and use these funds.

DR. DEES: Do you want to do 500 or do you want to do 450 so you can get a seed grant?

DR. KIESSLING: Yeah, let's do 450 so we can get two seed grants, two maybes, we could fund two maybes, or we have to cut the cores.

DR. KRAUSE: Is there some seed grant you desperately want to fund?

DR. KIESSLING: Well, no, but I think the seed grants are always a really big bang for our buck.

DR. KRAUSE: We don't know that. We haven't done the research yet for this other one.

DR. KIESSLING: Well, we've seen --

DR. DEES: (Indiscernible) just gives us 100,000? It gives 100, but --

DR. KIESSLING: -- yeah, but we got 100.

DR. DEES: So it's fair. So it gives us only -- as far as I can tell Anne, we've only got -- if we

do 450 we have room for one seed grant.

DR. HART: You're right, that's right.

DR. DEES: We do 450, because 100,000 and get 200,000 for --

DR. KIESSLING: Okay. So we could do --

DR. KRAUSE: I think 550 and then Stormy and David get to do their (indiscernible).l

DR. KIESSLING: -- I can't remember the seed grants anymore.

DR. DEES: And we've got no seed grants, right?

DR. KIESSLING: I can't remember the maybes.

DR. KRAUSE: I don't know, I'm just trying to imagine what they're going to do.

MS. MULLEN: Then I guess that goes back to looking at the budget and thinks that this is really going to be --

DR. KRAUSE: Yeah.

MS. MULLEN: -- but then is it going to support the work?

DR. KIESSLING: Everybody wants David to be able to come back.

DR. DEES: So I have a proposal then. Why

don't we -- can we for the moment say that we're going to give them 500, let's go then and look at seed grants and then we will come back based on how many seed grants we think we want to fund.

DR. KIESSLING: Well, I'd rather give them 450 and if we don't find a seed grant --

DR. DEES: And give it back to them?

DR. KIESSLING: -- and give it back to them.

DR. DEES: I'll accept that as --

DR. KIESSLING: I think it's easier to give than to taketh away.

MS. MULLEN: Can I just ask, when you look at the proportional cut there, and then we look at some of the other larger awards, if you're trying to make up a small amount of money could there be less impact to someone who's getting more?

DR. WALLACK: Yeah, I think you're right.

MS. MULLEN: What we have done in other years is just, I mean, you've got some other established grants here that if we took 50,000 from each one across the board, then we would not be cutting these ones $300,000 each.

DR. KIESSLING: Well, but we're cutting

them for two reasons I think. We're cutting them because they've got kind of pulled up, for good reasons, but they got pulled up out of order -- I don't know. I think it seems more fair.

DR. WALLACK: So there's six. So if we took -- if we took 20,000 out of each of those six grants. I don't think that it would substantially have any kind of adverse influence. I think I'd rather do it that way.

DR. KRAUSE: Which six are you talking about? So the six that are already --

DR. WALLACK: We have six established investigators at 750, right?

DR. KRAUSE: -- that are already -- right.

DR. WALLACK: So if we took, say, 15,000 out of each of those, that'll be 90,000. 90,000. We're taking 8,000 off the other -- off Redmond's. What we have to do is take 15,000 off the six established investigators and then -- and then the 8,000 off the Redmond grant and that brings us to where we have to be.

DR. GENEL: We know there's a seed grant that we really want to fund.

DR. KIESSLING: Yeah. I mean, we really have to review the maybes here.

DR. WALLACK: And Mike, that will give us

the money.

DR. KIESSLING: Yeah but we don't --

DR. HISKES: I always think of like it's $15 --

DR. GENEL: I'd like know whether there's a (indiscernible) behind it.

DR. HISKES: -- 15,000 is one third of a post-doc. 15,000 is almost the stipend of a graduate student. So, you know, that's a lot, the impact is a lot.

DR. KIESSLING: Let's look at the -- please, let's look at the seed maybes and see if maybe we don't want -- maybe we don't need it.

DR. FISHBONE: That's one question --

DR. KIESSLING: I don't remember which were the maybes --

DR. FISHBONE: -- turned back to the core, back to the core --

DR. KRAUSE: Yes.

DR. FISHBONE: -- one of which was rated extremely high --

DR. KIESSLING: I know David isn't here, but let's put him up there.

MS. HORN: I'm sorry. Could we just have one conversation, please?

A MALE VOICE: Let's bring that back to the seeds and then we'll have --

DR. KIESSLING: And then get rid of it again?

DR. FISHBONE: -- the one core was rated very highly and we gave him 500,000. The other core was not rated very highly and we wanted to fund it, but do we need to fund it at that same level?

DR. KRAUSE: I feel strongly that both core should get their 500K.

DR. FISHBONE: The same --

A MALE VOICE: I agree.

A MALE VOICE: Yeah, I agree also.

DR. FISHBONE: -- well, then, is there any point in evaluating -- will we be doing that each year?

DR. KRAUSE: I did evaluate -- seriously, Rhen He Xu's grant is very, very good and the concerns of the reviewer who gave it a less good score were really from a reviewer who I felt didn't fully understand the purpose of the cores.

DR. FISHBONE: Okay.

DR. KRAUSE: Because they're doing services, they're making IPS, they're doing the training, there's no wasted effort, and it's needed and it's used by

people all over. And they're now billing for their services, taking care of resource --

DR. FISHBONE: Then they deserve -- they deserve the better score.

DR. KRAUSE: -- there's been some nice specialization of the cores at UConn and Yale now, where Yale is working on the genomics, UConn is doing more of the maintaining of the IPS for people and it's growing in a really healthy way.

MS. HORN: So can I just ask if we should bring David back in?

DR. KIESSLING: Yeah, should we bring him back in for the seeds and then will kick him back out again?

DR. GENEL: We have five maybes here?

DR. HART: Yeah. Let's review the maybes.

MS. HORN: Okay. So we're going to move --

DR. HART: Let's review the maybes.

DR. KIESSLING: Because maybe this is going to go away.

DR. GENEL: I don't want -- I don't want to prolong this, but the real discussion is do we want to fund five more seeds or do we want to find one or two more established grants?

DR. HART: Or can we even find one seed we want to go with? That's right.

DR. DEES: The question is whether there's one seed (indiscernible).

DR. HART: That's right. Yeah. Let's review the seeds and see if we can answer that question. I think that'll draw everything else to a finish. If we decide on one or zero seeds we could finish everything else.

MS. MULLEN: Right. Do you want to take them in order, or is there just someone who feels very strongly that they want -- they have a seed that they would like to support at this point?

DR. KIESSLING: So I can't read that without my glasses. Somebody help me out here?

(Discussion off the record)

DR. FISHBONE: Those are the ones --

DR. HART: The maybes.

DR. FISHBONE: -- the maybes.

DR. HART: Yes.

DR. KIESSLING: Health Center 12. Health Center 12 is Wang?

MS. HORN: Yes.

DR. KIESSLING: Oh, this is this MS --

DR. HART: Yes. The irradiated MS cells, right?

A MALE VOICE: 12 and 9 are different researchers?

DR. HART: Yes. Same lab, same last name, different researchers.

DR. KIESSLING: So who reviewed the Wang?

DR. HART: I did.

DR. KIESSLING: Okay.

DR. HART: This was not only the question about irradiated MS -- MSC's derived from ESC's, whether that was even necessary and secondarily whether this post-doc, who's been in place since 2008 and was a seed awarded in 2010 has had enough productivity to justify a second consecutive seed award.

DR. KIESSLING: Okay.

DR. HART: Not on a clear path to career development, those kinds of things.

DR. KIESSLING: What do we think?

DR. HART: I stick by not --

DR. KIESSLING: Not funding it? Are you going to make that motion?

DR. HART: -- I move for a no on this one.

MS. HORN: Okay. Do we have a second?

A FEMALE VOICE: I second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Okay. 12-SCA-UCHC-12 is moved to the not fund category.

DR. HART: Right. The next one is 12-SCA-YALE-15, this is the Ren grant. Anne Kiessling and Paul Pescatello.

DR. KIESSLING: So this is a post-doc in Sean's (phonetic) lab.

MS. HORN: Yes.

DR. KIESSLING: We've had quite an extensive discussion of this. And we put it in the maybe because -- Paul, why did we put it in a maybe? Oh, we put in the maybe because we wanted to consider it with all of the other grants going to that lab.

DR. PESCATELLO: Right. I was originally a yes.

DR. KIESSLING: Yes. Because this is a very nice proposal. And so now that lab is going to have -- how much have we funded that lab?

DR. PESCATELLO: 750. Because we gave them the established grant.

DR. KIESSLING: He has an established grant

--

DR. PESCATELLO: And not the other seed.

DR. KIESSLING: -- and not his seed. So this would be $1,000,000 to that grant or to that lab.

DR. DEES: Almost.

DR. KIESSLING: Well, 950,000.

DR. DEES: I mean, again, it's not quite the same, right? Because now you're funding a post-doc and that's a different --

DR. PESCATELLO: That's what I think, that's the purpose of a seed grant.

DR. KIESSLING: Yeah.

DR. PESCATELLO: I was originally a yes on this one.

DR. KIESSLING: Because this is a very strong -- this is a very strong proposal.

DR. PESCATELLO: And my recollection of the discussion is that was the only reason why we put in the maybe because we wanted to look at the big picture.

DR. KIESSLING: At the big picture, right.

DR. HART: Well, we did. Now what?

DR. PESCATELLO: Now we fund it I think. I would do a motion to fund this.

DR. KIESSLING: Yeah, I mean, I think we do

too. So we did not fund his seed and we did not fund the other post-doc application for that lab. There were four applications for these guys. So I would like to fund this if we have enough money. This is really -- this is a very good application. This is taking advantage of that genetic disorder that leads to cardiomyopathy.

MS. HORN: So we have a motion -- a motion to approve, a motion to fund, a second, all in favor?

VOICES: Aye.

MS. HORN: Oh, sorry. Further questions?

DR. GOLDHAMER: So how much is he currently funded?

DR. KIESSLING: This is a post-doc.

DR. GOLDHAMER: Well, the lab I mean.

A MALE VOICE: This will make it 950.

DR. KIESSLING: Yeah.

DR. GOLDHAMER: That’s from -- if he has funding from us with the preview from last year as well?

DR. KIESSLING: Well, I looked at that.

DR. GOLDHAMER: How much money --

DR. KIESSLING: He’s a young investigator, he’s reasonably well-funded but a bunch of it is running out.

MS. MULLEN: I think you’re specifically

asking about funding from us?

DR. GOLDHAMER: -- from us. Yes.

DR. HART: And you're asking about the lab funding?

DR. GOLDHAMER: Yes.

DR. HART: I'm looking it up now. He has American Heart Scientist Development Award ending in June 2013. Yale Center for Clinical Investigation Scholar Award ending June 2012, this month. 10-SCA-35 from 2010, ending this summer, a seed grant. A KO-2 award running until March 2015. A established investigator award that was funded in 2011, scheduled to end September 2013. That's it.

DR. FISHBONE: Shouldn't the funding depend on the quality of the grant and the --

DR. KIESSLING: Yeah, but you know --

DR. FISHBONE: -- the P.I.?

DR. KIESSLING: -- we've had this problem before where we've, I thought, really overfunded some grants.

DR. GOLDHAMER: Quality certainly is a primary --

DR. KIESSLING: But this is also a really good grant. This got a score of two.

MS. HORN: Okay. So we had a motion -- we had a motion to fund and a second. All in favor?

VOICES: Aye.

MS. HORN: Opposed? Okay. YALE-15 is moved to the fund category.

DR. WALLACK: I don't have any enthusiasm to fund this.

MS. HORN: And Diane, this is yours as well.

DR. KRAUSE: Oh, I'm sorry. What are we talking about?

MS. HORN: UCHC-07, Rogina.

DR. WALLACK: I indicated I have no enthusiasm to fund this.

DR. KRAUSE: If there were money I would want to fund this, but I think we are already in the negatives with having available funds.

DR. WALLACK: So can we put this one in the reserve category?

DR. KIESSLING: This is Rogina?

DR. KRAUSE: Yeah. If I, you know, if I had to decide between Rogina and Wang, which were the two that I had back to back, I've been thinking about it a lot and I like the Rogina grant better, but I don't -- I mean,

I've seen it where all the --

DR. WALLACK: So Diane, let's put this in the reserve category.

DR. KRAUSE: -- yes.

DR. FISHBONE: Reserve, meaning if somebody doesn't take the grant?

A MALE VOICE: If someone else doesn't accept.

DR. FISHBONE: Yeah.

MS. HORN: Okay. So we have a motion to place the Rogina, UCHC-07 into the reserve fund for seeds. Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

(Discussion off the record)

MS. HORN: This is the Wang grant. Diane and Paul.

DR. KRAUSE: That was the one I was just saying --

MS. HORN: Okay.

DR. KRAUSE: -- between Rogina and Wang, they are both very good grants. I picked Rogina over --

DR. HART: So do you move for a no?

DR. KRAUSE: -- no. I move for a no.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Okay. Moved to no. And the final one is UCHC-13, Antic.

DR. HART: I mean, with these small grants we probably need two reserves.

MS. HORN: Yes, we should have two reserves.

DR. KIESSLING: Oh good. So, I move that the Antic grant become our second reserve.

DR. KRAUSE: I second the motion.

MS. HORN: Any discussion? All in favor?

VOICES: Aye.

MS. HORN: Antic grant is moved into the second, and is that in rank order then we have our reserve one and reserve two if a grant fails?

DR. HART: Yes.

DR. KIESSLING: That'll work.

DR. HART: Yes. So now we're back to the final established.

MS. MULLEN: Established.

DR. KIESSLING: So now how much money have we spent?

A FEMALE VOICE: 9.9.

DR. KIESSLING: And now David has to leave again?

DR. HART: 8.8 at this point. 8.9, 8.9.

MR. STRAUSS: 8.908.

A FEMALE VOICE: Check the cookies while you're out there and finish the cookies.

DR. HART: We took the 08 off.

(Discussion off the record)

MS. HORN: So Rick, what is our total?

MR. STRAUSS: 8.908 without any decisions on the change in the Redmond grant or the established.

DR. HART: So we have 900,000 if we take the $8,000 overage off of --

DR. KRAUSE: Okay. Let's take the $8,000 off and then we're at 450 and 450 with Chamberlain --

DR. HART: -- and then we're done.

DR. KRAUSE: -- and we're done. Great.

DR. HART: So what are you up -- so let's split it. So first take off the 8,000 and change off of the --

MS. HORN: So we have 8,900,000?

DR. HART: -- yes.

DR. KIESSLING: 8,000,000 only.

DR. HART: Yep. Which was that one -- the -- the YALE-01, disease directed grant, change it to 1.8 million even.

DR. KIESSLING: Yes. If we take 100,000 out of each core, we could fund one more seed.

DR. HART: But we didn't like any of the other seeds that much.

MS. HORN: Okay. So we already have in the disease directed 1,800,000, Rick, rather than --

DR. HART: 800,000 -- get rid of that last $800.

MR. STRAUSS: Sorry.

MS. HORN: -- that's okay.

DR. HART: Okay. Now we're good.

DR. FISHBONE: If we took 100 off each core, we could find -- we could fund --

DR. KIESSLING: One more seed.

DR. FISHBONE: -- one more seed.

DR. KRAUSE: And if we didn't fund a disease directed one, we could fund nine more cores, nine more seeds.

DR. HART: That's right.

DR. FISHBONE: Yeah, but we could fund another one we put in reserve.

DR. HART: No.

DR. WALLACK: You know, I think we're forgetting --

DR. KRAUSE: We're moving in the wrong direction.

DR. KIESSLING: Yeah, I think we're done.

DR. WALLACK: -- we had an inherent agreement that we were going to be funding $1,000,000 worth of cores.

MS. HORN: Well, there was no agreement. We agreed that we would -- up to $1,000,000.

DR. WALLACK: Up to -- up to.

MS. HORN: Yeah.

DR. HART: I'd like to move, please, that we fund the remaining two maybes on the established grant table at $450,000 each.

DR. WALLACK: Second.

MS. MULLEN: Is there any discussion of that?

DR. GENEL: Yeah. One is three years and one is four years?

DR. HART: We're not doing years.

DR. WALLACK: Not my problem.

DR. GENEL: You're not doing years?

DR. PESCATELLO: We're going to assume, for the record they're going to come back to us to modify.

MS. HORN: Yes. They will have to come back with a modified budget.

(Discussion off the record)

MS. HORN: Okay. So we have a motion and a second. Any further discussion? All in favor?

VOICES: Aye.

DR. HART: That's it, we're done.

MS. HORN: Well, we just have to go through and officially --

MS. MULLEN: This went from grant review to beat the clock.

MS. HORN: I'll get David and then we'll go through, if you don't mind, one by one and we'll vote them all in.

(Discussion off the record)

DR. GENEL: Before I forget, may I make a recommendation? And that is that next year that we request all investigators to specify the funding that they -- their lab, their group, or something like that, is receiving from the Stem Cell. I think there's a lot of

confusion this year because we did not have an aggregate -- one place where we could look to see where the funding from our program was going to groups and laboratories that are really closely affiliated with each other. I don't know quite how to define that, but I think we need to have something that requires a listing of that in one place where we don't have to --

DR. HART: It would be nice to have what previous funding we've had from the (indiscernible).

DR. GENEL: Yeah.

DR. HART: -- and what has come from that funding.

DR. KIESSLING: Yeah. We talked about that at a meeting. Somebody's got to work on that, right?

MS. HORN: We're talking --

DR. KRAUSE: They're two different things. I completely agree. So I have a list here of every Yale grant that's been funded that Paula made for all of the years and so I've seen how the funding, which I'm numb on, is continuing to go to certain labs. And you guys should be able to see that too. That's different from the outcomes analysis, which is a much bigger job.

A FEMALE VOICE: Just making a list of who got which grant.

DR. GENEL: And it's different than what the specific investigator may list as their funding also.

DR. KRAUSE: Because you see -- admit it's a post-doc and so --

DR. GENEL: Yeah, right. Yeah. I think we need to have a better handle on that.

MS. HORN: So I just want to point out, we do not have any established grants in reserve, we have only the two seeds in reserve.

DR. KIESSLING: Oh, so we need an established grant in reserve.

DR. KRAUSE: Or that we fund the two that we underfunded more fully.

DR. HART: Yes.

DR. KIESSLING: No. Let's see if we've got another one we like.

DR. KRAUSE: Okay.

A MALE VOICE: But there wasn't even another one on the maybe list.

DR. KIESSLING: Yeah, do we have another maybe?

DR. HART: We used all the maybes up.

MS. HORN: We did not. No, we just had nos.

DR. PESCATELLO: So we just had those two.

MS. HORN: We could have a motion that if a grant fails that we use that funding to fully fund the established grants that we did not. But it depends on when the failure occurs and it may be well down the road before that happens.

DR. KIESSLING: Yeah. That sounds complicated.

DR. GENEL: Why don't we just move the other seeds that we've rejected that were on our maybe list and have a lengthier seed?

DR. KIESSLING: Yeah. Does it have to be an established?

MS. HORN: No, no.

DR. GENEL: If we didn't have an established reserve and we basically funded them, why not use it --

DR. KIESSLING: For more seeds?

DR. GENEL: -- for more seeds?

DR. KIESSLING: Yeah.

DR. HART: But again, the other seeds, other than the two we put in the reserved list, there was really no real enthusiasm, there was no clear enthusiasm. There was a uniform lack of excitement. I'd rather pick

one of these established.

MS. HORN: So UCHC-12 we changed from a maybe to a no in the Wang grant. Any interest in having that be a reserve?

DR. KRAUSE: Sure.

DR. KIESSLING: Because you liked that one, right?

DR. KRAUSE: Yeah, but you know my opinion was that if there were extra funds it should go to the underfunded established investigator awards. Your opinion is that it should go to seeds and then you tell me, should it go to that seed --

MS. HORN: I think it is complicated, Diane. It could fail nine months down the road and we've already funded the established --

DR. KRAUSE: -- that should be the third seed in the list of backups.

DR. HART: So which one was it?

MS. HORN: This is 12-SCA-UCHC-12, Wang, and that was Ron Hart's and Gerry Fishbone.

DR. KRAUSE: The second Wang.

DR. KIESSLING: So if one established investigator award were not awarded, that's almost like three seeds, right?

MS. HORN: Yes.

DR. KIESSLING: So we need several seed backups.

MS. HORN: And we have two right now.

DR. HART: Three.

DR. KIESSLING: Three. No, we've got three.

MS. HORN: And this would be three.

(Discussion off the record)

MS. HORN: Okay. So, do I hear a motion to have Wang as a reserve?

DR. HART: As the third reserve.

MS. HORN: Third reserve.

DR. KIESSLING: That's J. Wang, right?

MS. MULLEN: Right. She gave the number.

MS. HORN: UCHC-12-SCA-09.

DR. HART: Yeah. Okay.

DR. KIESSLING: Oh, I thought we were talking about nine.

MS. HORN: No.

DR. KIESSLING: I don't have the (indiscernible, too far from mic.).

MS. HORN: Okay. But Dr. Hart, you --

DR. HART: Yes.

MS. HORN: -- okay.

DR. HART: As long as we specify third, yes.

MS. HORN: All right. So we have a motion to have that Wang grant as reserve number three. Do I have a second?

DR. WALLACK: Second.

MS. HORN: All in favor?

VOICES: Aye.

DR. HART: So if we pick out one more of the seeds, that could give us as much as 800,000 to use up a full 750,000 if that weren't awarded. It probably would be a good idea to have four just in case?

DR. KRAUSE: Then I propose it be the other Wang.

DR. KIESSLING: Wang and Wang as reserved?

DR. HART: UCHC-09?

DR. KIESSLING: Yes.

DR. HART: As the fourth reserve?

MS. MULLEN: And why would we not go with the issue of the established grant?

DR. KIESSLING: Because we didn't have any maybes. We already --

MS. MULLEN: But funding -- but we cut them

significantly.

DR. KIESSLING: -- it's just really hard I think to do that.

DR. HART: I think that's not --

MS. MULLEN: I'm asking. I don't know the answer. I don't know what. Is it hard?

DR. KIESSLING: Yeah.

MS. MULLEN: What's the difficulty?

DR. KIESSLING: Well, the state awards a contract and then --

MS. MULLEN: And then if you need to amend a contract you amend it. So I'm just trying to understand what the difficulty is.

DR. KIESSLING: -- well, I just think that would be hard.

MS. HORN: Yeah, I think it's a little complicated because they come back with -- they rework the proposal, they figure out what they can do over this period of time with this amount of money. I don't think it's impossible, I think it's something we ought to consider since we did -- we did slash does grants quite substantially.

A FEMALE VOICE: Can we hold on awarding those until we find out if everyone has accepted? I mean,

has accepted -- yeah, accepted.

DR. KIESSLING: Yeah, maybe we should wait and see if we have a problem.

MS. MULLEN: Well, we're trying to have enough so that we don't have to come back and say, we need to create -- generate more of a list. And I know we're at the point now where we're thinking, you know, in the hypothetical realm. I think to just be able to answer one way or another, do you at all want to consider being able to fund at a higher level the two established grants that we're funding at a much lower level would answer that question one way or the other and then move on to generating some other backup or reserved.

DR. DEES: If we lost an established grant would you rather -- I mean, we could then fully fund the two establish grants that we have partials on, or we could go down this list, down to the four we had -- we have to add one more, no we wouldn't have one more. So we have these three.

DR. FISHBONE: Could you stay in the category if a seed drops out fund another seed --

DR. HART: You'd rather it come easy. I mean, that's the question.

DR. FISHBONE: -- from established -- I

mean, I've never -- we haven't had anybody ever reject money in established or good grant, but sometimes a seed will get -- the post-doc will go somewhere else and then we would have to find another seed.

DR. DEES: I'm happy with that.

MS. MULLEN: Okay. So we need one more seed.

DR. HART: So we need one more seed.

DR. KIESSLING: Another Wang, there was another Wang.

DR. HART: But before that there was the Yale Liu that had a higher score. Is that went to be considered or should we just go right to the Wang?

DR. DEES: Well, you can do it either way.

DR. KIESSLING: You mean, the YALE-18?

DR. HART: Yes.

DR. KIESSLING: Okay. So that was Goldhamer and Anne.

DR. HART: Right.

DR. KIESSLING: And there was a reason that we voted no on that.

DR. HART: Yeah.

DR. DEES: Then why -- why don't we vote no so we can have clear conscience here.

(Discussion off the record)

DR. KIESSLING: Rogina is reserved, Wang is reserved.

DR. GOLDHAMER: Yeah. I reviewed that and I thought there was pause that I would feel more comfortable choosing another seed.

DR. HART: Okay. Sure.

DR. KIESSLING: So the next one would be Carson's, that went from a maybe to a no.

DR. HART: Well, all the rest of them are 2.5, so there's no specific order here.

DR. KIESSLING: No, but that one went from a maybe two a no, for some reason.

DR. HART: Several of them did. I'm just saying, (indiscernible). Now we are in the range everything else would be considered as two.

DR. DEES: We never got to the 2.5's and the Wang was a 2.5 as well.

DR. KIESSLING: Yep. That's right.

DR. DEES: And we had a maybe --

MS. HORN: That's right. We changed that to a no.

DR. HISKES: The YALE-20 we discounted because of overlap.

DR. HART: That's right.

DR. HISKES: But it was otherwise highly ranked --

DR. HART: That's right.

DR. HISKES: -- highly regarded.

DR. KIESSLING: And the Carson grant went from a maybe two a no.

DR. HART: Oh, that was the one with the Fragile X tremor where it was mostly biochemistry with a stem cells slapped onto it?

DR. KIESSLING: Oh, that's right.

DR. DEES: (Indiscernible) of the Wang, whatever it was, UCHC-09.

DR. HART: 09?

MS. HORN: Okay. That's Diane Krause and Paul Pescatello reviewed that. That is Wang.

DR. KRAUSE: That's the one I was recommending.

DR. HISKES: Diane, you put that in reserve at number four.

DR. HART: Number nine. Number nine.

MS. HORN: That's reserve number four?

DR. HART: Well, we didn't vote on it yet.

DR. DEES: We haven't voted on reserve

number four.

MS. HORN: Thank you. I thought I missed a whole chapter there. I don't have a reserve four yet.

DR. DEES: I'm moving that we pick that reserve number four.

MS. HORN: Okay. Do we have a second?

DR. HART: Second.

MS. HORN: All in favor? What we're voting on now is 12-SCA-UCHC-09, Wang, to move into the reserve four slot. Okay. All in favor?

VOICES: Aye.

MS. HORN: Opposed? Okay. Okay. So I have for reserve one is the Rogina. Reserve two is Antic. Reserve three is Wang. And reserve four is Wang. Wang-09. Okay. I think -- Rick, do we have a total?

MR. STRAUSS: Sure. 9.89.

MS. HORN: Well, that sounds good. Are we there?

MR. STRAUSS: We're there.

MS. HORN: All right. We're just going we run through the proposals, and we're going to take a vote on each one of the ones that we're going to fund.

MR. STRAUSS: Where do you want to start?

MS. HORN: Right at the -- it doesn't

matter, wherever you are. Are you on seed?

MR. STRAUSS: Seed.

MS. HORN: Okay. Can you read them out? I'm a little blurry.

MR. STRAUSS: What do you want to do?

MS. HORN: Can you just read out the grant number and we'll take the vote?

MR. STRAUSS: Okay. 12-CSA-YALE-02 (sic).

MS. HORN: We have a motion to fund this grant at $200,000.

DR. HART: So moved.

MS. HORN: Do I have a second?

DR. HISKES: Second.

MS. HORN: Anne Hiskes. All in favor?

VOICES: Aye.

MR. STRAUSS: 12-CSA-YALE-26 (sic).

DR. HISKES: So moved.

MS. HORN: Anne Hiskes moves to fund at $200,000.

DR. HART: Second.

MS. HORN: Ron Hart. All in favor?

VOICES: Aye.

MR. STRAUSS: 12-CSA-UCHC-6 (sic).

MS. HORN: Do we have a motion to fund at

$200,000?

DR. KRAUSE: I motion to fund that at 200,000.

MS. HORN: Diane Krause. Second?

DR. WALLACK: Second.

MS. HORN: Milt Wallack. All in favor?

VOICES: Aye.

MR. STRAUSS: 12-CSA-UCHC-15 (sic).

MS. HORN: Motion to fund 200?

DR. DEES: So moved.

MS. HORN: Dr. Dees. Second?

DR. HART: Second.

MS. HORN: All in favor?

VOICES: Aye.

MR. STRAUSS: 12-CSA-YALE-09 (sic).

MS. HORN: Motion to fund at $200,000?

DR. WALLACK: Move.

MS. HORN: Milt. Second?

DR. HISKES: Second.

MS. HORN: Anne Hiskes. All in favor?

VOICES: Aye.

MR. STRAUSS: 12-CSA-YALE-16 (sic).

DR. WALLACK: Move.

MS. HORN: Milt.

DR. HART: Second.

MS. HORN: All in favor?

VOICES: Aye.

MR. STRAUSS: 12-CSA-YALE-23 (sic).

DR. KIESSLING: So moved.

MS. HORN: Anne Kiessling.

DR. HART: Second.

MS. HORN: Dr. Hart. All in favor?

VOICES: Aye.

MR. STRAUSS: 12-CSA-YALE-15 (sic).

DR. KIESSLING: I move.

MS. HORN: Paul, Anne. All in favor?

VOICES: Aye.

MS. HORN: And the reserve grant, reserve one, 12 --

MR. STRAUSS: 12-CSA -- do you want to do it? Go ahead.

MS. HORN: -- no.

MR. STRAUSS: 12-CSA-UCHC-7 (sic).

DR. WALLACK: Move.

MS. HORN: Milt. Second?

DR. HISKES: Second.

MS. HORN: Anne Hiskes. All in favor?

VOICES: Aye.

MS. HORN: Reserve two?

MR. STRAUSS: 12-CSA --

DR. HISKES: That wasn't me.

MS. MULLEN: Oh, I thought you raised your hand.

DR. HISKES: No, no, no. I can't do it. I'll go to jail.

MS. HORN: Oh, okay. Anne Kiessling. Anne Kiessling. Okay. 12-SCA-UCHC-13 reserve two, motion to -- yeah, motion to give this $200,000?

DR. KIESSLING: So moved.

MS. HORN: Okay. Second?

A FEMALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And reserve four, 12-SCA-UCHC-09 for 200,000?

A FEMALE VOICE: That's reserve four.

DR. KRAUSE: I move.

MS. HORN: Reserve four. Diane. Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Okay. We are finished with the

seeds. Established, 12-SCB-YALE-10.

DR. DEES: Move.

MS. HORN: 750,000. Second?

A FEMALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: 12-SCB-UCON-02 for 750,000?

DR. WALLACK: Move.

MS. HORN: Milt. Second?

DR. HART: Second.

MS. HORN: Dr. Hart. All in favor?

VOICES: Aye.

MS. HORN: 12-SCB-YALE-01 for 750,000?

A FEMALE VOICE: Move.

DR. HISKES: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: 12-SCB-YALE-11 for 750,000. Move?

DR. HISKES: Move.

MS. HORN: Second?

A MALE VOICE: Yes.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: 12-SCB-YALE-06 for 750,000?

A FEMALE VOICE: Move.

DR. HISKES: Second.

MS. HORN: Second. All in favor?

VOICES: Aye.

MS. HORN: 12-SCB-UCON-01 for 450,000. Do we have a motion to accept?

DR. HART: Move.

MS. HORN: Second?

DR. DEES: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: 12-SCB-UCHC-09 for 450,000. Do I have a motion?

DR. DEES: Move.

MS. HORN: Second?

DR. HART: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Core facility, 12-SCD-UCHC-01 for 500,000. Do I have a motion?

DR. HART: Move.

MS. HORN: Second?

DR. DEES: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: 12-SCD-YALE-01 for 500,000. Do I have a motion?

VOICES: Move.

MS. HORN: Second?

A MALE VOICE: Aye.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And disease directed collaborative group proposal 01-SCDIS-YALE-01 for 1,800,000. Do I have a motion?

DR. HISKES: Move.

MS. HORN: Second?

DR. HART: Second.

MS. HORN: All in favor?

VOICES: Aye.

MR. STRAUSS: Did you want to put your, you know, the statement about the restriction on the funding in there?

MS. HORN: Pardon me?

MR. STRAUSS: Did you want to put your restriction on the funding not go to the St. Kitts' piece?

MS. HORN: Yes, we should note that for the

record that the 1,800,000 is not to be used for any funding that will be used for research performed outside of the state of Connecticut, specifically St. Kitts.

MS. MULLEN: Or travel.

MS. HORN: Or travel.

MS. MULLEN: Or travel related to that portion of the work to St. Kitts.

MS. HORN: Okay. Ladies and gentlemen, I think we are --

DR. WALLACK: Before you do, do we want to talk about two things, number one, are we meeting in August? And number two, about putting together how to implement the progress reports?

MS. HORN: And more importantly, I think we have a dear member who is departing.

DR. WALLACK: What?

MS. MULLEN: Anne Hiskes.

MS. HORN: Anne Hiskes, this is her last meeting.

DR. HISKES: My last meeting.

MS. MULLEN: Thank you for staying in town long enough to do this with us.

DR. HISKES: Oh, you’re welcome.

DR. KIESSLING: Are you going to St. Kitts?

DR. HISKES: Well, that's an idea, but no, I'm moving to Michigan. I'm going to move into my cottage on Lake Michigan. I have accepted a position as Dean of Brooks College for interdisciplinary studies at Grand Valley State University. So I'm going home to the place where I grew up. My mother lives there, I have friends from college, friends from -- one of the faculty in my college will be someone who I came through kindergarten through 12th grade with. My PhD graduate student is in the philosophy department there. So it's a very good fit.

DR. KIESSLING: Old home week.

DR. HISKES: Pardon?

DR. KIESSLING: It will be old home week.

DR. HISKES: That's right.

A MALE VOICE: We'll miss you.

DR. HISKES: Thank you.

A FEMALE VOICE: We'll miss you.

DR. HISKES: So I've been working on this since 2005. Thank you.

DR. FISHBONE: I propose a vote of thanks.

DR. KIESSLING: Do we have a plaque ready or anything?

(Laughter)

MS. MULLEN: We're known to do things after

the fact.

(Applause)

DR. HISKES: Well, it's been a lot of fun.

DR. KIESSLING: An ethical plaque.

DR. HISKES: It would be unethical to accept it.

(Laughter)

MS. HORN: You've been a very big part of this since the beginning and it's much appreciated. We couldn't convince her to stay on and commute from Michigan.

DR. HISKES: Well, my new boss may not like that.

MS. HORN: That's right. Well, you're welcome back anytime. We do need to take public comment. So is there any member of the public who would like to make any comment? Hearing none -- I can't hear you.

MS. PAULA WILSON: I would like to (indiscernible, too far from mic.)

MS. HORN: -- I can't hear you. If you could just come up here if you would?

COURT REPORTER: Introduce yourself please, give your name?

MS. WILSON: This is Paula Wilson from

Yale. I would like to thank the Committee on behalf of the Yale Stem Cell Center for all your hard work in helping us get funding. Thank you.

DR. FISHBONE: Can I make one more proposal? To thank staff like C.I., Sarah, Emily, Rick and Terry from -- wherever they're from for their extremely hard work (interruption, change of tape) --

DR. HISKES: -- materials was vastly improved over previous years.

DR. KIESSLING: You didn't like the sticky papers on the walls?

(Laughter)

MS. HORN: That's right, our first one with all the yellow sticky's on the walls. Rick is so efficient. He has a proposal for all of you to sign and to fill out and he'll send to you on a review so that we can improve this part of the review and certainly do the same thing with the peer review and we'll take all of your comments for next year with the peer reviewers.

DR. KIESSLING: Are the peer reviewers being compensated?

MS. HORN: Yes they are.

MS. MULLEN: And I just thank all of you. I know it's hard. I think, once again, I've said

everything I have to say about integrity. The Department gets to administer this grant, and obviously we wouldn't be able to do what we do without what everyone else here contributes. So thank you very much. And in 10 minutes is the groundbreaking for Jackson. So for those of you who want to find money when they break ground you might want to go down the street.

A MALE VOICE: Marianne?

MS. HORN: Yes?

A MALE VOICE: I know my appointment runs out and I'm sure other people's appointment runs out. What's happening with those?

MS. HORN: Well we are -- yes, we're just assuming that you are appointed until you are either reappointed or your successor is appointed. So please, don't anybody else leave.

(Laughter)

MS. HORN: We are bringing all the pressure we can to bear and have made all kinds of suggestions for the vacancies and I appreciate the work that everybody's had to do this year with fewer reviewers and we'll do everything we can to get you back up to a complement for next year.

DR. GENEL: Is it worth giving an extra

thanks to our out-of-state colleagues who have traveled a little further than the rest of us to be here?

MS. HORN: Yes. Absolutely.

MS. MULLEN: Yes.

(Applause)

MS. HORN: And they need to get me their invoices for their overnights.

DR. KIESSLING: Do you think that the Connecticut folks appreciate what this little tiny fund has done for Connecticut?

MS. HORN: I do. You know --

DR. KRAUSE: We're going to make it even more apparent by doing this kind of survey on what the money is going to.

DR. WALLACK: So, to answer that question, when the Jackson Lab announcement was made it was particularly cited that this was an example of why Jackson was interested in coming to Connecticut.

DR. HISKES: And indeed we are connected.

DR. KIESSLING: The Jackson Lab staff is going to have appointments at UConn you think?

DR. HISKES: They're going to collaborate with the Health Center people.

A MALE VOICE: They probably have affiliate

appointments of some sort.

MS. HORN: So our next meeting is in August.

DR. HART: What's the date?

MS. HORN: I will send you an e-mail, third Tuesday, and we all need to start looking at rewording the RFP and where the program is going to go next. And Milt I think has a couple of -- two sentences Milt.

DR. WALLACK: The -- I think you said it all. I just want to make sure, I hope that we're going to do something about the progress reports that we in April discussed that we needed to have done. And I know that questions have been asked, to Anne's point, you know, with what has this provided for us? So it's provided that incentive for Jackson to come, but there are other people who asked the question, as they asked about California, so what have you done for me lately?

MS. HORN: Absolutely.

DR. KIESSLING: Why were there no grants from companies this time? We always have at least one. Nobody knows?

DR. PESCATELLO: Yes. It's some are early-stage. I mean, it's just the research is still --

DR. KIESSLING: Do we have hopes?

DR. PESCATELLO: -- yes, I mean, but it's -- and I can say I'm super impressed with the quality of the research, but it's still very early. You know, it's basic research, and early-stage research, and especially in this environment now, I mean, companies and venture capitalists are looking for later stage, you know, more later stage than ever before actually.

DR. WALLACK: So, can I just say one other thing? And that is that I've never sat in a group that can debate the way we debate and walk out totally hand-in-hand and feeling good about each other. And a lot of that has to do not only with all of us here, but you two guys sitting at the head of the table. And so we really appreciate the two of you and what you guys do for all of us. So thank you.

MS. MULLEN: Thank you.

MS. HORN: Thank you.

(Applause)

MS. MULLEN: And if there are -- based on this experience and the constraints that we felt with regard to the use of the dollars, if you want to individually, or as a group, send recommendations to the Commissioner that we need to take forward in anticipation of next year's legislative session for any changes, do it.

You're invited to do that. I can't tell you what to say, I won't even tell you what not to say, just if you have --

DR. KIESSLING: We can write you a letter that recommends a 10 percent increase in the budget.

MS. MULLEN: -- you can write me whatever you want.

A FEMALE VOICE: Think big.

MS. MULLEN: You know, or, you know, the whole issue of out-of-state use of resources and other considerations. Anything else that you think this deep into the program the legislature needs to consider. This is the time to do it. We need a motion to adjourn.

A MALE VOICE: So moved.

A FEMALE VOICE: Second.

MS. MULLEN: Thank you all.

MS. HORN: Thank you very much.

MS. MULLEN: All in favor?

MS. HORN: Yeah, yeah, all in favor.

(Whereupon, the hearing adjourned at 5:25 p.m.)