VERBATIM PROCEEDINGS

CONNECTICUT STEM CELL RESEARCH ADVISORY COMMITTEE

COMMISSIONER JEWEL MULLEN, CHAIRPERSON

JULY 19, 2011

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. . .Verbatim Proceedings of a meeting of the Connecticut Stem Cell Research Advisory Committee held on July 19, 2011 at 8:53 a.m. at the Farmington Marriott, 15 Farm Springs Road, Farmington, Connecticut. . .

MS. MARIANNE HORN: Good morning and welcome to our 2011 grant review. Thank you to people who have traveled a great distance and to all of you who have done the hard work of reviewing these grants. We still have some work to do in terms of getting ourselves connected to the Internet. Ann, I have you over here.

DR. ANNE HISKES: Oh, thank you.

MS. HORN: And I think as the first order of business let’s go around the table and just introduce ourselves. I know many of you met Commissioner Mullen at the last meeting, but some of you are here for the first time.

CHAIRPERSON JEWEL MULLEN: And so am I, for the second time. Hi everyone.

DR. MILTON WALLACK: Milt Wallack.

DR. HISKES: Anne Hiskes.

DR. ROBERT HART: I’m Ron Hart.

MS. CHELSEY SARNECKY: Chelsey Sarnecky.

DR. GERRY FISHBONE: Gerry Fishbone.

DR. MIKE GENEL: Mike Genel.

DR. DAVID GOLDHAMER: David Goldhamer.

DR. TREENA ARINZEH: Treena Arinzeh.

MS. HORN: And from the public?

A MALE VOICE: (Indiscernible, too far from mic.)

A MALE VOICE: Can they identify who they're representing please?

MS. CAROLINE DEALY: Caroline Dealy, UConn Health Center (indiscernible, too far from mic.).

MR. DAVID BAUMAN: David Bauman, University of Connecticut (indiscernible, too far from mic.).

MS. ISOLDE BATES: Issie Bates.

MS. PAULA WILSON: Paula Wilson, Yale Stem Cell Center.

VOICES: (Indiscernible, too far from mic.)

MS. HORN: So this morning -- and Dr. Dees, Dr. Mullen, our Commissioner. At the last meeting we discussed a slightly different way of handling the grant discussions this morning and that was to take some cutoff point, somewhere between 15 and $16,000,000 was the figure tossed around, and draw a line there where those grants

would be put into a, should we call it presumptively fundable category? That doesn't mean that they will all get funded because we only have $9.8 million to fund so there will need to be discussion of those grants. So that's one part we need to discuss.

The other part was that any reviewer with a grant that fell outside of that cutoff line could move to have the Committee consider that grant for discussion and inclusion in the presumptively fundable category. Does that comport with what we decided last time? Okay.

So then once we have that presumptively fundable pool the committee needs to determine how to go through those grants, in what order, and the length of time for discussion in terms of making decisions to bring us down to the $9.8 million that we have available.

DR. ROBERT HART: Marianne, I'm sorry. The one real problem with that approach though is the question of whether to fund some of the larger grants and that would make a huge difference on the other grants and so it almost seems as though if you set by score alone a threshold you're either assuming inclusion or exclusion of some large grants that we kind of need to deal with separately.

MS. HORN: Well, I think that could be part

of the process of looking at what's in that presumptive pool and saying, you know what? We don't have any of the particular type of grant and here's an excellent one that we -- I think we ought to consider.

DR. ROBERT DEES: Or we could make the cutoff point low enough.

A MALE VOICE: None of us would.

DR. DEES: Maybe. Then there's a -- we have a sheet that Chelsey sent us the other day and there was a cutoff point of about 16,000,000. We could even -- if we take out all the big grants there's still more than $10,000,000 worth of stuff, so it seems like that's a reasonable cutoff point to do what we determine is the best.

MS. HORN: So I'm hearing $16,000,000? Is that what you had sent out Chelsey? 16?

DR. DEES: Well, there's a number of lines she sent on that whole chart that she sent us and one of them is 16,738, which --

MR. ROBERT MANDELKERN: Point of information. This is Bob Mandelkern.

MS. HORN: Yes?

MR. MANDELKERN: Nobody is coming through except yourself.

MS. HORN: Okay. That is a problem with the phone Bob, I'm sorry. So we'll have to ask people to speak up. It is a U-shaped room and we'll try to keep you in the loop the best we can. We're trying to move the mic. here, or the speaker.

DR. ANN KIESSLING: Are these on? Are the microphones on? They're not going to make us any louder? Okay. Could I offer an alternate to money as a concept? I think most of us are a little more familiar with using a priority score sort of as a cutoff and when I went through these lists I realize it's all about the money, but when I went through this list yesterday I reviewed all of the applications that I was assigned that had a score above 4.5 and I agreed that all of the grants that I was assigned that had a score above 4.5 should go into the not fundable category. Not because they're not worthy grants, but because there were other grants that are above those.

A FEMALE VOICE: Can we just check in and see whether he can hear you now?

DR. KIESSLING: Can you hear me Bob? Anyway, that would be my argument, that instead of talking about funds talk about a peer review priority score and then try to whittle down from there and the one that I would suggest is a priority score of anything that scored

worse than 4.5 go into the not to be funded category unless someone wants to pull it up. That would leave us with 44 applications to discuss.

DR. HART: And that makes sense as well because there's a kind of natural break point scoring at that level as well.

DR. WALLACK: I would endorse what Ann just presented. I would also as we start though like to point out that if we wind up granting -- doing our grants on the basis of the amount of dollars that are being asked for, as an example, established investigator $750,000 and so on and so on, that I think that we're only going to be awarding potentially between 15 and 18 grants at the most and we've had this discussion before at the tail end of the meeting as we tried to figure out what we can include or not. I'm offering to suggest right now at the beginning of the meeting that we consider because of the numbers that are in front of us that we consider lowering the amounts that we will be awarding.

So for example, if you have a established investigator who's asking for $750,000 I would recommend that we lower that amount by about 100,000, even $150,000, because otherwise we're not going to be able to establish an expanded pool of researchers, we're going to be very,

very restricted in what we're presenting. And I think -- so that would be one recommendation or one thought that I'm making. The second thing is that I think that it's important to proceed on a certain basis and I would take -- I would want to start personally with the established investigators and leave some of the other grants, I'm talking specifically about the core grant, grants for later in the process, and I'm saying that because if you recall when we sent out the RFA we specifically noted that the funding of cores is not going to be a priority in this cycle of funding.

So those would be two recommendations. To cut the amounts, even the seed grant amounts and if we did that I think that we'll probably wind up being able to fund instead of 16 or 15, 18 grants as many as 22 or so grants or 23 grants. I'd rather see a greater pool of researchers and in talking to some of the researchers I don't think that that would make it impossible for those researchers to proceed with their projects. That would be my recommendation.

CHAIRPERSON MULLEN: We have two different approaches with the mindfulness that all of us have to uphold, which is that on either side we have to make sure that we're not sprinkling funds in a way that we've

awarded something but not actually given people the potential to do something sustainful and, you know, I live in the resource allocation, figure out your priorities world, even more strongly now as you all know, so I think that while we start with merit and priority score, if that's the way we start, there's that other piece because I agree with you, we're trying to expand, but to an end point that we also want to make sure there's the potential for. So that the resources really also have their biggest spend and it might be more about the density of the funding or the quality of it rather than the quantity of it that gets us where we need to go.

DR. FISHBONE: Gerry Fishbone. If I can make one point? I asked Warren Wolschlager last year how come every grant for say established investigators come in at exactly 750,000? I asked, is there some, you know, is there some reason that everybody needs exactly the same amount of money? And he said to me, duh.

(Laughter)

DR. FISHBONE: Like say you'll give up to that amount people come in for that amount and I'd like to ask some of the scientists, is it valid that everybody needs that kind of money or can they do what they're saying they want to do for less?

DR. HART: Yeah. I mean, you always wish you had more money than you would even offer. But you'll always do with what you can get.

DR. GOLDHAMER: Yeah. I'll say the $750,000 limit for an established grant is not a huge amount of money when you take off the 25 percent overhead it really allows you to buy supplies and mice, hire a technician and maybe one post-doctoral slot. So it is a fact that whatever the limit is set at scientists will ask for that limit. I think at this limit through it's very reasonable that this amount of money should be asked for for a grant of the scope that the established investigator grants are.

So I think we should be mindful of Milt's point and look to see if there's ways of expanding the pool of funded grants. I don't think I would be in favor of kind of a non-priority decision to do that, but as we see the pool of grants and which ones we'd really like to fund if there's -- if it's impossible without cutting then I think we should at that point consider some kind of across the board cut to bring in some of those grants that would not be funded otherwise.

A MALE VOICE: Yeah, I agree.

DR. WALLACK: That's sort of a sense of --

that's the flavor David of what I was trying to say, but I just want -- the only reason I put it out there early this time is that we've addressed this subject later and if we're -- as we're looking at these if we can keep what you've just said in mind I think it might not in an attempt to dilute the pool because some are very close, but maybe have quality and still expand and have it both ways. So I would be fine with what you just said.

DR. GOLDHAMER: And one more point. Since I at the last meeting suggested this concept of going by dollars to establish a cutoff really what I intended was that we go by priority score. But being mindful of the dollars. So, you know, so it's not -- so I'd like to kind of recharacterize what I had said. So we go by priority score but we have to be mindful that, you know, once we get up past 16,000,000 or maybe, you know, that's a little -- it's an arbitrary cutoff, but after some point we're getting down into priority scores that really are not going to be competitive unless there's some reason for the Committee to kind of push for a grant even though the reviews were not great.

So where the cutoff is is a little bit arbitrary. But the point was that I thought we could be more efficient by going in order of quality of grant and

stopping at some point where we can be rest assured that -- that, you know, we've collected the best grants and now -- for consideration and now we have to make final decisions. I happen to think from looking at the cutoffs that, you know, for instance, a 3.5 is a reasonable cutoff and suggest 4.5. That's a little bit arbitrary. At least with my pool of grants the ones that are 4 and 4.5 have major flaws or very significant flaws relative to the ones that scored better. So from my own, you know, I haven't looked at everyone's grants, but from my own grants they wouldn't be competitive. So I -- that's why I kind of had, you know, asked for this provision that any grant at no matter the score be assessed, or be brought up to the Committee if the reviewers thought that it was warranted. But not to go too deep into the pile on every single -- for, you know, and look at every single grant.

DR. WALLACK: Just to follow up on what David said in that regard as we begin, again, I would also endorse the 3.5 number. If we can have the ability to bring others into it, it would be fine, that it's necessary, and I will personally give you two grants in that regard, yeah, two grants. They're both established investigators. So for the record Marianne, I would endorse the 3.5, but I would also ask for the inclusion in

that 3.5 of Nelson SCB15, who has a 4.0.

CHAIRPERSON MULLEN: I don't think we're -- we're not there yet.

A FEMALE VOICE: No.

CHAIRPERSON MULLEN: In terms of the agenda.

DR. WALLACK: Oh, okay.

CHAIRPERSON MULLEN: We're still doing process. Thank you. But hold that -- hold that thought.

DR. WALLACK: Okay.

CHAIRPERSON MULLEN: Thanks. So we have --

DR. KIESSLING: Are you going to go to 3.5?

CHAIRPERSON MULLEN: No.

DR. KIESSLING: No. Okay.

CHAIRPERSON MULLEN: There's too many seed grants in the fours.

A MALE VOICE: We've got at least four. 4.0 and under.

CHAIRPERSON MULLEN: Yeah.

A MALE VOICE: How about 4.0? With pulling things out and lower if necessary.

DR. KIESSLING: The other three are all seed grants. All four point -- down to 4.5 is seed grants.

DR. GOLDHAMER: And the significance of having seed grants in that range is what?

DR. KIESSLING: I think the seed grants are really -- have been very powerful instruments in this state and very few seed grants made it in the top tier. I don't know why, but if you want to fund a reasonable number of seed grants, which have been very profitable and very innovative for the Connecticut funds you need to go to 4.5.

DR. GOLDHAMER: There's at least 15 or 16 seed grants in that top tier up to 3.5, which is well beyond the amount that we funded seed grants in the past.

DR. KIESSLING: It all shakes out in the discussion.

DR. GOLDHAMER: I understand, but I don't think it's the case that there's not many seed grants in the top tier.

CHAIRPERSON MULLEN: So is it possible to start with four and see where we are?

DR. WALLACK: Well, we can start with four and if somebody wants to bring in --

DR. KIESSLING: We can split, right.

DR. WALLACK: -- if they want to bring in something they can.

DR. HART: The seed grants ending at four total 4.2 million. The seed grants totaling ending at 4.5 total 5.8 million.

DR. KIESSLING: No, no, ending at 4.25. Yeah.

DR. HART: Well, 4.25 ends in 4.8.

DR. GOLDHAMER: It's not written into the RFA, but in the past $2,000,000 has been kind of the target or at least the minimum amount allocated for seed grants.

DR. GENEL: Are you including the group, the clinical application within that Ann, or just the group grants?

DR. KIESSLING: I just -- I just did a -- I looked at where we could sort of -- I hate to use the word, triage, but that's what we're going to do if we make this decision, where we should start discussing and we've got 79 applications. If we want to talk about roughly half of them the break off point is somewhere between 4 and 4.25. And then I noticed that the 4.25s were all seed grants. I then looked at --

DR. GENEL: Oh, seed. I'm sorry. Seed grants.

DR. KIESSLING: -- they're all seed grants.

I then looked at all of my 4.5 and above for my own group and realized that I agreed with the peer reviewers and I didn't see that there was any reason to dip into that group for discussion. So my motion would be that we only discuss openly grants between -- that have scores better than 4.5 and that scores worse than 4.5 that the investigators get the peer review comments, but that we not spend time today deliberating those roles.

A MALE VOICE: Is that greater than or equal to or less than?

DR. KIESSLING: It's just because the 4.25s are all seed grants.

CHAIRPERSON MULLEN: Are you including 4.5 in the discuss or not?

DR. KIESSLING: No. No. So can -- 4.5 or worse would be triaged, the investigators -- and that's not to say about the Meriden Science, the investigators would get the peer review comments. Unless someone else was assigned an application that they really think should be discussed I agree with the peer review for all of my assignments that were 4.5 and above. So my motion would be to triage or not discuss applications that have a score worse than or equal to 4.5.

DR. HART: Second.

MS. HORN: All in favor?

VOICES: Aye.

DR. GENEL: 4.25?

DR. KIESSLING: 4.5.

DR. GENEL: 4.5? Well, we voted so I won't argue. But I count 14 -- I count 14 seed grants that are over 3.5 and that's 2.8 million. And I think it's unlikely we would even fund that many seed grants, but whatever. I won't prolong it, let's just get on with it.

CHAIRPERSON MULLEN: So I have just one other process question. If we are the point of funding an established researcher at less than the 750,000 magical number are we looking at their budgets and telling them what we are and are not funding? And is that happening today or is that happening after?

DR. WALLACK: After.

DR. KIESSLING: Can I make -- I think one of the things that we need to know about the established investigators is how much money do they currently have from us?

DR. GENEL: Right. I agree.

DR. KIESSLING: So I think we've got to put -- like for instance, we have two applications from a couple of relatively senior scientists and we have to put

both of those applications I think in a context of their total picture from Connecticut.

CHAIRPERSON MULLEN: That sounds reasonable. Chelsey would have that figure.

MS. HORN: Right. I know Chelsey was --

DR. WALLACK: So to facilitate the process though today I'm not sure if we felt that we wanted to cut 750,000 to say 650 if we have to tell them what they want to do. I think maybe what we can do is okay the grant at a certain number, it goes back to that lab, that researcher, but we also I think today will probably be establishing a bullpen of researchers and if -- if say Dr. Jones cannot do that project at 650 instead of 750 we might want to reconsider advancing him to 750 or possibly going to the bullpen.

MS. HORN: What we've done in the past is when we've made across the board cuts is send a grant back, it's approved, but the budget gets sent back to the investigator and they resubmit a budget to the Committee that is then approved by the Committee. They certainly can come back and say I don't want your $650,000, but that hasn't happened yet.

DR. WALLACK: It's never happened. And that -- and to the point that Gerry was eluding to that's

exactly the point that no one has ever turned down our offer Marianne, at a lower number.

DR. FISHBONE: Well, I think most of the established investigators have like three aims and it would seem to me that if they chose to they could do two of the three aims.

DR. HART: Certainly if the budget's cut it would be fair to ask the investigator to revise the aims I'm sure.

DR. FISHBONE: Yeah, that's fine.

DR. HART: So they're not held accountable to something they can't afford.

DR. FISHBONE: Yeah.

MS. HART: Okay. The internet problem appears to be hotel-wide. So they're working on it and --

DR. KIESSLING: Do we get a discount?

MS. HART: -- we're not paying for it anyway.

DR. FISHBONE: I'm wondering, can we cut back a little on the air conditioning just because of the noise level? It makes it a little hard -- or I could move down the table I guess so I could hear everybody. Is anybody else having a problem?

DR. KIESSLING: I'd like to make one more

general comment. This year we received, and unfortunately they're higher than our cutoff, but we received three -- we've received four applications from industry, if Chondrogenics is really industry, and I think that's a new record, isn't it? I don't think we've ever gotten so many applications from industry before. So even though three of them are not going to get discussed today I really want to commend those companies for doing this and I always encourage those companies to try to find a partner in an institution to help them get this work funded, because this -- getting these companies funded was a major discussion point for the voters of Connecticut to fund this work. So what Connecticut people are trying to -- citizens are trying to do is fund their biotech industry and I think that the fact that every year we get one more application from an industry is very promising and I don't want those people to get discouraged.

A FEMALE VOICE: That's a good point.

DR. WALLACK: So just to pick up on what Ann said. Would it be possible for us to at some point consider having a workshop for business and industry and devote that session specifically to business and industry so that they can understand? Because I think that some of the problems in their presentations has been in format so

they can better understand. I would recommend that in light of what Ann you brought to our attention, that we in the fall or sometime soon, establish a workshop so that whoever is interested, and that would I think also be welcoming to business and industry and let them know we really care about them participating.

CHAIRPERSON MULLEN: That sounds like a great agenda item for the fall and I just want to check in with you all who want to leave and have all of our work done today that we do periodic time checks since we're in the process discussion and to our grant review discussion so I don't know if we'll be able to expound on what your recommendation is but it's a great recommendation. But I also just want to call our attention to the time.

MS. HORN: Very good. I have a question on -- in terms of process. We have established a less than 4.5 as the priority score for us.

CHAIRPERSON MULLEN: Equal to or less than.

MS. HORN: Okay. Equal to or less than 4.5?

(Indiscernible, multiple voices)

MS. HORN: Okay. So less than 4.5 will be considered. The order in which they are considered, I heard one person put forward established grants as the

starting point, is that the consensus of the group, to start with established?

A FEMALE VOICE: That works for me.

MS. HORN: Okay. And then next would we want to go to the group grants, they seem to be a high priority for the group --

A MALE VOICE: I'm sorry Marianne?

MS. HORN: -- the group grants would be -- would be -- could be next?

A MALE VOICE: And then disease directive?

MS. HORN: Including the disease directive, yeah. And then perhaps either seed or core. Core was our lowest priority.

DR. WALLACK: I would recommend seed after disease directed groups because the core, as you just indicated Marianne, they were notified that that would be our least priority for this cycle.

MS. HORN: Okay. And then we can discuss if we want do the budget cutting as we're discussing the grants or what, do we save that to the end and do the budget cutting at that point. Along the way if people do have grants outside of that 4.5 and would like to have them included and discussed let's start the discussion for example with the established investigators, but start the

process with that by hearing from the Committee what other grants they would like to add in and then we'll do the old established investigator pools.

CHAIRPERSON MULLEN: That sounds reasonable. Are we clear?

A MALE VOICE: Yep.

CHAIRPERSON MULLEN: We're good? Okay.

MS. HORN: So Chelsey, what we're going to attempt to do is --

MS. SARNECKY: I'm sorry. I've been out of the room and I'm just trying to figure out what's going on here.

MS. HORN: -- it goes in many directions starting with the establish investigators.

MS. SARNECKY: Okay.

MS. HORN: Less than 4.5 score --

MS. SARNECKY: Okay.

MS. HORN: -- and at the outset we will have -- hear from the Committee members if they would like to add any grants to that discussion and then we'll go through the grants one at a time and determine whether to continue having progressively fundable category or to move them out.

MS. SARNECKY: Okay.

MR. MANDELKERN: This is Bob Mandelkern.

MS. HORN: Hi Bob.

MR. MANDELKERN: I'm unable to understand or follow the conversation and I don't see how I'll be able to vote on anything because not intelligible coming through. I don't know whether it's the system or what, but nothing is coming through that I can understand.

MS. HORN: Okay. I think I'll move the phone back up to the front table and then try to interpret to you the bottom line of what we're doing, is that okay? You're not going to be able to hear much of the discussion I'm afraid unless we walk the phone around and we have not got people available to do that.

A MALE VOICE: We can all talk as loud as we can.

MS. HORN: We'll all talk as loud as we can.

MR. MANDELKERN: Well, if I can hear what's going on (indiscernible, telephonic).

DR. FISHBONE: Marianne? Are we going to go through the established investigators in order or in order of ranking? Like if we just go through the list and stop at --

MS. SARNECKY: Where are we drawing the

line?

MS. HORN: Under 4.5.

MS. SARNECKY: Under 4.5.

MS. HORN: Is it easiest Chelsey then to do it according to ranking or numbers?

MS. SARNECKY: It's up to the Committee. I can do it either way.

MS. HORN: Okay Bob. So here's where we are. We are starting with the established investigator priority scores of less than 4.5. To add to the -- Committee members are able to nominate other scores with -- other grants with a higher score and add that to the pool and then they will be discussed individually according to score. And we're going to try to pass the phone around Bob. It's not a perfect system and I'm sorry, but we'll try to pass the phone around to whoever is presenting.

MR. MANDELKERN: Yes. My vote is needed to pass something.

MS. HORN: Absolutely. Your input is needed too.

MR. MANDELKERN: My vote may be necessary. When you're speaking now I'm having a hard time understanding.

MS. HORN: We're having a little problem with our internet connection, so that's delaying us here, but we're going to plow ahead. Okay Chelsey, are we set to go?

MS. SARNECKY: I think we are.

MS. HORN: Okay.

MS. SARNECKY: I think we're all set. I have up here on the screen, this is the first group of grants that we're going to be looking at. Everything -- would you guys prefer to do it by score or by --

A MALE VOICE: I would like scores.

MS. SARNECKY: -- by score. Okay. Great. Did you hear that we're going to be doing by score?

MS. HORN: Okay. Now from the Committee are there grants that score beyond four that Committee members would like to add to this list recommend that we review?

A MALE VOICE: Just one thing. SB28 is not Yale University, it's Wesleyan.

A MALE VOICE: She said 3.5 gets included.

A MALE VOICE: No, but -- no, it's listed as Yale but it's Wesleyan.

A MALE VOICE: Oh, right, right. Yeah.

MS. HORN: So Chelsey, the correction there

would be Wesleyan University.

MS. SARNECKY: Thank you.

MS. HORN: Okay. Anything else? May it all be so easy. Anybody else want to nominate an established investigator grant to be added to this presumptively funded list?

A FEMALE VOICE: Well, I don't think you should take presumptively funded.

MS. HORN: Oh, okay. I was trying discussible.

A FEMALE VOICE: Discussible.

MS. HORN: Discussible, okay. We're trying to keep people's expectations lowered, but --

DR. HISKES: We always do that.

MS. HORN: -- yes, alright.

A FEMALE VOICE: What was your word?

MS. HORN: Discussible. Discussible. Okay, in the discussible pile. Anybody else?

DR. HART: I'd like to nominate Ren He Xu, that's B06.

(Off the record)

MS. HORN: Okay. Chelsey, did you get that?

MS. SARNECKY: I did. I added Dr. Xu,

11SCB06 to the list as Dr. Hart requested.

MS. HORN: Alright. Any further nominations to this list? Okay. Hearing none --

DR. KIESSLING: Is C-N-N HOT capital letters?

A MALE VOICE: Lower case.

MS. HORN: Then your pleasure in terms of discussing any of these grants for possible not funding or possible funding at a lower level. Would you like to start with the lowest scoring grants or the highest?

DR. HART: I think some of that may come out in discussion of the grants especially for the one I wish to cut.

MS. HORN: So do you want to start with 4.5 and work down?

A MALE VOICE: Why don’t we start with the highest ones, the best grants?

MS. HORN: Okay. So 11SCB19, Yale University, Sandra Wolin is the P.I. for $750,000, a peer review score of 1.5. And the reviewers?

DR. HISKES: I’m one of the reviewers.

DR. KIESSLING: I’m the other, the reviewers are Anne Hiskes and Ann Kiessling.

DR. HISKES: Hi. This is one of the

highest rated grants at 1.5. Sandra Wolin is the P.I. She's described as a veteran researcher. She's very experienced in this area. The title of the project is Mechanisms of RNA Surveillance in Human Embryonic Stem Cell -- Human Embryonic Stem Cells. The objective is to investigate how non-coding RNA surveillance pathways protect tests from potentially deleterious RNAs. The reviewers, and I concur with their opinion after reading the grant is that it's extremely well thought out, extremely feasible, and very, very important in the future of human embryonic stem cell research. That we know how to control and identify these RNAs that are destructive. I defer to the scientist to elaborate.

DR. KIESSLING: Yeah. This is a really nice grant. So this is a good example of -- what is the history of Dr. Wolin with Connecticut monies? Does she -- I didn't look at this budget page carefully. Does she have prior funding from us?

MS. SARNECKY: I believe she does, but I unfortunately can't confirm that right now.

DR. KIESSLING: Okay.

(Indiscernible, too far from mic.)

DR. KIESSLING: Right. But then I don't -- because we're all trying to pull that up. If we don't

have a hard copy of the grant --

MS. HORN: We do. We do. Chelsey, do we have a hard copy of her grant?

MS. SARNECKY: Yes.

A MALE VOICE: Weren't the reviewers asked about overlap in NIH grants?

DR. KIESSLING: Yeah. There was some -- I know there was a couple of questions about overlap with one of the aims and something she's already funded.

DR. HART: She had a stem cell research seed grant from us ending in May '11 on nuclear RNA surveillance. She says it funded the preliminary data in the current application.

DR. HISKES: Okay. That's why she has good preliminary data.

DR. KIESSLING: Yeah.

DR. HISKES: Which is one of the strong arguments in favor of this particular grant.

DR. HART: And the MIH grant that she has is on middle cost extension. It would have expired in April '11.

DR. HISKES: And it's a related NIH grant to RNA quality control.

DR. HART: Oh, I'm sorry. I'm reading the

wrong one.

DR. KIESSLING: Is this -- is she asking for three years of funding at 250 per year or two years?

DR. HART: Four years. She's asking for four.

DR. KIESSLING: Oh, she's asking for four years?

DR. HART: Yes. 180, 190 a year.

DR. HISKES: She's asking for 1.8 months of her own time and 3.6 months of another person and a post-doc for 10 months. So three individuals working on the project.

DR. FISHBONE: I think this is clearly a grant that we would want to fund and I think Chelsea and others review of the budget and the overlap and could take care of that. But I think we have to be more careful -- just one procedural thing. I don't think we should use the word, recommended for funding, because what happens in the end is sometimes some of the ones that we recommend for funding we have to take out for lack of money and maybe using a term like fundable, you know, this is a fundable grant, because we've had problems where people come back to us and they said, at the end of the day you said I was getting funded and then I see I'm not on the

final list.

A FEMALE VOICE: Right.

DR. HART: Chesley has categories list of yes, no and maybe. So if you just said, put it in the yes category?

A FEMALE VOICE: Yes.

DR. HISKES: Yes means fundable.

DR. HART: Yes means intentionally.

DR. HISKES: And then when you have to make hard choices you can go by --

DR. FISHBONE: Well, clearly this is going to be one that’s way up there.

DR. HISKES: -- right. And a strong track record should not be held against someone I guess.

MS. HORN: In the report she’s asking for four years.

DR. HISKES: I know.

MS. HORN: Okay. So -- did you hear that Bob?

MS. JUNE MANDELKERN: She wants to know if you heard that. I’m sorry, this is June, but -- yes, he did hear that.

MS. HORN: Okay. Good. Okay. Is there any objection to this grant being placed in the fundable

category?

DR. GENEL: Move the grant being placed.

MS. HORN: The next grant for review, 11SCB04, UCHC, Gordon Carmichael for $750,000. Peer review score 2.5. And the reviewers?

DR. GENEL: Well, I'm one reviewer. I think this is a good -- I thought this was a good example of the impact of the stem cell program because this is an established investigator who has been previously funded, who was building on previous research that we had funded to study the impact of double stranded RNA in stem cells. It's enthusiastically reviewed at a 2.5 and I think it moves into the upper category.

DR. FISHBONE: I agree.

MS. HORN: Do people want to say anything about the budget as we go through?

DR. GENEL: It's four years at 750.

MS. HORN: Four?

DR. GENEL: I think it's four years if I looked at it correctly.

MS. HORN: I think the RFA reads up to --

DR. GENEL: I'm sorry, three years.

MS. HORN: -- it's asking for three years?

DR. FISHBONE: Both reviewers said the

budget was appropriate.

DR. GENEL: Appropriate, yeah. No, I agree with my colleague on the left in terms of the size of the award.

MS. HORN: So is there any objection to this grant being placed in the fundable category? Hearing no objection it will be placed in the funding -- fundable category. The next grant up for discussion is 11SCB08, UCHC.

MR. MANDELKERN: The grant number?

CHAIRPERSON MULLEN: 11SCB08, UCHC.

MR. MANDELKERN: Chondrogenics grant. I'd like to make a comment.

MS. HORN: Okay. This is Hicham Drissi is the P.I. and the peer review score is 2.5. Go ahead Bob. Were you one of the reviewers?

DR. WALLACK: No.

MS. HORN: The reviewers on this grant?

DR. WALLACK: Wallack and Arinzeh.

MS. HORN: Wallack and Arinzeh. Okay.

DR. WALLACK: I thought that this is a very, very worthy grant.

MR. MANDELKERN: (Indiscernible, telephonic) what about escrow (indiscernible, telephonic).

DR. WALLACK: Bob, just let me just make the presentation and then Treena can follow up and you can comment and that may make it easier. I think it's a very worthwhile grant. The purpose is for the application to generate articular like chondrocytes from embryonic stem cells and this is the main thing for cartilage repair use. It follows on a lot of very, very good work that has been going on at the Health Center for the last few years. David Rowe was funded at $3.2 million I believe. Ann, you asked about previous funding for tangentially associated kind of work.

And the -- all of the peer reviewers are very, very positive about the grant. It's a strong application and I would be in favor of funding this grant. However, this is an example because of the strong core support and the strong backing that we've provided for this area in the past and for the groundwork that's been laid that we fund it not at $750,000 but rather at no more than $650,000. So I endorse funding it, but at a figure of $650,000.

DR. ARINZEH: So I agree that funding the work. I think it's a very interesting proposal and the reviewers are very favorable. And it also brings together a really nice team of investigators going from very senior

to junior -- junior staffing there, so I think that's great. And it's fine if there's a reduction in the overall budget as well. So I'm agreeable to that.

DR. WALLACK: The co-investigators are Ren He Xu and Jay Liberman, we are all familiar with and Dr. Nair (phonetic) as well as the collaborator on it. As Treena said, it's a very strong team.

MS. HORN: Bob, did you have a comment on this grant?

MR. MANDELKERN: No. My comment was Chondrogenics. Is there any mention of escrow? Because we have the experience of voting to fund commercial grants and then finding that there was no escrow in place and we had to withdraw the grant and not fund it?

MS. HORN: Right.

MR. MANDELKERN: I don't see in this Chondrogenics if there's any mention of how escrow approval is going to be sought?

A MALE VOICE: This is not Chondrogenics.

MS. HORN: No, this isn't Chondrogenics Bob. When we get to that point, if we get to that point, that's a good discussion to have. But this -- this is UCHC. It's an established investigator grant 808. Okay. So is there any objection to placing this grant in the

fundable category at $650,000? Okay. Hearing none we'll move onto the next grant, which is 11SCB23, Yale University, Flora Vaccarino. Did you hear that Bob? 11SCB23, Yale University, Flora Vaccarino at 2.5 peer review. Now the reviewers on this one, Ann Hiskes and David Goldhamer.

DR. GOLDHAMER: Alright. So this grant is tied for second best established investigator grant. Dr. Vaccarino is a professor in the Department of Neurobiology. She's an excellent productive investigator and she's assembled a high quality interdisciplinary team for this work. The title of the grant is Differentiation of Human iPS and ES Cells into Functional Neurons. So the rationale for this project is the understanding that iPS cells are going to become increasingly important in the future, but that iPS cells so far have demonstrated more variability in terms of their capacity for neuronal differentiation. And so what she would like to do is to compare in a systematic way ES cells to iPS cells in terms of their ability to differentiate both in vitro and perhaps more importantly in vivo after transplantation.

And so what I -- what I liked about this project is although it's not groundbreaking in terms of innovation, a lot of people are looking at neuronal

differentiation, I thought the care and the quality of the evaluation of acquisition of the neuronal phenotype was better than most other grants that I have seen or work that I've seen. The reviewers -- the sentiment of the reviewers can be encapsulated by the comments of reviewer two who said that the application is from a strong team and presents supported preliminary data for the project. The likelihood for success appears high. They say that comparing iSP NeoCells is not particularly innovative, but it is important in determining the use of iPS cells as an alternative to ES cells.

So I was in favor of this grant. The plan was well conceived and they're all quality researchers and it scored well so I was in favor of putting this in the yes column. It's a three year established investigator grant. I will say that Dr. Vaccarino has had or is coming to the end of a three year E.I. grant, I believe it ends in August. But on a related, but distinct project. I don't believe there's publications from that E.I. grant yet, but again, the work is not overlapping. She's going to put 10 percent effort on the grant and her co-investigators are putting five percent effort, which is appropriate for the scope of this grant. So in summary I favored a yes for this application.

DR. HISKES: I think David did an excellent job of summarizing the strengths and fundability of this grant and I recommend that it be put into the yes column.

DR. HART: Can I ask a question David?

DR. GOLDHAMER: Yes.

DR. HART: There's been obviously a number of studies differentiating iPS into neurons and several publications comparing different sources of iPS. What makes this one different from the others?

DR. GOLDHAMER: Yeah. I mean, I think the limitation of this work is that it's not terribly novel. What I think is different though is the types of analyses that are done to really phenotypically classify the neurons that derive from iPS NeoCells. There's electrophysiology, there's electron microscopy, there's functional assays, in vivo after implantation into mice, there's a number of things that are done that goes well beyond what kind of the average paper does in terms of marker characterization in vitro.

Of course a lot of studies go beyond that, but I think in terms of the scope and the integration and the types of analysis that she is proposing it goes beyond most studies of this sort.

DR. HART: I don't want to belabor this too

long, but there have even been publications showing that cells from very different sources can be pushed into their own differentiation efficiently even regardless of their native potential. So it seems like I wonder whether this is going to really advance the field?

DR. GOLDHAMER: I mean, I -- you know, I think you've hit on the one aspect that is not -- is not a strength of the application. It's not terribly innovative. Both reviewers though did feel that it was -- they were important experiments that were worth doing. You know, and again, it comes down to the level of detail that they're putting into actually describing phenotypically what the cells become.

DR. HISKES: Well, the reviewers describe it as not innovative, but necessary. Someone has to do this.

DR. GOLDHAMER: I mean, okay, so -- I mean, you can always make the argument -- they're using three iPS lines and two ES lines. And so if they want to really understand the variability of iPS cells in neuronal differentiation they may not get there with looking at three lines. But the kind of work that they propose and the level of the detail of work it would be really impossible in a three year grant or a four year grant to

look at many more iPS lines than this. So I don't know if it's going to answer one of the questions they wanted to and that is to define the variability neuronal end point phenotypes, but it will give a very clear idea at least for some iPS lines and ES lines how true to the native phenotype, neuronal phenotype these cells can be differentiated into.

DR. HART: And just lastly, are they doing epigenetics as well, or not?

DR. GOLDHAMER: There is no epigenetics.

DR. HART: Okay.

DR. WALLACK: May I?

MS. HORN: Yes.

DR. WALLACK: Yeah. I would endorse funding this grant as well. However, since this team has -- is coming off funding from a previous grant and since it's a three year grant I'm going to recommend that we fund it at a level of $600,000, not $750,000.

MS. HORN: Any comment by the reviewers?

DR. DEES: Why 600 Milt?

DR. WALLACK: It's a three year grant and I'd like to see them -- in my mind Richard if I'm looking at $750,000 grant, and forgive me for, you know, not digging deep into the specific budget, it's about $200,000

a year times four and it's 800,000, so 750,000 and this being a three year grant, again, without digging deeply into it I think I'm comfortable in asking the researcher if they could do the proposed work at $600,000. That's how I came to that number.

DR. DEES: Okay. I just wanted to know what your logic was.

DR. GOLDHAMER: Yes. Well, I'll comment on that. So I have looked at the budget. I think 600 it would be difficult to do this project. There are three -- there's a P.I. and I believe two co-investigators. Neither co-investigator is asking for any salary. The P.I. is asking for 10 percent. And the other salary support goes to one post-doc and 65 percent of another support staff. And the supply costs, including mouse costs are 40,000 a year, which is not excessive. So I think if you went to 600,000 there would have to be very significant change in scope or in staff.

So, you know, yes, she has had support from the State. It was on distinct work and so I'm not sure that that should enter into the decision to reduce this particular grant.

DR. WALLACK: David, would you be -- do you think that there's room at all to move that number down

from 750?

DR. GOLDHAMER: I mean, it -- I think --

DR. WALLACK: Alright. Let me make it easy -- let me make it easy for you.

DR. GOLDHAMER: -- I would say no.

DR. HART: Yeah. The argument is that the depth of this is the strength of the proposal. The depth is the amount of work that's being done.

DR. GOLDHAMER: I mean, if we decide as a Committee at the end of some kind of across the board cut to fund other grants that would be one thing. But I don't think that this particular grant should be targeted for reduction.

DR. WALLACK: Would you be willing to do this? To accept the passage of this with an asterisk that if we have to come back to grants that would be one that we would come back to just so that we have a memory of what -- where we can come back to possibly?

CHAIRPERSON MULLEN: Isn't it that we might come back to any of them?

A MALE VOICE: Well, yes.

CHAIRPERSON MULLEN: So how about if we keep going?

DR. WALLACK: Okay.

DR. FISHBONE: Yeah. I have a little concern that we may be getting a little bit arbitrary by saying this grant we could cut. Because most of us I think have not read all the budgets of all the grants and I just feel uneasy having to vote on something where I don't even know what the factors are.

MS. HORN: Sure. I just thought as we went through if there were particular reviewers who had that come to mind that this was an excessive budget we could highlight that as we did in the grant above.

DR. FISHBONE: I'd be more comfortable with that than, you know, and I'd like the people who are making the presentation to tell us what the reviewers thought about whether the budgets were appropriate or not.

MS. HORN: So is there any objection to placing 11SCB23, Yale University, Flora Vaccarino, in the fundable category at $744,446? Hearing none. Okay. The next grant is 11SCB11, UCHC

DR. GENEL: Well, I'm one of the reviewers.

MS. HORN: I'm sorry. I'll just do it for Bob. 11SCB11, UCHC for $570,000, David Han and he's received a three from the peer reviewers.

DR. GENEL: Milt, I think he was listening to you because he didn't ask for 750,000 and moreover it's

four years, not even three years. So I mean on the basis of efficiency we ought to fund this.

DR. WALLACK: Then the lunch that I had with him paid off.

(Laughter)

DR. GENEL: This was very well peer reviewed. It's basically a study of what was called, a very interesting term here, Vostal Proteinal (phonetic), and basically the mechanisms of activation of those factors, intercellular factors that are necessary for pluripotency and the most impressive part of the grant was the paper in science signaling, which I had not seen, which was -- is a real tome, it's 15 papers in science of the early studies of Vostal Proteinal analysis, a T-cell receptor signal. So it's very -- it was very well reviewed. I think it ought to be in the yes category.

MS. HORN: Okay. And your fellow reviewer?

DR. GENEL: I'm not sure. The fellow reviewer is -- the fellow reviewer is Ann.

DR. KIESSLING: Oh, is that me?

MS. HORN: Dr. Kiessling.

DR. GENEL: You're the fellow reviewer.

DR. KIESSLING: I thought this sounded familiar.

(Laughter)

DR. KIESSLING: I didn't actually pick upon the fact that it was a four year application though, I was thinking it was three. So yeah, I agree. I think this is -- this is a very good study and one of the reviewers was a lot more enthusiastic than the other. So I definitely would put this in the yes category.

MS. HORN: Any objection to placing 11SCB11 at 570,000 into the fundable category? Hearing none. 11SCB16, UConn, $744,013, Rachel O'Neill, peer reviewed at three. And the reviewers, Dr. Dees?

DR. DEES: So they were listening to you, 744,013. This grant is a very sort of basic science proposal to look at the role of certain small RNA molecules and regulating genes in both cell recognition and differentiation. The peer reviewers think the project is both unique and innovative, though one of them had some worries about whether some of the techniques involved really work. This is a pretty important basic science project. The tie to therapy is pretty distant here, I don't know how much we want to emphasize that. I was looking at a bunch of grants myself, they were all established investigator grants, they were all rated 3.0, and so this is the one of those grants that I thought was

most distantly related to therapy. So it's going to be a long time before this has therapeutic implications. So I was sort of leaning more towards maybe here rather than a clear yes.

MS. HORN: And who else reviewed this grant?

DR. GENEL: I was the other reviewer. Well, I'm not sure that the direct applications of clinical care is necessarily a factor. It's -- this was very well reviewed, a three is a very good score. I think it's 1.5 in the old version or something like that if you can translate that. I would put this in the fundable category.

DR. FISHBONE: May I make a comment? The second reviewer sounded not very happy with it. The differential strategies are flawed, unclear why he's doing certain things. One thing that concerns me a little bit is that we don't know the scoring of the individuals, the two reviewers. We only know the composite and you can have somebody giving it a seven and somebody giving it a two and you would end up with --

DR. GENEL: 4.5 though Gerry.

DR. FISHBONE: -- thank you. But it's a little bit disturbing to me that -- I'm not saying what we

should or shouldn't do with this grant, but the second reviewer had a lot of problems. And I think we have a mechanism Chelsey where you can get a third reviewer in the process if the two are far apart?

MS. SARNECKY: I would defer to Marianne.

MS. HORN: Yes. And that was done. That was done in the cases where there -- the reviewers were far apart there was a third reviewer assigned to come to an --

DR. DEES: We can infer they weren't that far apart.

DR. FISHBONE: They weren't that far apart. Okay. My case rests.

DR. GENEL: Well, I highlighted the first reviewer, enthusiastic about this unique proposal. That's pretty high praise.

DR. DEES: What did the second reviewer say?

DR. GENEL: Innovative proposal.

(Laughter)

A MALE VOICE: He loves applause.

DR. GENEL: I mean, highly innovative. I mean, this is the second reviewer. One had --

MS. HORN: Okay.

DR. GENEL: -- okay. If you want to put it in the maybe category for now I don't care.

DR. DEES: No. I was just making a point about the process.

MS. HORN: Any comments on the budget?

DR. DEES: It's a four year grant, so it's not an unreasonable amount of money. As I say, I can't look at those budget lines myself and say if it's reasonable or unreasonable because I don't do the science.

MS. HORN: So am I hearing that this should go into the maybe category? Is there any objection to it going to the maybe category?

A FEMALE VOICE: How many years? I'm sorry.

A MALE VOICE: It's a four year grant.

DR. FISHBONE: Yeah. I withdraw my comments. I think it should be fundable.

MS. HORN: Okay.

DR. FISHBONE: I just have a problem when one reviewer says it's not very good and the other one says it's great.

MS. HORN: Okay. Is there any objection to this grant going into the fundable category?

DR. WALLACK: So moved.

MS. HORN: Okay. So 11SCB16 is moved to the fundable category.

MS. SARNECKY: Fundable?

MS. HORN: Yes. The next grant, 11SCB18, Yale University, and I'm not going to do well with this name, Yibing Qyang, peer review at three.

DR. DEES: I'm one of the reviewers on that one as well.

DR. HISKES: The name sounds familiar. Yes, I'm also a reviewer of this. Go ahead.

DR. DEES: This is another four year grant. This goal is to produce heart muscle cells from human embryonic stem cells and human induced trotuck (phonetic) cells that can be transplanted to hearts to help patients who have only one heart ventricle. It will be done in mice, the study will go in mice planting cells that actually pop as opposed to synthetic cells that are currently used. The peer reviewers were generally quite favorable, one is really enthusiastic the other has some worries about the tissues they're using and what the use of the human cells in a mouse model would tell us since the mouse versus human models are very different in the cases of hearts.

It looks like it may overlap somewhat with

the current RO-1. But this one is clearly close to therapeutic uses and so more in line with our kind of overall goals so I was recommending a yes.

DR. HISKES: And I think the objections to this grant from the reviewers' point of view are pretty trivial. They shouldn't use that cell line, they should use this other cell line. So I can't think of a major weakness.

DR. FISHBONE: I have that she has a current RO-1 application in that would overlap.

DR. DEES: Yeah, it's an application pending. Yeah, it's an application -- she doesn't have this RO-1 --

DR. FISHBONE: Right.

DR. DEES: -- and it would overlap with it if she's gotten the RO-1.

DR. FISHBONE: Is that something we can do something about subsequently if she gets the RO-1?

DR. DEES: I mean, even if this application was written shouldn't they know already right, whether she got this RO-1 or not?

DR. FISHBONE: Yeah, couldn't we check that out? If she was funded under the RO-1?

DR. GOLDHAMER: Well, we're going to have a

waiting list, right, of some grants that will be bumped up if one isn't accepted? So I think that would take care of that. I don't think we need right now to make that decision.

DR. HART: There needs to be a mechanism where if she did receive the RO-1 we would -- we'd find out about it and make our decision based on that.

DR. WALLACK: This is one that we might want to consider the budget and I say that mainly because of what I'm reading on the primary reviewer. That he has -- that person, the reviewer has some question about what seems like overlapping with past funding as well as the RO-1 consideration and I don't know if I would be uncomfortable. I don't think I would be uncomfortable if this would be a grant that we would lower to at least $650,000 and it could possibly be lower, but I would certainly recommend that as a starting point, 650.

CHAIRPERSON MULLEN: Have we decided that we're going to discuss the dollar amount now or we're just trying to decide what to do with the applications?

DR. GOLDHAMER: I had one question about the grant itself before the budget. So can you clarify for me in this grant, is the investigator going to make -- they're making cardiomyocytes from ES cells, or iPS cells,

is that right? And the reason I ask -- and if that's true I'm wondering if the reviewers mentioned -- I'm wondering if the reviewers questioned the production of cardiomyocytes versus cardiogenic progenitor cells. Most people who are doing this kind of work now are making progenitor cells, which have greater capacity to differentiate into not only cardiomyocytes, but also into support cells of the heart. So there's a move towards the use of progenitors and I just was wondering if reviewers question that and whether that was seen as a limitation? I didn't read the grant, so if the reviewers didn't pick up on it I'm not going to, you know --

DR. DEES: You're asking scientific questions of a non-scientist.

DR. GOLDHAMER: I'm just asking if the reviewers mentioned anything of that sort?

DR. KIESSLING: I just read the review, the answer is no. The reviewers are split. One's very enthusiastic the other one is moderate.

DR. WALLACK: Marianne, just a procedural question, point of order if you will. What are we doing, and I know we've had this question come up in the past, in this particular grant one of the collaborators, Darryl Cotton (phonetic), is from Boston University, from out of

state. I know that that effected the Parkinson's grant that we funded a few years ago and we reduced it because we had to cut out certain things that were happening out of state. In your opinion how do we handle the collaboration here with Darryl Cotton from Massachusetts?

MS. HORN: I can check on this. I think we looked at this when this grant first came through because I had a similar concern about where the research was going to be conducted and I can double-check. But I think we were reassured that the research was going to take place in Connecticut but with collaboration with the Boston scientist.

DR. DEES: There's no money going to the subcontractor, there's no money going somewhere else.

MS. HORN: Right. So we can double-check on that. It is a concern. We do want the research being done in Connecticut at some extraordinary reason for it not being done here.

DR. WALLACK: Okay. We discussed that in previous grants.

MS. HORN: Correct.

DR. GOLDHAMER: I'd like to make another comment. So if the reviewers didn't say anything about this concern I'll withdraw my concern on that issue. I'm

wondering if we, you know, some of the -- some of the three grants that scored a three are going to be funded and some will not be funded, okay? I'm wondering when one of us notes, you know, considerable disagreement between the reviewers that maybe we asterisk those grants. Because those are probably going to be ones that we want to take a more careful look at because we necessarily have to not fund some of the 3's or some of the 3.5's or --

A MALE VOICE: Agree. Good point.

A FEMALE VOICE: I agree.

DR. GOLDHAMER: So that would be adjusted and then -- and then this one as well?

DR. KIESSLING: Maybe they should go in the maybes.

A MALE VOICE: Well, that would be another way to --

A MALE VOICE: Why not put it in the maybes, that's what it's for.

DR. GOLDHAMER: Well, that's -- I'm fine with that. Yeah.

DR. HISKES: But then it becomes important to look closely at the nature of this agreement.

DR. GENEL: I think that makes -- I think that makes a great deal of sense. And I would move the

other one into the maybe category too.

DR. WALLACK: So you would then put O'Neill in the maybe as well?

DR. GENEL: For the same reason.

DR. WALLACK: Right.

DR. GENEL: That's the right way to go.

DR. WALLACK: I wouldn't go for those, exactly.

MS. HORN: Okay. Any objection to moving O'Neill to the maybe and Qyang to the maybe? Okay. And we will check at the break about the RO-1 funding issue, whether that has happened or not, and we'll bring that information back. Okay. The next grant is 11SCB20, UCHC for 750,000, Hector Aguila, and the priority score is three.

DR. ARINZEH: Oh, I'm on that one. I'll just summarize it. This is a three year grant and the proposed work is to address cell based treatments for osteopetrosis, which is actually a rare bone disease and results in increased bone density due to dysfunctional osteoplasts. So they're going to use -- generate iPS cells and then evaluate them and these are going to be from patients that have this congenital osteopetrosis. So the reviewers are actually not so favorable, they were so-

so. And so I was surprised that they didn't give it a worse score because they said it wasn't innovative, it was, you know, low to fair innovation significance. There really aren't a lot of specifics about potential problems, mutations of the iPS, cell derivation, some other comments coming from these patients. Aim Four, which is a correction of the osteoplast defect. This wasn't really detailed well in the grant.

The second reviewer was a little more favorable, but also cited some additional weaknesses in that, you know, the P.I. didn't really show the iPS -- there should be more preliminary data available there. They just felt that was a weakness. So I thought, you know, based on that the scores probably should have been worse. They also didn't provide IRB and escrow approvals, or at least they were pending or just nothing. Nothing was there in the proposal about that.

DR. HISKES: University of Connecticut never approved his escrow approval in advance of the funding of a grant.

DR. ARINZEH: But should it state in -- I've seen in other proposals where they at least say it's pending or it's being --

DR. HISKES: Well, that's just our policy,

you know, it has a different policy.

DR. ARINZEH: -- okay.

MS. HORN: Yeah, we do demand that before we would sign a contract with them, but we haven't required it as a part of their proposal.

DR. ARINZEH: Okay.

DR. FISHBONE: I'd just like to ask a sort of philosophical question. That a few of these grants deal with extremely rare diseases, osteopetrosis I think fits into that category. And I would wonder, you know, if the research -- thinking of the fact that we're allocating these grants on the basis of money that is being allocated by the State, by the people in this State, I wonder about the research, it's not that it's not good research, but research on extremely rare diseases unless it adds to the sum total, you know, to the knowledge about how cells work and so on. I just, you know, I know we have Angelman's Disease and a few others that are quite rare and I just wonder if this is the best use, nothing to do with the science, if it's the best use of State funds.

MR. MANDELKERN: I would like to contribute because I was one of the reviewers with Dr. Arinzeh. Of course you have to look at the fact that there are two proposals from the same reviewer that have been given the

same score and my feeling was that B21 is described as having the potential that could lead to therapies gives it greater importance than B20 and I would certainly feel that we should not push forward two yes's for the same researcher and give him double dipping so to speak. And so my feeling, and I think Dr. Arinzeh agreed, that only one of these proposals should be funded and I felt that maybe the 21 rated a slightly higher maybe than the 20 did.

DR. ARINZEH: Alright. So my recommendation was going to be maybe for this one and then as we get to 21 it's also going to be a maybe.

DR. KIESSLING: So can I answer Gerry's question about -- so the advantage of rare diseases is they frequently give us some really useful information into common diseases. So a rare disease is, you know, sometimes a very interesting genetic defect. It's clearly some kind of defect in a non-redundant gene property. So the fact that this is a rare disease is probably -- it could be a really good model for bone remodeling in general. That's usually the justification for --

A MALE VOICE: There's always that piece made by the P.I.

MS. HORN: Yes Milt?

DR. WALLACK: From another perspective. I don't have a problem funding the rare disease directed project also because very often that rare disease becomes a very significant public health issue and a tremendous burden to the community in order to take care of that problem. So besides what Ann said there's a pragmatic I think approach often that helps me get through the idea that I don't have a problem funding it.

DR. ARINZEH: I guess we're pointing in the maybe category I think because of the way the reviewers were not actually very favorable and that's what it's coming down to. You know, agreed that investigating rare diseases there's potential there to get some value information, but the reviewers just thought this investigator may not be, you know, able to do it.

DR. WALLACK: So Treena, would you have any problem in putting that -- I would think that that's one that we can put in the no category to be honest with you because they're already receiving significant other funding for similar work. This project does have significant weaknesses and I don't -- it would be my proposal to put it in the no category especially picking up on what Bob said that 21 seems to be either -- certainly a maybe, 21 is certainly a maybe. To me this

would be a no.

MS. HORN: Dr. Hart?

DR. HART: I think on the topic of rare diseases I agree with Ann, but the problem of course is the P.I. has to make the case as to why a study of this rare disease has a value either for financial impact upon the community or on some future biological problem. And I didn't read the grant obviously, but if the discussion hasn't brought that up yet it concerns me, number one. Secondly it's clear from reading the review that the score does not match the descriptors for that score. And so the tone of the review sounds like a worse scored grant. On that reason alone I agree that we should put this -- number 20 into the no category.

DR. WALLACK: I would move no on 20.

MS. HORN: Any objection to moving 20 to the no category? Hearing none it will be moved to the no category. The next grant is 11SCB21, UCHC, 750, Hector Aguila, peer review score three.

DR. ARINZEH: Okay. So this is the same investigator again and it's a three year grant. This is more of a development grant where he's looking to develop an array of antibodies for embryonic stem cell derived progenitors obtained during development. So he's trying

to look at identifying, you know, varying stages of development of these ESCs, these novel antibodies. So the reviewers -- well, there's actually only one reviewer I think on this.

A MALE VOICE: No, it's got two.

MR. MANDELKERN: I was a reviewer.

DR. ARINZEH: Well, the peer reviewers. I only saw one. Because there was actually some other ones there, but they were referring to the B20 I think proposal. It's a little confusing. Maybe I was looking at the wrong one, but the reviewer's comment was very favorable. They only -- they just had a very mild minor weakness there about they should look at progenitors from iPS. So other than that this is very favorable. This P.I. does have -- has funded work from -- it has a stem cell core, but that's coming to an end and a flow cytometry core. But he's a productive associate professor in immunology. So I think, you know, this is a development grant, it could have high probability for commercialization I think of these antibodies. If he's able to identify an array of antibodies of -- for these E.S. cells during development I think that would be of benefit. So out of the two, I guess that that was a higher maybe.

DR. HART: I want to just add a bit of perspective to this -- these two projects in particular bring up the topic -- the reviews bring up the topic that hasn't been discussed yet and I just want to point out a great deal has happened in the field of induced pluripotent cells over the past year. And it's difficult because these were written in December and we're reviewing them in July and a lot has changed in the last few months. So one of the criticisms I see, in the previous grant especially and mentioned briefly in this one, is the idea of using blood cells to make iPS cells. That was only published last fall. So a number of labs were jumping on trying to adapt that technology. It isn't yet widely used, it should be very shortly. And so criticizing them for not having preliminary data, making blood cells into iPS, is unfair although not unreasonable.

The other topic that I just want to point out because it's going to come up a few times is genomic stability. There's a comment here about genomic stability and that's been a huge issue in the last four or five months. It's been found that induced pluripotent cells have genomic rearrangements as they become iPS cells and that is a great concern for cellular therapy. No one has any answers yet but there are some people -- reviewers for

this seem to comment that they're aware of genomic instability problem and yet back in December no one knew about this. So if you see something about genomic instability please give it a little bit of leeway.

DR. ARINZEH: So Ron, those are comments for the previous proposal, just so you know.

DR. HART: Yeah. I saw a little of it here.

DR. ARINZEH: Yeah.

DR. HART: He's definitely stronger in the first one, yes.

DR. ARINZEH: Okay. Because he's actually -- he's just using a standard ESE.

DR. HART: I thought he was using monosytes, no?

DR. ARINZEH: That's with the other proposal.

DR. HART: Oh, okay.

DR. ARINZEH: So that's where the confusion was.

DR. HART: How about 21?

A FEMALE VOICE: No, no, no, 21 --

DR. HART: 21 uses monocytes according to the review.

A FEMALE VOICE: -- it uses monocytes to make iPS cells.

DR. ARINZEH: No, this is an ESC proposal.

DR. HART: Then -- okay, then the reviews are screwed up. I'll just look at the reviews. I'm sorry.

DR. ARINZEH: 20 was pure embryonic stem cells and that's where the confusion was as well between the two proposals from this guy.

DR. KIESSLING: So do we have the review for 21?

DR. ARINZEH: If you go -- it keeps going down there's only one review for this proposal, for 21. It's a secondary reviewer.

DR. HART: That's 21.

DR. ARINZEH: 21 has two reviews.

DR. HART: 21 has two reviews.

DR. ARINZEH: So go to the very last one.

DR. HART: No, no, 21 has two reviewers listed. There's a secondary review halfway down the second page.

DR. ARINZEH: Yeah, but that's probably the one that's applicable. I just can't --

DR. HART: Yeah, there it is.

DR. KIESSLING: So this is not the review for 21?

DR. ARINZEH: -- that's the review. Okay. That's the one then.

DR. KIESSLING: So that's using iPS cells though.

DR. ARINZEH: No, that's ES.

DR. HART: They've successfully used it in the past. Chelsey, isn't this the grant where I got involved because there was a review for one grant put onto the review for the other grant, that the reviews were messed up?

MS. HORN: Yes.

DR. HART: And that they had -- there was --

DR. ARINZEH: This is?

MS. HORN: Yes.

DR. HART: -- so I don't know which copy you're all looking at. But the reviewers made a mistake.

DR. ARINZEH: Yeah, this is a mess up. So if that secondary reviewer is correct for this 21 --

DR. KIESSLING: So where's the first reviewer for 21?

DR. ARINZEH: -- there isn't one.

A MALE VOICE: There's not one.

MS. HORN: There actually is one that I sent to you Chelsey and was sent to Dr. Aguila as well.

DR. ARINZEH: So that suggestion about iPS is just a suggestion. We should look at it and look into it.

DR. HART: Okay. Then I was confused as well. Those points still stand overall through.

MS. HORN: I can read the primary reviews for 21 if anybody's interested. Bob, did you have any comments on this?

DR. ARINZEH: Well, we had discussed it prior to the meeting. He said he wanted -- this was much more favorable, higher maybe.

DR. WALLACK: So is this going in the maybe category?

DR. ARINZEH: It's in the maybe.

A MALE VOICE: Still a maybe.

DR. ARINZEH: Still a maybe, yes.

MS. HORN: So we will without objection move this to the maybe category. This is a three year grant?

DR. ARINZEH: Three year grant.

MS. HORN: Okay. Now I want you to know

we're about halfway down this category. It's about 10:20. If people need to take a break there are refreshments behind you and, you know, take a break when it's convenient. But I think we'll just kind of push on if that's okay?

A MALE VOICE: Yep.

MS. HORN: Okay. The next grant is 11SCB22, Yale University for $750,000, Scott Swenson with a peer review score of three. And the reviewers, Dr. Dees?

DR. DEES: I'm one of the reviewers. The goal of this grant is to use induced pluripotent cells to create liver cells from patients with an inherited liver disease to better understand what exactly is going wrong. Hopefully these can then serve as a model for developing drugs and other kinds of treatment. The peer reviewers think this proposal is solid, well conceived, with particularly important results though there were some worries about developing the induced pluripotent, although these are your words, they're not mine, to maturity and what exactly those cells would tell us. One is worried why there's not a whole lot more preliminary data. Actually you can look at that and tell me if that's the summary of their problems.

They said -- this is a quote and I felt this was worth putting in. The proposal is intended as an extension of work already underway in the applicant's research group, so it may not be that he was being highly innovative or having the capability of generating essentially novel results, but this should not detract in any way from the proposal's quality, the development of interesting preliminary data from the ongoing research and increases the probability of producing information that could lead to useful new treatments for liver disease.

This grant on whole is -- you can see the therapeutic value of this, so it has some really sort of direct therapeutic value so it bumps it up a little bit in my book. There's oddly not a letter of support from Dr. Park, who is one of the collaborators so I was a little worried about that. I wasn't quite sure. So I was tentatively wanted to say yes to this.

DR. FISHBONE: I was the second reviewer and I'll comment on the secondary reviewer's comments, which this has potential significance and will potentially shed light on interesting roadblock. Considering he is an established investigator there's a (indiscernible, too far from mic.) of preliminary data. Only proposes to study one line of HS cells and iPS cells. Needs to further --

need to characterize differentiation efficiency by staining cells and mark the markers to accurately assess differentiation. In other words, the second reviewer is not very positive about it.

DR. DEES: Less enthusiastic, yes.

DR. FISHBONE: Yeah. Same kind of problem, split reviews.

DR. KIESSLING: Is it three year or four year?

DR. FISHBONE: I'll tell you in a minute.

DR. DEES: Let me look.

MS. SARNECKY: I have a three year. Oh, no, I'm sorry.

DR. FISHBONE: It brings up an interesting question --

MS. SARNECKY: Four.

DR. FISHBONE: -- it's a four year. This Doctor, In-Hyun Park, is a co-principle investigator. He is on about six other grants. He has letters of support for all kind of people and I'm a little bit concerned. We were talking about this just a little bit before that Dr. Park is -- I just have some concerns about some of his applications. He seems to be on an awful lot of other projects. I don't know if that's good or bad, but do you

have some thoughts on Dr. Park, Milt?

DR. WALLACK: I'm sorry?

DR. FISHBONE: Did you have some thoughts on Dr. Park who is a co-investigator on this grant?

A FEMALE VOICE: He's asking for 10 percent salary.

DR. WALLACK: Yeah. I did have some issues with Dr. Park and his involvement in the grant becomes very frankly a negative for me.

DR. FISHBONE: Okay.

A MALE VOICE: Because?

A MALE VOICE: Why?

(Laughter)

DR. HISKES: Could someone go through his -- I can't get to the edge of that so I can't access his bio. So if we're talking about --

DR. KIESSLING: He just did a post-doc with George Daily (phonetic).

DR. HISKES: -- oh, he's a post-doc. Okay.

DR. KIESSLING: But he's on a lot of grants this time.

DR. WALLACK: He is involved in a lot of grants across the board. He has the -- he has his own grant as you can see, SCB17 --

DR. HISKES: Okay.

DR. WALLACK: -- and he's also involved with a seed grant and I just have some philosophical issues about his involvement with the other grants, his involvement with that grant, and my understanding of this group's intent in doing the seed grants category is contrary to what at least from my perspective he should be doing. If he's an established investigator then the idea of seed grants for an established investigator was supposed to be for people who were in fact senior investigators who wanted to become involved with stem cell research or young investigators wanting to enter the field. Both those individuals wanted to --

DR. HISKES: So go to the field or just --

DR. WALLACK: -- right. And to me this is playing the system a little bit. I'm sorry I have to say that.

DR. GOLDHAMER: So what is his role -- I didn't -- I missed it if it was said. What is his role on this one?

DR. FISHBONE: Co-P.I.

DR. GOLDHAMER: But specifically what is he doing? Is it in the personnel justification?

DR. FISHBONE: He will be responsible for

the overall design of the proposed work. This is Dr. Park, directing it's execution in the financial administration and analysis of the work. He will devote 10 percent effort on this project.

DR. GOLDHAMER: That sounds like the P.I.

DR. KIESSLING: He's a DNA methylation expert.

DR. FISHBONE: So Co-P.I.

A MALE VOICE: He's the Co-P.I.

DR. HART: So the reality is this is a young investigator just recruited from one of the world's top laboratories probably based on funding from this group. So he's being used as a tool by many researchers because of his expertise as a co-P.I. to help their projects succeed. I don't see the downside of that.

DR. GOLDHAMER: Well, that's why I asked what his role was. I thought you'd say, well, he's going to be technically the person that does the DNA methylation work and then some effort on the grant for his expertise would be appropriate. I was just surprised when you said that he's actually in charge of overall design and the -- it sounds like the description of a P.I.

DR. HART: And let me just finish the thought. The idea that a person like this would be asking

for a seed project you can certainly very well criticize that on it's programmatic merits alone. But as a co-P.I. on this project I don't see a problem with it.

DR. KIESSLING: Well, he's a co-P.I. on several.

DR. HART: I don't see a problem with that.

MS. HORN: What we do with the facts we have on this grant and decide --

DR. FISHBONE: Could I just make one point? The two co-P.I.s are responsible for exactly the same things. Scott Swenson will be responsible for the overall design, so will Dr. Park be responsible for the overall design. Directing this execution of financial administration. Both of them have exactly the same role. One's 10 percent effort for salary, the other one is 25 percent. And neither of them will actually be doing any of the work, they have 100 percent Ph.D. post-doctoral associate who is to be announced, to be named, who will devote 100 percent to the project. There's just something about it that doesn't quite sit right, you know, with me. You guys have no problem?

DR. HART: No.

DR. FISHBONE: They're both doing exactly the same thing, one is to pay them for both doing the same

thing?

DR. KIESSLING: I think it would be worthwhile to find out how many grants Dr. Park is on.

DR. FISHBONE: How many grants that --

DR. KIESSLING: He's on. He submitted two of his own, he's co-P.I. on this one, how many others is he co-P.I. on?

DR. WALLACK: I don't know the number Ann, because I didn't tally the number, but in going through all of the seed grants I believe that he appears on a number of seed grants.

DR. GOLDHAMER: The problem is then if the -- if he's removed and the grant falls apart because he is the reason that, I mean, he's one of the reasons that the grant scored what it did, his expertise he brings to the table. And so -- so you have to be careful that -- I don't see how you then fund the grant if you have a problem with this person having effort as a co-P.I. on the grant.

DR. WALLACK: So just from -- David, from a philosophical perspective, how do we feel about the whole idea of a person who's categorizing himself actually as an established investigator, I have no problem with that, and what Ron said I wouldn't disagree with. But at the same

time he's coming in asking for his own seed grant.

DR. KIESSLING: We had another investigator --

A MALE VOICE: That's what we're discussing --

DR. KIESSLING: -- we have another investigator who's done that.

DR. WALLACK: We do, I know that. That's Ted Rasmussen, and I was in --

DR. KIESSLING: No. We have another one.

DR. WALLACK: -- there's at least three or four.

DR. GOLDHAMER: I think the issue of a seed grant that really has to be justified. It has to be a really new area for that. It has to be a new area, it just can't -- so I would agree, but this I don't have a problem with. If the science is good, if it was scored well, if it was reviewed well, and his expertise is essential for the successful completion of the work then I --

DR. WALLACK: I guess it gets down to the point that forgetting the merits of what he's bringing to the table, and David, I hear what you're saying, that he has an expertise from George Daily's lab and so forth, if

the person is somehow not -- I don't know how to say this, I'm trying to be kind. Is not proceeding along the lines of what we at least expect for him to proceed then there's an implication there to me at least about the individual I'm talking to. And it doesn't speak to the highest level of confidence in the individual and I'm -- so does it bring into question my feeling about how he's going to approach things in general?

DR. GOLDHAMER: I missed part of that argument. So why is confidence in him questioned? Because of what?

DR. WALLACK: He's involved in a lot of projects.

DR. GOLDHAMER: Well, you know what? You know, funding is really had to get and most people's careers are cobbled -- where funding is cobbled together for, you know, five percent effort on this and 10 percent on that, you know, it's really hard to fund a lab on, you know, very few people can get two or three, you know, NIHRO-1's to fund their lab. They get a little bit of maybe part of a program project, a little bit of effort here and there. So I think -- so that's a reality of how people fund their labs. But again -- so again, I don't have a problem with this. I do potentially have a problem

with the seed, although I haven't reviewed that grant.

DR. HISKES: I want to speak in favor of Mr. Park's involvement in this grant and any others he may have applied to. I think it's a non-issue. Seed grants are another issue. One, he's been recruited to Yale for a certain purpose. He's a young professor trying to achieve tenure. He needs to get as much funding as he can. He doesn't know what's going to bear fruit or not bear fruit. So he's putting on a lot of teams and it's sort of the institution's responsibility to enable their young -- their new young professors to participate in teams, support them in getting funding so that they can succeed, so this is what you -- how you foster the careers of young professors.

MS. HORN: Okay. I think we need to cut off the discussion.

DR. HISKES: So I think it's a non-issue. He should be -- being put in on a lot of grants, be included in a lot of teams. Some of them are going to get funded, some of them aren't.

DR. HART: And realize this is very similar to the situation of Ren He Xu. This is a person who is critical to a lot of projects.

DR. HISKES: Yes, right.

DR. KIESSLING: Only one reviewer mentions Dr. Park's positive involvement in this project and both reviewers talk about the big weakness in this project is the whole project is based on one cell line.

DR. HART: Well, that's serious. That's another issue.

DR. HISKES: But that's a substantive issue, not a personnel issue.

DR. HART: That's right.

DR. HISKES: And I think we should concentrate on those kinds of issues.

MS. HORN: So do we have a sense this grant should end up in the maybe category, is that the consensus of the group?

DR. FISHBONE: I feel that way as a reviewer. And it bothers me that two co-P.I.'s are supposed to be doing exactly the same thing and they, you know, elucidate --

DR. DEES: I mean, I was the other reviewer. I mean, I was tentatively saying yes on this. I'm okay with maybe.

MS. HORN: Is there any objection to this being placed in the maybe category?

A MALE VOICE: Chelsey already did it, so -

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(Laughter)

MS. HORN: Hearing none. She's going to keep us on track here. 11SCB24, UCHC, $750,000 for Xue Jun Li, peer review three. The reviewers?

DR. HART: I actually focused my efforts on those that I felt were going to be on the bubble because we need decisions on those and so this is one of those I put a little more effort into for that reason. This is from UConn Health Center. Both the P.I. and the collaborator are from Department of Neuro Science. It's to look at development of cortical motor neurons, upper cortical neurons from the brain heading down to the spinal cord to control movements. And what was one of the nicest parts about the project is they focused on a specific rate disease, hereditary spastic paraplegia, which would provide useful genetic material for investigating the problem that will apply to many other diseases such as ALS, primary lateral sclerosis, peripheral neuropathies, which are much more common, MS, even spinal cord injury. So they've previously demonstrated that the ability to produce cells that resemble deep layer cortical precursors and they're now working on turning those into the appropriate types of neurons and this is a very tricky

game. Many people are asking similar questions on a variety of different varieties of neurons.

Without going into the details the reviewers branded the project as the dirty word, ambitious, and it really is. They found confidence that the P.I. collaborator would have success with the proposed work and would be highly significant, my italics here, should a phenotype arise and that's the key issue. There's no guarantee that they will be able to reproduce the degenerative phenotype in these cells as much as one would like to see that happen.

The criticism was the P.I. was previously funded for a very similar project on spinal motor atrophy, I'm sorry, I wrote the abbreviation and so I'm stumbled on the full term. It's unclear whether progress has been made on that project and whether there's any potential overlap. It would seem reasonable that many of the preliminary data in this project came from control experiments in the SMA project.

The P.I. came to the Health Center in 2007. He's had two first authored publications (indiscernible, too far from mic.) since then. He's contributed to high impact studies from colleagues. A senior author manuscript is impressed in a good journal. This is an

ambitious and powerful project focused on a widely impacting degenerative disease and an important cell. That's the positive. I'm concerned that each aim must be successful for the subsequent aims to be attempted, which is always a very big criticism at a program like NIH where if you're building a whole house of cards and the first one doesn't hold up and you're in trouble.

A more limited pilot skill project would have generated a great deal more enthusiasm from me, let's put it that way.

DR. DEES: I don't have too much to add. I mean, the peer reviewers did think this project is well designed and significant, were worried about whether these goals can be really be met. They were worried about the key parts of the project with all the differentiating of these cortical motor neurons. So but I was -- I liked it that the impact for therapy was I think fairly clear so you can see how was going to impact the disease model pretty easily. So again, I was on the tentative yes part myself. So I would say given where we're going it would be one -- and this one is one where we might come back -- when we come back later consider whether a reduced scope might be appropriate because early parts of the project are more important to prove and then later parts of the

project would depend upon those earlier parts of the project. So it might be appropriate to consider that later.

DR. GENEL: Well, would you fund say two years or would you --

DR. DEES: That's possible. We should I think when we come back discuss.

DR. GENEL: -- we haven't done that in the past, but you know --

DR. DEES: We can talk about that.

DR. KIESSLING: Is it a four year application now?

DR. HART: I think it is.

DR. DEES: Let me double-check. Yeah, I don't have it in front of me at the moment but I think so.

MS. HORN: I have it. It is a four year Ann.

DR. DEES: So I think that's something we should discuss later.

DR. HART: Yes.

MS. HORN: You're leaning to putting it in the maybe with further discussion?

DR. HART: Yes. Is it worth -- can we have a note on that, might be worth --

DR. DEES: Maybe defines.

DR. HART: Maybe defines that. Okay.

MS. HORN: I can make a note that --

DR. KIESSLING: Well, why don't we just discuss it and then we're done with it?

DR. HART: Well, I don't think we can be done with it is the problem.

A FEMALE VOICE: It depends on the other ones.

DR. HART: Yeah.

MS. HORN: It might not even come up for a discussion before you reach that level.

DR. HART: Yeah. That's why I say it's discussible later I think. Yes.

MS. HORN: We'll make a note that this should be discussed as possibly being funded for a two year grant as opposed to four and put it in the maybe category?

DR. DEES: Put it in maybe and then with a note that --

MS. HORN: Okay.

DR. DEES: -- possibly --

DR. WALLACK: Marianne?

MS. HORN: Yes?

DR. WALLACK: What about the amount of funding for that grant? And the reason I'm asking is that on a cover sheet that the researchers submitted on 1/10/2011 that person was asking for the stated amount on the board of 750,000. But then on 1/13/2011, and I don't think it's just been a transposed figure, it became $570,173. So the final amount that the person asked for was almost $200,000 less than what's on the board.

DR. DEES: I'm sorry. Where are you getting this from?

DR. WALLACK: On SCB24, the one we're discussing now I think, right?

A MALE VOICE: But that's budget year three.

DR. WALLACK: What's that? The requested amount that I have here is 570,173.

DR. HART: Then when you go to year four it's the cumulative budget is 750,000.

A MALE VOICE: He's got something with some other member altogether.

DR. DEES: I don't know where you're putting -- where is this number coming from?

DR. WALLACK: I'm reading it right off the submission. On the budget, the 750.

(Discussion off the record)

MS. HORN: Is this something that we could discuss off line and then when we come back to discussing this grant and whether it's two year funding we can get an accurate figure?

DR. WALLACK: Is there a way for -- Marianne for us to put it up there a question on the math also then?

MS. HORN: Yes. We've got a question there for two year funding and we can put another note on the amount. Sure. Okay. The next grant, 11SCB28, Wesleyan, 750,000, Laural Grabel, 3.5 is the peer review.

DR. ARINZEH: So this is a four year grant, again, established investigative grant, and she is looking to promote the integration of ESC derived moral progenitors into a lesion (indiscernible, too far from mic.) campus using math models of temporal lobe epilepsy. So she wants to look closely at the relationship between angiogenesis and survival and integration of these moral progenitors and she will characterize really that throughout her specific aims are to look at that relationship, angiogenesis. And so the reviewers thought this was innovative and, you know, just some minor weaknesses -- I believe there were minor weaknesses here

about -- about how this could be manipulated in disease setting, which was one of the comments, and applicability to treatment of epilepsy. This could be broader -- and my thing I think it could be broader than epilepsy. I mean, if she's able to really characterize that there is some link there performing engraftment with angiogenesis I think that would be a good innovative approach there.

So -- and the secondary reviewer thought however that was a weakness in that they haven't really shown yet that that's vascularization is a problem. So, you know, you can go both ways always. The P.I. has extensive experience. I don't think there are any issues with the P.I. The collaborators also provide a lot of expertise in neuronal cell culture and other characterization, electrophysiology but they just didn't have the C.V.'s there, I didn't see C.V.'s for the collaborators.

But again, I think overall the proposal is innovative and should be funded is my recommendation.

DR. GOLDHAMER: Alright. I'll add a little bit. So this team Laural Grabel leads this team, it includes Jan Nagalie (phonetic) and Boster Erin (phonetic) all of Wesleyan. They have had funding in the past and still do have funding from the State. There is no overlap

though with the current proposal. In fact, the prior funding has set the stage for this grant. So in prior funding Laural Grabel had funding to derive neurons from ES cells and that grant ended. And then Jan Nagalie received funding I believe two years ago, possibly last year, to check -- to use the epilepsy model, the seizure model, ES cell derive neuron implantation to see if they can effect outcomes in the seizure model. So in the course of that work they discovered that the vasculature, the blood vessels invaded the grafts and there seemed to be some stimulatory effect of the cells implanted on the vasculature.

And so what I liked about this was that most of the studies, you know, are involved in directed differentiation of ES cells or iPS cells to certain cell types and they're characterized, they're implanted, there's not nearly as much attention paid to the response of the host and one of the key aspects of the host response has to be vascularization of the implanted cells in order for them to survive and incorporate into whatever structure, in this case the brain. So I think that's why the investigators thought this was innovative because it took an approach in terms of looking at the host response that is less well studied than -- less well studied in the

field.

So this was the only grant, although it kind of scored a little bit lower, it was the only grant that I reviewed of any score that had no criticisms of the science. There was some questions about how relevant this may ultimately be to this disease and you won't know that until you see the data, you know? So I didn't really put too much weight on that criticism. But it was the only grant that did not have any scientific flaws mentioned by the reviewers.

So it's a really good, excellent team. I thought it was a novel set of experiments and I had thought this was a yes.

DR. WALLACK: And I would endorse the idea of the two reviewers' suggestion of funding and it does exactly what Ron had said that he hoped would see happen and that is this is an example of the building block process and she's building on published information and to me it's -- I would endorse the funding of this grant.

DR. GENEL: I think there's an additional factor and that is that this is the only application from Wesleyan in the whole crop and that I think that some diversity in terms of where we put our funding is also of value in and of itself. The science being appropriate I

think I'd lean over towards that type of diversity.

DR. GOLDHAMER: Just a comment about the budget. I thought it was appropriate. The collaborators do not ask for a salary and the budget line items seemed appropriate for this kind of work.

DR. HART: It didn't automatically total up to 750,000.

DR. DEES: I'm just curious, do you have any speculation about why it didn't score better given --

DR. KIESSLING: I think the secondary reviewer is mistaken. So the secondary reviewer clearly was not as enthusiastic. The first -- the primary reviewer was really enthusiastic. The secondary reviewer says that there's no data to indicate that defective vascularization is limiting for CNS repair in any current cell therapy paradigm. I don't think that's true. So I think -- I don't know why the secondary reviewer threw that in, but I also think it's not accurate.

A MALE VOICE: I think -- okay, well, that's --

DR. GOLDHAMER: Well, it's a very difficult thing to prove one way or another whether or not the reason for failure was sought. So I agree with you that it's a completely open question and so I --

DR. KIESSLING: Right. So that probably really brought it down because the primary reviewer is very enthusiastic.

DR. DEES: Right. So that actually makes things good.

DR. FISHBONE: It's also cross-institutional, which I think is a very good thing too.

DR. GOLDHAMER: There's a Yale investigator who's an expert on angiogenesis who is part of the project.

DR. HISKES: So I have a question. So if in a case where maybe a secondary reviewer just doesn't know the field very well and --

DR. KIESSLING: Or has a bias.

DR. HISKES: -- or has a bias and makes an assertion like this is there a mechanism where the reviewers come together and then talk this out?

DR. KIESSLING: No, we're the mechanism.

DR. HISKES: We're the mechanism. Okay. So that's a very good point.

MS. HORN: The peer reviewers do get together and if there is a severe discrepancy between one reviewer and the other they talk about that between themselves and then they talk about it at a meeting where

the --

DR. HISKES: But there's not a place where the first reviewer might say to the second, you're just off the wall --

DR. GOLDHAMER: Oh, there's a place, yeah. There's plenty of places to tell a reviewer they're off the wall.

DR. WALLACK: And I believe in our system we also allow for tertiary review and so that would help mitigate that as well.

DR. GOLDHAMER: But this is not one of those cases.

DR. WALLACK: No, no.

DR. GOLDHAMER: There was no question about the science. It was just one wasn't clear on whether this was going to be long-term therapeutic relevance, but I'd say it's way too early to evaluate that anyway.

DR. FISHBONE: So can we just move to put it in --

MS. HORN: I'm hearing consensus to put it into the yes, any objection? Hearing none put it to the yes. 11SCB05, UCHC for $750,000, Stormy Chamberlain, peer review score is four. And the reviewers are?

DR. GENEL: Well, I'm one.

MS. HORN: Dr. Genel?

DR. GENEL: The reviews are positive but not enthusiastic. The score is I think below what I would regard as the priority line. I'd just move it to the no category. The other reviewer is welcome to -- whoever that is.

MS. HORN: Other reviewer on this?

DR. GENEL: Oh, I think it was Bob Mandelkern.

MS. HORN: Okay. Bob?

MR. MANDELKERN: Yeah. Mike and I agreed on this completely and I have the same recommendation that Dr. Genel did.

MS. HORN: Okay. Further discussion? Hearing none this grant will be moved to the no category. The next grant is 11SCB15, UConn, $750,000, Craig Nelson, scored four with the peer review.

DR. HART: This is Dr. Genel and myself. This is somewhat of a special case. I've seen a total of three different versions of this grant so far. I believe the reviewers saw the shortest version of this grant.

MS. SARNECKY: One of the reviewers saw the full version and one reviewer saw --

DR. HART: Oh, that actually helps a lot.

That helps a lot, no doubt. Okay. So to give every possible, you know, advantage for the problem I went through last night and read it in as much detail as I could and tried to be as careful about this as we could be.

DR. KIESSLING: Why were there so many versions?

DR. HART: One doesn't know that answer.

MS. SARNECKY: It could be an internet glitch the way it was downloaded on the computer. It had been downloaded multiple times in different ways. So some of it got chopped off for one reviewer.

DR. HART: It was worse than that though because some had different page numbers than others.

DR. GENEL: The page numbers don't match.

DR. HART: Yeah. But let's move on because we're not going to fix that right now.

DR. GENEL: But whatever.

DR. HART: So the score -- the score that was given by the reviewers is four and I'm going to remind you that that score is labeled as very good, moderate impact, strong with numerous minor weaknesses, just to keep in mind as we go forward here. I completely discounted a few of the comments from one of the reviewers

that had something to do with things that were missing. So that's not a concern. The point is to generate endocrine pancreatic organoids. These are little lumps of tissues that could serve to treat diabetes if transplanted and they would generate them from both ESC and IBSC as models of development for possible transplant therapy. My one complaint about the background is that while diabetes is obviously a major disease there was actually little tie in to human health impact in the grant itself. But that's minor.

Most -- the reviewers -- I'm sorry, I'm working off the screen instead of paper because I wrote this last night. The reviewers were not enthusiastic since work by others is in progress and it is not clear how these approaches would be brought and clear advance. The reviewers complained there was an assumption that neurogenics grew, and two, did not convince the reviewers as a justified direction and they targeted it as ambitious just to summarize what they gave us as their major concerns. One of the major concerns from the reviewers was that other labs had worked in this topic for some time and one reviewer was not convinced the plan would provide a significant advance to the field.

I think a little of that is unfair. There

certainly are a lot of laboratories trying to find a way to treat diabetes with stem cells for sure. There are actually a surprising number of publications that use the term, organoids. Almost none of those in the last 10 years has had anything to do with pancreatic tissue, so in that respect it is somewhat novel. So that criticism I think should be erased.

Now I get into the meat of the project. There is essentially three components. The first is to optimize the differentiation condition, which is critical for this. They focus first on gene expression patterns and second on insulin response. Unfortunately in these experiments the descriptions of what was going to be particularly varied and particularly assayed was very vague and hard to judge on that basis. It certainly needs to be done to optimize these cultures before anything to be worthwhile could come of this. But I was just disappointed in the fact that I couldn't tell exactly what they had in mind in this grant.

The second aim was about artificially expressing a particular transcription factor in neurogenic three that the reviewers claimed was not fully justified as a master regulator and I didn't worry too much about that one. And three is really the strongest part of the

grant where once they've obtained these lumps of tissues they'll very, very rigorous and very nicely determine exactly how functional they really are in a series of assays. They were very well described.

So, you know, putting all of that together the beginning of the grant was somewhat weak. The end of the grant was somewhat strong. It's a novel topic, it's an important topic. And one last problem. Nelson was a co-P.I. with Carter in a prior seed grant from this group, a topic very similar to aim two generating it's lymph producing cells from -- excuse me, embryonic stem cells using neurogenic three and I'm sure there's, you know, some of the preliminary from this grant came from that seed grant and so forth. But that project I don't see any publications that mention that outcome either as neurogenic three or as beta cells or as organites. So I really wonder about the productivity in this seed project in the past.

So overall the concept of building organites is novel. Preliminary results suggest it may be effective and it certainly needs to be developed, it needs to be optimized. The existing grant as written would probably not be competitive for funding on it's own merits in this category, but if it were a seed grant I think it

would be very highly considered. And of course they've already had one bite of the apple as being a seed grant.

So it's a little bit of a tough, you know, you're on a knife edge here. But I would -- I feel as though the topic is novel enough, the direction is of high enough impact. They've gotten far enough with the preliminary results to suggest that this is worth supporting. I don't see the value of supporting the entire project as it was proposed because of the flaws. Dr. Genel?

DR. GENEL: Well, we've had a lot of discussions in the last 24 hours.

DR. HART: That's why I was so long.

DR. GENEL: And I think in essence I think we agree. The only thing I might add and I think we might come back to this later is that we consider this very much like we consider the B24 and that is not consider it not for full funding, but perhaps consider it for a shorter period of funding --

DR. HART: Partial funding.

DR. GENEL: -- and then with an opportunity I think both grants could come back with their intermediate progress and then make a determination. That's something we haven't done before, but I think it's

something we might want to consider.

DR. KIESSLING: Does this use HES cells or iPS cells?

DR. HART: All preliminary data is on HES pretty much. It's proposing to use iPS primarily.

DR. FISHBONE: Can I ask a question? You indicate that aim three sounds like a very good aim. Is it dependent on aim one?

DR. GENEL: Yes. Which is another reason I think not for funding the -- for funding --

DR. HART: If aim one doesn't work you can't do aim three.

DR. GENEL: -- so I would say let's, you know, we consider funding with a -- some sort of a requirement for an interim report at some critical point of view or I don't know, or something like that. We can discuss it.

A MALE VOICE: That's a good idea Mike.

DR. GENEL: We can discuss the mechanism later.

DR. HART: I think that's right. I think again, I feel very positive with partial funding.

MS. HORN: Okay. So are you recommending a maybe funding?

DR. HART: I think by the definition what we've been calling here let's use a maybe category.

MS. HORN: -- okay. With partial funding perhaps contingent on a satisfactory progress report before release of the rest of the funding?

DR. HART: Two year funding. I mean, you know --

DR. GENEL: If we do it this -- if we do this way let's say perhaps either one or both grants then I think we ought to do it the same way.

MS. HORN: I mean, we have not done anything like that before, if we do decide --

DR. GENEL: Well, I know that. That's why I'm --

MS. HORN: -- yeah.

DR. HART: But I think, you know, the other way we can approach this too is we can offer a reduced budget in total and let the P.I. tell us how they'd like to handle it.

MS. HORN: Right.

MS. SARNECKY: We have done that in the past where we've reduced funding and the P.I. comes back with an alternative plan on how they're going to use that funding based on the initial aims that they had proposed.

DR. HISKES: That's better than dictating.

DR. HART: That's right. That's right.

MS. HORN: Okay. The next grant is 11SCB17, Yale University for $750,000, In-Hyun Park, peer review score of four. The reviewers?

DR. GENEL: I'm listed as a reviewer, but I'm going to bow out, I have a conflict.

MS. HORN: Oh, yes you do. That was not --

DR. GENEL: I'm happy to comment. I know another fellow and so forth and I'm happy to comment.

MS. HORN: -- you have a conflict. Thank you.

DR. GOLDHAMER: Alright. So will start and finish I guess. So this is an established investigator grant. The title is, The Role of DNA Methylation in Human ES Cells and iPS Cells. So it's -- it's thought that DNA methylation is a determinant of gene expression, usually repressive, usually it turns off genes and there's a lot of effort being put in to understand and characterize the pattern of methylation across the entire genome, a global approach to defining the methylation pattern --

MS. SARNECKY: Excuse me. I'm sorry to interrupt. I just want to note that this project has indicated that there's proprietary and privileged

information so if you're aware of where that is in the grant if you could keep those comments to a minimum, unless we need to go into some sort of --

DR. GOLDHAMER: -- I'm not aware where that is. I don't think I will be saying anything that is confidential.

MS. SARNECKY: -- I just wanted to put that on the record.

DR. GOLDHAMER: Thank you.

MS. HORN: It should be bolded in the proposal.

MS. SARNECKY: And underlined in the grant.

DR. GOLDHAMER: I thought that was for emphasis.

(Laughter)

A FEMALE VOICE: Those are the really good parts.

DR. HISKES: That's the novel part.

(Laughter)

DR. GOLDHAMER: So anyway, the correlation between DNA methylation and gene expression has been around for years and years and so it's an important problem. What I saw as the problem in this grant though is that much of the types of analysis that he plans to do

has been done by many groups already. This is not -- and therefore it's not new and it's not novel. And that was reflected in at least one reviewer's comments. The first reviewer thought that the proposal was highly significant and important to know differences between ES cells and iPS cells and they had a criticism that they should have expanded the project to look at more epigenetic changes than just methylation.

Personally I didn't think that was a big criticism. You do what you can do and he's an expert on methylation and this is what he's doing. But the second reviewer was much more critical predominantly because of the lack of novelty of the proposal because of what I just said because there's really a great deal of information about methylation during ES cell differentiation. And so he felt that it was -- or he or she felt that it was unlikely to shed significant light on reprogramming process or improve the process.

And so the reviewer was not positive about aims one or two. The reviewer was more positive about aim three, which started to look at interactions between the methylations that are involved in -- that catalyze the addition of methyl groups to DNA to get at the mechanism, so the reviewer was more positive about aim three, but

really didn't like aims one and two.

It had a score of a four and I agreed with the criticisms of reviewer two. I mean, it was a pretty well put together application, but I just didn't feel with it scoring fairly low and with the criticisms of reviewer two that a lot of what is proposed has essentially been done and there's always unique aspects to any project, but has essentially been done, that this warranted funding. And I had recommended or I do recommend that this go into the no category.

MS. HORN: Further discussion? The consensus is that it is placed into the no category?

DR. WALLACK: I would go with no also.

DR. FISHBONE: I just have one question.

MS. HORN: Yes?

DR. FISHBONE: Is aim three dependent on aims one or two?

DR. GOLDHAMER: No. Aim three is not dependent on aims one or two.

DR. FISHBONE: I thought aim three was a very good project, worthwhile.

DR. GOLDHAMER: Yes. I mean, I have -- one reviewer specifically commented that they thought aim three was the strength of the proposal. The other

reviewer did not make that -- did not say that.

DR. FISHBONE: Is it worth giving less money directly into aim three?

DR. GOLDHAMER: I mean, I think this approach of funding parts of projects may in certain unusual situations be appropriate. I think it's a slippery slope to start cherry picking aims from grants to fund. So I don't think that I would recommend that for this grant.

MS. HORN: Okay. Any further discussion? Okay. The next grant is 11 --

DR. WALLACK: Could I ask a question though separate from the specifics? In the formatting of the grant request we have a certain discipline that we've tried to go by. There are a couple of applications that have come through that has not coincided with what we've asked for. This particular grant, for example, on the it's own lay summary of what his grant was all about it didn't coincide with the tenants of what we had asked for. Is there a way of getting back somehow to the appropriate -- and he's not the only one, there are a few of them who didn't format their grants properly, at least properly from our perspective. Can we get back to the institutions and make sure that they go by the guidelines that we're

setting down?

MS. HORN: We could certainly collect that feedback and meet with them and talk about any common issues that there are in terms of what we're seeing in the applications.

DR. WALLACK: Okay. I think it's important to do.

MS. HORN: I mean, we try to go through them for major flaws that would make them not reviewable, but we don't fly special --

DR. WALLACK: Well, this is clearly outside of the realm of what we expect to see come back to us.

MS. HORN: -- okay. The next grant is 11SCB26, Yale University, $750,000, Weimin Zhong, four is the peer review score. Reviewers?

DR. HISKES: I'm one and David is one.

DR. GOLDHAMER: Do you want me to go?

DR. HISKES: I'll go first and then you can elaborate on the --

A MALE VOICE: Which one?

MS. HORN: 26, SCB26.

DR. HISKES: -- scientific -- more scientific insight. So the title of this project is Mechanism for Balancing Stem Cell Self-renewal and

Differentiation During Human Neuro Development. So this investigator wants to investigate mechanisms that control the self-renewal differentiation of neuro progenitors and in particular he's looking to assess the role of Numb proteins. I'm not familiar with Numb proteins myself. But he wants to investigate the role they have in neuro-genesis. He thinks that by investigating this they may discover novel regulatory mechanisms, may lead to applications of exogenous stem cells in neuro disease and shed light on mechanisms of central nervous system repair. So these are some of the strengthens that the first reviewer sees.

He's done preliminary work in mouse and now wants to move to human cells. What's interesting is that this person was part of a hybrid grant funded by this particular Connecticut program in 2006. That grant was discontinued because the major P.I., Dr. Schneider, left Yale for Stamford. And this grant then seeks to extend the work of that previous grant.

This is a case where three -- a third reviewer was brought in to mediate a dispute between two reviewers. The first reviewer did not say anything negative at all about the grant. Talked about it's potential, considered -- the budget was fine, thought the

proposal to discover novel molecules in stem cell regulation could yield important insights into stem cell regulation. The second reviewer was very, very brief. Says the proposal examines the potential role of Numb and Numb anal in neuro-genesis, not convinced of either rationale or approach. Additional weaknesses are the P.I.'s lack of expertise in neuronal differentiation of human pluripotent cell. No collaborator with adequate expertise was listed. And this was a very, very brief summary. It doesn't say why he or she believes the rationale isn't there.

So the third reviewer is brought in. Sort of defends moving to the human from the mouse at this point and so this is a natural progression, it makes sense. So basically a descriptive review. It doesn't really address the strengths. So the rating of four I guess is sort of an average of a positive and negative and then something that's sort of neutral, neither enthusiastic nor negative. So I don't know what you're -- so I think, you know, it's probably risky to fund.

DR. GOLDHAMER: So I'll just say a couple of things. First of all, it's an important problem. When cells divide asymmetrically one stem cell goes back and reoccupies the stem cell lesion as a stem cell and the

other ones goes on and does something, differentiates it, progresses. And this seems to be controlled by proteins that include Numb and this was really a major contribution of this investigator in prior work that showed localization of Numb to one of the two daughter cells and what he's trying to do is to understand the mechanism of Numb localization because that will -- to understand the mechanism of asymmetric division. So the problem is very important.

The work that is described is, you know, pretty similar to work he's already done, but he now wants to apply it to human ES cells and, you know, I think by and large experiments are okay except I really couldn't get past this discrepancy in the reviewers with one reviewer being -- not mentioning all the reviews were short, you know, and one reviewer said the experiments are well thought out and well designed and reviewer two really disliked it on multiple levels. They questioned the rationale, they, you know, the design, everything was questioned. And the third reviewer unfortunately made very few comments that would allow us to differentiate between the first two, but the third reviewer did make one important comment and they said that the Numb expression pattern wasn't clear in his preliminary data for human

cells and that interpretation of all aims will require better data on localization. So localization of Numb and being able to localize it with high resolution is essential for this and that wasn't demonstrated in the preliminary data.

I don't know if I would totally kill a grant on that alone, but given this very large discrepancy between reviews and the fact that their reviewer didn't really clarify the issue except to raise one more criticism I really lean towards no on this.

DR. HISKES: Well, this gives arguments.

DR. GOLDHAMER: A four, you know -- you know, we're discussing the fours, but most fours are going to end up outside of the funding range and I didn't see anything in the reviews, in the third review that would lead me to say, okay, this is a four but there's really mitigating circumstances that should elevate it. So for that reason I kept it as a no.

DR. WALLACK: So I totally agree David and Anne about the no category. In this particular instance though, and I don't know what you've done in the past, is there a way that we can somehow reflect back to the researcher and the fact that there's some apparent lack of strength in certain areas that he has and this is an

instance where the use of collaborators may have picked up on that and perhaps as he goes forward in the next cycle he may want to consider that. I mean, that would be from my perspective a constructive management of this.

DR. GOLDHAMER: I think that's really the job of mentors and so forth.

MS. HORN: And I believe in the audience this feedback will --

DR. HISKES: That's right. That's what I was going to say.

DR. GOLDHAMER: Okay. Okay.

MS. HORN: There are representatives from both institutions. But good point. So I'm hearing a no placement for this grant. Any objection to that? Okay. That will be placed in the no category. The final grant in this established investigator category 11SCB06, UCH, 750,000, Ren He Xu, 4.5 is the peer review.

MS. SARNECKY: This grant also notes proprietary information.

MS. HORN: Okay. Thank you.

DR. HART: What are we up to number on this, 06?

MS. HORN: 06, the final one that's there. Who are the reviewers?

DR. HART: That was me.

MS. HORN: Okay. Dr. Hart?

DR. HART: I was the one that asked this to be pulled out and looked at. And I pulled it out of the pile for three short reasons. One of course is just out or respect for the P.I. and the contribution this person has made to the overall groups in Connecticut. Secondly, because the reviews to me sounded more positive than the score and third, because it's a collaboration between three groups, Ren He Xu, the Stem Cell Corp., Sue at Yale and Lou at Advanced Cell Technologies. So there's involvement from a biotechnology company here as well. So programmatically that to me was a plus.

Now as to the science their goal is to explore and define value of ESC derived MSC in the treatment of Multiple Sclerosis. There's been some history that transplanted MSC cells, which are adult stem cells derived from either bone marrow or some other source may be effective in treating auto immune diseases like MS. However, it's hard to get enough of them to be effective. These folks looked at this as maybe there's a larger and more expandable source than ES cells. So the reviewers note clear relevance to the disease and the fact that they're on a track toward a therapeutic potential. They

view -- oh, and they note that in this case where all cell transplant stories here you can transplant a tree without grafting it to the host, which should be helpful. The cell is only going to be around for a short period of time, if they're rejected it's no big deal or if, you know, it's not a big rejection, let's put it that way.

The complaint however the project is not highly novel and whether the EAU model -- the animal model of multiple sclerosis is called experimental allergic encephalopathy. And it's whether that model is totally appropriate here. The reviewers complain that targeting the initial phase of this disease may not be as good a model of human disease elapsing EAE, which is probably true. There's a lack of details in the protocol of the plan, it doesn't give a clear study of -- picture of how the study will generate useful data was one of the criticisms.

So I should have rated this numerically slightly better than the reviewers did based on the judgement of minor versus major flaws. The way that it's written up and the way I look at the proposals I certainly agree that the complaint about the animal model should have been considered but to me that's the only really substitute complaint. And so at this point I'd like to

see discussion of this in the maybe category just -- it may not make it at all, but I'd just like to see it discussed.

DR. GENEL: What's the budget?

DR. HART: No, I haven't been looking at the budget.

DR. GENEL: Because the secondary reviewer calls it a seed grant.

DR. KIESSLING: Right. A seed grant.

DR. HART: Oh, yeah. I think that's -- so this is a good point to point out is the reviewers really have been lacking in this round and this is yet another example where there's, you know, a factual misstatement in the reviews so it's clearly not a seed grant.

DR. GENEL: Okay.

DR. KIESSLING: But you think this review goes with this grant?

DR. HART: I think so.

DR. HISKES: Well, that could just be a mental blip. I'm guilty of these all the time.

DR. HART: Yeah. But there's been this pattern this year of some of the reviews have been descriptive and not critical, etcetera.

MS. HORN: Yes Bob?

MR. MANDELKERN: I'm a reviewer on this grant and I thought that it had significance for (indiscernible, telephonic) possibilities for disease treatment. It seems to me that the score of 4.5 was extremely severe and it warranted better consideration especially with Ren He Xu as the P.I. Given possible great value, successful research and having given leadership evidence I would propose giving this a maybe even though 12 out of 28 established have scores of 3.5 or better.

DR. KIESSLING: Can I ask what the other funding is now for this investigator?

DR. HART: That's going to take a second. Ask another question while I look.

DR. KIESSLING: Chesley might know.

MS. SARNECKY: I don't know off the top of my head unfortunately Ann.

DR. FISHBONE: This reminded me a little of the Abbott and Costello thing of, Who's on First.

DR. HART: We can certainly bring that up during the discussion of maybes. I can be ready for that.

DR. KIESSLING: Is this a four year grant?

DR. HART: Yes.

DR. WALLACK: To Ann's point though, again,

as with Chesley I'm not sure either specifically but I know -- I think I remember that in the last round of this -- or the round before last, the one we were here we denied him funding in a very, very in depth conversation. So I hear what you're asking Ann and it's not like he's been just run through every time at all.

MS. HORN: Okay. So then I'm hearing recommendation for maybe?

DR. KIESSLING: This had a contract to Yale -- back to Yale?

DR. HART: Well, he's at the Health Center.

DR. KIESSLING: He is, but I think part of this grant he's got -- it looks like he's got a contract back to Yale.

DR. HART: He does have a subcontract to Yale, yes. Yes, he does.

DR. KIESSLING: I mean, nobody's a bigger fan of Ren He than myself, but I don't -- we need to know how much money he's got right now.

DR. HART: He's -- okay. He's just finished up a previous established investigator grant on May 1st of '11. The core facility goes through '13. He's a co-P.I. on another established investigator grant that goes through '13 from Strean Hastada (phonetic). What

else is listed? That's it. That's all he lists.

DR. KIESSLING: And what is their core grant situation right now? We re-funded them for two years, three years?

DR. HART: Through 6/13.

DR. FISHBONE: Last year, wasn't it?

DR. KIESSLING: And that was their second round of funding I think.

A MALE VOICE: That was two years ago.

A FEMALE VOICE: Two years ago.

DR. FISHBONE: Two years ago. Okay. But does that help him in any way in his individual grant?

DR. KIESSLING: Yeah, no, it does. Sure.

DR. FISHBONE: I mean, financially is there --

DR. HISKES: Well, I mean, the core grant supports the development of new studies (indiscernible, sneezing) lines, maintaining stem cell lines.

DR. FISHBONE: But it shouldn't deny somebody from getting his own grant to do his own work.

DR. HISKES: Not totally no.

DR. HART: It's a three year project. Sorry.

DR. KIESSLING: A three year project. With

a three year contract back to Yale?

DR. HART: One, two, three, yes.

MS. HORN: I'm hearing consensus for maybe and come back and have further discussion on this? Okay. This grant will be placed in the maybe category. And that's bringing us close to 11:30. I don't know what your preference is at this point, whether to move onto the next category to finish with this, to stretch and have lunch and come back?

DR. WALLACK: Would it be possible if we took a stretch break and then finished the group diseased category before lunch?

A MALE VOICE: Sure.

DR. WALLACK: Okay?

MS. HORN: What time is lunch?

MS. SARNECKY: We do have lunch set up for between 12:00 and 12:15.

MS. HORN: Oh, fine. I thought it was 11:45. Okay, perfect. That sounds good. Let's take a little break and then come right back and proceed with the group grants.

(Off the record)

MS. HORN: Chelsey, we're still with the same phone?

MS. SARNECKY: I had asked for someone to come down, so if we could either give him another few minutes or just go on and --

MS. HORN: I think we should get started.

DR. GENEL: Yes. Yes.

DR. KIESSLING: I agree.

MS. HORN: Okay. And at some point I'm going to slip out before noon and I'm going to make the decision that we are not coming back tomorrow, so that means everybody needs to really fulfill that promise of just keeping our eye on the prize and moving alone. Otherwise we have to pay for a whole other day, so --

DR. GENEL: We wouldn't want to do that.

MS. HORN: -- not if we don't have to. Okay. So we're going to move onto the group category.

MS. MANDELKERN: Hello?

MS. HORN: Hi June.

MS. MANDELKERN: Yeah. I thought I lost the connection.

MS. HORN: No, we're just getting the group category up on screen. Okay. We have two. One with a peer review score of seven. What is your pleasure on this?

DR. GENEL: The only one that was higher

was a seed grant at eight. I think we don't need to discuss this.

A MALE VOICE: Did we go past that?

A MALE VOICE: We had a policy of 4.5 or under.

MS. HORN: Okay.

MS. SARNECKY: So I'm going to remove this and we will discuss this one.

MS. HORN: There we go. 11SCC01, Chondrogenics, Inc., Caroline Dealy is the P.I.

DR. DEES: I'm one of the reviewers.

MS. HORN: Okay.

DR. FISHBONE: I'm the other. Do you want to start?

DR. DEES: This is a -- parts of these studies is to determine how best to use embryonic stem cell derive chondrogenic cells to facilitate cartilage repair in joints using a mouse model and then to expand it to new embryonic stem cell and use pluripotent stem cell lines. Additional assess the best methods for maximizing cartilage repairs in mice. Intent to perform anal trials necessary for regulatory approval of the techniques used in anticipation of commercial marketing.

The peer reviews, there's only one peer

review, is that right?

MS. SARNECKY: That's what I have in here.

DR. DEES: The peer review is very enthusiastic about this grant, only that the mouse model has some inherent problems with scaling up to larger mammals and humans. The peer reviewer also noted that the induced pluripotent studies seemed to afterthought they weren't quite as well integrated through the whole project but still worth doing.

Now this is actually a little bit funny here because this is listed under group grant where maximum funding is 1.5 million, but on the other hand this is clearly a disease model, so I think it just got mis-classified. So I think the 1.6 is probably alright. This is using a collaboration of an academic group and a new file technology group company that's been trying to definitely market this because the point of this whole study is to do the preliminary trials for FDA funding -- FDA approval of this kind of therapeutic technique. So in some ways this is really a kind of project that we've been looking for. It's integrating the academic side, the bio-technology side, it's clearly disease directed, it seems to be just the sort of thing we're looking for. It gets a pretty good high score, so I would say yes.

DR. FISHBONE: I thought it was an extremely well written grant, very extensive and yet explained everything very well. And which it says a very good collaboration between the UCHC and Chondrogenics. It was a little bit difficult for me to figure out who was getting paid for what in the way it was broken down, you know, a portion of funding was going to UCHC to fund the researchers with portions coming from Chondrogenics that we were paying to them. There's sort of a subcontract of the 1.6 million of 1.1 million to UCHC in that the funding, you know, the salaries --

DR. DEES: I mean, that's just -- the funding was going to Chondrogenics and then they were subcontracting most of the work out to UCHC.

DR. FISHBONE: -- yeah, yeah. But, you know, there was no problem with it, it just was a little hard to follow. But I thought it was an extremely good grant and I would be very comfortable recommending it highly for funding.

DR. GENEL: What is the overhead that we're asking a commercial company to pay, the same?

MS. SARNECKY: What was the question? I'm sorry.

DR. GENEL: What's the overhead to

Chondrogenics?

MS. SARNECKY: Does somebody who reviewed this grant want to help?

DR. FISHBONE: I don't know, it's like we're giving it to Chondrogenics and they're giving most of it back to UCHC, but I don't know what the overhead is.

DR. GENEL: Well, my question is, who pays the overhead?

A MALE VOICE: Meaning indirect?

DR. GENEL: Yeah. Is it to -- is it UCHC's overhead or --

DR. FISHBONE: If you can figure that out be my guest.

DR. DEES: I have to say I don't have any idea.

DR. GENEL: Well, yeah.

DR. FISHBONE: I'm sure it's clear to them, but it's not clear -- budget justification.

DR. GENEL: I mean, Dealy is on the faculty at UCHC, isn't she?

DR. DEES: Yeah.

DR. HISKES: And she's been on stem cell grants before.

DR. DEES: Right. And she's also the

scientific advisor to this company, so the money's coming through this Chondrogenic company, but it -- I mean, the way their budget is structured she's not getting money there, she's getting money --

DR. GENEL: Subcontract from UCHC.

DR. DEES: -- same thing -- I mean, I'm looking at this and I'm not sure what I'm saying it's --

DR. FISHBONE: Yeah. Funds for 20 percent of her effort are requested on the UCHC subcontract and I think -- how many months is she asking?

DR. KIESSLING: It says that Chondrogenics was founded with assistance from the University of Connecticut Center for Science and Technology Commercialization. Is that new?

DR. FISHBONE: No, no, that's been there a while. She's requesting 2.4 months of salary per year and it's under subcontract from UCHC. I don't see a budget from Chondrogenics.

DR. DEES: There is one.

DR. FISHBONE: There is?

DR. DEES: Yes.

A MALE VOICE: Chondrogenics is the primary contractor, UHCH is the subcontractor.

DR. DEES: Yeah. It's page one of three --

four.

DR. FISHBONE: Oh, Chondrogenics, yes. She's not getting any funding from them.

DR. DEES: You see, she's not getting any funding through Chondrogenics. They're paying for some materials and some of the technicians and probably (indiscernible, too far from mic.) and then the UCHC subcontract she is giving 2.4 months a year, so 20 percent.

DR. HISKES: Well, she's acting as a consultant then and being paid as a consultant.

DR. FISHBONE: Yeah, technician and two programmers are being paid for under the Chondrogenics part, but that's still coming from us, right? I mean, everything on here is coming from the Connecticut Stem Cell Fund and Chondrogenics is asking for --

DR. DEES: Well, it's 1.6 million and 1.1 is going -- is subcontracted out to UCHC.

DR. FISHBONE: 1.6 and how much is going -- 1.1 goes to UCHC?

DR. DEES: Yeah.

DR. WALLACK: So Marianne, somebody if they can explain this to me I'm still very, very confused with the numbers here because on the grant request that they

sent in, that Daily sent in, Dealy, on 1/13 she's indicating that she's -- the amount requested is 1.6 million. Literally the next day she's requesting 1.1 million.

DR. DEES: No, I think that's --

DR. WALLACK: Well, I don't understand. No, I mean, it's right here.

DR. FISHBONE: What does it say at the top? You know, one says Chondrogenics the other one says UCHC subcontract.

MS. HORN: Could I make the recommendation that we -- it seems that we have a consensus to move this into the yes category and that we come back and revisit this level of detail? We also do have some UConn people who might be able to give us some factual information on the relationship without getting into any of the merits or --

DR. DEES: I think it's actually pretty clear. I mean, there's two cover sheets here, one is basically for the Chondrogenics grant, which is the main grantee, they're asking for 1.6 million and then there is a subcontract in UCHC that is for 1.1 million. I mean -- so 1.1 of the 1.6 is going to UCHC as a subcontract of this general thing, but it's going to Dealy in her

capacity as director of research for this start up.

DR. HISKES: So she'll be paid as a consultant.

DR. DEES: She'll be paid in her capacity as a UCHC researcher subcontractor.

DR. FISHBONE: Yeah. She's getting no money from Chondrogenics.

DR. DEES: She's getting no money from Chondrogenics directly.

DR. FISHBONE: But other people like a technician, two programmers, are being funded by Chondrogenics.

DR. HISKES: So part of her salary then to the Health Center will be paid by this?

DR. DEES: By this, yes.

CHAIRPERSON MULLEN: Now you ask whether or not answering these questions now is going to help us determine whether or not this application is a yes, no or maybe because then I'll feel more comfortable about the time that we're spending on this portion, something for everyone.

DR. KIESSLING: The biggest problem with this application --

MR. MANDELKERN: I have one comment on this

grant.

MS. HORN: Please.

MR. MANDELKERN: Remember some years ago we voted to fund a commercial grant for $1,000,000 and we never were able to give the money because they never came up with an escrow and the question of escrow approval on commercial projects has not been resolved in my mind, nor is it resolved in this particular grant. I think that must be taken into consideration.

DR. DEES: I don't think it's a problem Bob.

MR. MANDELKERN: They made no notice of it.

DR. DEES: It's not a problem here because the UCHC people are going to handle the escrow because all that work's going through UCHC.

A FEMALE VOICE: Correct.

DR. KIESSLING: The other particular thing, I think everybody's very enthusiastic about this project. The problem is that it's 16 percent of our total money. So we need to understand it.

CHAIRPERSON MULLEN: I understand that. I totally get it. All of this -- all that we've looked at so far I don't know, it might be 80 percent of our total money, if not 100 percent. So we are triaging, right?

Who didn't want to use that word before? I just used it. So we're still going through our first round so that we can then get to these other details. But I want us to be able to at least get through the first round because we're going to come back to these considerations again as we're weighing one against the other. That's all.

MS. HORN: So I think the consensus is that we move this to the fundable category.

DR. DEES: Yes.

MS. HORN: And now we have about 20 minutes. Is the sense of the group that we move onto the core grants?

DR. GENEL: Well, don't you have the disease directed?

MS. HORN: Did we not --

CHAIRPERSON MULLEN: Established group seed for additional considerations was the breaking that I had.

MS. HORN: We did the group, correct?

CHAIRPERSON MULLEN: Right.

A MALE VOICE: These are the disease directed group grants.

A MALE VOICE: We didn't do the --

CHAIRPERSON MULLEN: I'm sorry.

MS. HORN: There's only one so may be we

can --

A FEMALE VOICE: There's three.

A MALE VOICE: There's only one above the cutoff.

MS. HORN: Okay. Was there any other disease directed group grant that we wanted to have the group take a look at other than the one that met the cut?

DR. FISHBONE: Well, we have those still -- we've got a rating of two in the disease oriented.

MS. HORN: Three.

DR. FISHBONE: Three, I'm sorry.

MS. HORN: Yeah, and we have that one up there. And we have two others that are 5.5 and one is 5.25. Is there any sponsorship from the group here to bring those into the, you know, fundable discussions -- discussible? Okay. So then we are looking at the 11SCD1S -- ISO2, UConn, $1,747,172, Urs Boelsteril, three is the peer review. The reviewers?

DR. WALLACK: Want me to go first?

DR. KIESSLING: Yeah, go ahead.

DR. WALLACK: Okay. The project's purpose is to reprogram patient derived skin fibroblasts to iPS cells, to differentiate them into hepatocytes and to use those cells to assess genetically determined pre-

dispositions to drug induced liver disease. So basically it's a method to help in the treatment of liver disease. It has some significance in what can come out of it in that it can improve our understanding of the genetic mechanisms that predispose to drug induced liver therapy and could have a significant potential of major clinical significance.

It has a strong team of collaborators. The only question that we have -- that I have on it, and we discussed this a little bit before, is on the budget considerations. But we can -- Ann, after you comment on it if you want to comment on it, so I'm recommending that we fund this grant and we can come back to the budget considerations based upon some recommendations that one of the reviewers has put forth.

DR. KIESSLING: So this -- actually I thought this was a very interesting disease directed application because it's directed not only to people who have idiosyncratic liver responses to various kinds of medications and diseases, but it also is going to provide testing models for drug companies to be able to test their combinations on a liver. So this not only has both human clinical application, but it's going to be very useful if it works to testing applications to drug discovery. So I

was really excited about this.

I thought the reviewers' comments were a lot more positive than a 3.0 score indicates. They -- the first reviewer is quite enthusiastic about it and the second reviewer is a little bit worried because one part builds upon another part. But I thought based on my other peer review comments that this was -- I was surprised it only got a ranking of three, because they seemed more enthusiastic than a three.

We do have some budget concerns though because this is a big chunk of money and one of these investigators has another application before us.

DR. WALLACK: Well, it's not only that, but one of the peer reviewers has a question on the budget for the functional analysis portion and whether or not the time involved with the researcher's time could be in fact better -- reduced and better focused. So again, we're saying the same thing about strongly endorsing it being funded. Dr. Mullen is clear. But we do have a concern about the budget, not based upon our own looking at it, but also the reviewers.

MS. HORN: Okay. I hear consensus for placing this into the --

DR. HART: Just one question.

MS. HORN: -- oh, I'm sorry.

DR. HART: For those of you who read the grant was there, I mean, is this totally on -- this isn't drugs of abuse or is this therapeutic drugs?

DR. KIESSLING: It looks like it's going to be a general predict liver toxicity kind of program. But they're taking advantage of the fact that some people seem to have -- what is the disease? DT -- DILI, Drug Induced Liver Injury. So they've got -- they're taking specific cells from those folks and comparing them with folks who don't have Drug Induced Liver Injury.

DR. HART: Is there any consideration of the background for the wealth of knowledge of the G-watt (phonetic) studies on drug injury?

DR. KIESSLING: I think so and they're going to -- well, I can't say.

DR. HART: Because it worried me that it sounded like they weren't viewing at all the genetics that have been known on this. They're dealing with very few numbers of samples.

DR. KIESSLING: They have -- they talked about some prior genetic studies.

DR. HART: Okay. As long as they're aware of them.

MS. HORN: Okay. So am I now hearing consensus that this should be placed in the fundable category? Okay.

DR. WALLACK: Just they reference Dr. Krueger's lab, Ron, in that area that you're asking about.

DR. HART: Okay. Good.

MS. HORN: Okay? Chelsey, is lunch available?

MS. SARNECKY: They said between 12:00 and 12:15.

A FEMALE VOICE: We've only got two more.

MS. HORN: Oh, I'm sorry. Yes, let's finish up. I'm sorry. We've only got two more, let's finish up the two, yeah. Okay. 11S -- 11SCD, UCH, 176,735, Janet Hager, peer review score of four. And the reviewers?

DR. KIESSLING: Oh, I'm one of those. This is -- I'm happy to talk about this. This is an application from somebody who wants to set up a micro ray screening core. The reviewers were sort of moderately enthusiastic about this. I don't think this area -- considering everything else we've got on our plate I don't think this area requires a separate core. This is not a big deal technology. It's not even the most recent

technology. So although I understand how important it is to monitor the stem cells my recommendation for this application would be to not fund it.

DR. ARINZEH: I'm on the other one, I mean, I'm the other reviewer. I mean, I guess by the reviewers' comments they thought that the micro ray technology that they'd want to have and the scores actually aren't that great, they need to be a little more advanced with the technology. So that would be my other -- I guess the other ding there, so I would say, no, not to fund.

DR. KIESSLING: There are lots of labs that can do this.

DR. ARINZEH: Yeah.

A MALE VOICE: There are lots of core facilities that you can hire.

MS. HORN: Okay. So consensus is to not fund, to be placed in the no category. The next grant is 11SCD, Yale, $2,499,791, Haifan Lin, peer review of two. The reviewers?

DR. GOLDHAMER: I'll start. Alright. So the background is that a core grant of 1.8 million to support the Yale Stem Cell Core Facilities was funded in 2008 and that is coming to an end this year and this present application requests 2.5 million over three years

that begins in October, I think October 1, for continued support of three of the four cores -- to fund three of the four cores that are part of the stem cell core facilities and that would provide funding until September 2014. So the three components are continued operation of the human ES cell Polter (phonetic) Laboratory, continued operations of the cell imaging core and continued operations of the genomics core. There is also a fax, a self-sorting core, that is stated as not -- they're not requesting funding for that. That on cost recovery basis they get the cost of running the core back from users.

So the three cores, ES cell core, the cell imaging core and the genomics core have been used greatly. So I'll just give you an example. That human -- and this is noted in the application, the ES cell core they say provides infrastructure for 30 labs at Yale to do human ES cell work. They've trained 84 investigators in 30 departments and they're also now training investigators in iPS technology, RNAI knock on approaches as well. So it's a very active core and it clearly serves an important purpose for the -- particularly for the Yale community, but it's stressed that other investigators in Connecticut can use the facilities. I wasn't quite clear on how much it's used by people outside of Yale though.

The cell imaging core they have a confocal microscope that's used seven days a week and something like 250 hours a month and what they're requesting, and this is the only equipment that they ask for is one additional microscope in year one. High quality inverted florescence microscope, not a confocal microscope, but a microscope that can serve the needs of many people, not all of the people who use the confocal need the confocal and this microscope will take some of the load off the confocal microscope.

And then they asked for continued support of the genomics core in the way of funding the technical director of that core. So all of these technologies are essential for stem cell research, there's no question about that. And the cores have done an outstanding job at training and facilitating stem cell research. I should also add that there's outstanding leadership. Haifan Lin is director, Diane Krauss is associate director. So clearly the core has accomplished and continues to accomplish what they have set out to do.

I'll just raise one issue that the reviewer mentioned and that is, and I'm quoting, the weaknesses are that there is no coherent plan for the future of the cores, no justification for use of new equipment, although

I think there was justification for the microscope and that was the only new equipment. But no strategy on long-term viability of the cores. And so I'm not -- so what I think they -- so funding from the State is not going to last forever and there has to be away to I think make the core self-sufficient. If that's by recovery of funds, by user fees or what have you. And so I think -- so I'm very supportive of the core, it's done an outstanding job. The question is, how much money should the State put to cores? A $2.5 million price tag is extremely high and I would hope to see that in the future they move towards ways either through Yale support or user fee support, some way to make this more self-sustaining without the operations being entirely or mostly dependent on State funds. So I think in -- that's kind of my overall feeling of this application.

DR. ARINZEH: And I agree. I was the second reviewer on that too. I agree with those comments. I think, you know, they did lay out that equipment purchase was critical for that microscope because it allows now for real time imaging, so that's a benefit of that. The reviewer was a little bit off there with that. But -- yeah, but the reviewers were critical on the proposal itself, the way it was written. They didn't

really step forward, you know, they really didn't -- they only talked about contributions that it's made to the, you know, Yale community and things like that. So reviewers were critical on that.

I don't know, but is it a maybe -- I guess it's in the maybe based on -- or maybe a reduction in the amount? I think the amount that they are proposing is to help -- is the support personnel majority and then also -- and then supplies and things like that.

DR. GOLDHAMER: Yeah, personnel, some supplies, equipment contracts, maintenance contracts. So, you know, so I agree with the one aspect of the reviewers' criticisms that there has to be some forward looking as to how this would be self-sustained. I didn't really agree, you know, they said that there's no coherent plan for the future of the cores. I'm not exactly sure what that means. I don't know if they wanted to spell out in more detail how the cores would be used. I personally if that's what they meant don't think that's a criticism. They -- the director and associate director know the state of stem cell research, they know what's required, they've brought in the right expertise and equipment to do state of the art work. So I don't think there has to be a lot of specific detail on how the equipment will be used. The

researchers know they're being surrounded by the best equipment and they'll use it appropriately.

But I do think we need to seriously think about how to fund, to what extent it should be funded and how this can become more self-sustaining. So I would give it clear yes, but I think the budget has to be really looked at. How much we're wanting to expend on this needs to be discussed.

DR. KIESSLING: Do they talk about Yale's contribution, financial contribution to the core?

DR. GOLDHAMER: They do. So let's see, I'm not sure I'm going to remember all of the details, but for instance I believe the fax floor was set up by Yale. I think they've put the outlay of funds to buy the fax machine. There was one other case -- one other expenditure that I'm not recalling that was required for setup, but I don't remember what that was. I think it was the genomics core that some of that money came from a hybrid. This is what it was, some of the money came from Mike Schneider's -- what was it called, the hybrid grant that we used to have? And some of that was also matched by Yale funds. And one other less -- a little -- a specific point about the budget that I wanted to raise is it does say throughout that the fax core will not -- that

they're not requesting funds for the fax core, but under the budget they do request salary for the fax technician, so there was a discrepancy there.

DR. FISHBONE: I just have a question. If you establish a core, which I think was one of the original needs for this, at what point does the State's responsibility for continuing to fund that core end? You know, we obviously have a limited amount of money, a limited time span that we can be funding. At some point it would seem that they have to have some way of continuing and I think maybe that's what the -- they were asking in the --

DR. GOLDHAMER: Right. And that's what I tried to articulate as well, yes.

DR. FISHBONE: -- yeah.

MS. HORN: So are we hearing a consensus to put this in the fundable and come back for further discussion on the --

DR. WALLACK: To pick up on Gerry's point though, that was part of a conversation that we had about nine, 10 months ago, and the conversation had to do with the fact that -- Ann, I think you were part of the conversation two years ago, and that is that there has to be some limit to our responsibility for funding the cores.

And there has to be other ways -- and we agreed to that. And in the RFA this year it says specifically that cores will not be a priority in this cycle. We said that. We all agreed upon that.

If we fund this grant as it's being requested it's going to be 25 percent of our entire distribution. Again, having said that it's not going to be a priority for us. And I think Gerry to your point there comes a time when philanthropy for example, has to be -- and again, you have brought that to our attention vis-a-vis what's happening in California. Philanthropy has to be I think a part of the answer to your question. And fortunately for Yale philanthropy is contributing at this particular point I believe to things having to do with the core.

So well I agree totally with what David has said and I am a huge supporter of what is going on at the Center and I'm even a larger supporter of what the University has done remembering that they created the Amistad building not by accident but because of the opportunities that we were bringing to them vis-a-vis stem cell research. They don't have the whole building but they have a good 30 percent I would imagine, one floor and other spaces. So Yale has been great, but we only have

$10,000,000 -- $9.8 million, this is 25 percent. We've said there's a limit and maybe there has to be discussion about redirecting how cores are going to be sustained. So I think your question is a very, very valid question.

A FEMALE VOICE: Do you want to put it in maybe?

DR. WALLACK: I would put it in maybe because I think we have to consider it on the basis of all the things that I've just articulated, what Gerry's eluded to and what we've discussed as a group in the past.

DR. GOLDHAMER: Can I make a couple of comments? I completely agree and I was leading towards that point that this is unsustainable to completely or mostly fund cores. I still would vote in putting in the yes category but with a serious discussion about budget. I think if it was completely cut off this would probably be catastrophic, but there has to be a period of time where there is kind of incremental or perhaps more than incremental, but some reduction and give Yale a chance to recoup some of that money. I think it would be very, very difficult to not fund it and expect Yale overnight essentially to come up with 2.5 million.

CHAIRPERSON MULLEN: So here's my observation. We decided at the beginning that we were

going to access applications within categories and place them within categories. So if we're just looking at this little batch then we can say, yes, no or maybe within this batch because we're still going to come back to a bigger conversation.

A MALE VOICE: Yes.

CHAIRPERSON MULLEN: Which should still -- yeah --

DR. DEES: There's some point in having this conversation now because look, how we decide what to do with this grant is going to impact everything we do. There's so much money on the line here. So I mean, I think it's worth talking -- to go ahead and decide, you know, we're going to fund this grant X amount and then -- because we're going to have to make other decisions elsewhere and if we think -- and I think everybody agrees that we ought to give them some money because this core is so important. The question is, how much? And I think this is worth doing, going ahead and doing it now. I think that means we discuss this one first when we come back.

CHAIRPERSON MULLEN: Right. So what's being -- yeah, what's the end point of this conversation for this moment is my question?

A FEMALE VOICE: We don't know yet.

DR. GOLDHAMER: So is --

CHAIRPERSON MULLEN: Well, we need to establish how far we're going, that's right.

DR. GOLDHAMER: -- the definition of maybe is that maybe we're going to reconsider for the amounts.

CHAIRPERSON MULLEN: Right.

A FEMALE VOICE: I don't think we can come up with an amount yet. I think we need to as we started out prioritize the other categories, see which ones we want to fund there at whatever -- those amounts and then see what's left over and that's what they get.

CHAIRPERSON MULLEN: David, can I ask you, what funding do they have right now and when does it stop?

DR. GOLDHAMER: The money ends I believe in September, maybe September 30th.

CHAIRPERSON MULLEN: Of this -- of 2011?

DR. GOLDHAMER: Of this year.

CHAIRPERSON MULLEN: And they don't have anything left over?

DR. WALLACK: No, no. I believe there's been philanthropic support.

DR. GOLDHAMER: I was just talking about State funding.

DR. WALLACK: I understand.

DR. GOLDHAMER: I don't really know about --

DR. WALLACK: But we're talking about sustaining the core and I could be wrong, but I believe there's philanthropic support that has recently been provided that will be supporting the core.

DR. GOLDHAMER: -- that I don't know. There were statements made that that is a goal is to increase that component. I know they're working towards that. I just don't know where they are.

MS. HORN: Can I just interrupt here and be the bad guy? Because I'm really hungry and I have to go tell them about tomorrow. So can we put this into the fundable category with the understanding that we come back and we have this whole budget discussion and we don't have to fund it in any particular amount?

DR. KIESSLING: Let me make one last comment about that then. Because we -- our whole mission was to send a very clear statement with this RFA. I was surprised to see this core in this application. We sent a very strong signal with that RFA that cores were not going to be a priority. And I don't know if we want to put this in the yes or the no category at this point because I

think they've had a year to realize that this might not get -- and we've also funded them twice already, right?

MS. HORN: So then maybe we put them in the maybe category and come back for a larger discussion?

A FEMALE VOICE: Well, there's some yes, there's some no's.

MS. HORN: I know. We're just trying to come to consensus here.

CHAIRPERSON MULLEN: Are the no's movable to something else so we can move on for now? If not --

DR. WALLACK: Well, can we have -- can we vote on it?

CHAIRPERSON MULLEN: Sure.

DR. WALLACK: We're going to call -- what was your recommendation?

DR. GOLDHAMER: My recommendation was, yes, but with a budget discussion. If that means that becomes a maybe then I'm comfortable with the maybe.

MS. HORN: And you were a maybe?

A MALE VOICE: Maybe.

DR. HISKES: I vote yes with the caveat that my yes means we're going to look at the budget very, very carefully.

A MALE VOICE: Understanding that's a

maybe.

MS. HORN: Okay. And you're a maybe Doctor?

A MALE VOICE: That defines maybe a maybe.

MR. MANDELKERN: Mandelkern votes yes.

MS. HORN: Okay.

A FEMALE VOICE: As long as we're clear.

A MALE VOICE: Okay. That's right.

MS. HORN: And Dr. Dees?

DR. DEES: Maybe is fine.

MS. HORN: Maybe is fine. Maybe?

A MALE VOICE: Maybe.

MS. HORN: I think --

A MALE VOICE: I abstain.

MS. HORN: -- you abstain -- oh, that's -- yeah, okay. Thank you. I think the maybes have it. We're lunch time so we'll place it there, come back -- do you folks want to have a working lunch? I don't want to --

A FEMALE VOICE: Sure.

A MALE VOICE: Sure.

DR. HISKES: I can do two things at once.

(Laughter)

MS. HORN: Thank you.

A MALE VOICE: Are we eating lunch in here?

MS. HORN: Yes. We're going -- Bob and June, we're going to go grab ourselves some lunch and bring our lunch back here and continue working. So we'll be back in about 15 minutes or so.

(Whereupon a lunch break was taken.)

MS. HORN: We're coming back to look at the seed grants, looking at the grants that are below 4.5 and hearing any grants from the group that they would like to add to this pool that would be above the 4.5, 4.5 or above. So does anybody have a grant that they would like added to this discussible pool? Milt, did you have one grant that you had mentioned?

DR. WALLACK: It's already been added. Yeah, it's already been added.

MS. HORN: Okay.

DR. WALLACK: When you went over four.

MS. SARNECKY: Which one was it?

DR. WALLACK: In these two it was SCA03 and SCA40 in this category. It was from the last category that I was talking about that was Nelson, SCB -- Craig Nelson, 40, that was the one, 4.0. But you already put him I think on the maybe list.

MS. SARNECKY: So thing that scored 4.5 or

a less favorable score?

DR. WALLACK: Correct.

MS. HORN: Okay. Was there something with the Carter grant that anybody wanted to bring forward? No? Okay.

MS. SARNECKY: I'm sorry. I'm just double-checking my -- we're including 4.5 in -- we're not including? Okay. Just checking. Okay.

MS. HORN: Okay. The first grant is 11SCA37, Yale University, 200,000, Shanqin Guo, 1.5. Who were the reviewers?

MR. MANDELKERN: Arinzeh and Mandelkern. I'll start it.

MS. HORN: Okay. Go ahead. You're on.

MR. MANDELKERN: The reviewers felt it was excellent total and an experienced P.I. Investigate detail of understanding and maintenance of ATSC. All favors were excellent and the science was strong. Peer review rating of 1.5 was among the best of all 79 proposals. Recommendation is to fund with the score of PR 1.5.

MS. HORN: Okay. Thank you.

MR. MANDELKERN: Did it come through?

MS. HORN: It did. Thank you.

DR. ARINZEH: I agree. The investigator is looking at micro RNA and looking at how that can direct human ES cells into hemopoietic cells. And so the reviewers are very favorable for the (indiscernible, too far from mic.) expansion of these cells. And again, it's actually from a junior faculty member and with an excellent track record so far. So I vote to fund the grant.

MS. HORN: Okay. The consensus is to place this in the fundable category. Is there any discussion? Hearing none we'll move onto the next grant. 11SCA35, UConn, 200,000, Theodore Rasmussen, peer review score of two. The reviewers?

DR. KIESSLING: This is one of mine. This is one of the highest scoring grants. This is a very nice seed type project to look at cell cycle control focusing on a gene that this investigator had actually discovered was important to the cell cycle. So I can't remember if he has prior funding though. I don't know quite why this is a seed and why this is not an established investigator grant and it could be that -- it's possible just because this is a new project and he needs to get a little more into it. I don't know. But I recommend that we fund this seed grant not knowing exactly why it's not a higher level

grant.

MS. HORN: And the second reviewer?

MR. MANDELKERN: I was the second reviewer on this and the score of two by the peer reviewers is the second best among 49 seed grants. The sense of Rasmussen's previous work on (indiscernible, telephonic) to human model, strong (indiscernible, telephonic) and great rationale. It says will provide important biology for ATSC, could have an important impact on human pluripotent stem cell biology. I recommend we fund.

MS. HORN: Okay. The consensus is --

DR. WALLACK: Question?

MS. HORN: -- yes?

DR. WALLACK: It goes back to something that we were discussing earlier in the day. I think it's appropriate to put it on the table now. Marianne, maybe you can elucidate this, and that is when we established the category of seed grants as I recall there was to bring new investigators into the field and to then give opportunities for senior investigators who have already been involved in research who wanted to transfer their efforts into stem cell research.

MS. HORN: Yes. They could -- it was for established investigators new to stem cell research or

developing new research directions for their stem cell research.

DR. WALLACK: Well, wait, wait. New directions I think outside of stem cell research.

DR. KIESSLING: No, it was new direction -- yeah.

DR. WALLACK: Within stem cell research?

A FEMALE VOICE: Yes.

DR. KIESSLING: The idea was that if you didn't have enough -- if the criticism that you were going to get was that there was not enough pilot data then you needed to fund a post-doc to get you the pilot data.

DR. WALLACK: So how does that -- how does that validate the fact that Ted Rasmussen, who I think is a great researcher, and I think it's really fantastic that we have him in the state, he's been a great advocate legislatively for us. I mean, he does all the right stuff. But he's an established investigator. If he had one of his post-docs or somebody like that that he is collaborating with I understand what you're saying Ann.

DR. KIESSLING: Right. No, I mean, I think that is -- we've got two or three applications like this this time.

DR. GENEL: Yes, there's another one coming

up.

DR. KIESSLING: Yeah, there's two or three. So if we want to put this in a mega category to see, I'm happy to do that because we've got some established investigators that have put in seed grants.

DR. WALLACK: Yeah, I agree with that.

MR. MANDELKERN: Both of the reviewers who reviewed the Rasmussen proposal were very positive and recommended funding themselves and I think it's possible that Rasmussen just wanted to go to this new direction and keep it small and just have a seed grant in this new direction whereas you might share in much larger projects of loop nature. So I see no reason to refuse to fund to $200,000.

MS. HORN: Well, how about if we put it in the maybe and come back and have this discussion more thoroughly about whether this is actually new direction or whether it is research that he is building on and perhaps not appropriate for a seed grant?

DR. WALLACK: I would be in favor of maybe.

DR. FISHBONE: Also you're concerned about making that decision at this moment in the process. It's probably something that should be --

MR. MANDELKERN: I'm for putting it in yes.

MS. HORN: Okay, we do hear you on that.

DR. FISHBONE: -- it probably would make sense to look at it much earlier in the process and say, you're in the wrong category rather than now.

DR. KIESSLING: Well, some investigators gave us two grants this time. We didn't have the chance to do that. They submitted two applications this round.

DR. FISHBONE: Yeah.

MS. HORN: Okay. So is the consensus we'll put it into maybe and revisit those issues?

A MALE VOICE: Okay.

MS. HORN: Okay. The next grant is 11SCA01, UCHC for 200,000, Kristin Martins-Taylor, 2.5 peer review.

DR. GENEL: Well, this is a post-doc in Mark LeLand's (phonetic) lab who actually had done work previously in the Stem Cell Center on epigenetic changes in stem cells who is moving over to do work related to Prader-Willi Syndrome, which is a genetic disorder with a deletion of the paternally derived portion of chromosome 11 -- 151113 at the long arm -- the long arm of picture chromosome. And the proposal is to use iPS derived stem cells from patients with Prader-Willi Syndrome and use these to then determine the changes, the epigenetic

changes that occur comparing them to programmed stem cells from normals to see whether or not there are some unique factors related to this.

It's highly reviewed. I think this is precisely the sort we're talking about the intent of the -- of the seed grants this is precisely the sort of individual it's intended for. So I would say it moves into the fundable category.

DR. HART: Yeah. This is a post-doc even though it's within a larger group. One of the keys is they've already published creating the ISP line from a deletion based patient but they are not proposing to also add the maternal uniparental disomy, which is more of an epigenetic effect so they get a breadth of disease covered and what was key was one of the reviewers completely missed the main point of the grant, which was that the snow RNAs that are coated within this region are hypothesized to effect genes outside the region. One of the reviewers didn't get that at all. And in fact, most of the criticism -- it was highly reviewed but most of the criticism that did exist in my mind was based on ignorance of the reviewers. They really didn't understand RNA seek and a few other related technologies. Felt as though there was almost no substantive criticism here whatsoever.

So I'm in favor of yes.

MS. HORN: Further discussion? Okay. The consensus is to move this grant to the yes category. Next grant, 11SCA33, Yale University, 200,000, Peter Amos, peer review score 2.5.

DR. KIESSLING: David and I are the reviewers on this. Do you want me to go or do you want to go?

DR. GOLDHAMER: I can go.

DR. KIESSLING: Okay.

DR. GOLDHAMER: This is an application from the post-doc who is in the lab of Yibing Qyang and I'm probably saying that wrong, he was a new assistant professor at Yale. The title is, The Role of Endocardial Cells in Human Down Syndrome Related Heart Defects. So the background is that 40 percent of Down Syndrome individual have heart septal defects and there's a cell tied to the endocardial cell that's responsible for making the septum that separates the atria from ventricles. But in Down Syndrome patients they're unable to do this effectively for unknown reasons and so the hypothesis that they're going on is that there's a defect in the interaction of endocardial cells with certain matrix proteins, collegian type six is one in particular that

they are interested in.

So -- but it's very hard to get tissue and so they're trying to model this by using iPS technology so they have gotten samples from a Down Syndrome patient in fibroblast and they're in the process of making iPS cells. Preliminary data shows that they've probably made an iPS line. And the P.I. in the lab is experienced in cardiogenetic differentiation from ES cells I believe it is. So they plan to make endocardial cells from iPS cells and then they have in vitro models to look at the function, the behavior of the endocardial cells, their migratory behavior, their interactions with collegian type six and so forth. So it seems to me to be an understudied area and quite novel. The reviewers rated it highly. It got a score of 2.5. The reviewer one thought it addressed an important problem and that the experiments were innovative and reviewer two said, considered the studies very straightforward and exciting.

There were some concerns. One concern is that they're only planning on using iPS cells derived from one patient and I don't know why that is. That does seem to be a limitation to me as well and that's not explained. And then there was some other issues concerning a reporter system that they used to identify the endocardial

cells based on GFP expression. But these are -- these kinds of reporter ES cells and iPS cells are becoming more and more common and it's probably not a big deal.

But there are some uncertainties. But I thought it's the right lab to do this work. The person, the P.I. is -- or the lab head is experienced in cardiac differentiation. It's an important problem and both reviewers liked it so I had recommended this for a yes.

DR. KIESSLING: And now again, the reviewers give it very high marks for innovation. They give it very high marks for importance and significance and potential impact and there are a few minor criticisms as David points out. One he did mention is that there was no discussion of evaluating the cells in terms of genomic stability and how this system might be used to develop patient specific therapies. Notes that chromosomal imbalance syndromes would be a significant challenge of otologist tissue repair. But that's sort of down the line. So I think this is an exciting and important project and I would recommend that it be funded.

MS. HORN: Any further discussion?

MR. MANDELKERN: And I was the second reviewer.

MS. HORN: Oh, I'm sorry.

MR. MANDELKERN: I confer with Dr. Hart's recommendation with a yes recommendation.

MS. HORN: Okay. Very good.

DR. WALLACK: Can we just make sure that there's clarification that all of the work will be done in Connecticut? Again, with one of the collaborators being from B.U.

MS. HORN: Okay. We'll make sure we check that out. Remind me of that. So the consensus is to place this into the yes category. Okay. And the next grant, 11SCA34, Yale University, $200,000, Pascal Drane, 2.5 in peer review. Mr. Mandelkern?

MR. MANDELKERN: I mixed my reviews.

MS. HORN: That's okay.

MR. MANDELKERN: I apologize for that. This is a review investigating gene, H2A-X in determining embryonic stem cells fate. Importance of the gene seem to be great and successfully yield important data to facilitate the relevance of iPS cells. There's a score of 2.5 and it reaches 14 out of 44 reach such scores. Therefore I would recommend yes for funding on this grant.

MS. HORN: Thank you.

DR. HART: This is a new investigator working at a lab of another faculty member who has I guess

had funding from us before that also is a K99 and IH on similar topics. But it's clear this person is starting to head out on their own. This histone variant H2A-X is actually a very exciting new direction for science and for this group as well. There's some quite revolutionary work from a number of systems showing that histone changes must occur to turn a cell into a pluripotent cell, so this is likely to be one of the many players in that game.

What was particularly interesting about this grant, and I hate to keep saying this over and over again, the reviews were unusually weak in that the reviewers again didn't seem to understand the technology that was being done, the criticisms were really out of left field. So realistically this grant should have scored higher even than it was scored by these reviewers. The details that were picked on were just totally either impractical or don't apply here. So I think that this for sure should be in the yes category.

MS. HORN: Okay. Any further discussion? Hearing none we'll place that in the yes category. The next grant 11SCA15, Yale, 195,251, Rong Fan, 2.8 peer review.

DR. KIESSLING: I'm one of the reviewers on this and I think Bob Mandelkern is the other.

MS. HORN: Okay.

DR. KIESSLING: This is an interesting application that's essentially from a very, very senior researcher that's been packaged with a different principle investigator. So this is essentially a project of Sherman Weisman (phonetic) and it's been packaged as a principle investigator for Rong Fan, who is going to commit almost no time to this and doesn't ask for any salary support. Now Sherm Weisman has been around a very long time, he's got to be in his early 80s or mid-80s, right?

But what they want to do is important. They want to try to figure out how to more reliably differentiate cells into mesenchymal or some kind of bone marrow stem cell, that's the purpose of this project. They're going to do a lot of molecular profiling, they're going to do some interesting studies that they're all very well equipped to do, but they have two years of research planned here and they've got less -- a total I think of less than half an FTE to do the work.

So I think the biggest -- I want to put this in the maybe category because I think we want to talk about this. I don't know who's going to do this work or exactly how they're going to get this project done because the budget -- and that was a primary concern of the

reviewers, they couldn't figure out how the budget was going to work. The weaknesses are primarily related to the commitment of personnel to carry out these studies, this seems inadequate. It is also unclear why Dr. Fan is the P.I. relating Dr. Weisman since Dr. Fan is barely committing any time or effort to this project. So let's put this in the maybe category for the moment.

MS. HORN: Okay. Bob, did you have some comments?

MR. MANDELKERN: Well, my comments were that it was an important grant. Steven and I discussed it. We had some questions about the placement of Dr. Weisman and Dr. Fan in various positions, but we thought that the significance of the work that they wanted to do in gene and proteins associated with differentiations of hemopoietic cells was important and that the grant should be funded.

MS. HORN: Thank you. Was there any concern about this being appropriately a seed grant? Okay. So the consensus is then to place it in the maybe. Any further discussion? Okay. We'll put it in the maybe. And the next grant, 11SCA28, UCHC, 200,000, Xin-Ming Ma, 2.8.

DR. DEES: I'm one of the reviewers. So

these experiments they're designed to test the role of the expression of a particular gene in the formation of synapses as precursors to treatments for schizophrenia. The role of stem cells here is going to be first to use embryonic stem cells to characterize the expressions of gene in the neuron formation and then to derive and also to derive pluripotent cells in schizophrenics and controls to see what the differences between those types of cells is going to be.

The peer reviewers were really quite open. This is a -- the P.I. here is someone who has mostly been involved in neuro-science research and has collaborated -- is collaborating with someone who's more involved in embryonic stem cell research, so it's someone who's kind of moving into embryonic stem cells or into stem cell research.

The peer reviewers were quite favorable, offered the experiments were quite, "potentially high impact." And they thought the scientists were really well positioned to do what appears to be a fairly ambitious study for a seed grant. There's -- I have one little oddity here. They say this does not involve human subjects but they're getting their stem cells from patients so they're not doing their experiments on people

on the one hand, but there's going to have to be some IRB involvement here. It wasn't clear to me that they realized that there had to be IRB involvement. I'm sure they must know that, but it was a little disturbing there was no discussion of it. I was -- wanted to recommend a yes for this.

DR. FISHBONE: I was the secondary -- excuse me, secondary reviewer and I would agree with much of what Richard said. The only question I sort of had was that there -- one of the comments that was made was she was -- she has long-standing expertise in studying this (indiscernible, too far from mic.). I wondered if it should be a, you know, a seed grant or here it is as a seed grant. I think it is worthy of funding.

DR. DEES: My impression was that the work was not in stem cells, it was in cell biology.

DR. FISHBONE: It says she has long-standing expertise in studying calorin (phonetic).

DR. DEES: Right.

DR. FISHBONE: But, you know, I think it's a worthy project and worthy of the funding. She's spending 25 percent of her time on the project, which is okay.

MS. HORN: Okay. Any further discussion?

The consensus is then to put it in the funding category. Okay. Fundable. And the next grant is 11SCA07, UCHC, $200,000, Gordon Carmichael, peer review of three. Dr. Hart?

DR. HART: This is me and Dr. Genel. It's a score of three. This is from an established professor investigator exploring a new direction at UConn Health Center. Interesting topic, it's epigenetics like some of the others we've seen, but it's unusual in that it's the H-1 protein. H-1 is not a component of the core histone, it's a linker between them and it's not in the past been considered important because it was thought to be more dynamic. But we found two minor variants of H-1 genes that are expressed in pluripotent cells specifically and show that they're regulated appropriately on different occasions, which is very interesting.

Hypothesized these variants might be important for maintenance of pluripotency. This is a very, very broad hypothesis due to the pilot nature of the project. The reviewers liked the novelty of the topic calling H-1 variants overlooked in human pluripotent cells and likely to lead to new and novel important insights, yada, yada, yada. Naturally the weaknesses the variants may have no discernible impact on pluripotency at all it's

at this point not proven that they're required for or important to pluripotency yet.

The P.I. currently has an NHRO-1 in contention for renewal on a different topic. An NSF award unrelated topic and just finished or is finishing up now an award from our organization on a different, but also epigenetic topic. Due to the speculative nature of the project and this is a senior investigator that is logically a new project but not really so different I'd put it in the maybe for the moment.

DR. GENEL: Yeah, I would agree with maybe. We have them on the fundable category for a established investigator grant to look at epigenetic mechanisms in induced and stem cells and so forth. I believe in maybe for the time being, but I think when we get to the cut -- the other thing is this is for a post-doc to be named also. So --

DR. HART: Yeah, I mean, realistically if this came from a post-doc named Carmichael --

DR. GENEL: -- if it came from a post-doc who's there, yes.

DR. HART: -- you would probably give it a higher, but --

DR. GENEL: Yeah.

DR. HART: -- and it shouldn't really be that big of a difference because he'll find a good post-doc.

DR. GENEL: Well, I know, but yeah.

DR. HART: But what are you going to do?

MS. HORN: Okay. Any further discussion? So we're going to put this in the maybe category?

DR. GENEL: I'd move it in the no category frankly I think. We're going to have to make a cut somewhere.

MS. HORN: Okay. So is the consensus maybe?

DR. HART: I like maybe at the moment, yeah.

MS. HORN: Maybe for the moment. Is that what the consensus is?

DR. GENEL: Alright.

DR. HART: He doesn't get the other one.

(Laughter)

MS. HORN: Alright. The next grant is 11SCA44, Yale University, 200,000, Zheng Wang, 3.3.

DR. HART: That's me again. This is from a post-doc at the Yale Stem Cell Center and Genetics Departments. Already has -- this person is already

identified by GMY knock down screen novel regulatory pathways in human embryonic stem cells and has pulled out from those screens two genes that are -- when they're inhibited increase the growth rate of stem cells and those are P53 and C1249. P53 is exceedingly well known and highly studied and it's been published and known that knockdown of P53 enhances the efficiency of iPS formation. That was published over a year ago I believe. The other gene's function is completely unknown. So there's not so much of a hypothesis here, it's just a goal to find out what these things were doing in this situation.

The reviewers were not terribly helpful. I hate to keep saying this over and over again. There was no concrete reasons why it was scored the way it was other than vague labels of novel factors that might be useful. There were some minor criticisms that is kind of ridiculous given the page limitations. They wanted a lot more detail in techniques which are very commonly used.

The one reviewer -- one reviewer was able to generate a reasonably good hypothesis that the P.I. did not come up with, which I thought was very interesting, and these are -- the collaborators included Ki Hong Che (phonetic) and Sherm Weisman again. The P.I. has six publications all in 2007 in secondary journals but nothing

since joining Yale as a post-doc in 2007. It's a highly competitive field. The P.I. hasn't published since 2007. One of the two genes selected for further study is already very highly studied and already published upon in similar situations.

While the project is very technologically elegant I'm concerned that this is heading nowhere. The lack of hypothesis, the laundry list experiments doesn't help. So I really recommend at this point putting this in the no category.

MS. HORN: And who is the second reviewer?

DR. FISHBONE: Yeah, the primary reviewer says the proposal was not well checked, seems to have been prepared in a hurry, full of typos making it very hard to read. Hopefully this will not correlate with the way the applicant conducts the experiments, which is sort of like the kiss of death. You know, I have nothing really to add from your excellent review of the budget.

MS. HORN: Okay. Any further discussion?

DR. FISHBONE: It's another one of these examples where the words say one thing and the scoring numbers say something else, you know?

MS. HORN: So the consensus is to move this grant to the no category. If they left it to you to give

it the score you thought it really deserves -- if they left it to us to give it the score it really deserves?

DR. FISHBONE: Yeah. There's nothing about it that says it's better than, you know, many -- a lot of the other stuff that we're looking at.

MS. HORN: Okay.

DR. KIESSLING: How many reviewers were there, peer reviewers?

DR. HART: Two.

DR. KIESSLING: No, no, I know that.

A MALE VOICE: In the whole group?

MS. HORN: I believe there were 10 altogether.

A FEMALE VOICE: Oh, wow.

DR. KIESSLING: Okay.

DR. FISHBONE: It's a lot of grants to review.

MS. HORN: Yeah, we need to --

DR. KIESSLING: That would only be 16 grants.

MS. HORN: We can have up to 15 that we can appoint and that would be a great idea I think for next year if you guys could recommend some people to --

DR. KIESSLING: They only had eight to be

primary reviewer for and eight to be secondary reviewer for. And they have three months to do it or something, right?

DR. HISKES: We each had 16 ourselves.

DR. KIESSLING: Right.

DR. HISKES: So the same load.

DR. KIESSLING: Well, no, that's a different level. It's a very different level.

DR. HISKES: But they have to do it in more detail, right.

DR. GOLDHAMER: Weren't three people lost at the last minute? I mean, there was some turmoil. There was some at the last minute I think.

MS. HORN: Well, we need to look at the allocation and experience too of expertise when we get the grants in and see if there are particular reviewers we should add if we get a lot of grants that are slanted in, you know, certain directions.

CHAIRPERSON MULLEN: If we could just -- if this is something that we should really tackle early on in a Board meeting this fall and maybe take a look at.

MS. HORN: Okay. So we placed 44 into the no category. 11SCA03, UCHC, 200,000 --

A MALE VOICE: Now you're on a roll.

MS. HORN: -- Alissa Resch, 3.5.

DR. HART: My third of three in a row.

MS. HORN: Okay.

DR. HART: This was scored at 3.5. It's from a post-doc at UConn Health Center in the Graveley (phonetic) lab. And actually this just as an aside Dr. Resch was listed as a funded post-doc on Dr. Martin Taylor's project. So there is overlap here.

The project is identification of regulatory mechanisms controlling protein expression for MR&A, and I highlight that, protein expression, because most people don't do that. This person points out that most gene expression studies focus on MR&A levels and not necessarily what is translated into protein. There's a high discordancy between protein levels and RA levels and this project is going to start to attack that in this system. So she's going to R&A seek, total R&A, small R&A's as potential regulators, and footprint ribosomes onto R&A's to identify which ones are actually in ribosomal translated complexes, which is novel.

So this is really a discovery project, lacking a true hypothesis by the nature of the project. The reviewers laud a systematic approach, the feasibility to studies. Oh, I should say too, the background of this

P.I. is primarily bioinformatics and it shows. It's very, very strong in bioinformatics, which is necessary for a project like this.

A couple of criticisms from reviewers were very minor in my opinion, that lack of knowledge about embryonic stem cells. There's plenty of knowledge in that environment. She's in with her collaborators and co-P.I.'s for that. I don't think that's a fair criticism. And in fact, again, the reviewers seem to be ignorant of some of the issues. They were complaining that ribosomal R&A levels may contaminate the preparation and based on what was proposed that was not really a problem.

It was odd though that one of the methods listed for the ribosomal footprinting can't possibly work the way that it was written in the grant and must be a mistake. But again, this is a bioinformatics person, I'm not too concerned, it's a very knowledgeable laboratory.

He has been a post-doc at UConn Health Center since 2009, has two manuscripts in prep in this short period. Previous publication record is good including a recent BMC genomics first author article, which is highly competitive. The Graveley lab is highly experienced and productive and an excellent place for the work. I think this study while lacking a hypothesis is

ideally used in existing strength, the stem cell core at the R&A seed facility for bioinformatics capability to generate a highly useful and important set of predictions. It deserves a much higher score than it was given, so I vote yes.

DR. DEES: You would have thought that this person has all these resources surely somebody should have checked this grant. It has what you'd think is really obvious errors.

DR. HART: Yeah. It was in a flow chart too.

DR. DEES: Which makes me worry. I mean, you're basically saying, this is a great lab so we'll assume this is all going to work out, but that's kind of unfair, isn't it?

DR. HART: It is to an extent. I mean, let's face it. You do have a little bit of bias based on the track record of a group and these guys have demonstrated that they can really do stuff like this.

MS. HORN: Is there another reviewer?

DR. HART: Dr. Genel?

DR. GENEL: Well, it seemed to me that the peer reviews were split. The one that -- reviewer number two was pretty negative while reviewer number one was sort

of moderately positive and she's been a post-doc for a hell of a long time, albeit that she's sort of shifted -- sort of shifted fields. You know, I'm lukewarm I would say. I would put it in a maybe category.

DR. HART: Well, I was actually trying to skip more of my criticism of the reviewers but now that you've given me the opportunity --

(Laughter)

DR. HART: -- the first reviewer gave like no good reason why the proposal was not ranked higher, it was very bland. The second reviewer complained about a lack of stem cell experience and a lack of track record, not being ready for an independent P.I. position. This seems really unsubstantiated.

DR. GENEL: Yeah.

DR. HART: She shifted from a Ph.D. in biochemistry to post-docs in bioinformatics where she's been productive and some very good journals.

A FEMALE VOICE: And probably pregnant.

DR. HART: And finally, the reviewer complains about lack of preliminary data for a seed grant and I think that's (indiscernible, talking over each other).

DR. GENEL: If I said that I'd be arrested,

right? Who is reviewer number two who gives all these lousy reviews?

DR. HART: We need to get a T-shirt, Reviewer Number Two.

(Laughter)

MS. HORN: Okay. Now we have one reviewer strongly supporting and one for a maybe. Any other comments?

DR. GENEL: You can put it in the yes category.

MS. HORN: In the yes?

DR. GENEL: Well, I think we're going to need to cut -- we're going to need to make a cut at some point, but I don't think we're there yet.

DR. HART: This should be high enough in the pile that it really shouldn't be a question of that.

MS. HORN: Okay. So we'll put it in the yes category. And the next grant, 11SCA12, Yale University, 200,000, Jun Yu, 3.5.

DR. GOLDHAMER: Alright, so I'm a reviewer and Bob as well. So I'll start. So the title of this grant is Functional Evaluation of HESC Derived Skeletal Muscle Myocytes in Treating Muscle Degeneration Caused by Peripheral Arterial Disease. So the background is that

PAD, Peripheral Arterial Disease is caused by occlusions of blood vessels and that results in ischaemic damage to tissues like muscle, okay? So therapies to date have focused on restoring blood flow, but less attention has been paid to the muscle itself so this is common in elderly patients because of the ischaemic muscle environment the muscle degenerates and then it doesn't regenerate appropriately as it would in a younger person. And so what this investigator would like to do is to produce skeletal muscle cells from human embryonic stem cells and then test them functionally in mouse models of skeletal muscle ischaemia.

Okay. So I think that the goals are important and reviewer one called the research significant and far reaching. But reviewer one did have significant concerns and I'll just quote, the reviewer said, "However, there are significant questions as to the feasibility of the differentiation, the marking scheme, and transplantation experiments that all diminish expectations for success."

Reviewer two was a little more positive. I have to say that I agree with reviewer one on this and specifically it's extremely difficult to make skeletal muscle cells from human embryonic stem cells or mouse

embryonic stem cells for that matter. And so I really don't have any confidence and there's no preliminary data to suggest otherwise that they'll be successful in step one.

There's one published report that shows this -- that this can happen, although a lot of people have tried to reproduce this and it hasn't been successful in most people's hands, including my own.

Also the measurement of engraftment is done -- is kind of a cursory experimental plan and I get the feeling that the investigator doesn't know that much about muscle biology. For instance, they plan to inject myocytes into muscle. Myocytes are differentiated muscle cells and myocytes would never be used for this kind of application. So that is a terminology issue, but it tells me that maybe the investigator is not that up on muscle -- on skeletal muscle. And the C.V.s suggest no apparent prior experience or track record in muscle biology. So I was very concerned that although it's an important problem that there would be roadblocks to success and I was not favorably inclined towards this project. So I rated this a no.

MS. HORN: Okay. Bob?

MR. MANDELKERN: What was your final

recommendation David?

DR. GOLDHAMER: It was a no.

MR. MANDELKERN: Well, I had originally been intending to recommend maybe on this grant, but Dr. Goldhamer convinced me to put it in the no category reluctantly and so I'll go with the no category.

MS. HORN: Okay. Any further discussion?

DR. WALLACK: It's the first time I've ever heard Bob Mandelkern forego his own opinion.

MS. HORN: You were very persuasive Dr. Goldhamer. Okay. We'll put this in the no category.

MS. MANDELKERN: Who said that?

DR. GOLDHAMER: Milt said that. Bob's good friend.

MS. HORN: Okay. The next grant, 11SCA18, Yale University, 200,000, Stephanie Halene, 3.5.

DR. GOLDHAMER: Milt, that's you and me. Would you like to start on that? I have to --

DR. WALLACK: Okay. I found the grant to be a very interesting and innovative grant with potentially high significance. It proposes to generate iPS cell lines from Myelodysplastic Syndrome patients, which is related to acute Myeloid Leukemia. The reviewer though makes an interesting observation and that is that

it might have been a stronger application if the researcher had gone directly to hemopoietic cells taken directly from the patients. So the reviewer I think is pointing out, and there are some other weaknesses as well, is that the researcher could be well advised to redirect in the next cycle the approach that's being taken for this subject.

So I certainly would not go past maybe on this one, but I would certainly want to hear from David also.

DR. GOLDHAMER: Yes. The problem -- so in this condition, in the syndrome the hemopoietic stem cells or progenitor cells don't thrive, they don't proliferate well and there's a general syndrome of symptoms associated with it that include susceptibility to infection and bleeding and so forth. So there appears to be, and this happens after chemotherapy or radiation therapy, so there's probably -- and it's very heterogeneous syndrome as well so not one cause. So there's probably genetic damage to the stem cells or progenitor cells, they don't proliferate well and there might be other defects as well and then it leads to these downstream effects.

So one reviewer questioned why this can't be done directly with hematopoietic stem cells and this

wasn't maybe approached as directly as it should have been in the application, but I think the reason is that these cells just don't do well and it would be very difficult to grow them up in culture, to modify them, to manipulate them because of proliferation defects. Having said that, the same concerns apply when one considers whether iPS cells will be -- we will be able to make iPS cells from these damaged hemopoietic cells because of the proliferation problems. And the investigator to their credit addressed this head on and said, you know, this really could be a problem. But there was no work around and so I was really worried that this is just a very difficult project that's high risk.

And the other thing that concerned me somewhat, and the reviewer pointed this out, is that the various tests that they want to do in vitro it's not clear what relationship the perimeters that they plan to study in vitro have to the disease in patients. And so the reviewers again, thought it was overall an important problem but had significant concerns and I came down on the side of saying that probably a no is warranted for this.

DR. WALLACK: And David, I certainly was on the fence even to put it in the maybes so that I can

certainly go with a no as well on this particular grant.

MS. HORN: Any further discussion? The consensus is this will be placed in the no category. The next grant is 11SCA22, Yale University, 200,000, Jie Xu, 3.5.

DR. HISKES: We're the reviewers.

DR. ARINZEH: Yeah, do you want me to go?

DR. HISKES: Go ahead.

DR. ARINZEH: Okay. Well, the work is by a post-doc. The work will involve investigating the role of lin28 in human ES cell differentiation into embryonic cardiomyocytes. And so they're looking to understandable lin28 and which is involved in the survival of as we know ES cells and so they have various aims and plan to look into that.

The reviewers' comments were not favorable and so the score doesn't seem to reflect that. Again, another case of that. So they, you know, they said that the -- well, the post-doc really does not have any experience in ES cells, cardiomyocytes, really all of the work that's being presented here. He or she just started I guess, well relatively just started in November of 2010 and so all of that experience is coming from the mentor who has the background of lin28 but the post-doc's

background is in cord blood, mesenchymal stem cells and cancer stem cells for like cancer and ischaemic stroke applications.

They also thought that though they said that -- it looks as though the lab mates produced the preliminary data, that was something the reviewers said. Thought that there should have been some preliminary data showing the lin28 that's actually expressed in human cells. So I think that work was in MS cells, so -- so, you know, so there's some major -- I feel these are major weaknesses so I felt the score should have been worse. So I say no as a recommendation.

DR. HISKES: So I was -- there's nothing, no strong argument to be made here. The criticism -- so the lin28 I guess is known to exist in mouse cardiomyocyte cells and so the question was whether the mouse cells and the human cells are close enough so that then you can infer that lin28 will be a factor in human cardiomyocytes as well. And if that's not the case then there's nothing to study and so they had wanted to have some other evidence that lin28 was at least present in the human cell. So I, being a non-scientist, I don't know how good that argument from analogy is, present in the mouse cardiomyocytes therefore likely to be a factor in human as

well.

MS. HORN: Okay. So am I hearing --

DR. HISKES: But that would be a fatal flaw if lin28 is not present, then there's nothing to study.

DR. ARINZEH: That's right. They don't present any alternative approaches of things that they would do.

DR. HISKES: Yeah, right. So I'd say no.

MS. HORN: -- any further discussion? The consensus is no, place this in the no category. And the next grant is 11SCA40, Yale University, 200,000, Sumati Sundaram, 3.5.

DR. WALLACK: So I think I'm on this Marianne. I thought it was a very good proposal, lots of significant value. It has to do with the engineering of vascular grafts and it opens potentially a whole generation of implantable vascular grafts. It seems as though the P.I.s had the ability to achieve their goals. There's strong preliminary data. There's a clear strategy in place. I actually thought that the 3.5 was low for this particular grant. I would have had it rated higher or better and I would vote in favor of granting this -- approving this grant.

DR. GOLDHAMER: I was the other reviewer on

this. I had a little bit of a different opinion. First of all, this is a great lab. It's an important problem. It's right at the intersection of basic science and translational science. That was all great. The lab has in the past used smooth muscle cells to make vascular grafts and they have made progress in generating smooth muscle cells from ES cells, I believe, and/or iPS cells. So that's all great.

But when they use these smooth muscle cells to make vascular grafts in their bio-reactors the grafts failed, okay? So there's a number of reasons why this could be, but it's unclear the difference between their HSC derived smooth muscle cells and peer populations to smooth muscle cells that they get from rat or other organisms.

So what bothered me about this is that their one over-arching hypothesis, and they don't really consider others, is that it's simply because their mix of cells derived from ES cells is partly smooth muscle, about 50 percent, and partly something else and they blame the failure entirely on the fact that they're not working with pure population of smooth muscle cells. So the entire grant is based on a generation methodologies to engineer the ES cells so that they can then purify the smooth

muscle cells and then test that purified population.

Now it bothered me that in the preliminary data they had the means very easily to -- their hypothesis is that they make smooth muscle cells in their ES cell derived cultures and then the smooth muscle cells are overgrown by other non-smooth muscle cells and that's why the system fails. They could have in a week determined if that was true and they used very indirect ways of approaching that problem. They could have just done immunohistochemistry and counted cells and known over time if their smooth muscle component decreased. So I had very mixed feelings on this grant because it's a great lab and an important problem. You know, I'm swayed. Initially I said no and I think maybe that's a little harsh because they have made progress and I think, you know, if they're smart they will figure out some of these things and come up with alternative hypotheses if their initial one is not true. It could be that it's the immature status of the smooth muscle cells rather than their representation in the cellular mix that's the culprit.

So, you know, at face value I said no, but given that they've made progress on similar types of things and it's a seed grant I was -- I'm swayed to at least be not so hard on them. So -- and Milt -- and Milt

really liked it.

(Laughter)

DR. DEES: So you're saying we like this lab and so we're going to give it this money and even though the grant sucks --

DR. GOLDHAMER: My esteemed colleague Ron Hart, didn't you use a similar argument just a few grants ago?

DR. HART: Absolutely.

DR. GOLDHAMER: But the thing is -- so it's partly --

DR. DEES: With a big smirk from me.

DR. GOLDHAMER: -- yeah. I mean --

DR. KIESSLING: Don't read between the lines.

DR. GOLDHAMER: -- yeah.

DR. DEES: Well, you're saying Laura Nickelson you have confidence in and -- who was the collaborator and that they'll work it out.

DR. GOLDHAMER: So the experiments are appropriate, it's not like there's technical flaws in what they want to do, I just think their overriding assumption is to simplistic and one of the reviewers commented on that as well. And if they -- so -- and I will say

although their overriding hypothesis -- I'm talking myself into a better kind of evaluation, although the overriding hypothesis is that it has to do with representation of smooth muscle cells in the mix they do state in their pitfall section that this might not be the case and if it still fails after purifying the population that they will devise ways of generating better smooth muscle cells by maturing them. So there's immature smooth muscle cells and more mature muscle cells than smooth muscle cells that can be distinguished by certain markers they express smooth muscle acting versus some other markers like calphonen (phonetic).

So they know that it's a potential -- so they're -- so they know that their hypothesis may not be correct and they're willing to try other things if it comes to it. So I was a little put off by the hypothesis being so limiting, but I think it's good research and so I would come down after this long-winded discourse and say maybe.

DR. WALLACK: And I'm still in the yes category, but I think that that's because I'm 72 and David's 45 so that I'm closer to the utilization of this work.

DR. GOLDHAMER: We're a little closer in

age than that.

MS. HORN: Okay. I'm hearing a consensus for maybe then?

DR. WALLACK: Well, I would still --

A FEMALE VOICE: (Indiscernible, talking over each other).

DR. WALLACK: -- no, no. So in a serious vein --

MS. HORN: Yes.

DR. WALLACK: -- so I would still push for the yes because the reality is I think that this is precisely the kind of reason we have the seed category, to work through these kinds of initial problems and the risk factor here is potentially very little for the potential gain that we may have. So from my perspective because of the significance of it, because of the P.I.'s ability to achieve goals, because of the strong preliminary data whether or not they've listened to whatever that's been all about, they're cognizant of it at least and because of the clear strategy I still would come down on the yes. But, you know, that's what we're all about, we have different thinking.

MS. HORN: Further discussion?

CHAIRPERSON MULLEN: It sounded to me as if

we're going to end up somewhere between a low maybe and no. So it's hard for me to figure out how to be between a yes and a maybe at this point as we look at all of the other considerations.

DR. WALLACK: Well, I can go for a maybe for the time being.

MS. HORN: I'm hearing a consensus for maybe. Thank you.

A FEMALE VOICE: Is it going to come down to a yes?

DR. WALLACK: I was hoping for a yes.

MS. HORN: Okay. The next grant is 11SCA11, Yale University, 200,000, Jing Zhou, four peer review.

DR. HISKES: I have the name but I have a 13 by it, maybe I'm wrong. Probably I'm wrong. With Gerry? So I can begin. The P.I. is an associate research professor at Yale in anesthesiology. She has a Ph.D. in mechanical engineering, which informs this particular project. The title of the project is, Artificial Microfluidic Vessels to Direct HES Differentiation into Smooth Muscle Cells via Integrating Dynamic Mechanical and Chemical Hues.

The objective is to develop artificial

microfluidic vessels to see how really mechanical forces in the location of cells next to each other influences the differentiation and survival of smooth muscle cells. This might be very useful for coronary bypass surgery. She has very good preliminary data.

The reviewers described this as interesting and significant, but both reviewers expressed concern about the clarity of the protocols used and the likelihood of giving significant data. They say that the project is over defined and it tries to test too many variables at once. So there seems to be a question about the logic of the project and also, you know, a question about the clarity of the conception in the writing.

DR. FISHBONE: Yeah. I had the same feelings from the reviews, they doubt the efficiency of what they're doing. How to identify the purity of the targeted stem cell population is another concern. Trying to test too many unknown factors. You know, they're saying it significantly can broaden the knowledge of HESC differentiation mechanism, but I have a feeling that neither of the reviewers are overly enthusiastic about it.

DR. HISKES: So to me it looks like a no. No one -- the reviewers have not made a strong argument in any way.

MS. HORN: Further discussion?

DR. FISHBONE: I guess the main problem lies with the probability of successful data generation. It would have been easier to assess if the protocols had been better described. It doesn't sound like a lot of enthusiasm for the project.

DR. HISKES: No. You know, it's a very, very looking at individual cells and the mechanical and chemical forces on these cells to see what happens.

MS. HORN: So I'm hearing place this in the no?

DR. FISHBONE: No.

DR. HISKES: Correct.

MS. HORN: Okay. We will do that. Okay. The next grant, 11SCA23, UConn, 200, Bahram Javidi, four is the peer review.

DR. ARINZEH: Okay. This is -- they are proposing to develop photonic biosensor microscopy system. So it's a three dimensional -- they call it three dimensional digital holographic microscopy and optical coherent summigraphic microscopy system. That's a lot of stuff. So it's a highly sophisticated advanced microscope, okay? More or less. And they want to use that to characterize ES cell differentiation. They're

going from the undifferentiated to differentiated states, so developing actual, I guess, optical markers for that differentiation process.

And so they have a lot of technical information then about that system. The P.I. is a distinguished professor and has over 650 publications and so he's very well known for this type of, you know, technology. He's an electrical engineering professor.

So the primary reviewer and the secondary reviewer thought this was novel because it is a non-destructive, you know, system where you can monitor the cells over time and if you're able to come up with some markers and look at differentiation using this that would be great. But the reviewer did bring up that, you know, there isn't -- there doesn't appear to be a collaborator on the team that provides the biological expertise. So they don't have this -- and what's not in the proposal is about correlating differentiation influence with some of the, you know, whatever you're getting in the microscope with actual molecular descriptions of the cells. So doing that type of work would be needed.

And so the reviewer, primarily reviewer thought it was just, you know, if you kind of watered down a little bit with the microscope technique is just

characterizing cell morphology more or less as a descriptor differentiation. So for the prior reviewer it wasn't as enthusiastic. The secondary reviewer really didn't have anything negative to say.

So the score seems like what it is. So my recommendation is a maybe. So I don't know if you want to --

DR. HART: I agree with what you bring up. The only big issue that I found and one of the reviewers picked out as well is that they're not looking at individual cells, we're looking at more follow through colonies and there's a great deal of heterogeneity within the colonies for crying out loud. So I couldn't -- I would look through it several times to try to get through the engineering and the optics of it, which I don't know if I get the optics, but I was looking for a clue as to what they thought they could measure that would really help us in any way. I couldn't find anything. That's my worry.

DR. KIESSLING: You don't think pretty colonies are better than ugly colonies?

(Laughter)

DR. HART: No. No, I don't.

DR. ARINZEH: I'm not an ES expert, but if

you separate them from the colony doesn't it divide them --

DR. HART: You have to go in the colonies.

DR. ARINZEH: -- you have to go in the colonies. Okay.

DR. HART: Alright? You know, I was worried about what this really is going to accomplish.

A FEMALE VOICE: And maybe if it's --

DR. HART: I couldn't find it. And at least one of the reviewers couldn't find it either.

DR. ARINZEH: I guess when you have a secondary reviewer being so enthusiastic, I mean, this reviewer is kind of like go for it, it's novel, it's great.

DR. HISKES: It's fascinating.

DR. KIESSLING: Hope that this novel approach, although exploratory and risky will be successful?

DR. ARINZEH: Yes.

DR. HART: Yes, but not sure what success means in this system, that's my problem. And sure, it's great technology, great engineering, what's going -- how is he going to move the field of stem cells forward? I don't get it.

DR. WALLACK: So if we have these questions doesn't that maybe mean since we're going to have to make the cuts someplace that this one would be a no?

DR. HART: Well, this being -- while not a stem cell researcher it clearly involves -- he's clearly working with a stem cell group, but it's not very obvious here, but he's clearing working with a stem cell group. Being such a senior researcher I would give him an extra ding for not telling me what I need to know here and put it to the no.

DR. FISHBONE: It sounds like they have a wonderful technology and they're trying to find some way to use it and this may not be the most applicable way to --

DR. HART: And the worst part about saying no is that most of the money really, there's a little bit of equipment in there, but most of the money is to hire two graduate students to really do the program, do the work, but the work is going to be imaging and writing algorithms to describe the colonies. And I don't get what that get us. That's my worry.

DR. HISKES: And it won't pay off.

DR. HART: Yeah. If the P.I. had given me a good reason why that would help, why that would do

anything, I'd go for it.

DR. ARINZEH: Yeah. I don't have a proposal in front of me. I mean, they showed some preliminary data. There are -- you are able to see some distinctions between cells and those colonies. But how much depth I guess is probably the question.

MS. HORN: Consensus?

(Laughter)

A MALE VOICE: It looks like a no Marianne.

MS. HORN: Treena, is it a no?

DR. ARINZEH: I can live with a no.

MS. HORN: Okay. The consensus for this is to move it to the no category. The next grant is 11SCA24, UCHC, 200,000, Jay Lieberman, the peer review score is four.

DR. HART: Same two. Do you want me to go first? Want me to do this one first?

DR. ARINZEH: Go ahead, you go.

DR. HART: Okay. This is a very accomplished orthopedic surgeon at UConn Health Center who wishes to develop a combination of growth factor and iPS to come up with novel therapies for bone fracture in non-unions where you've got to clamp, you know, through hardware, chunks of bone together to get them to reform

that missing gap. He's got a history with growth factor induced therapies in these situations and wants to add the cellular component to it at this point as well.

The reviewers identified this as an ambitious project with a potential for direct application for development of novel therapies. It's something that, you know, again, if you buy the idea of these cells being close to being ready for therapeutic transplant it's almost ready to be used if there's any success whatsoever.

The applicants are highly experienced in bone repair. It's reasonably innovative quotes according to the reviewers. The criticisms includes the proposed use of a novel expression control system that was apparently developed by either them or a friend of theirs to attain long-term expression of growth factors and there's no consideration -- there's no proof whether that's going to be effective or not. Furthermore, they use a viral promoter that's likely to be epigenetically methylated and silenced over long-term expression the reviewers pointed out.

The reviewers also note that osteogenesis from MSC has been demonstrated but that ESC derived osteogenesis is more difficult according to the reviewers. There's a vague description of the iPSC to be generated

and a lack of iPSC characterization. Particularly cariotypic and genomic which is recently of great concern. So it's -- well, let me let you go next.

DR. ARINZEH: I'm in agreement. I think, you know, because this is right up my alley, this is kind of what I -- this is my area of research actually in the bone repair. So Lieberman is very well known and he does a lot of this kind of stuff and with genetic modification. He's done a lot with the mesenchymal stem cells and I think he has a grant now with just the ES cells and so he's just kind of moving now into the iPS and is trying to use similar types of technology here.

But so I agree with the reviewers in that this is, you know, he may not have worked out issues there with the iPS and the reviewers are concerned about his lack of experience with the iPS and maybe being concerned here. So I think that's where kind of this lower score is coming from. And again, pilot data is something they suggest having some additional pilot data. But it's a very strong group.

DR. DEES: But this is a very established researcher --

DR. ARINZEH: He's established.

DR. DEES: -- but a core seed grant move

into iPS stuff.

DR. ARINZEH: iPS, right. He doesn't have iPS.

DR. DEES: That seems like an appropriate use of a seed grant. Is that right?

DR. ARINZEH: Yes.

DR. DEES: Do we expect the same preliminary data? I mean, because he had a mixture, right?

A MALE VOICE: Yeah, that's the problem.

DR. DEES: Right, because he's established on the one hand and on the other hand he's very --

DR. HART: We just had a case of that you answered about a post-doc who submitted a grant a month after they had come to the lab and was criticized for having data (indiscernible, too far from mic.) the lab, but that was the situation, they just showed up, wrote the grant, submitted it and there we are. Here's someone who's whole career has been on things related to this topic and now they're using same cell type and suddenly they're eligible for this grant. We expect a little bit more sophistication coming into the room from this guy. That's all.

DR. HISKES: Is it going to work?

DR. HART: I don't know. What do you think? Do you think it's going to work?

DR. HISKES: Do you think it's going to work?

DR. ARINZEH: You know, he's shown --

DR. KIESSLING: If it works is it important?

DR. ARINZEH: -- I mean with other stem cells has very nice pre-clinical data using these types of factors.

DR. KIESSLING: If it works how important will that be?

DR. ARINZEH: Well, bone is a tough area because there are a lot of products out there that are used to regenerate bone. These critical size defects, which I think is what he's referring to here, which usually shows in his models, they are challenging to repair. But, you know, there is a company or two out there that have very good products that are doing extremely well and these are just using growth factors to treat those defects. Or the surgeon will use allografts, auto grafts to repair the defects and it's okay. I mean, the percentage of defects that actually don't repair is relatively small when you talk to surgeons. So I guess

it's -- I don't know, it's kind of --

DR. WALLACK: So clearly we have something that's on the fence here. I wonder if the fact that there's some tangential connection to Drissi, who is his collaborator, Drissi's work that I think we funded at SCB08 or proposing to fund, I'm wondering if since a lot of that work -- some of that work may already be done in that other grant if we can therefore since we're having such a difficult time move it to the no since we're not going to lose a whole lot by doing that?

DR. HART: Let me ask that same question a different way. This particular researcher, this particular group, what's the effect if this $200,000 project doesn't get funded, does this work stop?

DR. ARINZEH: I don't think so. This guy is well funded.

DR. HART: There's my answer.

DR. WALLACK: So that's about what I was asking.

DR. HART: If it was up in the two's I would change my opinion, but being here and being on the fence I'd rather give the money to an up and coming young post-doc.

DR. WALLACK: Then think about it as a no

then Ron?

DR. DEES: I think at this level of scoring it would have to be a very good reason for moving it up.

DR. HART: Up meaning to a yes?

DR. DEES: Right. You know, funding, and it doesn't sound like that's been presented.

DR. KIESSLING: It's not like we're moving it down.

MS. HORN: Okay. I'm hearing a consensus for moving this grant to the no's? That will go to the no category. The next grant is 11SCA36, UCHC, 200,000, Blanka Rogina, peer review of four.

DR. KIESSLING: This was one of my applications to review. This is a really fun proposal from a drosophila scientist who is looking at a gene called INDY, which stands for I'm Not Dead Yet.

(Laughter)

DR. KIESSLING: So the INDY gene is -- it's in the mid-gut of drosophila, it keeps their guts alive. She wants to look to see exactly --

(Telephone recording)

DR. KIESSLING: -- we're talking about INDY. But I think that this -- there's little reason to move this into the funding category as the reviewers point

out because this investigator has not really shared with us how her work is going to relate to either any kind of human disease or any -- certainly any embryonic stem cell research. So this is a wonderful basic drosophila project and if this scientist could relate it to even growth and longevity of ES cells in culture it would be useful, but that's not part of this application. So I think all things considered this is going to have have to go in the -- INDY is going to have to go in the no category.

A MALE VOICE: It is dead then.

DR. KIESSLING: It is dead.

MS. HORN: Is there a secondary -- or second reviewer?

MS. MANDELKERN: If you'll allow this breach of protocol could I just speak for Bob just a moment? He did discuss this with Ann and he's just not available at this moment and not to hold you up. But he did discuss this with Ann and I think you agreed on the vote of no and did I hear you correctly?

DR. KIESSLING: Yes.

MS. HORN: Okay. So the consensus is --

MS. MANDELKERN: (Indiscernible, telephonic testimony).

MS. HORN: -- thank you. The consensus is

that we move this to the no category.

DR. KIESSLING: This is a wonderful project, but not for this group.

MS. HORN: Okay. 11SCA39, UCHC, 196,836, Jonathan Covault, the peer review score is four.

DR. KIESSLING: This is also one of my applications to review. This is a much -- this was much tougher for me to review because I think this is a really good approach. So this is a psychiatrist who studies alcoholism and they are --

DR. GENEL: Also a geneticist.

DR. KIESSLING: -- he's a geneticist, right. And they are interested in deriving a bank of iPS cells from alcoholics and from non-alcoholics and attempting to derive -- to differentiate those iPS cells into neurons to see if there's any way that this approach is going to in any way provide a model for alcoholism. And they do a nice job of pointing out not only the substantial social and the economic impact of alcoholism as a disease in this country.

They have already collected a bunch of skin samples. They've got quite a bit done. The goal of this project is actually to see if they can differentiate these iPS cells into any kind of functioning neuron.

The reviewers were pretty split on this. One of them appreciated how important the work was and how good the investigator was and the other one -- and the other one really thought that it was going to be highly speculative. Thought that the process they were going to use to differentiate them into neurons was too tedious and they didn't know how this was going to work.

I -- my take on this is that this is a really important problem and this I think is a good example of a seed grant. And they are asking for support. I can't remember exactly what they are going to do with the money, but I think what they're going to do is really just support their culture and a person to help with the culture project. And if this would work, if they could actually develop -- use iPS cells, which I think is also this is a good application of iPS cell technology, they could actually derive lines of neurons from iPS cells from these two groups of people it might be very helpful.

DR. GENEL: They already have lines on five alcoholics.

DR. KIESSLING: They have some lines, right.

DR. GENEL: So they want the money to get three additional lines and do the comparative -- and then

do the comparative studies. I won't add anything. I agree completely with what Ann said. I think this is the prototype of what we had in mind when we created the seed grant.

DR. KIESSLING: Right.

DR. GENEL: Yet it's speculative. So what?

DR. HART: I'm kind of smiling at all this because since the deadline for this grant program there was an RFA from alcoholics to do exactly this for an R-21 program that would award six projects. So I wouldn't be surprised if they applied for that as well. But it was exactly this.

DR. GENEL: Exactly this?

DR. HART: I mean, you could have written the RFA based on what you just said about this grant.

DR. KIESSLING: So I would recommend that this go in the yes category.

MS. HORN: Any further discussion? Okay. Consensus is to put it in the yes category.

DR. KIESSLING: It's not even quite 200,000.

MS. HORN: The next grant is 11SCA41, Yale University, 200,000, Jean-Leon Thomas, four peer review. Who has this for a review?

DR. WALLACK: I do.

MS. HORN: Okay.

DR. WALLACK: Who else has it? I think I do. The notes that I have on it are that it might have value in a therapeutic approach for brain repair or treatment of nerve degenerative diseases. But -- but the project as outlined has many weaknesses, many problems to it, and I -- without going through all of the peer review comments on the weaknesses would jump to the idea that I would recommend not funding it, do not fund this.

MS. HORN: Ann, I think you are the other reviewer?

DR. KIESSLING: Me? Am I?

DR. HISKES: It's not me.

MS. HORN: No, Ann Kiessling.

DR. KIESSLING: Oh, I remember this. I'm sorry. Yes. Yes. This had -- this had some problems. Yeah. Yes. So this is a -- there's not an argument to be made to move this project into fundable. That's basically the way to put it.

A MALE VOICE: It sounds like we're done.

MS. HORN: So the consensus is to move it into the no category?

DR. KIESSLING: Yes. This is an

interesting project but it's not fundable the way it's written now.

MS. HORN: Okay. Thank you. 11SCA42, Yale University, 200,000, Xin Ge, four is the peer review.

DR. DEES: I'm one of the reviewers. I'm not sure who the other one is.

DR. FISHBONE: I'm the second.

DR. DEES: This study is to develop techniques to produce smooth muscle cells from reduced pluripotent cells to enhance research into supra aguilar (phonetic) aortic stenosis. The peer reviewers thought the studies were very global and important though they didn't think they were being particularly innovative about them. And one noted that there was a better technique available for doing work that they had proposed. So it wasn't quite clear to me why this got as bad a score as it did on the one hand and I'm worried because one of the grant reviewers got the sex of the applicant wrong so it made me worry about whether they were reading the applicant page very carefully so it made me doubt where that score was coming down. I'm not sure what to make of it. I don't have the scientific background to be able to say they're wrong about the science or something. It just made me worried about what we were getting from the peer

reviewers.

This grantee is a post-doc, fairly new to this lab, so I was in the maybe category because it seemed like (indiscernible, too far from mic.) reviews.

MS. HORN: Dr. Fishbone?

DR. FISHBONE: Yeah. I didn't think the reviewers were very positive. They say that it's straightforward in theory but excessive and complicated experimental. Concern about the assessment of the SDAS, IBSC's in terms of their micro-mutations ongoing analysis, etcetera. It's important but very little innovation. There are numerous studies underway that focus on patient-specific IBSC's and they don't know where they're getting their cells from.

The secondary reviewer says it's not clear what's the source of the cells. Litany viral vectors for reprogramming are obsolete. It doesn't sound to me like they were very impressed with the grant.

DR. DEES: I mean, it struck me that they didn't say as many negative things as I would have expected.

DR. FISHBONE: I don't think there's any reason to move it forward ahead of other grants.

DR. DEES: I'm okay with that.

MS. HORN: So the consensus on this grant is no. Any further discussion? Okay. We'll place that in the no category. The next grant is 11SCA45, Yale University, 200,000, In-Hyun Park, with a peer review of four.

DR. KIESSLING: This is the project that we just needed to -- was just discovered had no reviewers, right? Is this it Chelsey?

MS. HORN: That's correct, yes.

DR. KIESSLING: So this is the seed grant from Dr. Park and it's title is he wants to look at the role of methylating -- CPT methylation in Wet Syndrome, which is an interesting syndrome to study. It's a common retardation syndrome in females and there's actually a lot of laboratories studying this because it looks like it's going to lend itself to dissection of why this mutation causes the --

DR. GENEL: The geneticist I think at Baylor is the woman who got --

DR. KIESSLING: -- who discovered it?

DR. GENEL: -- yeah, and who I think has got some big (indiscernible, too far from mic.) prize or something recently.

DR. KIESSLING: Yeah. Well, anyway there's

also a few labs in Boston that are also working on this. The project has a couple of aims and the peer reviewers were not enthusiastic about this project partly because one of the aims is to improve the protocols to generate cerebella neurons in HES cells and he sort of goes through just some kind of standard rhetoric about doing it as if somehow applying these in his laboratory is going to make a difference.

And then the second one is to dissect the regulatory mechanisms and if aim one doesn't work then aim two is not going to work. So I think the enthusiasm for this project which appears to be rather quickly described wasn't high on the part of the reviewers and unless we can identify the model of Wet Syndrome as being super important I don't know that we're going to be able to move this up to fundable. I'm willing to put this in a maybe category while we consider everything else, Dr. Park's other grant.

DR. WALLACK: So am I the other reviewer on this?

DR. KIESSLING: Yes. Chelsey asked us to do this yesterday.

DR. WALLACK: Right. So I would actually vote to keep it in the no category. The project has a

number of weaknesses. One issue for example is that Dr. Park and his immediate co-investigators lack the expertise to generate the neurons from the human embryonic stem cells. The -- another comment is that the proposal is not focused and did not take full advantage of it's potential.

One of the things that the second reviewer also had significant -- found significant weaknesses in the proposal. And my feeling is, as Gerry has indicated before, that it has to have real compelling reason to move it into a possible funding category and I just don't see that in what I'm reading. There's also an indication that, and I could be wrong on this, Ann, I'm going to ask you to help me out with this, but did they reference a published paper?

DR. KIESSLING: No. I don't think so.

DR. WALLACK: No?

DR. KIESSLING: Maybe I don't have that -- oh, wait a minute. No, they missed a paper. Yeah, they missed a paper.

DR. WALLACK: Right. So what happened is that the -- in putting the grant together there was a paper that was supposedly written pretty much about -- around the same kind of thing that they're doing and there's a sort of criticism or a citing on this that maybe

that should have been cited.

DR. KIESSLING: Right.

DR. WALLACK: It wasn't cited. So the fact that it's got a lower rating, the fact that there's no compelling reason to move it and the fact that, you know, I have these other issues with it I would really want to keep it in the no category.

MS. HORN: Okay. Further discussion?

DR. KIESSLING: I'll go along with that.

MS. HORN: Okay. Then that will go into the no category.

DR. KIESSLING: What happened to A42?

MS. HORN: We just don't have our transcriber here. Chelsey.

DR. KIESSLING: Oh, Chelsey.

MS. HORN: Yeah. So we'll try to check. 11SCA02 is the next grant, Yale University, 200,000, Anna Kloc, and it's a 4.3 peer review.

DR. HISKES: I'm one of the reviewers.

DR. FISHBONE: Do you want to go ahead?

DR. HISKES: Okay. So the P.I. on Kloc is a new post-doc in Natalia Ivanoff's (sic) at Yale. The title of the project is, The Role of DTDPPA2 Lineage Specification of HES. What she wants to do is -- she's

very interested in events regarding the separation of the three primary germ layers, the endoderm, mesoderm, ectoderm. DPPA2 is a gene that regulates this differentiation and it turns out that knock outs of DPPA2 in mice embryonic stem cells showed severe defects and differentiation and can't become neuro-ectoderm. So she wants to investigate the role of this particular protein in the ectoderm lineage. And to look at the role of this in lineage specification and pluripotency, identify this protein in controlled molecular networks that regulate development and wants to then look at the third aim is whether this protein improves iPS generation as well.

The reviewers -- reviewer number one describes this as a very significant project, will lead to deep insight into neuro-ectodermal differentiation. Says the P.I. has done relevant preliminary work with DPPA2 knock out in mice. And then the reviewer number one has a few things he or she would like to add to the project. Namely questions the significance of the level of knock out achieved and would be to titrate levels of DPPA to determine whether this effect occurs. So that's something that could be included in the protocol.

Wonders why the P.I. uses a certain thing to help grow HES's, but again that's sort of a minor thing

that can be adjusted. So reviewer number two is very positive -- or reviewer number one is very positive. Reviewer number two doesn't say anything specifically negative about the project but rather says that the post-doc and the mentor are not experienced in the area and therefore is skeptical. And I'm not sure about the validity of that criticism.

The mentor, Natalia Ivanoff (sic) has a list of publications about, I don't know, looking at the genetics of stem cell differentiation, and so I would have to defer to a scientist to asses the validity of that criticism. That neither have experience in this area so it's not going to work.

DR. FISHBONE: Yeah. They say lack of evidence in experiencing -- in experience of the culturing and using human embryonic stem cells.

DR. HISKES: But I don't know if that's true.

DR. HART: Natalia Ivanoff (sic) was a key part of the Maska's (phonetic) lab and moved to Princeton to work and was the very first lab to really knock down kind of wide scale, she was involved in pluripotency and huge screens with embryonic stem cells. So that's definitely not true.

DR. HISKES: I think it's a bogus criticism.

DR. HART: Not to pick on the reviewers.

DR. HISKES: No. So I just question the validity of that and --

DR. FISHBONE: That was reviewer number two again.

DR. HISKES: -- and confirm skepticism so I would put it yes.

MS. HORN: Put it a yes. Dr. Fishbone?

DR. HISKES: That's my recommendation.

DR. FISHBONE: I had mixed feelings about it. I was a little bit convinced by the reviewers which apparently was not correct that they had no experience in this. It's hard for me to evaluate the project because it's an area that I didn't know much about. But the other thing they say is the mentor is turning out of funding and what will her role be, is that a valid -- I mean, is there a reason to do it for the funding category at a 4.25?

DR. HISKES: Well, the mentor is what, Natalia Ivanoff (sic)?

DR. FISHBONE: Yeah.

DR. HISKES: Ivanova?

DR. FISHBONE: Yeah.

DR. HISKES: So I presume she'll be funded sometime.

DR. HART: We chose not to review because of the cutoff we didn't look at one of her grants that she was a full investigative grant I reviewed and it's -- one of the things about that grant that concerned me was that she didn't have any publications since 2008 when she moved to Yale. So I suspect it's a funding situation as well.

DR. FISHBONE: And I feel I would need advice from somebody in the field on this one because I don't know that I can really evaluate it and we can't trust the reviewers. What did you feel about it, should it be moved up? I'll make it your fault.

DR. HISKES: Well --

DR. KIESSLING: Should we put it in maybe and we can -- some of us can look at it? I didn't look at this grant.

DR. WALLACK: I would put it in maybe for another reason also and that's the presentation of the grant. I mean, I know we referred to some of the sloppiness sometimes in the presentations of the grant and this presentation had some awkwardness to it and I would endorse the maybe also.

MS. HORN: So it sounds like the consensus

from the group is to put into the maybe, perhaps do a little review over the coffee break and see if we can discuss it during the next round.

DR. WALLACK: Yeah.

MS. HORN: Okay. Thank you. Okay. So the next grant is 11SCA21, Yale University, 200,000, Erica Herzog, 4.3. And Dr. Arinzeh and Hiskes are the reviewers.

DR. ARINZEH: I can start. Okay. So this investigator is going to be looking at the biology of fibrocytes, which she believes contributes to the condition of Scleroderma. So where you have -- where you get fibrosis in organs, in particular, 70 percent form in lung disease. So she thinks this cell type is a contributor to that. And she's going to look at different factors, additional proteins that also may be involved in their biology differentiation.

So I don't know, I mean, I'm not familiar with this cell type, fibrocyte, but I'm assuming that it's not a stem cell so I'm not really sure if it's quite applicable to what we're going to be funding here. The reviewer doesn't mention any of that, but maybe I'm off and I don't know if any other researcher is familiar with this cell type? But I did a quick review myself in the

literature just to see and people are describe it as being a progenitor of -- it's derived from the hemopoietic stem cell turns into a fibrocyte, so I'm just -- I don't know. So besides that the reviewers also were not favorable, so they cited a bunch of weaknesses in that experimental design, rationale, things like that were not clearly spelled out.

So they found some major weaknesses there, so I would say no for funding.

DR. HISKES: Again, it's, you know, the reviewers were not particularly positive about -- about the logic of this. They didn't think it was well thought out. During nebulous experiment (indiscernible, too far from mic.). I would concur with a no.

MS. HORN: Okay. The consensus on this seem to be put it in the no category. And the last grant, 11SCA38, Yale University, 200,000, Julie Ann Sousa, 4.3 is the peer review.

DR. WALLACK: So it's an interesting proposal to treat hypoparathyroidism. The grant however has many weaknesses. There's lack of preliminary data. It has budget questions and I would vote no.

A MALE VOICE: I was the second reviewer and I agree.

MS. HORN: Any further discussion on this grant? The consensus is no, it'll be placed in the no category. And I would suggest we take a five or 10 minute break. There are some cookies and drinks behind us and come back and figure out where we go from here.

(Off the record)

A MALE VOICE: So Marianne, have we finished now officially?

MS. HORN: Have we finished? Are we at 9.8 mil?

DR. KIESSLING: Round one.

MS. HORN: I think we're at 20,000,000, so we've got a little work to do.

DR. KIESSLING: We're still at 20,000,000? Can we ask for more money? What was that about philanthropy?

A MALE VOICE: We're at $9,000,000?

MS. HORN: We are at $9,000,000.

A MALE VOICE: Just for the yes's.

DR. KIESSLING: For the yes's, oh my gosh, we're done.

A FEMALE VOICE: I say we keep it and call it a day.

DR. KIESSLING: Oh, is this for all the

yes's?

A MALE VOICE: That's for all the yes's.

MS. HORN: So if we look here Dr. Hart and Dr. Dees prepared this amazing spreadsheet. Oh, it's just him?

A MALE VOICE: You're giving me credit.

CHAIRPERSON MULLEN: I'd point out something that is a positive on it. What was announced in the paper from Friday was the $9.6 million cut to public health for the State budget. So I just want to point out that this funding that we can award really does, as you know, but I'll just reiterate, represent a very strong commitment from the government, from this administration to this work because we just -- not because, I'm saying this because if you look at all the programmatic cuts and layoffs that we announced they totaled $9.6 million just about. So just perspective. Just perspective.

All the conversation about the scientific merit and the future impact for population is something that I think we can also just keep in perspective as we do this. And if anybody asks, since I'm a primary care doctor who, you know, has prevention as a middle name, I can, you know, attest to the thought that has gone into all of this from everyone and I appreciate that. So I

won't be mad, but I just want -- I might as well just pause and put that out there.

DR. WALLACK: And we appreciate that also.

A MALE VOICE: 30 percent of the budget is the two grants.

DR. HISKES: Yeah. I want to look at that.

DR. FISHBONE: Could we look at some of the bigger grants and see whether they need all the money that is allocated?

A MALE VOICE: So the disease grant, of course their committee asked for this year knew.

A FEMALE VOICE: Yes. So we should talk about the next step.

A MALE VOICE: And the truth is both of these grants are disease grants.

DR. WALLACK: Now that we're going back could we possibly -- I know in the past we have looked at the possibility of keeping the seed grants at approximately 20 percent I think, $2,000,000.

A MALE VOICE: 2,000,000 as I recall.

DR. WALLACK: $2,000,000 and so can we possibly go back to the seed grants and see where we are with that?

DR. KIESSLING: We're at 1.4

DR. WALLACK: 1.4?

DR. KIESSLING: 1.4 yes's in the seed grants. Seven yes's and five maybes.

MS. HORN: We did take that limit out of the RFP. I don't know that that reflected a decision on the part of the Advisory Committee to not be quite so tied to the 10 percent going to that.

DR. WALLACK: No, I understand, but I mean, just as a starting point that would give us at least a framework to work within. So if we have seven, does anybody mind going back to finish the seed grants?

MS. HORN: We did.

DR. WALLACK: No, I'm talking to finalize it.

MS. HORN: Oh. Well, we thought maybe what we would do is revisit some of these big grants so we know how much money we have.

DR. DEES: Well, if we're going to fund seed grants we have to cut some of the big ones.

DR. KIESSLING: We have to cut some of the big ones.

DR. DEES: Okay. I mean, we've got about $1,000,000, we're at 8.9, is that where we are? We're at nine effectively, so we've got $800,000. So we can fund

four more seed grants with the money we've got without doing anything. If we didn't mess with anybody's grants we could give four of the five maybes. Why don't we do that first?

DR. KIESSLING: Well, I think we should go back to the yes's and finalize our yes's then you know what you can do with the maybes.

DR. HISKES: I don't think we should -- I think our primary focus should be quality, should be the quality of seed grants and not say, well, we've got to do 10 so let's find 10. So maybe there aren't 10 that we'd want to fund.

MS. HORN: And I think what the priorities were for this year was the disease directed group grants?

A MALE VOICE: Right.

DR. DEES: Yeah, so let's start there.

(Indiscernible, multiple voices)

DR. DEES: Well, if you wanted to do something, I mean, the one grant, the Chondrogenics grant was placed in the group grants, which has a 1.5 limit. So we could say, well, you asked for a grant that was 1.5 so we'll give you 1.5.

MS. HORN: That's true.

DR. KIESSLING: So can we just go through

the big yes's and see if we want to do anything with those budgets? And then we can come up with a new bottom line.

DR. HISKES: Right.

MS. HORN: Is that acceptable to the group? We'll revisit the big numbers?

MS. SARNECKY: I'm just going to highlight them both so --

DR. KIESSLING: Well, the top one, shall we start with the Wolin grant? That's $750,000, is that three years or four years? I think that's me. Is that me? I think it's me.

MS. HORN: That is you and Anne Hiskes.

DR. KIESSLING: Yeah. I think it's us Anne.

DR. HISKES: Okay. Let me look.

DR. KIESSLING: I've got it here somewhere.

DR. FISHBONE: Who had Wolin?

DR. KIESSLING: I did.

DR. FISHBONE: Do we have that information up there? I'm concerned about (indiscernible, too far from mic.) going up and down.

A MALE VOICE: It's four years.

DR. KIESSLING: Okay. So that's -- that was one of our highest scoring grants and she's asking for

a reasonable amount of money for four years, so my recommendation would be to not touch that.

MS. HORN: Alright. For the next one?

DR. KIESSLING: SCC01.

DR. FISHBONE: That's a combination of the Chondrogenics and UCHC.

MS. HORN: So it's Dees and Fishbone.

DR. KIESSLING: Does it have two reviewers?

DR. DEES: I was one. No, it does not have two peer reviewers.

DR. FISHBONE: This is three years.

MR. MANDELKERN: Are we allowing threes?

DR. FISHBONE: Three years for the Dealy budget.

MS. HORN: They were discussing 11SCC01, Chondrogenics, Caroline Dealy.

DR. FISHBONE: Yeah. Which the subcontract to UCHC was 1.123 million.

DR. WALLACK: So at best there's going to be a very, very difficult rationale for cutting any of that, is that right?

DR. KIESSLING: Maybe not.

DR. WALLACK: Well, for the most part Ann. Not across the board. Not across the board. I know in

the past we've done this and every time we've done it it's been accepted. It has not interfered with the system. If it's a three year grant and not a four year grant and it is 16 percent of our budget, I mean, I don't know -- I can't scientifically tell you why we should cut it, but I think maybe it's the kind of decision from a pragmatic standpoint that we have to do in order to again, increase the pool of researchers. And I would recommend that we agree on an amount, if $500,000 is an amount that we feel that we can reduce this by maybe that's a starting point. And I can't give you a more rational reason for it other than for the fact that I know something like that has to be done.

DR. KIESSLING: Was there a ceiling in the RFA, any kind of ceiling?

MS. HORN: This is a group grant and technically the funding limit on it is 1.5 million.

DR. HISKES: Is there a limit on disease grants?

MS. HORN: And the disease grant was, let me just check those figures.

A MALE VOICE: 2,000,000.

DR. HISKES: Okay.

DR. WALLACK: So this is already above the

amount?

MS. HORN: It looks like the researchers misclassified it. Let's see. Group grants 1.5 and the disease directed collaborative group project award up to 2,000,000.

DR. WALLACK: Marianne, just to get the conversation going I'm going to --

DR. KIESSLING: And how many years?

MS. HORN: Four, four years.

DR. WALLACK: -- I'm going to recommend that we reduce it by $500,000.

DR. HART: What if instead -- what if instead --

CHAIRPERSON MULLEN: If I could just point out just for one second? I'm sorry.

DR. HART: -- sure. No problem.

CHAIRPERSON MULLEN: I encourage us to try to stick to one train of thought at a time so that every valid consideration can be fleshed out the way it needs to. I just -- it's hard for me personally to track when we go from one bit of a conversation to another and I'm not sure we do justice to what anybody's trying to present. Now I understand that in discourse sometimes means that people are going to say different things, but

we've put a lot into this process and I want us to think we still have some framework that we're following for this portion of the discussion as well.

And I will tell you what the rank ought to be in consideration. I hear you talk about for example increasing the pool. Well, that's one consideration, but I don't know that that's the number one priority. So all of this is about increasing a pool and job creation on the foundation of good science, the scientific merit and future benefit for the population. So that being said let's see how we can keep the conversation going, okay?

DR. HART: Okay. I understand Milt that your goal is to do some cutting to try to extend the pool somewhat and I don't disagree with the concept of course, and of course we've got to be careful about that that we don't ruin one project to save another. Since this year we worked to introduce the idea of these disease group grants and this is the theme of what we were proposing to accomplish this year I think we ought to set a goal that we have a good large chunk of funding this year go toward that goal. Right now we're over 30 percent of our budget, so maybe that's not the right goal, but let's start with that number.

If we're going to do some cutting I would

argue that we should do less cutting from those that have been deemed to be the most scientific worthy and the most highly rated. So for example, Chondrogenics --

A MALE VOICE: So goal directed?

DR. HART: -- yes. The Chondrogenics one is not the highest rates of these projects. The one thing that we could pull out of our hat if we wish to cut a little bit would be to say, well, they actually applied for a grant that's a $1.5 million limit. We can say, well, that's all we're going to give you and we'd be within our rights to do so I think. And that would be by our consideration full funding. Okay? That's a small way to take a small cut.

A MALE VOICE: Okay.

DR. HART: And then you might consider a little deeper cut in a lower graded one to be balanced. But I'd say maybe 25 percent of the total budget this year to go to these two grants would not be out of line.

DR. KIESSLING: This is a beautiful grant.

DR. HART: Yeah. That's why I'm saying that. I'm arguing for very little cut here.

DR. KIESSLING: I'm looking at the budget now.

DR. WALLACK: So Ron, I would as a starting

point I can understand that and go for that.

DR. HART: So if we recommended on SCC01 to fund it at the theoretically the limit of $1.5 million for this program that would be acceptable?

DR. WALLACK: I would endorse that.

MS. HORN: Okay. Is that the group consensus here, to reduce this budget to 1.5 million? Any objections? Okay.

DR. FISHBONE: I have one other point at this moment. The other big grant, which is pending over us sort of like a large umbrella, is the core grant for Yale, which is 2.5 million. We might be able to look at that.

DR. HART: Right. Well, right now that's not even in the yes category yet.

DR. FISHBONE: It's in the maybes?

DR. HART: Yeah.

DR. FISHBONE: So I think it was my sense of the discussion was it was probably going to be in the yes, but with a significant budget adjustment. Is that wrong?

DR. HART: So right now then with the two large projects in the yes category we're at 32 percent of the total budget for those two things, right? 3.2

million, I'm rounding us to 10,000,000 just for convenience sake. Do we wish to look at the DIS02 project and look and see if we can reduce the total effort on that?

A MALE VOICE: I think we have to.

DR. HART: Okay.

MS. HORN: 11SCDIS02.

DR. WALLACK: I think Ann and I were.

A FEMALE VOICE: Or do you want to just go in order? Do you want to look at this --

DR. HART: This is such a big chunk it changes all the other decisions.

A FEMALE VOICE: -- okay.

DR. HISKES: I think this is a good systematic change.

DR. HART: Let's set our percentage goal for this category and then move on.

A MALE VOICE: I agree.

DR. HART: This decides everything.

MS. HORN: Bob, we're looking at 11SCDIS02, the other disease directed group grant.

DR. WALLACK: So in this particular grant one of the -- to be a little more substantive on it we have a recommendation or one of -- the second reviewer

indicates that there might be able to be a reduction in the grant. And so this one we might be able to reduce. Ann, what would you be comfortable reducing it? But I definitely think there's room to reduce it.

DR. KIESSLING: Yeah. Right. I'm looking at the budget right now. This is only a three year grant I think.

DR. HART: It's going to have to be a little arbitrary unfortunately.

DR. WALLACK: Well, that's what I said before. It's all arbitrary.

DR. DEES: If we put it in at 1.52, would that be --

DR. KIESSLING: Well, this one evidentially has a cap of 2,000,000.

DR. HART: Right. But you have your choice.

DR. WALLACK: Yeah.

DR. FISHBONE: I propose to put this at 1.5.

DR. HART: That would give us a total of 30 percent for the large so far.

DR. FISHBONE: That's what you were looking for, isn't it?

(Indiscernible, multiple voices)

DR. HART: Well, I mean, I was wondering if we could get to 25, that's my -- I'm just asking, I'm not telling you.

DR. WALLACK: That's a good point. So guys?

CHAIRPERSON MULLEN: One person at a time please.

DR. WALLACK: Go ahead Ann. Do you want to do it?

(Telephone recording)

MS. HORN: We're really having a lot of activity here, so --

DR. KIESSLING: I wanted to kind of review this budget for a minute. At some level you might be able to argue that you could use the reviewers' comment and cut this back to the same amount of the other ones.

DR. HART: There you go.

DR. WALLACK: That would still be 30 percent though. Ron, what was your suggestion a moment ago? 25 percent?

DR. HART: Well, I was asking whether it was possible at 25 percent just in the idea of broadening the base, but that's a decision for the Committee.

DR. WALLACK: I can see us cutting this one. This is a two year grant Ann?

DR. KIESSLING: No, it's three years. That's what I was trying to find.

DR. WALLACK: Three years?

DR. KIESSLING: I think it's three years.

DR. WALLACK: Based upon the peer reviews recommendation --

DR. KIESSLING: The other consideration for this grant is that one of the investigators also has a grant. So one of the investigators here is Dr. Rasmussen and I don't know what the outcome of his other --

DR. HART: He's in the maybes, currently maybe.

DR. KIESSLING: -- he's currently maybe. Okay.

DR. HISKES: So we're not allowed to talk about this now?

DR. KIESSLING: No.

DR. HISKES: However, were I to speak I would say --

(Laughter)

DR. KIESSLING: You can tell me.

DR. HART: So --

DR. KIESSLING: Let me see -- let me see what the budget is here. Yeah, the seed grant from Rasmussen, I think it's actually quite different. So they're asking for a post-doc and four graduate students. And what did the reviewers say that they thought --

DR. HART: -- it reduced -- that their functional analysis could be reduced to one to one and a half persons to do focus studies on monocondral (phonetic) activity.

DR. WALLACK: Right. So how much would you be able to cut on that basis?

DR. GENEL: Not a heck of a lot.

DR. WALLACK: It's a lot.

DR. GENEL: No, I don't think so.

DR. WALLACK: No?

DR. FISHBONE: Your post-doc associate -- one post-doc associate for 12 months is 44,000.

DR. KIESSLING: It's only 38 in these budgets.

DR. GENEL: Well, I'm looking -- it just happened where I opened the page. But it's in the -- you knock off 1.5 you're not going to get to where we were.

DR. WALLACK: What are you saying Mike, we have to cut more off or what?

DR. GENEL: Yeah, more. No, I mean, if you -- what did the reviewers say, they could cut back personnel by one and a half?

DR. FISHBONE: One to one and a half.

DR. GENEL: Well, that's 50,000, 60,000.

DR. KIESSLING: So this is a three year grant --

DR. GENEL: I don't know, maybe with some overhead, it was 100,000.

DR. KIESSLING: -- this is a three year grant just like the other one.

DR. FISHBONE: At 1.5 you'd be giving them 500,000 a year.

DR. WALLACK: Right. Right. So do you want to then recommend the 1.5?

DR. HART: Why don't we say 1.5 for now and see where we are and then we may temper back and revisit it?

DR. WALLACK: Right. I think that's a good idea.

DR. KIESSLING: I actually think that's going to probably just about -- going to get back to 1.5 people because they've got four or five people each year. They've got four graduate students and a post-doc every

year it looks like. I'm trying to figure out what the company's budget is. Minor, I realize it's minor.

DR. HART: I'm sorry, what are you looking at?

A MALE VOICE: That's the company's budget exclusive of cell.

DR. KIESSLING: Oh, no, that's right. This isn't the company budget, this is three separate budgets, isn't it? Okay.

DR. WALLACK: So Marianne, why don't we put it at 1.5 for now and we'll -- we can leave it open still?

MS. HORN: Okay. So the consensus is to cut this -- the grant to 1.5 million.

DR. WALLACK: Right.

MS. HORN: Is there any opposition to doing that and revisiting it as we move along?

DR. KIESSLING: Yeah. So that would be 30 percent of our budget because this is actually like four or five big projects.

DR. HART: Yeah, it is and so, you know --

DR. DEES: And it's four or five big projects about what we said we wanted --

A FEMALE VOICE: Wanted to review.

DR. HART: What are we going to say, that,

you know, that we spent $3,000,000 on disease and teams to solve diseases.

DR. WALLACK: Right.

DR. HART: That's the right answer.

DR. WALLACK: That is good.

DR. FISHBONE: Disease oriented. So that gives us about 400,000 to put in one thing.

DR. HART: Yeah, it's two seed grants.

MS. HORN: Alright. So what is our strategy from here on in?

DR. KIESSLING: So I think we want to look at the big grants, the 750,000 grants. I think they're for four years or three years.

DR. HART: We already looked at Walin. We're down to Drissi.

MS. HORN: Okay. So we're revisiting the established grants.

A MALE VOICE: And Drissi we've already cut back.

DR. HART: That one's already been cut. So now we're down to Vaccarino.

MS. HORN: So we're looking at 11SCB23, Vaccarino. It's currently at 744,446.

DR. KIESSLING: This is a stretcher, we can

get out the stretcher.

DR. GOLDHAMER: This was the grant that had 10 percent effort by the P.I. and one post-doc and 65 percent of another staff member. And 40,000 a year in supplies that includes mice.

DR. KIESSLING: This is three years, right?

DR. GOLDHAMER: This was three years, it did not seem to me to be an excessive amount of -- excessive budget for what they're trying to do.

DR. HISKES: The reviewer says the consumable costs seem relatively low compared to other costs.

DR. KIESSLING: I don't know how a mouse got to $23. Okay. If there's nothing --

DR. GOLDHAMER: It's also among the higher rated grants as well.

DR. KIESSLING: -- yeah, exactly.

MS. HORN: Okay. So Carmichael, the consensus is then not to change the budget there. 11SCB04, Carmichael.

DR. KIESSLING: That's a four year grant.

MS. HORN: Four year grant for 750,000.

(Indiscernible, multiple voices)

MS. HORN: I'm sorry, we need to keep

things straight for the record. What was the decision and the consensus on Carmichael?

DR. KIESSLING: It's a four year grant. I would recommend it stay.

MS. HORN: Okay. Is that the consensus that we leave this budget alone for now?

A MALE VOICE: Yes.

MS. HORN: Okay. Further discussion? Okay. Hearing none, 11SCB11, Han at 570,000.

DR. GENEL: That was for four years as I recall. I'll double-check that.

MS. HORN: That's a four year grant for 570,000. So consensus is to leave that where it is. The next grant down, 11SCB28, Wesleyan, 750,000, this is Laural Grabel.

DR. HART: Established, a four year grant.

MS. HORN: A four year grant. Okay. The consensus is to leave this unchanged?

DR. KIESSLING: It is a four year grant?

DR. HART: It's four years, yes.

A MALE VOICE: What's our total now?

A FEMALE VOICE: We're at 8.6.

A MALE VOICE: Okay. Now we have some room to deal with some of the seeds.

(Indiscernible, multiple voices)

MS. HORN: Do you want to visit the rest of the established?

DR. HISKES: Yeah. I'm worried about the Yale core.

DR. HART: So now that there's 1,000,000 there and with the statement that Yale gave us that with partial funding they can't do anything. That was in their -- that was in their statement.

DR. KIESSLING: What did they say?

DR. GENEL: What was the statement?

DR. HART: In their grant they said without salary support they would close.

MS. HORN: Okay. So we again for the record we're discussing 11SCD02, Yale University, the core grant for just under two and a half million dollars. It's a maybe grant currently.

DR. KIESSLING: That sound like a threat.

DR. HART: I mean, they've been very successful. They've done a lot of good things. They've -- they knew going into this round that core grants were not a high priority this year for us and I might want to -- it's slow to pull up again one more time, but I remember we looked it up specifically in the justification there

was a statement saying the fact that they would just --

DR. GENEL: What exactly did the RFA say?

MS. HORN: I'd be happy to read those sections for you. Okay. This is from the little framework that I pulled out for the core facility awards. These awards are intended to provide shared core facilities for stem cell researchers at eligible Connecticut institutions, hospitals or companies. Core funding is not a priority for this round of funding. Some additional core funding may be considered for applications with novel or unusual scientific merit. Applications will be considered for additional support for expansion or enhancement of already established cores that will be made widely accessible to the Connecticut stem cell research community and that are likely to advance stem cell research throughout the state.

Proposals must include an explanation of the need for a new core or expansion of an existing core along with estimates of likely capacity and usage. Previously funded cores should provide specific details in their budget justification about the necessity of additional funding, including explanations of how new and existing funding will be integrated without overlap. Funds may be used to cover equipment, salaries or other

costs associated with establishing and operating cores.

Cores will also be allowed to establish a reasonable fee for service schedule in order to recover additional costs associated with their operation. Proposed fees must be specified and approved by these institution, hospital or company.

DR. HART: Can I read a couple of sentences from justification? Under budget justification --

A FEMALE VOICE: What page?

DR. HART: -- page 76 under senior personnel. The personnel salaries requested in this application are calculated to cover the three year period from October 1st, ’11 through 9/30/14. It’s important to note that without the requested funding the YSCC will not be able to continue the current operation of the HESC core laboratories.

DR. FISHBONE: What would happen if you were to fund them for one year to give them --

DR. KIESSLING: We said that -- we said that we would only fund additional stuff. I mean, I think we made it really clear we weren’t going to just continue to fund the core as it is.

MS. HORN: But I think there is language in there that says we would continue to fund existing core’s

operations.

DR. KIESSLING: Really? I didn't hear you say that.

DR. DEES: Yeah, I mean, the way I heard you say that you could shoehorn it in there but it was a little --

DR. KIESSLING: I thought we were going to --

DR. HISKES: Can you just repeat it Marianne?

MS. HORN: Some additional core funding may be considered for applications -- no, applications will be considered for additional support for expansion or enhancement of already existing cores that will be made widely accessible to the Connecticut stem cell research community and that are likely to advance stem cell research throughout the state.

DR. HISKES: Enhancement.

MS. HORN: Right. For enhancement of already established cores.

DR. FISHBONE: Could I ask a question?

MS. HORN: Yes.

DR. FISHBONE: Do you have the numbers if you just funded personnel for one year?

DR. DEES: We did -- it was at roughly 750,000.

DR. FISHBONE: That would allow them to continue for one year and they would have that period to look for other sources of funding.

DR. KIESSLING: Gerry, according to our RFA what we really could fund is their new microscope.

DR. FISHBONE: Yeah, but it's easier to get for example the $1.5 million it's a lot easier to get a donor for a microscope than it is to pay salaries to lab techs. I think.

DR. KIESSLING: I don't know. I mean, we had this conversation last year.

DR. HART: Total salaries and wages is with fringe is 451 for the first year.

DR. KIESSLING: Okay. I mean, we had this conversation last year that we don't want to continue to fund the cores.

CHAIRPERSON MULLEN: What's the other support for their work then?

DR. KIESSLING: They've got -- I saw a paragraph --

CHAIRPERSON MULLEN: (Indiscernible, talking over each other).

DR. KIESSLING: -- no, they've got a bunch of people giving them money. They've got --

A MALE VOICE: They have philanthropic support?

DR. KIESSLING: -- right.

CHAIRPERSON MULLEN: Right, but that's maybe -- maybe they could talk to their funders about using some of what they're getting to support their -- it sounds almost like it's all for salary. Right?

DR. KIESSLING: Yeah. Core funds are almost always for salary.

DR. FISHBONE: But they don't need 450,000 you're saying a year?

DR. GOLDHAMER: Without even calculating the institutional support, the indirect costs. Over three years I calculated I think 1.4 million of the 2.5 went to salary and fringe.

DR. KIESSLING: Yeah. The cores are almost all salary.

DR. GOLDHAMER: So divide that by three approximately -- it's pretty near. And there's 10,000 for travel, 17,000 for computer services, stuff like that. 53,000 for supplies and then 150,000 for the microscope and a few other pieces.

DR. FISHBONE: Can I make a point? I may be way off target here, but if people get funding -- if you have $10,000,000 to give for this year and people come or us for four years of funding it's like, you know, we're taking money out of what we can give to this year in order to give them for the next four years. So obviously the more years you apply for the longer until they have to come back and ask again. But, you know, maybe with core for example if we could fund something for one year and say, you know, we just don't have enough to give you for three years in this year's budget. I don't know, how does the State budget, do you just give out what you're spending this year or do you give out four years' ahead?

CHAIRPERSON MULLEN: Well, people might get a grant that they hope will be a multiple year grant, but every -- funding every year, funding is contingent upon available resources and, you know, I think everybody who has to write or respond to RFPs knows that sustainability is what people look for in the applications as well because the resource allocation discussions get really, really tough and so they can get philanthropic support, they're not eligible for Federal funds?

DR. GOLDHAMER: No, they can get both.

CHAIRPERSON MULLEN: So --

DR. GOLDHAMER: But they receive --

DR. KIESSLING: Well, Federal funds are iffy.

CHAIRPERSON MULLEN: Right. I'm just reading what's involved, the priority for Connecticut Stem Cell Research Grants Program is to support research on human embryonic stem cells that's not currently eligible for Federal funding. That we also have --

DR. HART: That's not the case anymore here. That was when there was no embryonic stem cells --

CHAIRPERSON MULLEN: -- oh, really?

DR. HART: -- very few embryonic stem cells --

CHAIRPERSON MULLEN: So I can cross this out?

DR. HISKES: No, no, no. Not everything is legal.

A MALE VOICE: It's back in court.

(Indiscernible, multiple voices)

CHAIRPERSON MULLEN: Alright. Okay.

DR. WALLACK: So we're trying to figure out, aren't we, how we can keep them in operation?

DR. GOLDHAMER: Right. That's what I'm --

DR. WALLACK: Right. And if they have --

and we have limited dollars and we made a statement that we did not want to do this funding this year, I mean, and if we know they already -- it's been all over the Internet that they already received 1.5 and as I read that Internet blurb, blog, whatever, it seemed as though it was going to be going for some -- in some manner to core.

MS. HORN: I think we have to stay away from things that we really don't have factually before us --

DR. WALLACK: Well, I can let you read the thing right now.

MS. HORN: -- in the grant?

DR. WALLACK: No, in the publication.

MS. HORN: Oh, okay, that's fine. Okay, sorry. I thought it was something you were reading from outside.

DR. WALLACK: So I guess what I'm saying is we're torturing ourselves with the idea that we're going to do something contrary to what we had wanted to do and we don't have the money if we do that to fund a lot of research that we wanted to fund. So maybe what we have to do is come to some kind of compromise on this and certainly the 2.5 is beyond our means. I don't know if -- Gerry you're trying to direct our thinking to the fact

that if the salaries are picked up at 750,000 --

DR. FISHBONE: Or whatever it was.

DR. WALLACK: -- well, that's what I think I heard.

DR. DEES: Yeah, I said that and maybe that's not quite right. But the salaries for one year.

DR. FISHBONE: For one year.

DR. DEES: Salaries for one year, what was the core, 51?

DR. HART: Plus indirect 500,000.

DR. DEES: So half a million.

DR. WALLACK: So what if we then -- I'm uncomfortable having them come back every year. What if we try to put aside $1,000,000 -- $1,000,000 for two years, they can use that as they want.

DR. DEES: Actually, I'm clear, except let's do it one year. I mean, we gave them the shot across the bow saying this is not our priority anymore, right? So they should be looking for other funding and I guess I'm okay with let's fund them for another year and say, you've got to do it this time because you ain't getting anymore.

DR. WALLACK: So Rich, you're saying do the 500,000 for the one year?

DR. DEES: Yes.

DR. WALLACK: Okay.

DR. DEES: Now hang on. The --

DR. KIESSLING: Well, why not give them what they requested in year one, which is -- it's a little more, was it 780?

DR. DEES: -- what they requested was 906,000 for one year.

MS. HORN: In year one?

DR. KIESSLING: Yeah, because they want their microscope.

A MALE VOICE: They want a microscope.

DR. KIESSLING: You see the only thing in our RFA that we said we would do is expand -- is help them expand. I thought the RFA, at least I know from our discussion last year it was really clear to everybody that we didn't want to continue to fund the cores that we had, you know, we'd put in all this seed money, I mean, we've given them what, $5,000,000?

A MALE VOICE: 4.3.

DR. KIESSLING: $4.3 million and we want to fund the work, not the cores. So I mean, I thought the RFA was clear on that. If Marianne thinks that there's wiggle room in there and it sounds as though we were

willing to continue to fund their core then maybe we have a different problem, but I thought it was really clear.

MS. HORN: I think it's difficult -- I think it's difficult to separate out some of what the -- it does say expansion or enhancement of already established cores.

DR. KIESSLING: Right.

MS. HORN: So to the extent that they have figures that are a little muddied because they have to continue operating part of it in order to enhance this. So that's where it becomes a little blurry.

DR. WALLACK: Marianne, maybe Rich has the right idea. To give them the 500,000 for the one year because the second reviewer on the grant did indicate that they had to come back with a strategic plan with an idea of how they're going to be managing the core from a financial standpoint. This gives them, as Rich, I think you're trying to strive for, the ability to continue this year, come back next year with a plan.

DR. KIESSLING: Or not come back next year at all.

DR. WALLACK: Or not come back at all.

(Indiscernible, multiple voices)

MS. HORN: Just one person at a time

please.

DR. GOLDHAMER: I don't think we should restrict it to salaries alone, there's supplies, there's service contracts. If we're going to restrict this to one year it should be -- it should be I think full funding for a year and we should also note that they do plan expansion and offering new technologies. It's just not articulated very well exactly how this is going to be rolled out and what the detailed plan is. So that makes it a little more difficult to discuss.

DR. HART: And also, think about this from the fact that the P.I. of this project has three RO-1s and a large project grant already from NIH --

DR. KIESSLING: Planning award.

DR. HART: -- yeah, planning award, thank you. And is this going to -- and you've got success now. You've got a number of stem cell laboratories at Yale because of this core facility. If we say, okay, we should fund them for one year at the requested level that choice is not just out of the vapor saying give them $1,000,000, it means take that away from the possibility of funding five more seed projects, if you want to pick a number.

DR. KIESSLING: Right.

DR. HART: Okay? So either you fund five

seed projects or you don't fund five seed projects. If you don't fund the five seed projects and you put $1,000,000 in this project I can see at this point calling the Yale Stem Cell Center a success from our point of view and good luck and goodbye and you're ready to go off on your own.

DR. GOLDHAMER: Well, I don't agree. I don't think --

DR. KIESSLING: I do. I agree.

DR. GOLDHAMER: -- I don't think we should do that so cut and dried. There's a lot of people at Yale now, 30 labs that on some level or another depend on this core and if tomorrow that core has no funding, you know, Yale over time I'm sure can find ways in cost recovery, through donations, can find a way and needs to find a way to fund the core. We all agree on that. The question is do we cut off funding immediately and completely or do we give them a little more time to reach that point? And I would be in favor of giving them a little more time.

DR. WALLACK: I'm hearing that this feeling of funding them for this year, and I'm hearing --

DR. GOLDHAMER: I think Ron was suggesting --

DR. HART: Well, that's your proposal.

DR. KIESSLING: That's not coming from me either. We gave them a year last year, we made it really clear, we have some really good projects we'd like to fund, and I think Yale can take this package and say to somebody and say, we need this.

DR. GOLDHAMER: I think -- sorry to interrupt. I think then if that's the case then we need to go through each of the Yale grants that we're planning on funding who depends on that core and now reevaluate it and decide can they do that work with the assumption that the core no longer exists? Because a lot of people they don't have expertise in stem cells or they need the technologies from the core and if the core isn't there then I would want to go back to each of those grants and say, now I don't think you can do this because the core doesn't exist. We have to assume it doesn't. They may find out ways to keep it up and running.

DR. KIESSLING: But David, they knew this last year.

DR. GOLDHAMER: I understand. But here we are today with many, many labs that are dependent on it and I just don't feel like we should pull the plug completely.

DR. KIESSLING: When does their current

funding run out?

DR. HART: So in the beginning when the core was initiated one of their primary goals was to train scientists in growth of stem cells, they've done that, right? In the beginning one of their goals was to provide some technical support services. So are they actually handing out cultures at this point to individual labs? I think that's still true, does that seem to be true?

DR. KIESSLING: Yes.

DR. GOLDHAMER: They're new investigators and, yeah.

DR. HART: They're doing like sequencing as part of this other side component of their main project. They've still go the instrument, that's not going to stop. When do you pull the Band Aid off is my question?

DR. GOLDHAMER: Well, they have to find ways -- no, the instrument is not going to disappear, but the technical director may disappear. I mean, somewhere the money -- I don't think it's a viable option for the core and all of it's infrastructure and all the related facilities to just disappear. They have to be sustained. And it may be that if they got no funding from this Committee Yale would find a way to fund it, we just don't know that and I think it's risky at this point to say, no,

you're done. So I would -- I think a year is a good compromise. It gives them -- I understand that they should perhaps have come at this differently given what the RFA said this year. But here we are with a decision to make and I think pulling the plug could --

DR. WALLACK: So can I try a compromise and we can vote on it? I mean, it's going to come down to that because we can go back all day. What if we funded them for one year, $500,000, with a narrative about what we're all saying here that this is something that we're going to ask them to do in the future to look elsewhere to sustain the fund -- the core. This way we give them more than Ann thinks we should or Ron. I would recommend that we try to take a vote on the 500,000 for one year.

DR. GOLDHAMER: Good compromise when nobody's happy, right?

DR. WALLACK: Well, no one's going to be happy either way.

DR. FISHBONE: I would agree with that and also say there will be no more funding.

DR. WALLACK: Right. That's fine.

CHAIRPERSON MULLEN: So next year how do we avoid having this conversation? Because technically every application that we reviewed today could have included

that little sentence, if you don't give us -- what it boils down to, it's all up to you whether or not we survive. This work cannot continue. And if so, if that message came through last year and we're saying, okay one more time, I sort of get it. But on the other hand, you know, how would we do this if everybody had said that now?

DR. WALLACK: I think there's a way to get around that and that is that I don't believe that they took as seriously as they might have taken what we wrote in the RFA.

CHAIRPERSON MULLEN: Is that our issue? I'm not -- I'm just trying to push the conversation --

DR. DEES: So I think the answer is we say next year we are not funding core facilities, period, just take them out.

DR. WALLACK: I agree.

DR. KIESSLING: I mean, the spirit last year was that we didn't want to not fund some new innovative technology if it was going to really enhance the core. That was the spirit. We had no intentions of continuing to fund the entire core.

CHAIRPERSON MULLEN: Okay.

DR. KIESSLING: That was the conversation last year. So if we didn't make that clear in the RFA we

need to make it clear now and I think that would still be the spirit. If there's some new technology that shows up that, you know, costs -- people use once a month you would like to have it in that core. But other than that we in no way want to be responsible for their dissolving.

DR. DEES: I guess -- and I want to rephrase that. I want to like take out the core language so that they don't get the wrong impression, right? So we can say, look, we're not funding cores and we can have some provision for --

DR. WALLACK: And in fact we basically said that but some people weren't paying as much attention to that. It's obvious that we did not get the same number of core requests as we've gotten before so the message was gotten. It wasn't gotten across the whole spectrum. That's why I think the transition year might be -- no one's going to be thrilled with it, I mean, but at least it gets us, you know, backed in some way.

DR. HART: So let me actually complete the picture if that's your proposal. So your proposal right now is $500,000, that leaves enough room -- look at the top of the maybe list, only for the seed grants, there are three seed grants that are fairly high in scoring. One there, there and there, and the rest of them are fairly

down -- farther down the list. It almost fits.

DR. WALLACK: Okay.

DR. HART: So that means we fund three more seed grants only.

DR. KIESSLING: And none of the other maybes.

DR. HART: And none of the other maybes if that's the case. That's the price of doing the 500,000, just to be clear.

DR. GENEL: Yeah, well, in all fairness -- in all fairness there are one, two, three, four, there are six grants at a three level. I guess that's the only seed, is that your point?

DR. HART: Yeah. I was just looking at the seeds separately.

DR. GENEL: That's the only seed at the three.

DR. DEES: No, there's --

DR. HART: Are we funding him already?

DR. DEES: -- Carmichael and Rasmussen we're funding. Rasmussen is getting funded through one of the other grants.

(Indiscernible, multiple voices)

MS. HORN: One at a time please.

DR. WALLACK: I agree. Ron's argument is a very powerful argument because if you notice where's Nelson?

DR. HART: Below.

DR. WALLACK: Right. And if you notice, we said very positive. I mean, I have to tell you from a very personal standpoint I feel very badly if he was not able to get his funding.

DR. KIESSLING: Or some funding.

DR. WALLACK: Or some kind of funding for his project.

DR. GENEL: Yeah. I would suggest we deal with the rest of this and then come back to that.

DR. HART: We also don't have enough dollars left to get that far down the list almost no matter how we do it.

DR. KIESSLING: Well, we cannot fund Rasmussen and Carmichael because we've already funded them elsewhere.

DR. HART: Okay. Then that's another proposal.

DR. KIESSLING: So those can be moved to the no category.

DR. HART: But now --

DR. KIESSLING: Is everybody comfortable with that?

DR. HART: -- the Rasmussen one, the seed Rasmussen grant, did that really scientifically -- was that distinct from the larger grant he was a part of?

DR. KIESSLING: I think it is distinct.

DR. HART: But that doesn't matter to you?

DR. KIESSLING: Well --

A MALE VOICE: We're making bad choices.

DR. HART: No, no, I just want to be clear that we understand what we're doing, that's all.

DR. DEES: I mean, I think there's a reasonable argument here that you only get -- even if you're doing great stuff on two different things we're only going to give you one.

A MALE VOICE: Right, right.

DR. HART: And that's one of our rules here. That works.

DR. DEES: It's not an unreasonable thing for us to say. We'll give you this much, but we're not going to --

DR. KIESSLING: I think we should raise our debt ceiling.

(Laughter)

DR. GENEL: You know, the reality is in a large laboratory things are not quite that distinctly separate as it might be portrayed on paper.

DR. DEES: So then the question would be -- the question will be -- there's a question on the floor. The question on the floor was to fund them for 500,000 for one year.

DR. WALLACK: With a note that that was the end of the funding.

DR. HART: For the purposes of seeing how far the budget goes why don't we model that on the screen and continue working?

MS. HORN: Okay. So the consensus for purposes of this exercise is that we would fund 11SCD02 for $500,000 for one year.

DR. HART: And now take the other conditions one at a time. Rasmussen, if you choose to say that the left route has already been funded to the larger grants -- I'm not going to make that --

DR. WALLACK: Yeah. He's in the -- he's in the diseased directed grant. He's in --

DR. HART: -- yes.

DR. KIESSLING: What is that, is this a different project?

DR. HART: It is a different project.

DR. WALLACK: BIC02, right.

MS. HORN: Yeah. I think you need to be very careful that we're funding the best science and that if this person's last name was something different and they had distinct projects that we would fund them both.

DR. WALLACK: Well, we were happy with the science of 02.

MS. HORN: And we don't handicap them because they happened to put in two excellent grants.

DR. DEES: I think -- Marianne, I actually disagree with that.

MS. HORN: Okay.

DR. DEES: I think there's a reason to say, look, we want to spread this money around and so if you give us two excellent projects we will fund one of them, but we will not fund both of them.

DR. GENEL: I agree with that. I agree with that. And I don't think the difference between a two and a three is that great that it would make all of the difference in terms of whether we fund it or not. That's what our job is.

DR. KIESSLING: We're already funding the best -- we can't fund all of the best, that's the problem.

If we could fund all of the best science --

DR. FISHBONE: And one includes the 500,000.

DR. KIESSLING: Yes.

DR. FISHBONE: Fund 1,000,000 includes the 500,000.

DR. KIESSLING: Yes.

DR. GENEL: After all, we're down to 4.5 on maybes, I mean, which we all agree is fundable. So --

DR. KIESSLING: The caliber of the applications has improved enormously.

DR. GENEL: -- so, I mean --

DR. WALLACK: So what else are we looking to cut now?

DR. GENEL: -- well, I think I'd rather look at what we want to put in to cut --

DR. WALLACK: So where do you want to go Mike, do you want to go back to the seed or not?

DR. GENEL: -- no, I want to go back -- first of all I'd like to go back to Nelson, B15.

DR. WALLACK: You want to go to Nelson?

DR. GENEL: Yeah. I'd like to do that.

DR. WALLACK: I would make the argument of at some point trying to fund Nelson.

DR. GENEL: Well, I would -- I think Ron's suggestion was that we only -- that the first aim was the aim that we ought to fund and that a message could be sent either -- was the wrong message --

DR. HART: I want to be clear that I thought the good first aim was the thing to do but I don't want to impose that upon it.

DR. GENEL: -- okay.

DR. HART: So I think partial funding would be a good idea, but I would leave that for the P.I. to decide how to deal with that.

DR. GENEL: So whatever the rationale --

DR. HART: Five points for the Board.

DR. GENEL: -- whatever the rationale.

DR. HART: Yeah.

DR. GENEL: There are two ways of doing it. One would be simply to fund it say at half and just -- and let the investigator come back with, you know, with a budget, which I'm fine with.

DR. FISHBONE: Didn't we say that everything was dependent -- we're talking about Nelson now?

DR. GENEL: Yeah.

DR. FISHBONE: Everything was dependent

upon aim one being achieved.

DR. GENEL: Before going forward, yeah.

DR. FISHBONE: And so maybe we could fund the one year for aim one for $250,000 and then come back if that is successful.

DR. GENEL: My recollection was he was asking for four years, am I wrong?

DR. WALLACK: So Gerry, that would probably --

DR. GENEL: Is it three years? Was it three years?

DR. WALLACK: -- that would be a good approach to it.

DR. GENEL: Well, I'm okay with that.

DR. WALLACK: And if you prorate that he's still getting for the first year basically what he's asking for.

MS. HORN: I'm not sure how this is going to play out. 11SCB15 we're proposing that a certain amount of money be spent and if it's spent well then he comes back? I'm not clear.

DR. HART: I think the award is just the $250,000 and he can reapply for grants.

MS. HORN: Because this money is allocated

it's gone -- we don't have carry it over that way?

DR. WALLACK: But it's for one year.

MS. HORN: Correct. Okay. So for one year. And then he'd have to reapply.

DR. WALLACK: Then he comes back to us next year.

DR. HART: Well, it was a four year request.

DR. GENEL: It was a four year request.

DR. HART: And totaled about $200,000 a year roughly.

A MALE VOICE: So you're really thinking one year at $200,000.

DR. HART: Well, the only problem with that is that there was a key piece of equipment that he proposed to buy that really would be important for everything else he wished to do. So 250 might be a good compromise, he wouldn't be cut off so drastically.

DR. WALLACK: So can we do that? Do we all agree about the 250 for him? So let's do that one.

DR. GENEL: Let's model it and then I mean we can -- we can come up with the fine tuning of the language if we need to.

DR. KIESSLING: What about the Hugh grant?

MS. HORN: Okay. Just -- if we could just establish some process that goes logically from how we're listing these grants besides somebody liked it that would be really good.

A MALE VOICE: It sure would.

MS. HORN: So we've got Nelson 11SCB15 and the proposal that was adopted by consensus is to fund it for one year for $250,000. Now I would propose that we go back and we're revisiting established grants that we go back up to the ones that are in the maybe column and decide whether we want to fund them or not and proceed down that list.

DR. KIESSLING: O'Neill would be next then?

DR. DEES: Yes.

MS. HORN: Okay. 11SCB16, UConn, Rachel O'Neill for $744,013. Currently in the maybe, peer review three.

DR. DEES: I was one of the peer reviewers there. This is a very basic science oriented grant and for myself it wasn't one of my high priorities. I looked at a number that were in the three range and this is one I was going to put below the line. I'm happy leaving it.

DR. GENEL: Yeah. I mean, I think this is what Ann was referring to, I think we have a lot of good

science we just can't fund it all and we're going to have to make decisions. I think, yeah, it was very, very basic.

DR. KIESSLING: Oh, but this was a human ES cell grant.

DR. GENEL: Rachel O'Neill, this was the small RNA and there was some discordance between the reviewers. The secondary reviewer comment, differentiation strategies are flawed, because purifying, enriching and cell types are not proposed. There's a couple of other comments here. I mean, there was -- that's how we got to a three I'm sure, there was some discordance in the reviews.

A MALE VOICE: So what do we want to do with that then? Do we keep it in or not Rich?

DR. GENEL: I thought we were going to leave it off.

DR. DEES: I would keep it out.

A MALE VOICE: Keep it out?

DR. DEES: That's my recommendation.

A MALE VOICE: So let's move to keep it out.

MS. HORN: It's the consensus that we move this to the no funding category.

DR. KIESSLING: This is hard.

A MALE VOICE: They're all hard.

MS. HORN: Further discussion? Any further discussion? So we'll move this to the no funding.

MS. SARNECKY: Would it be visually better if I actually moved it over?

A MALE VOICE: Yeah, it would be.

DR. FISHBONE: I have at the risk of being unimported I have another question that I sort of brought up before and that is, you know, we don't have enough money to fund all the good grants you want to and yet we're funding people out for four years and this -- in a field that is changing extremely rapidly. I mean, Ron's made the point that between the time that people send in their applications and now there have been major changes in stem cell research. And I'm wondering if it makes sense with the shortage of funds to fund people for four years rather than, you know, have them come back in two years for additional funding? Because they've got several aims which are largely sequential and it may be that at this point in time it may look very good what they're going to be doing three years down the road, but in three years it may not look that good. So what will they do? They'll move it into something else if things have

changed.

But I'm just wondering if we can achieve the same thing by funding people for two years. I know the researchers don't like this, they always shake their heads when I say that, but --

A MALE VOICE: You'd spend all your time writing grants.

DR. FISHBONE: -- yeah, but that's what you do anyway isn't it? Don't you do that for NIH as well?

A MALE VOICE: And you're always in danger of not getting anything out of talented people to do that.

DR. GOLDHAMER: If you get funding for two years then you'd have to start writing your grant after one year to get -- so there's overlap in funding.

DR. FISHBONE: How about three years instead of four years? I mean, do you know what you're going to be doing four years from now?

DR. GOLDHAMER: The RFA does say up to four years so to now say that we're not going to fund more than three years I'm not sure that that's a good strategy.

DR. HART: No. But if we're looking for strategies to -- if we're looking for strategies to cut budgets and extend how many grants can be funded that might be one strategy is to go from four to three years on

some of the lower scoring ones. But that's the best I can come up with. And, you know, even now I'm a little uncomfortable, but --

DR. KIESSLING: The ones that are -- the established investigator grants that are four years and they're $750,000 those are really cost effective.

DR. KIESSLING: That's, you know, not even $200,000 a year so these people have really thought it through and they're going to be able to build a team and know they have that money. They can even train graduate students. You've got four years of funding, you can train somebody.

MS. HORN: And remember last year we funded them for $1,000,000 so we've already cut them back by 250.

DR. KIESSLING: Well, I think unless there's something about the application, like the one that we just talked about, the Nelson one, it seems like to me like 750,000 for four years is really cost effective. As much as I would like to stretch these funds.

DR. FISHBONE: Well, by the way, that makes our grants the only thing you can be sure of in this state that you will have a job for four year, you know, it'll be funded.

(Laughter)

DR. GENEL: Well, the other thing to keep in mind if I calculate correctly we just have four more years of authorized funding.

MS. HORN: That's correct.

DR. GENEL: This is -- this is just four more years I believe.

MS. HORN: At most.

DR. GENEL: You're not doing anybody a favor by funding them for three years. They can't be --

DR. WALLACK: But even if it lasts until we get the grants --

DR. GENEL: -- but that -- well, okay.

DR. WALLACK: So Marianne, can we move to 18?

MS. HORN: Well, let's just finish up on 11SCB16. The consensus was that we move the O'Neill grant from maybe to no?

DR. WALLACK: No, right. We did that. So we're at 18.

MS. HORN: Okay. So we're moving on to 11SCB18, this is from Yale.

DR. WALLACK: Did we ever find out about the RO-1?

MS. HORN: Yes we did. I have a note here

from Paula and it says that this RO-1 has a start date of April 2012. It has not been reviewed yet and therefore they don't know if it will be funded.

A FEMALE VOICE: Did that help?

DR. WALLACK: No. I wish she said something else.

MS. HORN: I'm sorry.

DR. FISHBONE: Could you punch up for two years and see if she gets funded?

CHAIRPERSON MULLEN: Was that one of the reasons it was a maybe though? Is because of that question that was answered?

DR. WALLACK: Yeah.

A MALE VOICE: Well, that was one of the reasons.

CHAIRPERSON MULLEN: Right. But does that move it all now that you know that?

DR. GOLDHAMER: I don't think that should be a reason for it to be in the maybes. It should be on scientific merit. They'll rebudget as needed and make sure there's no overlap, give one grant back, so partial funding from one of those grants. So I think that has to be dealt with at the time they hear about it.

DR. WALLACK: So can I make a suggestion at

18? The -- it seems like a strong grant. They -- the reviewer -- the reviewers themselves talked about the budget as possibly having overlap.

DR. HART: It's overlap in that RO-1.

DR. FISHBONE: And also it passed funding.

DR. HART: It's an RO-1 that hasn't been looked at yet.

A MALE VOICE: With a current RO-1 application.

DR. HART: Right. So they have an application that (indiscernible, too far from mic.) RO-1 for pretty much the same sort of stuff. It hasn't been reviewed yet and don't know if it's ever been funded.

DR. DEES: But otherwise this is a fairly strong grant. It has -- the things I liked about it was it was really directed towards (indiscernible, too far from mic.). But I mean, it was a fairly clear translation.

DR. HART: This is another one of those too where the second reviewer says that lengthy viral vectors are obsolete in the programming. I don't know where that's coming from. I don't know what planet they're on.

DR. KIESSLING: They were obsolete for about a month I think.

DR. HART: I don't know. Maybe that was the month. It's just odd.

MS. HORN: Okay. So this grant is currently in the maybe column.

DR. WALLACK: So Marianne, do we have to then decide whether to move it into the yes column and then decide on the amount?

MS. HORN: You have to decide to do something with it, yeah.

DR. WALLACK: Right. So I don't think I'm the -- I'm not the -- who was the --

MS. HORN: No, this is Dees and Hiskes.

DR. WALLACK: -- so can you guys help us by making a recommendation?

DR. HISKES: I'm going to go look at the budget.

DR. DEES: It's a four year grant. It's pretty hard to cut out of the budget. I mean, I think this is where we make the decision about whether we want to -- can we fund this with -- no, we don't have enough money to fund this even in full. So we couldn't fund this at a full rate anyway.

DR. HISKES: It's looking at tissue engineered grafts for correction of heart anomalies.

DR. FISHBONE: Would you make it a three year cutoff? I mean, it's going to be above the -- it's going to be above our max at four years.

DR. DEES: So I mean, the real impression here now I think actually is not this, I mean, we can leave this in maybe for now. The question is do you want to fund these seed grants in priority?

DR. HART: Well, the problem is there are four established investigator grants at a priority score of three, all in a row, all for $750,000 a year and we can't quite fund one of them to completion.

DR. DEES: That's right.

DR. HART: How are we going to deal with that?

DR. GENEL: Yeah. And of the seeds that are up there the top two are in well funded laboratories.

DR. HART: That's right.

DR. GENEL: One in fact for a post-doc that's yet to be named.

DR. HART: We've already hit on arguments that those may not be good candidates for funding.

DR. KIESSLING: What about A15?

MS. HORN: A15, this is Yale University, Rong Fan, it's a maybe, 195,000.

DR. KIESSLING: This is that grant that's got such an odd budget going on.

DR. HART: What was the science again?

DR. KIESSLING: Well, this is the -- they're going to -- the science is neat. They're going to do podeomic (phonetic) on single cells, okay? It's technology, but that the P.I. is going to put in .04 percent effort.

A MALE VOICE: Ann is going to be doing all the work.

DR. KIESSLING: So there is -- the principle investigator is somebody named Pon (phonetic), the co-P.I. is Sherman Weisman and the other collaborator is the technician in Sherman Weisman's lab. He's a Ph.D. research associate, he's been there a long time. So it isn't clear why Rong Fan is the P.I. except he seems to know the microfluidics technology.

A MALE VOICE: It scored highly.

DR. KIESSLING: It scored highly. I mean, this is going to be neat. It just isn't clear who's at the helm. This was the -- the reviewers couldn't figure out who was going to do the work because there aren't enough people to do the work.

DR. HART: Now is that -- is that really

something that we should be so concerned about?

DR. KIESSLING: I don't know. Well, we can back him for a quarter of a post-doc, a 10 percent of Dr. Pon, half a percent of whatever this is, I can't quite ever figure out these grant-funded person runs. Half a month a year of Dr. Weisman and .04 percent or something of the P.I. who is not asking for any salary.

DR. WALLACK: That's -- .04 percent that's got to be a typo. No one -- that's a ridiculous effort so --

A FEMALE VOICE: You mean 0.4?

DR. WALLACK: They're saying the amount of time and effort --

DR. KIESSLING: No. He will --

(Indiscernible, multiple voices)

DR. KIESSLING: -- .09 academic months.

DR. WALLACK: Marianne?

MS. HORN: Yes?

DR. WALLACK: There's no way that we are going to be able to fund the maybes in the established investigator. So -- and I think we're getting pretty close to the number. Can we move away from the established investigator now and see -- go back to the seeds and see if there's one or two that we can get back

from the maybes if anybody feels strongly?

A MALE VOICE: That's kind of what we were just doing I thought.

CHAIRPERSON MULLEN: We're right in the middle or somewhere in the midst of discussing SCA15 specifically though, so --

DR. KIESSLING: Yeah, it's a seed grant.

DR. WALLACK: I guess what I'm looking to do though is to skip past the next seven or eight and -- because we're not going -- we're just torturing ourselves and go down to the seed portion.

DR. KIESSLING: No, no, that's where we are. We're at A15, which is a seed grant. That's a seed grant. It's not an established investigator grant.

DR. WALLACK: I know you brought that up.

CHAIRPERSON MULLEN: How about if we finish this piece of the discussion?

A MALE VOICE: Yes.

MS. HORN: And then I have another thought. I mean, we could just start at the top and move down the maybes sequentially leaving -- and doing the seeds first.

DR. HART: So we're on Fan.

MS. HORN: We're at 15, we're discussing whether this should be moved from the maybes.

DR. HART: Okay. Looking at the language and the budget justification for effort from the principles involved it's really saying that the P.I., Dr. Fan, will devote .09 academic month effort to these studies. I interpret that as meaning he doesn't need salary from this project to do it with all the other responsibilities listed as justification.

MS. HORN: But he's not asking for salary.

DR. HART: That's the point. So he's basically giving a token amount of effort to being part of the project because he's getting paid by somebody else, we don't know how, but his responsibilities are such that he's doing quite a bit for the project. So I don't see that this is really the problem. Whatever else you might want to find about the project I don't think that the effort of the P.I. on that particular case is a reason not to fund it. I think that based on the score I think we should move it to the yes. Based on the score and the other things that are available we should move it to yes, let's put it that way.

DR. WALLACK: So you want to fund it?

DR. HART: Yes.

DR. WALLACK: So make the motion to fund it.

DR. HART: I move to fund it.

DR. WALLACK: Second.

MS. HORN: Okay. We're not really making official motions but we are working by consent.

DR. HART: Right. Well, we just want to move through this.

CHAIRPERSON MULLEN: That's a very reasonable point. Is that clear? Good. I think we have a yes on this.

MS. HORN: So the consensus is to move 11SCA15 from the maybe to the yes, $195,251.

DR. HART: Now we've got what, pocket change left over?

A MALE VOICE: We can give one more seed grant I think.

MS. HORN: Okay. So I would suggest that we go to the top of the maybe list, which I believe is Rasmussen, that is 11SCA35, UConn, $200,000 and then we move down that list hitting the seed grants and see where we end up.

DR. DEES: The issue with the Rasmussen grant is not so much based on the science just with the peer score and what was said about it, although the science was pretty good, the question is are we giving

enough money to Dr. Rasmussen already or would it be more worthwhile to spread the money around?

DR. FISHBONE: Well, in the same vein that Ron just made. If the grant is worth doing it's may be worth funding. You know, if it's an important grant to do I don't see any problem with funding it.

DR. KIESSLING: We don't have enough money.

DR. FISHBONE: Well, we do. We do.

DR. KIESSLING: I know, but maybe that's not the one.

DR. FISHBONE: Is this the one.

DR. KIESSLING: Right. We can fund one more.

A MALE VOICE: What's the other one you would pick?

DR. GENEL: Well, the other one I think would be down -- would be down further. I can't speak to that. I'm just not inclined to fund Carmichael twice.

A MALE VOICE: I agree. Yeah. A senior guy.

MS. HORN: Rasmussen.

DR. GENEL: Huh?

MS. HORN: Rasmussen. We're talking about Rasmussen.

DR. GENEL: No, well -- well, Carmichael is the next -- Carmichael is the next seed grant and I'm just saying I'm just not inclined in this climate to fund him twice.

DR. HART: Can I bring up a point now? So the pickle we're in at the moment is that there's essentially enough money for one more seed grant. There are three of them available on the screen and so looking at just one of them in a vacuum doesn't help at this point because there's all these alternatives. Rasmussen, let's hold onto that for a minute. Carmichael, he's already got an established investigator grant. He's a senior investigator. This would be to fund an additional post-doc on an additional project, which was interesting and worthwhile, etcetera, but if we want to budget our resources this might be a way to cut. What's the case for the third one? I don't know that one, Sundaram?

MS. HORN: 11SCA40 is Sundaram.

DR. HART: What would be the argument for that one?

DR. GOLDHAMER: So this was the grant that Milt and I reviewed that they were -- the post-doc was making smooth muscle cells from ES cells and I was less favorable than Milt. I had originally said no and move it

to a maybe and there was problems in the reviews saying it was simplistic to think that their approach would work. But we both liked -- this was making vascular grafts and it was a very strong lab.

I looked at the P.I., the lab P.I.'s funding and they have funding from this Committee for another year to derive smooth muscle cells from ES cells. So the scope might be different. I don't know that this specific work, it probably wasn't funded in here, but it's very close. So I think this post-doc's work falls under the category of making smooth muscle cells from ES cells and they have another year of funding.

DR. HART: Okay. So having carefully considered the three options for the remaining budget --

DR. KIESSLING: We haven't. We haven't considered Anna Kloc.

DR. HART: -- well, I argue that that's far enough down the list of scores and it wouldn't be fair to give a 4.3 over a 2 or a 3.

DR. GOLDHAMER: In general I think. So we need a good reason not to hand a two to a three and take --

DR. HART: That's right.

DR. GOLDHAMER: -- and take a four or

higher.

DR. HART: I think it would be a real problem to go for a 4.3 over a 2.

DR. KIESSLING: Why? It depends on what they do.

DR. HART: Yeah, I know.

DR. KIESSLING: You're the ones who didn't like any of the reviewers.

DR. HART: Okay. Hang on. Hang on.

(Laughter)

DR. KIESSLING: Wait a minute. Let's just look and see why we left it in the maybes.

DR. HART: Alright. Let's revisit that one, Kloc. Which one?

DR. KIESSLING: A02.

DR. HART: A02.

MS. HORN: Anna Kloc, 11SCA02.

DR. HISKES: I was a reviewer. I thought that the reviewers' comments were primarily very strong. A few minor negatives that could -- you should do this rather than that and that person could do what is recommended. And that the criticism that neither the P.I. nor her mentor and whose last work experience in the area was not a -- was not a valid criticism. And it came to

substantiate my instincts.

DR. HART: Well, we've got the possibility of four good grants to choose from. That's always going to be the problem. There are possibly four good grants to choose from. Each one of them deserves funding, no question about it. Each one of them would be scientifically productive.

I could go for two possibilities in my own argument. One would be to say that having no good reason to choose a middle of the pack by score over a higher on the pact score I argue that Rasmussen, even though he's part of the disease oriented group, should be the one that gets this funding. But having said all of that I'm getting less and less comfortable with the idea of funding the Nelson grant for $250,000 at the expense of some of these. But that's -- I think at least we ought to deal with the first part of that.

DR. KIESSLING: Rasmussen has two or three other grants. If he wants to do this kind of a project he can.

DR. HART: Well, that's the same case with Carmichael, that's for sure.

DR. KIESSLING: That's right.

DR. HART: Okay? So keep making arguments

and go for another possibility.

MS. HORN: Do you want to revisit the Yale core?

CHAIRPERSON MULLEN: It's reasonable to revisit the Nelson question in light of all of this.

DR. WALLACK: Well, before we do the Nelson again, I mean, could we make the argument that Ted Rasmussen in fact is -- doesn't exactly fit into the seed category from what we expect as well as Carmichael? So in my mind I'm not uncomfortable removing those two.

DR. HART: Okay.

DR. WALLACK: And I'm not uncomfortable removing Anna Kloc because of the score. I come back to 40, Sundaram, because that is a young investigator.

DR. HART: That's a good argument.

DR. WALLACK: Got a good lab and it had very strong comments from the peer review people. So I'm not torn by the idea of proceeding, picking one, and I would pick CA40.

DR. DEES: You've convinced me.

MS. HORN: Okay. Could we go back up then and start with 11SCA35, Rasmussen?

DR. HART: So based on the -- we're voting for no on that one.

MS. HORN: Okay. The consensus is that we will move this to the no category. Is there any further discussion? Okay. We'll move that to the no category.

DR. HART: Let's finish the A's first.

MS. HORN: 11SCA15, Yale -- no, no, no, I'm sorry. 11SCA07, Carmichael, move that -- the consensus is to move that from the maybe to the no column. Is there any further discussion? Okay. Let's see, Kloc, 11SCA02 and the consensus is to move this grant to the no category. Any further discussion? Okay. That's moved to the no category. And let's see. I'll do the one that we wouldn't approve is 11SCA40, Sumati Sundaram, 200,000, moving that from a maybe to the yes column. Is that the consensus? Further discussion? Okay.

DR. HART: Now if we want the easy way out we take the small amount that's left over and add that to the Yale core facility and we're going to walk away.

CHAIRPERSON MULLEN: Any other discussion about Nelson? There was another question about Nelson. Is that settled yet?

MS. HORN: Well, I think somebody just raised the issue of how we got to revisiting that grant as opposed to some of the other higher scored established investigator grants.

DR. HART: So maybe now would be a good idea to go back through the other maybe me category grants to make sure that we really feel that those don't move to a yes category?

MS. HORN: Yes. Okay. So that is -- the first maybe, 18? 11SCB18, Yale University, Qyang. This is for $750,000.

DR. DEES: The truth is, alright, is that we're looking at these investigator grants unless we move other money around we could fund basically one year roughly. So the question is, is it worth covering that to cut something else? I mean, this grant I like (indiscernible, too far from mic.).

DR. KIESSLING: Yeah. Not fund the Yale core.

DR. DEES: Yeah. Not fund the Yale core. But that's what it comes down to. In order to fund these grants we have to just not fund the Yale core at all.

DR. WALLACK: So Marianne, you had -- we have SCB24 as a possible -- I don't remember the rationale, but are we talking about two year funding? So Rich, would that fit into what we might be able to do if we took that one and funded that one for two years?

DR. DEES: Well, it would be simpler to say

it would be better to fund that for $250,000 than the Nelson one at $250,000, which has a worse score.

DR. HART: And my argument with that one was that it would have been higher rated if it was more of a pilot oriented project because there wasn't as much preliminary data as would have been worthwhile for that big of a project. If there was no phenotype there was no project.

MS. HORN: Okay. We started with 18 and then moved to 24 because there was possibly a two year funding. Can we deal with 18 or do we need to do a comparison among all the other ones that are standing?

DR. HART: I think we have do this as a comparison.

DR. KIESSLING: They've got exactly the same score.

MS. HORN: Right.

DR. HART: Yeah. So all the three's.

MS. HORN: Okay. Any further discussion on B18? How about B21?

DR. ARINZEH: I mean, there was nothing in that grant --

DR. KIESSLING: We're looking at B24?

MS. HORN: 21, B21.

DR. ARINZEH: -- Agulla is the one that had the two grants --

DR. GENEL: That was the double --

DR. ARINZEH: -- yeah, the mixed up one and this is the one that had reviewers actually reviewing the wrong one. It was okay. I mean, it's still kind of maybe.

A MALE VOICE: Does Drissi's work cover any of what he's doing?

DR. ARINZEH: No. This one's, you know, this one's about the development of antibodies for trying to characterize differentiation of the ES cells differentiation. So he's just trying to develop an array of kinds of antibodies that he could, you know, potentially commercialize. So that's what he's trying to do.

MS. HORN: Any further discussion of 21? 11SCB22, Scott Swenson?

DR. WALLACK: So Marianne, if no one is speaking strongly in favor of it at this point don't we automatically have to put it into a no?

MS. HORN: I think we're just going to through them and see if there's any particular reason anybody would want to address the budget or anything else.

And if not then they should move back into the no.

DR. KIESSLING: The dredges, we're going through the dredges.

MS. HORN: Right. Okay. So I'm hearing nothing on Swenson.

DR. DEES: This is one of my grants too and I have to say I preferred giving money to 24 rather than 22. (Indiscernible, too far from mic.) 24 was more promising.

MS. HORN: 11SCB24 you're saying that was more promising?

DR. DEES: More promising than 22, yes. So given that they're scored equally.

MS. HORN: Yeah. This was the one where there was off in the right-hand column a two year possibility of funding.

DR. KIESSLING: 24.

DR. DEES: 24 was.

DR. KIESSLING: Was that based on a reviewer comment?

DR. DEES: I think it was based on (indiscernible, too far from mic.).

DR. HART: The reviewers called it -- the project ambitious and they pointed out that it would be

significant if they found a phenotype of their diseased IPS cells. And if they get a phenotype there would be no future in it. So that's why I pulled it out and said, well, maybe this would be a good idea to look at pilot scale approach.

DR. KIESSLING: This is an HES project.

DR. HART: ESC and IPSC. Yes, that's true, it's a mixture. By the third aim they're totally on IPS.

DR. GENEL: Well, the issue really is you have partial funding available for one investigator grant unless we want to give somebody 44,000, which I don't think gets very far. I think we have 9.8 is our limit. So -- and since none of the other investigator grants up there even came up for a discussion of partial funding we really have two grants that are there to choose between and --

DR. KIESSLING: Can we put them in our reserve pile?

A MALE VOICE: Yeah, put them in the bullpen.

DR. KIESSLING: We have a reserve in case something happens, right?

DR. GENEL: Well, but -- you want them both in the reserve? That's 9.756 I believe includes the

funding for the Nelson grant because that was put in. So that -- so at this moment the Nelson grant is yes at a one year funding. This is the one on the organoids that we discussed. So we have limited options unless we want to go back and revisit the whole, you know, the whole thing. So it's -- either we go with this and we have 44,000 we could slush or probably I suspect the Department could use that money for some of the administrative costs.

A MALE VOICE: Chelsey wants a raise.

DR. GENEL: Or what have you or CI could use the money since they don't get any anyway.

MS. SARNECKY: That's a fabulous idea.

DR. HART: If you were to stop here and say that there's nothing else worth awarding I would suggest bring whatever balance there is toward the Yale core just to make it --

DR. GENEL: Okay.

DR. HART: -- but that's just a way out.

DR. KIESSLING: Well, why not put it to Nelson?

CHAIRPERSON MULLEN: Why would we give it to Nelson rather than someone else? I'm just questioning, I don't know -- why would we give it to --

DR. GENEL: Well, there are a couple --

DR. HART: There are a couple (indiscernible, talking over each other) that we currently have allocated to Nelson. I'm talking if there's 44,000 left over.

CHAIRPERSON MULLEN: Right. But I'm getting to the -- what we're going to do to get to 44,000 left over.

DR. HART: Okay.

CHAIRPERSON MULLEN: And in that regard I just in terms of numerical analysis and hearing people's considerations wonder how we would have a bunch of maybes that remain unfunded or perhaps get partial funding and then have a lower ranked Nelson getting some funding. And I put that back at the group that if I were just looking at this I would be asking that question if I hadn't been sitting here all day and we should have that conversation in my opinion.

DR. HART: To turn down three -- four grants scored at three for a four score grant --

DR. KIESSLING: For one year.

CHAIRPERSON MULLEN: Right.

DR. HART: -- for partial funding, for one year --

DR. GENEL: Yeah, but we have to recall I

think that we felt that the first reviewer, who was clearly quite negative, did not receive the full grant.

DR. HART: -- I know. I know.

DR. GENEL: Well, I mean, that's how the 4.3 is derived. So if we discount that --

A FEMALE VOICE: That means a three?

DR. HART: Yeah, but that's the question because --

DR. GENEL: -- well, I don't know what he is, but -- and I thought the sense was that in favor of the grant. First of all, it's very much disease oriented.

DR. HART: -- so is 24.

DR. GENEL: Yeah, it is. Yeah. And that there was thought to be value in -- that was the rationale. You can make an equal rationale for any of these, but we're really down to a point where you've got to say, well, this is more compelling than the other.

DR. WALLACK: And that first reviewer clearly identified to pickup on Ron's observations throughout the day as being somewhat skewed in a way that we were comfortable with.

DR. DEES: Well, it wasn't necessarily the same person reviewing it.

CHAIRPERSON MULLEN: Right. And I have a

hard time with that if we don't apply that to every one of these that was --

DR. GENEL: Yeah, but in this particular case I think the --

DR. WALLACK: We've dealt with it case by case.

DR. GENEL: -- yeah. In this particular case Commissioner I'm afraid that the investigator was penalized by the reviewer not getting the full application.

CHAIRPERSON MULLEN: -- right. I hear that.

DR. GENEL: Which is why I -- which is why I discount that evaluation.

CHAIRPERSON MULLEN: Okay.

DR. WALLACK: The other thing is there was a break off there because the one year opportunity was goal number one. So it does work I think.

DR. GENEL: We have to make -- we have to make tough decisions that's all. And I can't say that -- I can't say that I feel the same way about it a week from now, but I mean, but we've got to make -- but we've got to make -- yeah.

DR. WALLACK: So Mike, how did you get us

to the -- that point? Can you run us through that again? You just made a statement to get us $48,000 --

CHAIRPERSON MULLEN: Can we stick -- before we get to that please --

DR. GENEL: Well, I was just saying -- commenting that there's $44,000 left over, but --

CHAIRPERSON MULLEN: -- can we finish this piece though?

DR. GENEL: -- forget about it.

CHAIRPERSON MULLEN: Whatever it is.

DR. GENEL: If we could agree that we have as reasonable a ranking order -- funding order as we're going to come up with we can play around with the margins. But anyway Commissioner, that was -- that was simply my rationale because deciding between things that are frankly very, very well balanced --

DR. HART: I only go back though to the contention about Nelson. When I went back and reread the grant and I went through my review of it I ended up including for all the faults of the short grant, etcetera, that the score ended up being appropriate because of scientific factors that were present in all versions of the grant. So my feeling about the partial funding was if we got to that point in the scoring that made sense this

would be a good candidate. At this point with what I see on the screen I'm uncomfortable with that because I feel like it's too far down in the scoring to warrant that extra bump of funding. I like the grant, I'd like to see it succeed. If there was enough money I'd fund it. But I don't like taking it out of order the way it is.

DR. KIESSLING: Can we go back to O'Neill then?

MS. HORN: And just keep in mind we need to have backup grants for each category.

(Indiscernible, multiple voices.)

MS. HORN: Or maybe five because maybe this is one of them.

DR. HART: Yes. Maybe this is one of them.

DR. WALLACK: Marianne, can I go back to something that Ron put on the floor before? And that is that maybe that even though -- and Rich, you were saying that we have to remember that our motive this year was disease directed. And frankly I was right there, I made that motion to the disease directed, so I'm in favor of this. But if we reduce the two disease directed so that it comes out at 25 percent, or 24 percent actually of our total --

DR. HART: We're at 30 percent now.

DR. WALLACK: -- that's what I'm saying, we're 30 percent. But I'm trying to find the money --

DR. HART: I see.

DR. WALLACK: -- I'm trying to find --

DR. KIESSLING: To fund one more.

DR. WALLACK: -- right, to fund one more. I'm trying to find the money. So that if we reduced those two to a very significant amount of our total budget, it's a powerful statement, 25 percent, that will free up what, about -- close to $500,000, take 250 from each.

DR. KIESSLING: And if we didn't fund the Yale core --

DR. WALLACK: And my friend on my left continues to --

(Laughter)

A MALE VOICE: This is the price of funding the Yale core.

DR. KIESSLING: This is the price of funding the Yale core. It's just I love the Yale core.

CHAIRPERSON MULLEN: I think that's reasonable. If we took -- well, let's go back grant by grant. Which his the most painful grant that we're not funding? I mean, apparently Nelson.

MS. HORN: Could I just make a suggestion

that the Nelson piece for 250 that we put that back into a maybe slot and come back to it and that would I think -- there was -- yes, I think that would make us happier.

DR. KIESSLING: Maybe for 250.

MS. HORN: Yes. And then what does that do to our total? Okay. And now we look at the disease directed reducing those by 250 each?

DR. WALLACK: 250 each, 500,000. So it brings us down to $9,000,000.

MS. SARNECKY: So we're going to bring this to 1.25?

MS. HORN: Okay. This is 11SCDI2. And 11SCC01 to 12.50. Okay. We're down to 9,000,000. Then I suggest we revisit the existing maybe grants --

A FEMALE VOICE: That scored three.

MS. HORN: -- that scored three.

MS. SARNECKY: So these right here?

A FEMALE VOICE: Yes. Well, no. (Indiscernible, too far from mic.).

MS. HORN: And keep in mind backup grants as we go down.

DR. WALLACK: So would it be possible to -- and I have a motivate obviously in what I'm going to say because I really would like to see the Nelson come back

for one year, that's okay, I mean, I'm not ashamed to say it. If we were to do the SCB24 for two years can we make that work and get that one as well as the Nelson grant out?

A MALE VOICE: Are those really the best two of that group to fund?

DR. KIESSLING: Yeah. Should we look at all the threes that are -- we've got a few minutes to --

MS. HORN: Look at the threes.

A MALE VOICE: It's only 4:30, it's not even dark out yet.

DR. KIESSLING: -- 16, 18, 21, 22 and 24.

DR. GENEL: I think we need to look at 16 again.

MS. HORN: Okay. 11SCB16, Rachel O'Neill, it had a peer review score of three. That's in the no, we moved that to the no. Yeah.

DR. GENEL: This is the grant to study --

MS. HORN: So we're not reconsidering that.

DR. GENEL: -- small RNA.

MS. HORN: 11SCB18, Qyang, had a three peer review score, maybe for 750. I think we really need to bring in our Connecticut specific criteria here and look at whether there's something in any of these grants that

we haven't funded yet.

DR. HISKES: Well, this is another heart graft project. (Indiscernible, too far from mic.).

DR. DEES: I can't remember how this worked. They were engineering these cells to puff the aorta, puffing --

DR. HISKES: Pulsative tissue engineered grant.

DR. KIESSLING: There's an idea the heart muscles develop best if we cut from the (Indiscernible, too far from mic.).

DR. HISKES: Lots of preliminary data. The reviewers say there's a high need for this project. So it has the right approach to making IPS because the reprogramming genes disappear, different location, youngish P.I. The other reviewer is skeptical about the use of fibroblast for pediatric surgery. Should use more accessible, more commercially available fibroblasts. But I don't (indiscernible, too far from mic.). He's afraid that mouse models may not be telling and you want eventually human parts. But maybe that's true with all experiments with mice.

DR. KIESSLING: What about innovation?

DR. HISKES: Well, innovative, well

designed, lots of preliminary data. So all the, you know, the checklist of what makes a proposal good is all positive.

MS. HORN: And we should also keep in mind is this anything that couldn't be funded Federally.

DR. DEES: That's not a problem here.

DR. HISKES: Yeah, they could be funded Federally.

DR. DEES: I mean, there's some embryonic stem cells --

DR. HISKES: Not all lines are --

A FEMALE VOICE: (Indiscernible, too far from mic.).

DR. DEES: -- yeah, I know it's back in court and then it falls apart and that would be probably the current (indiscernible, too far from mic.).

MS. HORN: Okay. Is there any strong consensus here for moving this grant from maybe to yes?

DR. HISKES: I think it's a solid grant.

DR. FISHBONE: This is Qyang,

MS. HORN: Yes, Qyang, 11S --

DR. DEES: Of the one, two, three, four, three's I reviewed three of them. This is my favorite of the three.

DR. HISKES: Well, I'm not allowed to compare. So, you know, what can I say? Were I to compare I would --

(Laughter)

DR. FISHBONE: I think it does have potential clinical application, you know, in terms of if you can make heart muscle or it may have some application. So I would support that too.

DR. DEES: That was actually why I had put it on the fund list.

DR. FISHBONE: Yes.

DR. DEES: (Indiscernible, too far from mic.).

DR. FISHBONE: Well, the entity is a very rate entity, single ventricle, but if you could learn something about, you know, cardiac dynamics that would allow you to be able to use it in a more, you know, extensive application it may be -- might be important.

DR. KIESSLING: Who is this person?

DR. FISHBONE: Qyang. There are a lot of collaborators.

DR. KIESSLING: Does he need the Yale core?

(Laughter)

DR. FISHBONE: Histor (phonetic) Brewer is

co-P.I.

DR. HART: Young investigator, assistant professor. Had a seed grant from us.

DR. HISKES: He was a post-doc at the Harvard Stem Cell Institute. Harvard Medical School.

DR. KIESSLING: He had a seed grant from us?

DR. HART: Yes. That has just ended. It just ended.

(Indiscernible, multiple voices)

DR. FISHBONE: Marianne, do we need a proposal?

MS. HORN: Yes we do.

DR. FISHBONE: I propose that we fund this researcher, Yibing Qyang, B18.

A MALE VOICE: How much?

DR. FISHBONE: I did my big, I'm proposing it, I'll leave the money part to you.

MS. HORN: Okay. We have a proposal to fund 11SCB18, Qyang, moving this from the maybe column to the yes column. The outstanding question is for how much?

DR. KIESSLING: Is this a three year grant or a four year grant?

A MALE VOICE: I believe it's a four year

grant. Let me just double-check. Four year grant, yes.

MS. HORN: Okay. So is the motion for 750,000?

DR. HART: What would it be like to fund this at 500,000?

DR. FISHBONE: That would set him back.

DR. HART: Programmatically in terms of what the budget is --

DR. KIESSLING: Or if you did it for 450 you could do another one.

DR. HART: -- well, that's what I'm trying to do.

DR. HISKES: Yeah, it could be another one. So let's see. Some money goes to Qyang, some goes to Brewer (phonetic), two post-docs, so the first year total salaries ranges fringe is 118,753. The total for the year is 187,000. So -- I don't know.

A MALE VOICE: You can do two years or four years.

DR. FISHBONE: Yeah. I think two years and then come back if you've got stuff worth --

DR. HART: And the advantage of a two year award here is that that doesn't mean a one year award would mean they have to come back this coming December and

apply for next year, that's too short to do anything like that. So two years is kind of the minimum to do anything effective.

DR. GOLDHAMER: I must have missed something. Why is cutting the number of years on this particular grant being discussed?

DR. HISKES: To fund another one at the same level.

DR. HART: It's among the lowest scored grants to try to find whether we could fund more than one. It's a question, not a proposal.

DR. HISKES: If we were to do 400,000 then we'd have 400,000 left.

DR. DEES: So two years at full funding here is 375.

DR. HART: So it would be more than they asked for per year for two years.

DR. FISHBONE: See how it goes and then come back if you're getting good results. I mean, this may be a blind end.

DR. KIESSLING: He's just at the end of a seed grant from us on this topic. So it would just carry him.

DR. HART: It's like a bigger -- another

seed grant.

CHAIRPERSON MULLEN: I understand that, I work for the State, as do some other people here. We don't usually give people more than they ask for per year. I just want to put that back out there.

DR. HART: Well, we being reasonable people --

(Laughter)

CHAIRPERSON MULLEN: Does it have a reason why we're doing that, that fits their budget?

DR. HART: Yes.

DR. HISKES: So I propose two years.

DR. HART: At 375?

DR. DEES: 375 would be two years.

MS. HORN: Okay. So the motion, and I think we'll make this a motion, is that we fund this 11SCB18 for $375 -- $375,000 for two years. Do I have a second?

DR. KIESSLING: I'll second that.

MS. HORN: Okay. All in favor?

VOICES: Aye.

MS. HORN: Opposed? Okay. That is --

A FEMALE VOICE: Why do you need a motion for that?

MS. HORN: -- I don't know why, I just felt like we were getting --

(Indiscernible, multiple voices)

MS. HORN: -- I'm just being arbitrary here.

DR. GENEL: Marianne, I should be listed as an abstention.

MS. HORN: Okay. And Dr. Genel is an abstention. Thank you. Alright. The next grant down then is 11SCB, UCHC, Hector Agulla, 750,000 again, peer review score of three.

DR. HART: And now there's no reason why that one is prioritized over the next one for any reason whatsoever.

DR. KIESSLING: That's the antibody grant.

DR. HART: Yeah.

MS. HORN: The consensus is then to move this to the no category? Further discussion? B22, Yale University, Scott Swenson, this is peer reviewed at three, 750,000, Yale University. Discussion?

DR. KIESSLING: This is a liver disease grant?

DR. DEES: (Indiscernible, too far from mic.).

DR. KIESSLING: Osteopetrosis. Osteoplast progenically. We looked at Agulla, 21?

MS. HORN: Who were the reviewers on this one?

DR. DEES: I was one of them.

MS. HORN: Okay. Dees and --

DR. DEES: I'm checking notes here. At this point my notes don't help me because my mind is completely fried.

MS. HORN: -- I'm sorry.

DR. HISKES: I don't think you should drive home.

DR. DEES: Yeah.

DR. KIESSLING: This may not be as strong a grant as number 24.

DR. DEES: Yeah. In my mind it wasn't as strong as 24.

DR. HART: I didn't read 22 but 24 I'd be very much in favor of half. So I guess I would go half on 24.

DR. KIESSLING: Yeah, 24 is a good project.

MS. HORN: Okay. So the consensus on B22 is to move this grant to the no category. Any further discussion? Okay. That's moved to no. B24, Li, peer

reviewed at three, 750,000, UCHC.

DR. KIESSLING: This is a good application.

DR. WALLACK: So Marianne? One of the questions that was stated about this grant is that the progress of the study -- of the previous study from 2008 is unclear. There was a question about moving forward with this grant, therefore about the validity of moving forward when their previous grant results have not yet been clarified.

DR. KIESSLING: Was it a seed grant?

DR. WALLACK: I don't know -- it was a similar study in 2008 and I'm not sure, I don't know if it was a seed or not.

MS. HORN: Dr. Hart, you were reviewing --

DR. HART: Yeah. I'm looking up past grants now. It was established. So that started in September '08 and it's on SMA using ESC.

DR. KIESSLING: Okay. She has funding through next August.

MS. HORN: I think there was discussion earlier that this be funded for possibly two years.

DR. HART: Yeah, the question is that or nothing.

DR. DEES: The two year, I mean, this

337,470.

DR. KIESSLING: What was it?

DR. DEES: 337,470. So this grant goes until next year Ann?

DR. KIESSLING: No. It's a different project. She has one grant that goes till next year. She has one, I mean, everything is --

DR. WALLACK: Are we looking at Li?

MS. HORN: Yes.

(Indiscernible, multiple voices)

MS. HORN: Do we have any sense of this grant? Anybody want to make a motion on this?

DR. KIESSLING: How about the one that's in press she's got?

DR. HART: Yeah, the one that's in press is close, but it doesn't seem to deal with us in that area. It says F2 regulates higher upbringing (indiscernible, too far from mic.).

DR. KIESSLING: I don't know. One paper it doesn't really --

DR. HART: The first one is, you know, again, for brain from IBS and it's a middle author paper. So I think being that the project itself was reasonably elegant and yet later aims depended on earlier aims if

there was any possibility of funding this one it should be for two years of the request. Among the other discussions we've had so far I still contend this is a good candidate for two year funding.

MS. HORN: Do you want to put that in the form of a motion?

DR. HART: Not yet.

DR. KIESSLING: We're going to balance this against Nelson, right?

DR. HART: Right.

CHAIRPERSON MULLEN: Balance it against putting some of the monies back that we took from somebody else.

A MALE VOICE: True.

CHAIRPERSON MULLEN: That's another way. Because we cut the others without really thinking about what those potential impacts are.

DR. KIESSLING: No we didn't.

CHAIRPERSON MULLEN: Oh, we didn't? I'm sorry.

DR. DEES: Well, we sort of cut the two big grants without really thinking about it.

DR. HART: It was a lot more money, that's all it was.

CHAIRPERSON MULLEN: Okay. So let's have a motion here just because it feels like it deserves a motion.

DR. DEES: The motion is we fund this for two years at 337,000, whatever the proposal is. Chelsey?

MS. SARNECKY: 337,470, which would leave us with a little over $80,000.

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

A MALE VOICE: Sure.

MS. HORN: You made the motion.

DR. HART: No, you made the motion.

MS. HORN: Oh, he -- I'm sorry. I'm sorry. Okay. So we have a motion and a second. Any further discussion?

DR. KIESSLING: I'm surprised he went above 375.

DR. HART: That's what they asked for for the first two years cumulatively.

DR. DEES: Yeah, cumulatively.

DR. KIESSLING: Oh, okay.

DR. HART: So we're funding it for two years and giving them what they asked for.

A MALE VOICE: Following the government rule and only giving them what they ask for.

MS. HORN: And this is the UCHC grant --

MS. SARNECKY: Quick question. The one that we just cut to 337,470, that's for two years?

MS. HORN: -- correct.

MS. SARNECKY: Okay. Just checking.

MS. HORN: Okay. So this is --

DR. KIESSLING: Then we can give $40,000 --

MS. HORN: -- this is the UConn grant. People who have the funds from UConn should not vote. All in favor of this motion please signify by saying yes?

VOICES: Yes.

MS. HORN: Opposed? And we have two recused. Okay. We are --

DR. KIESSLING: -- so we can give $40,000 back to the other two grants we just cut?

DR. WALLACK: So can I bring up the Nelson grant again possibly?

(Laughter)

MS. HORN: We also need backup grants in all categories.

DR. WALLACK: I understand but I've been talking about the Nelson grant as 80 for one year.

MS. SARNECKY: $80,997.

DR. WALLACK: And again, I don't think we

should hold him accountable for the process --

DR. HART: I think we gave him every consideration and we dealt with the issue already to tell you the truth. I don't think that is the issue. I think the multiple versions is the issue.

DR. WALLACK: -- well, I'm wondering though Ron if there isn't room in any of the other grants that -- to create space for that grant?

DR. HART: That's a different question.

DR. WALLACK: What's that?

DR. HART: That's a different question.

DR. WALLACK: Okay. Well, that's my question.

CHAIRPERSON MULLEN: Are you proposing that we go back through the entire list and find something to shave --

DR. WALLACK: No. What I'm proposing is that we can take a quick look at the -- what we've done so far.

DR. KIESSLING: Yeah, and I want you to defend my grants.

DR. WALLACK: And we're -- we need to pick up $180,000 and I'm wondering if there's not $180,000 in any of the other grants that -- or two --

DR. HART: Well, okay. So the one thing I see on the screen that I want to be reminded about why it's yes on the screen is the A39, that scored a four, that's got 196,000? And I didn't review it, I don't know anything about it, I just want to be reminded why that's on our list to be funded considering all the discussion we've just had.

DR. FISHBONE: Well, it's a seed grant.

DR. HART: Yeah. Okay. Is it a good one?

DR. FISHBONE: And a good one.

DR. HART: A four?

DR. FISHBONE: Studying IPS cells from alcoholics.

DR. KIESSLING: Oh, this is the alcohol syndrome.

DR. FISHBONE: This is the alcoholic study. I think if it were -- if it got -- if the scores were not as high as it might have been it was more because it was viewed to be speculative. But potentially very -- of great value.

DR. HART: I just want to be sure that we're not going too far down the list.

DR. FISHBONE: And this is an investigator not previously funded, not substantially funded. I mean,

we all agreed this was precisely the sort of stuff that we had established seed grants for.

DR. HISKES: Looking at the chart again let's think about the Laural Grabel grant. Arguments have been inconsistent over the course of this day. We would say, oh, it's a four year grant, therefore we're not going to -- and we've just been cutting four year grants. So do we want to revisit that and there's some equity among the other grants of the same rating.

DR. KIESSLING: It's a 3.5.

DR. HISKES: Yeah, 3.5 The argument earlier in the day, don't cut four year grants, that's four years, it's less money per year than if the amount asked had been for three years. But we've just been cutting four year grants on the grounds of trying to expand the number of people that get funded. So I'd like to revisit the Laural Grabel grant using the logic we've been applying.

MS. HORN: And that logic is?

DR. HISKES: That logic is can we fund another grant for two years.

DR. HART: Or not?

DR. HISKES: Or not. I have no opinion about the quality of the Grabel grant, vis-a-vis the

quality of the other grants we've cut.

DR. WALLACK: So could we fund the Laural Grabel grant for three years then?

DR. DEES: Well, we could. Is it appropriate?

MS. HORN: I think part of the argument for that one was that it was a grant from Wesleyan and an opportunity to derive funds to another institution. But it is a 3.5 five grant and we cut some three's.

DR. DEES: This was another case in which people thought the ranking was off.

DR. GOLDHAMER: Yeah. I reviewed this grant.

DR. KIESSLING: The reviewers were enthusiastic.

DR. GOLDHAMER: Yeah. This was the grant that didn't have a single criticism about the science and it was a big multi-co-P.I. team, they weren't asking for money for three of the collaborators. It would be difficult to do this research for significantly less than she asked for. So I'm not generally in favor of, I mean, I understand why we're, you know, giving partial funding just to try to find a way to fund quality science that didn't score quite as well. But in this case this grant

had -- there was no criticisms at all and I don't think there's a good justification to cut it.

DR. KIESSLING: Yeah. We talked about this. The score didn't match the enthusiasm.

DR. HART: Then that's fair to have it where it is then.

MS. HORN: So then the other proposal was that we take some of the remaining money and add it back to the disease specific grants, the disease directed grants since we cut 250 from there without talking about that a great deal.

DR. DEES: I move that we add the remaining money between the two disease directed grants.

DR. HART: Second.

MS. HORN: Discussion?

DR. HART: Because there's no good reason to do anything else.

MS. HORN: Seeing no further discussion all in favor?

VOICES: Aye.

MS. HORN: Opposed? Okay. The motion carries.

DR. HART: We might want to pick a few backup grants.

MS. HORN: You do need to pick out some backups, yes.

A MALE VOICE: Pickup meaning backup?

MS. HORN: We do.

DR. KIESSLING: How about the Nelson grant?

(Laughter)

MS. HORN: We have typically had two in the seed, two in the established. I think that's all we've done. We have not done --

DR. GENEL: I don't -- I don't think we've --

DR. WALLACK: I'll nominate Nelson for one of the backups.

DR. HART: At the reduced funding level or at the current?

DR. WALLACK: No, that's a very good question. I would recommend it at the reduced funding level because it would have a better chance of getting funding.

DR. HART: Plus, I don't think it's scientifically fair to give the full amount.

DR. WALLACK: Right.

DR. GENEL: So it would be a backup of what, 250? That was the number that we had up there.

DR. HART: Right.

DR. GENEL: Okay.

MS. HORN: Okay. Any further discussion? So Nelson -- what number is that? 11SCB15 is an established investigator backup grant at $250,000, funded for one year.

DR. GENEL: Rachel O'Neill.

MS. HORN: We're now looking for a second backup for established investigator.

DR. GENEL: This is one of the double-stranded RNA grants. I think this was the double-stranded RNA.

DR. HISKES: I would like to propose that for backup.

DR. GENEL: Yeah, I agree.

MS. SARNECKY: At full funding?

DR. GENEL: Well, it's backup -- it's going to be backup for what?

DR. FISHBONE: Chelsey, do you keep tabs on whether -- most of these people have applied to NIH as well? Do you keep tabs on whether they get funded by NIH?

MS. SARNECKY: No. No.

DR. FISHBONE: Because I think that would be important. You know -- no, this isn't for Chelsey,

this is for -- I think in most granting institutions you kind of try to keep an eye on are people getting double funded, are they -- have they put in NIH and are they getting funded by NIH. The institution I think would know that and I think that would be important to know because then you'd have a larger reserve list and use some of the money that's been given them to somebody that doesn't have funding.

MS. HORN: Okay. So the motion is for Rachel O'Neill, 11SCB16, for reserved established investigator grant at $744,013. Is there a second to that motion?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. SARNECKY: In the past we have picked out reserve grants and then put them in order of which one we wanted to fund before the other. Is this the order that we're doing it, the Nelson grant is first and then the O'Neill grant would be second?

MS. HORN: That would be up the group. The Nelson grant ranked lower.

DR. FISHBONE: I would suggest that because I think we have questions about ranking of the Nelson

established.

MS. HORN: Okay. So Nelson is one and O'Neill is two.

DR. GENEL: You know, it may depend upon what it's backup to. Why don't we just rank them -- why don't we just rank them together and if the question comes up then we'll have to decide? No? I don't know.

DR. ARINZEH: Then we have to come back here again.

DR. GENEL: Alright. I don't care.

MS. HORN: So we have one and a half established grants as backup. Is the Committee comfortable with that or do you want to go one more?

DR. GENEL: That's enough.

DR. WALLACK: No, that's enough.

DR. KIESSLING: How many do you usually need?

MS. HORN: We usually have two full established in case we have a failure of a grant.

MS. SARNECKY: Which has happened in the past.

DR. KIESSLING: But have you ever had more than one fail?

MS. SARNECKY: We've had one grant, a large

grant, not be able to get escrow approval and that was enough funding for two smaller grants.

DR. KIESSLING: Okay. So we need a third.

DR. HISKES: But that was because it was --

MS. SARNECKY: It was a private -- yeah.

MS. HORN: Well, we can go to seeds, we need a couple of seeds as well.

(Discussion off the record)

A FEMALE VOICE: We don't necessarily have to put seed grants on the reserve, do we?

MS. HORN: Well, if we have a seed grant that fails I think we should be able to pop one in.

A FEMALE VOICE: We might be able to fund the Nelson.

(Laughter)

DR. GENEL: I think for this one I'd just go back to priority score.

MS. HORN: Yeah, we had a couple that we --

DR. HART: If we go by priority score now we're going back to the issue of giving two grants the same --

DR. GENEL: Well, I know that, but as -- but I'm --

DR. HART: -- as a backup, yeah.

DR. DEES: And then there's other considerations here because now the backups -- the third backup is pretty far down. So I think anything that's already in the core --

DR. HART: So then how about if we make the motion that use the Rasmussen and Carmichael grants in that order as the backup seeds? Is that acceptable?

DR. DEES: Second.

MS. HORN: Any further discussion? Okay. Then let's get some numbers on those. The 11SCA35 is the Rasmussen grant for 200,000 and the Carmichael grant is 11SCA07 for 200,000 as reserve grants in that order. Any further discussion? All in favor?

VOICES: Aye.

MS. HORN: Opposed? Okay. We are almost there. What we need to do now is go through each one of the approved grants and have a motion, a second and only qualified voters voting on each one of those. Do people need to take a five minute break to stretch and come back and do that?

DR. HISKES: No.

A MALE VOICE: Let's just do it.

MS. HORN: No stretching, alright. Have you got the top of the list there Chelsey?

MS. SARNECKY: Yep.

MS. HORN: Okay. I'll need a motion for acceptance, a second and then a vote on each one of these. 11SCA37, Yale University, Shangqin Guo for 200,000. I need a motion?

DR. ARINZEH: I motion to accept.

DR. FISHBONE: So moved.

MS. HORN: Second. All in favor. This is a Yale University grant, so Dr. Genel is recused. All in favor?

VOICES: Aye.

MS. HORN: Opposed? And one recused. 11SCB19, Yale University, Sandra Wolin for $750,000?

DR. HISKES: So moved.

DR. FISHBONE: Moved.

MS. HORN: Okay. Second is Dr. Fishbone. This is a Yale University grant. Dr. Genel is recused. All in favor?

VOICES: Aye.

MS. HORN: Opposed? One recused. 11SCC01, Chondrogenics, Inc., Caroline Dealy, at $1,290,499?

DR. WALLACK: Move.

MS. HORN: Milt. A second?

DR. DEES: Second.

MS. HORN: Dr. Dees. And this is a -- everybody is able to vote on this, although there is a significant UCHC portion of this grant, so I think those folks should not vote on this. Correct?

DR. HISKES: I consider it one university.

MS. HORN: Yes. Yes. But this company is --

DR. HISKES: Right. That's UConn.

MS. HORN: -- yes, okay. So UConn voters are not voting. All in favor?

VOICES: Aye.

MS. HORN: Opposed? Motion carries. 11SCA01, UCHC, Kristin Martins-Taylor for $200,000. Motion?

DR. KIESSLING: I so move.

DR. FISHBONE: Second. Dr. Kiessling, Dr. Fishbone. UCHC voters are not voting. Dr. Hiskes and Dr. Goldhamer. All in favor?

VOICES: Aye.

MS. HORN: Opposed? Two recused. 11SCA33, Yale University, Peter Amos, $200,000. Motion?

DR. KIESSLING: I so move.

MS. HORN: Second? UC -- I'm sorry, this is Yale. Dr. Genel is recused. All in favor?

VOICES: Aye.

MS. HORN: Opposed? None. Dr. Genel recused. 11SCA34, Yale University, Pascal Drane, 200,000. Do I have a motion?

DR. HISKES: So moved.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Opposed? Dr. Genel is recused. 11SCB08, UCHC, Hicham Drissi, 650,000. Do I have a motion?

DR. FISHBONE: Moved.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: It's a UCHC, we have two recused. All in favor?

VOICES: Aye.

MS. HORN: Opposed? Motion carries. 11SCB23, Yale University, Flora Vaccarino for $744,446 and it's a Yale University grant. All in favor?

VOICES: Aye.

MS. HORN: Opposed? Did I have a motion from somebody?

VOICES: No.

DR. HISKES: So moved.

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Opposed? One recusal. 11SCB04, UCHC, Gordon Carmichael for $750,000.

DR. HISKES: So moved.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Okay. Two UCHC recusals. 11SCA28, UCHC, Xin-Ming Ma, 200,000. Do I have a motion?

A MALE VOICE: Make a motion.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And two UCHC recusals. 11SCB11, UCHC, David Han, 570,000. Do I have a motion?

A MALE VOICE: Move.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And two UCHC recusals. 11SCDIS02, UConn, $1,700,000 -- no, what's our final figure there? $1,290,499 --

MS. SARNECKY: And 50 cents.

A MALE VOICE: Move.

MS. HORN: -- and 50 cents?

MS. SARNECKY: Yes. But I didn't fix the decimal places to show on there yet, but there is an additional 50 cents.

MS. HORN: Do we need the 50 cents?

MS. SARNECKY: I was told to split it in half.

(Laughter)

MS. HORN: I see. I see. I think we can do away with 50 cents. $1,290,499, Urs Boelsteril, and we have a motion and a second. All in favor?

VOICES: Aye.

MS. HORN: And two UConn recusals. 11SCA03, UCHC, 200,000, Alissa Resch. Do I have a motion?

A MALE VOICE: So moved.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And two UCHC recusals. 11SCB28, Wesleyan for 750,000, Laural Grabel?

A MALE VOICE: So moved.

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: 11SCA39, UCHC, Jonathan Covault, 196,836. Motion?

A FEMALE VOICE: So moved.

MS. HORN: Second?

A MALE VOICE: Aye.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And two UCHC recusals. 11SCA35, UConn, 200,000, Theodore -- oh, I'm sorry, this is the reserve. Should we do those on our way through?

A FEMALE VOICE: Yeah. Why not.

MS. HORN: Okay. Theodore Rasmussen is reserve number one for 200,000. A motion?

A FEMALE VOICE: So moved.

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Two UConn recusals. 11SCD02, Yale University, Haifan Lin for 500,000?

A MALE VOICE: Move.

MS. HORN: Okay. And second?

A MALE VOICE: Second.

MS. HORN: And one Yale recusal. 11SCA15, Yale University for 195,251 --

A MALE VOICE: You skipped a vote there.

MS. HORN: -- I'm sorry?

A MALE VOICE: You skipped a vote.

MS. HORN: I skipped a vote?

A MALE VOICE: Yes.

MS. HORN: I did. I moved right beyond that. I'm sorry. Alright. Did we have a motion?

DR. HART: Yeah, we did and it was seconded.

MS. HORN: Alright. We had a second. Can we have a vote on the Yale core grant for 500,000? All in favor?

VOICES: Aye.

MS. HORN: And Dr. Genel is recused. Okay. Thank you. 11SCA15, Yale University, $195,251, Rong Fan. Motion?

A MALE VOICE: So moved.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: Okay. We had one recusal. 11SCA07, UCHC for 200,000, Gordon Carmichael, this is reserve two for the seed grants for 200,000. Motion?

A MALE VOICE: So moved.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And two UCHC recusals. 11SCB16, UConn, Rachel O'Neill, reserve number two for the established investigator, $744,013. And a motion?

A MALE VOICE: So moved.

MS. HORN: And a second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And two UConn recusals. 11SCB18, Yale University for $375,000, Yibing Qyang. May I have a motion please?

DR. HISKES: So moved.

MS. HORN: Do I have a second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And one Yale recusal. 11SCB21, UCHC --

A MALE VOICE: No, no, no.

MS. HORN: -- oh, I'm sorry. 11SCB24, UCHC, Li for $337,470. And a motion please?

A MALE VOICE: So moved.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And two UCHC recusals. 11SCA40, Yale University, Sundaram for $200,000. May I have a motion?

A FEMALE VOICE: So moved.

MS. HORN: Second?

A MALE VOICE: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And one Yale University recusal.

11SCB15, UConn, Craig Nelson, this is reserve one for the established investigators, $250,000. May I have a motion please?

A MALE VOICE: Move.

MS. HORN: Second?

DR. KIESSLING: Second.

MS. HORN: All in favor?

VOICES: Aye.

MS. HORN: And two UConn recusals. 11SCA02, Yale University --

A MALE VOICE: No, no. We're done.

MS. HORN: -- no. Okay. We're done. Thank you all very much. Anything we've forgotten?

DR. WALLACK: How many people did we fund, do you know the number of researchers that we funded?

MS. HORN: We can have that in just a minute I think.

MS. SARNECKY: 20.

DR. WALLACK: 20?

MS. SARNECKY: Yep.

MS. HORN: So Chelsey, can you just walk us through the process from here about how the people get notified?

MS. SARNECKY: Sure.

MS. HORN: Okay.

MS. SARNECKY: I will be notifying everyone that has applied to the program with either a sorry, you didn't make the cut, or a yes, you were funded, or a yes, you were partially funded. Please get me your revised budgets and/or science that goes along with those specific dollar amounts to me by a date chosen by this Committee if they want or I can just pick a date and we can go with that.

A FEMALE VOICE: You can pick a date.

MS. SARNECKY: Okay. So and then once we receive all of those revised budgets I will send them around to the Committee just as an FYI to review and then we begin the contracting process in which we request the money from the Department of Public Health, Connecticut Innovations does once we have signed contracts back from the universities, well, fully executed contracts with Connecticut Innovations and the universities or private company.

MS. HORN: And from the Department of Public Health we issue a letter of certification that has to be signed by the Commission indicating that everything is complete, that we have the completed escrow verification forms that are needed and completed

contracts. Well done.

MS. SARNECKY: Do we need a public comment period? I don't remember if we've done that.

MR. MARC LALANDE: My name is Marc Lalande. I'm the Director of the University of Connecticut Stem Cell Institute and I will also take the liberty of speaking for my friend and colleague, Dr. Haifan Lin, who is the Director of the Yale Stem Cell Center. We want to thank you very much for your work and especially for the awards. And Chelsey, I will be contacting at least the people at the University of Connecticut to tell them about this very good news. Thank you very much for looking at this. We greatly appreciate it and I can tell you that we're all working very hard to honor your commitment to us. Thank you very much.

A FEMALE VOICE: Can you get us some more money?

DR. LALANDE: I don't know. (Indiscernible, to far from mic.).

(Laughter)

MS. HORN: And to all of you thank you so much for your hard work. You just are a tremendous team.

A MALE VOICE: And thank you guys for making it happen, CI and DPH, we really appreciate it.

(Applause)

MS. HORN: So we'll meet again. When shall we meet again, September? We don't need to meet in August?

MS. SARNECKY: I think it would be a good idea if we did have a meeting. There's a lot of approvals that we need for previous years' grants, additional -- the Committee needs to approve annual reports and we have some personnel issues that need to be taken up. I can bring those issues to the smaller Grant Application Subcommittee, but I think there are a few issues that do -- that the full Committee does need to see.

MS. HORN: Okay. So we'll meet on our regularly scheduled August meeting, the third Tuesday of the month. Thanks very much.

(Whereupon, the hearing adjourned at 5:30 p.m.)