VERBATIM PROCEEDINGS

CONNECTICUT STEM CELL RESEARCH GRANT REVIEW

JUNE 7, 2010

8:30 A.M.

LEGISLATIVE OFFICE BUILDING
300 CAPITOL AVENUE
HARTFORD, CONNECTICUT

POST REPORTING SERVICE
HAMDEN, CT (800) 262-4102

RE: CONNECTICUT STEM CELL RESEARCH GRANT REVIEW
JUNE 7, 2010

. . .Verbatim proceedings of the Connecticut Stem Cell Research Grant Review, held at 300 Capitol Avenue, Hartford, Connecticut, on June 7, 2010 at 8:30 a.m. . . .

CHAIRPERSON ROBERT GALVIN: For those of you who aren't familiar with this room, the microphones only work when you press the little red button down and the light lights up. When you're through talking, if you don't shut your mike off, the next person can't -- it won't accommodate the next person, so you have to do it one-by-one.

And if you leave your mike on and mumble under your breath, it will be picked up, because these mikes in this room are very sensitive. We are in the Legislative Office Building. This is a public room, and you will see people wander in and out from time-to-time.

Some of them are curious about stem cells. Some of them are just looking for something else. So if you see people come in and sit down and get up, that's sort of the nature of the beast here.

The rules say that you can't bring food

into this room. I don't think anybody is going to yell at you if you bring a doughnut or something like that, but don't bring a meal back in here, or a big sandwich, although I see it done all the time when we're in session, but, for our purposes here today, don't do that.

The building closes at either 5:15 or 5:30, and there are no exceptions to that, so we will have to exit promptly at the end of our assigned time. We will have a 45-minute lunch break and two 10-minute breaks during the day. Marianne suggested, what, 11:45?

MS. MARIANNE HORN: As close to noon, wherever we get to.

CHAIRPERSON GALVIN: Yeah. When we can make a break that makes sense, as close to noon as we can, we will do so. The cafeteria is directly below us. The food is ordinarily quite good and very clean. You can make your own. You can get a sandwich. You can get a regular sit down meal, whatever you want.

There are bathrooms downstairs, but if you go out the door, the door to my left and take an immediate left, there are restrooms right there, so you don't have to go all the way down, up and down the stairs.

We have a great many grants, some of them of great merit, to discuss today. We are starting this

later in the calendar year than we thought. We were unaware that the 10 million dollars had been put in our account until one of our accountants noticed it.

It appeared in mid/late April, with no preamble. We had heard it was going to be five million. Sometimes it was nothing. We heard it was nothing, but we got to 10, and we have had zealous advocates.

We lost the money a couple of times and got it back, and we'll remind you all that next year, the next cycle is not very far away. I will also remind you that there will be a change in state government, and it's up to all of us, who are acquainted with, or asked to give aid and comfort to office seekers, to let them know that we certainly may be very inclined to do different things for them, but that we want our stem cell budget kept intact.

As you know, these are hard times, and there's no guarantee we'll have 10 million next year, but we've got 10 million now, and, so, we'll get on with the business of deciding which grants are going to be funded.

MS. LYNN TOWNSHEND: Good morning, everyone. My name is Lynn Townshend. Thank you for coming today to the 2010 Connecticut Stem Cell Research Advisory Committee grant consideration meeting. My apologies for my tardiness. We were transporting people

from the hotel over to the meeting.

There are 89 grants that will be considered today at 9.8 million dollars in grants and aid for Connecticut Stem Cell Research Fund or from that fund. These funding decisions are not binding until the final vote takes place.

As a committee, the right is reserved to change grant categorization. That is yes, no, or maybe, until the final and concluding vote takes place at the end of the meeting.

To the committee, good morning, and, once again, thank you so much for all of your hard work in reviewing all of this information, all of these grants in advancing stem cell research in the State of Connecticut. It is certainly appreciated.

Regarding the discussion and voting, please know that only committee members are eligible to vote on a grant, and they may participate only in the discussion of the grants for which they are eligible to vote.

If you are not eligible to vote on a grant, due to a conflict of interest, please do not participate in the discussion of that grant consideration.

The first two categories for consideration are those, today, are those of core and group grants.

Applications in these two categories, regardless of their peer review score, will be described by the team of committee members assigned to review that grant for a period of approximately five minutes.

The five-minute description period will be followed by a committee discussion period of about 10 minutes, after which Dr. Galvin will ask if there are any objections to placing the grant application in a particular category, that being yes, no, or maybe, as determined by group consensus. That's by the committee members who are eligible to vote on that grant.

If you have any objections and you are eligible to vote on a grant and wish to see an application placed in a category, other than that of the consensus of the eligible group, please make your objections known immediately.

That objection automatically places the application under the maybe category, so that this grant may be considered during the second phase of the process.

After all of the core and group grants have been considered, the maybe and yes grants from these categories will, again, be discussed with a four-minute time frame. The no grant applications will be eliminated. Again, that is not final until the final vote takes

place.

The remaining categories will be considered similarly, as outlined with the following time limits. Seed grant proposals scoring 6.0 or above will receive a one-minute description and discussion. Seed grant proposals scoring 5.9 or below will receive five minutes' description and discussion.

Established investigator grant proposals scoring 6.0 or above will receive a one-minute description and discussion, and established investigator proposals scoring 5.9 or below will receive five minutes' description and discussion.

Please do what you can to respect these time limits. I know that much discussion will be going on today. This was the time limit agreed to, approximately, by the committee, and, again, please express your objections and opinions according to the process in place that was decided at the last meeting.

Full funding considerations will be held until the end of the consideration of all grant categories. Roll call votes will be conducted only for final decisions regarding grant funding.

Because this is a public meeting, where most deliberations are to be heard by all, it is

imperative that committee members refrain from discussing grant applications among themselves, with others, such as audience members, or potential grantees, or DPH staff, and the media, if they are here, during breaks, lunch, or off hours tonight or tomorrow, if we move into tomorrow.

There may be a need for the committee to adjourn to Executive Session to consider a grant proposal or proprietary information contained in the proposal as pertinent to the decision making. During that time, the audience will be asked to leave the room and will be called back in when the Executive Session is concluded.

Two 10-minute breaks and a 45-minute lunch, as Dr. Galvin mentioned, have been planned during the course of the meeting. Lunch is on your own. There is a cafeteria, as he said, right below us, and your adherence to these time limits is also appreciated.

To the audience, lots of familiar faces over there today. Thank you for attending this open grant consideration meeting. As you've heard, there's lots of hard work to be done today, 89 grant proposals to be considered, and, again, very hard work to be completed by the committee members. We respectfully ask that conversation within the audience be kept to a minimum.

You are welcome to continue any

conversation in the hallway and return when you are finished. We thank you in advance for not addressing questions about grants under consideration to committee members on break, during lunch and between days of the meeting.

Should it become necessary for the committee to move into Executive Session, a period of two minutes will be allotted to allow audience members to move to the hallway, and, again, as I said, we'll notify you when the Executive Session has ended.

Finally, a period of public comment will take place at the end of this meeting after all grant funding decisions have been made. We ask that you refrain from comment until that time, unless specifically called upon by members of the committee for the purpose of clarity regarding a grant application.

At this time, if you would please silence your cell phones, Blackberries, laptops and other electronic instruments? It's much appreciated and away we go.

CHAIRPERSON GALVIN: I would just interject one remark. If you're in the cafeteria, there are lots of ears in the cafeteria, and you have no idea, I'm sure most of you don't, about who is sitting just behind you or next

to you, so I would suggest that you do not have any substantive discussions of the grants while you're in the cafeteria, even for coffee. It's not a private area at all.

Marianne, I cannot vote on UConn or Yale, and Marianne advises me that the individuals who can vote on Yale exclude?

MS. HORN: Dr. Genel and Dr. Latham. In general, there may be other people, who, on an individual grant, have a conflict, but I'm not aware of those. And then, on UConn, Dr. Hiskes and Dr. Goldhamer are excluded from UConn votes. Thank you.

DR. MILTON WALLACK: Milt Wallack. Are they going to be able to discuss the grants, Marianne?

MS. HORN: No. They don't take part in the discussion or the voting on those particular grants where they have a conflict.

CHAIRPERSON GALVIN: Let's go.

MS. TOWNSHEND: The first grant for consideration this morning is 10SCD01, Dr. Antic. The title is Stem Cell Physiology and Core Chemistry, the institution is UConn, the peer review score is 2.0. This is a core grant, and five minutes of description by the grant -- do you have a list of that? Would you be able to

provide me with that list? Thank you, Darling.

That would be Fishbone and Hart. Five minutes of description, please. Kiessling and Latham. I apologize.

DR. STEPHEN LATHAM: Sorry. I'm one of them. I think Ann might be the other on this.

MS. TOWNSHEND: Kiessling and Latham.

DR. LATHAM: And I'd appreciate it if Ann would go first.

DR. ANN KIESSLING: This is an interesting core grant application from not a really established investigator, but somebody who has a strong background in neurophysiology.

This is an interesting idea. The score that we see, this 2.0, is quite a bit higher than the enthusiasm reflected in the criticisms of the grant reviewers, and, when I looked through this, I actually had some of the same concerns, so although it's scored at 2.0, what they say and what I take from this is a little bit more like a 2.5 or so.

This is a very large amount of money. It's $600,000, I think, and they're proposing to establish a neurophysiology core, so that stem cells that are differentiated from any source, embryonic stem cells, IPS

cells, can be tested for real nerve function, and this is a really good idea.

The common use of simply gene expression to decide something that's going down a neural pathway has sort of run its course, and now what we really need are some very fine-tuned methods for seeing if the cells that are created can actually conduct nerve impulses, that sort of thing, and he's got about six different ways that they're going to do this, but I think this needs to be considered, in terms of the other, some of the other really large grants we have, and I would, at this point, not recommend anything, except a maybe.

CHAIRPERSON GALVIN: Further comments?

DR. LATHAM: Yeah. Steve Latham. I was actually inclined to put this in the yes category, because although -- the main criticism that I worried about in the peer review was the question of how this core facility would be made available to researchers elsewhere in Connecticut.

Part of the proposal outlines, mentions by name the various researchers around Connecticut, who are doing research that might benefit from this core, but the question is whether the functionality of this core can actually be delivered reasonably and efficiently to

researchers off site.

Having said that, though, I thought that the peer review, even at Ann's modified 2.5, was the best score of all the proposals I was given to review, and I also thought that it sounded like the peer reviewers all thought that the basic idea was a very good one.

On the other hand, I'm well aware of my status as a layperson, and if Ann wants to put it in a maybe, I'm happy to join her in that as a bottom line recommendation for now.

CHAIRPERSON GALVIN: Do we have a consensus to put it into maybe? Further comments?

MR. ROBERT MANDELKERN: While I respect Dr. Kiessling's input on it, this grant for $600,000 for a core, which is a new core, received the second highest score out of 89 grant applications. The only one before it is a 1.8, and I think that this has some significance.

And he does talk about fee-based, the use of the measurement core, and I feel that given the importance of measurements and the going forward, that a reasonable amount of $600,000 for a new core is reasonable, and I would prefer to see it in the yes category.

CHAIRPERSON GALVIN: Well that's five

percent of our budget, so go ahead, Paul.

DR. PAUL PESCATELLO: I just have a question for the non-laymen. Is this core, is this infrastructure really something that we need to duplicate in Connecticut that's not available for the scientists to use from other providers?

DR. KIESSLING: I'm happy to answer that. What he's proposing are methods that are not available in standard laboratories, especially standard stem cell laboratories. They're going to do some electrophysiology that is not routine and that a lot of cell biologists don't really understand how to do, so, no, this would be a unique resource.

I think they have some discussions in here about how they would share it. I was actually just trying to go back through and look for my notes on the budget, and it's well written, but it's a lot of, it's a huge percentage of this budget, and, so, I'd kind of like us to hear from some of the other large applications before we make a final decision on this one.

CHAIRPERSON GALVIN: Milt?

DR. WALLACK: I think there's value in establishing this core, and I certainly would agree to leave it in the maybe category.

I'd like to ask the question, however, if my memory serves me correct, when we put out the RFP for this round of grant requests, I seem to remember that we specifically indicated that it would be our preference, and I'm addressing this, I guess, to Marianne, that it would be our preference if we could hopefully not fund cores, except if it was a situation that supplemented what was already existing or was crucial for that core going forward.

So I just want to put that on the table, if my recollection is right, but I certainly would agree to keep it in the maybe category with reservations.

CHAIRPERSON GALVIN: Core funding, these are from our notes, 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 merits. Your memory is correct. Ron?

DR. RONALD HART: I notice that the reviewers pointed out that there was no oversight committee proposing the grant. If it were to be funded, could we impose one that included all of the sites that are funded statewide to try to encourage collaborativity?

CHAIRPERSON GALVIN: I'm not sure I understand your question.

DR. HART: The grant, itself, did not include a scientific oversight committee, which is common for a large core like this.

CHAIRPERSON GALVIN: Got it.

DR. HART: I'm asking whether we could impose one, require that one be appointed if this were funded.

CHAIRPERSON GALVIN: We can do pretty nearly anything reasonable that we'd like to do.

DR. HART: Well I'm suggesting it.

CHAIRPERSON GALVIN: For the money, you can say this is what we expect.

DR. KIESSLING: I don't want to imply any kind of negative anything about this core. My concern is the size of the budget and what else we have before us and since I haven't read all the grants in detail, and I know some others have pretty good scores.

There's a paragraph in this grant application that says, "Explanation of the need for a new core," and I think this is appropriate for everybody to hear. This is from the investigator.

"Although we are aware that core funding is not a priority for this round of funding, we feel that the proposed facility has enormous potential to advance stem

cell research throughout the state.

So far, we have witnessed the development of three core or semi-core facilities. The UConn stem core provides frozen and fresh stem cell lines, feeder lines, and some basic testing.

The translational genomic's core performs micro ray studies. The flow cytometry facility, which is not exactly a core that we funded, but exists, performs sorting and separation of fluorescently labeled cells.

None of these three core facilities is dealing with basic aspects of cellular chemistry and physiology," and that's correct, so it's really going to be a matter of whether we're going to balance this particular technical advance, which is going to, undoubtedly, be a big help to the neurophysiology or the people who were studying neuronal development against some of the other big, nice grants we have.

CHAIRPERSON GALVIN: Okay. We've spent twice as much time as we allocated already. Okay, well, we're up on the 10-minute level now. Are we ready for a consensus vote? It's going to be a long couple of days if we spend this much time on each individual grant.

MR. MANDELKERN: Thank you, Dr. Galvin. This is a unique grant, and I would like to just point out

that it is only 60 percent of the dollars of an established investigator grant, and it is, of course, three starter grants, which I've lost the word.

So in terms of the dollars for what is being proposed, I think it's a unique function, and I would still go along with the maybe, but I think, in the later discussion, these facts should be born in mind.

CHAIRPERSON GALVIN: Do we have a consensus to put it into maybe, or do we have further comments? It's a maybe. Let's move on.

MS. TOWNSHEND: Next grant is 10SCC01, Dr. Rachel O'Neill. The title is Neuron Differentiation of Human Embryonic Stem Cells and Patient Derived IPS Cells. The peer review score is 4.3. Five minutes' description, 10 minutes' discussion, and this one is Dr. Fishbone and Dr. Hart.

DR. HART: I guess I've been elected to start this one. This is a very nicely outlined group grant from Dr. O'Neill and colleagues, proposed to find what they call a complete understanding of gene expression patterns in stem cells and induced pluripotent stem cells.

The reviewers were very thorough in their consideration, and they had a lot of very complimentary comments, including that it was an excellent group grant,

however, they identified a number of shortcomings scientifically, primarily issues of biological replicates and a little bit of broad scope and hard to find focus within the description, so the score ended up at a 4.3.

Even though this is proposing to use embryonic stem cells, one of our criteria for funding, although I believe the lines that are proposed in here are all NIH eligible, there's not a direct strong connection to human health, another one of our criteria, and, so, I propose a no for this one.

CHAIRPERSON GALVIN: Further comments? Second reviewer?

DR. GERALD FISHBONE: I have nothing to add significant to Dr. Hart's comments. There were a significant number of negative comments from the reviewers, which I think like what are they going to do with all the data that they collect? It didn't seem to be leading anywhere, so I would agree with his assessment.

CHAIRPERSON GALVIN: Okay. Further comments? Are we ready for --

MS. TOWNSHEND: Discussion?

CHAIRPERSON GALVIN: Okay.

MS. TOWNSHEND: Consensus of the recommendation of the peer review team to place this in

the no category? So moved.

Next grant considered is 10SCC02, UCHC, Molly Brown, and the title is Cancer --

A MALE VOICE: Molly Brewer.

MS. TOWNSHEND: Brewer. Apologies. Cancer Stem Cells as Tumor Initiating Cells in Breast and Ovarian Cancer. The peer review score is 4.0, and the considering team is Kiessling and Pescatello.

MS. HORN: And I would note that this has claimed proprietary information is included in the grant. It is marked in bold in the grant, so if you can avoid discussing that, we would appreciate it. If you need to go into the proprietary information in detail, we will have to go into Executive Session. Thank you.

DR. KIESSLING: This is kind of a confusing application, actually, and I, again, think that the score that has been given it is a little bit higher than their comments.

One of the big problems with this application is that it stated several times in the application that cancer stem cells are mutated stem cells of that tissue that go on to form tumors, and I think that there’s a lot of evidence, as the reviewers point out, that that’s not necessarily the case, that cancer stem

cells may actually arise from dedifferentiation.

So there's several aspects of this grant that are a little bit not behind the times, but you think that this group has pulled together in an effort to apply for stem cell funds for a project, which is really cancer-based, and I think there's also a fair amount of money available for these studies from other organizations.

I would actually put this in a no funding category, unless somebody has strong objections.

MS. TOWNSHEND: Paul?

CHAIRPERSON GALVIN: Paul?

DR. PESCATELLO: I agree with that analysis.

MS. TOWNSHEND: Discussion? Is there a consensus in the group to put this in the no category? So be it.

Next grant under consideration is 10SCC03, Yale University, Valerie Horsley, Emerging Roles of Biochemical and Mechanical Environments During hESC Cell Fate Determination. The grant is peer reviewed score at 3.8, and the team is Goldhamer and Mandelkern.

MS. HORN: And, again, proprietary information has been claimed in this grant. Thank you.

DR. DAVID GOLDHAMER: I'll start on this

one. So in this grant, this is a four PI interdisciplinary team. There's two biologists, an engineer and a physicist, and the goal, as they stated, is to interrogate and manipulate mechanical forces of human ESCs during directed differentiation into two tissue types, keratinocytes and neuronal cell fates.

So there's an increasing body of work that suggests that the sub straight that cells grow on, its stiffness, its elasticity, can affect differentiation, and, so, what they would like to do is to address this issue in human embryonic stem cells to see if they can push embryonic stem cells to a greater extent than now possible down the keratinocyte or epidermis pathway and the neuronal pathway.

So this is a really good grant. It's very well written. It is topical, in the sense that other types of cells have been shown to be affected by sub straight elasticity and stiffness.

I did have issues, though, and this kind of mirrors the reviewers' comments. So the problem is that this is a relatively new area, and it is true that a couple of other cell types have been shown to be coaxed or affected by sub straight. This has not been shown in embryonic stem cells.

So the problem is that although this a worthwhile application, the reviewers, and I concur with this, thought that this was probably not ready for a group grant, that this is more exploratory.

In my opinion, this would be a terrific seed grant to just get some baseline information. They don't have an idea at this point whether their cells will grow well or differentiate well using these special sub straights that they're using for the first time.

So it's a $2,000,000 grant, and aim one is dependent on being able to get ES cells to grow and differentiate, and they haven't shown that yet.

So I did have mixed feelings about this, because it was very well written, and it's a really great team of investigators, but it just didn't seem ready for, as the reviewer said, ready for prime time for a group grant anyway.

One reviewer commented that additional convincing preliminary data would be essential for this group research grant. So because of those concerns, despite the fact that I thought the grant was well written, I put this in a no category.

CHAIRPERSON GALVIN: Very thoughtful comments. Thank you. Any other comments?

MR. MANDELKERN: When I first reviewed this grant with Dr. Goldhamer, I was inclined to put it in the yes category, because I went to the other side of the coin, the positive things that the peer review said about the investigators and the need to investigate kind of a new field of what happens to embryonic stem cells, but Dr. Goldhamer convinced me with his science that maybe it wasn't all that great, in spite of the fact that of the three group proposals that reached us this one received the best score.

So I think it would probably be appropriate to keep one group alive and put this in the maybe, in case we decide we do want to fund what I think is the best of the three group proposals.

MS. TOWNSHEND: Is there discussion among the group?

DR. GOLDHAMER: I'll just make a couple other comments. First of all, yes, it did score the highest. I'm not sure, realistically, if there's a real difference between a 3.8 and a 4.3, in terms of measuring quality of grant, based on that narrow range.

Just to put this in perspective, as well, I counted that there are 16 established investigator grants and 19 seed grants that scored better, so I think that

needs to, you know, this is a different category, but there's competition for limited dollars, that we have to keep in mind that taking this grant means that better scoring grants, significantly better scoring grants, don't get funded.

So, again, I -- and I just want to correct or clarify one thing that Bob said about my perspective. I didn't have an issue about the quality of the science, per se. It's laid out very nicely. It looks like a very good team. It just seemed quite risky to devote $2,000,000 to a grant where they haven't taken the first step and shown that ES cells can even differentiate on these different sub straights that they want to test.

If it was a seed grant, an exploratory grant, I'd say it would be a slam dunk. I just thought that, for this mechanism, that it was premature.

CHAIRPERSON GALVIN: Thank you, once again, for your thoughtful comments, and I think, speaking generically, that we have I don't think favorably considered two-step grants, i.e., I'm going to be able to do this, but I have to be able to do that first, and no one else has done that, whatever it is, and I think that, I don't know if David has been with us for all of those, but I think, generally speaking, the group has felt that

those kind of stepped things relying on an initial step, which was unproven or theoretical, have not been very favorably considered.

Second reviewer? Any other comments? Mr. Mandelkern?

MR. MANDELKERN: No other comments. I've made my point of view clear.

CHAIRPERSON GALVIN: Okay. Any discussion among the group as a whole? If not, do we have a consensus that we will assign a no value to that grant?

MS. TOWNSHEND: Are you saying there's not a consensus? This moves into the no category.

CHAIRPERSON GALVIN: That's a no.

MS. TOWNSHEND: That concludes core and -- help me here. Group. Thank you. With your permission, with the permission of the group, we will move on to seed, the seed grant category. Is that correct? Thank you.

CHAIRPERSON GALVIN: Are we all on board? We're moving on to seed grants? I notice that there are, at least in this initial bunch, there are a good deal of very low ranking grants. I'm not sure. We will spend as much time as the group feels they need to spend, but our rules are usually a minute for six or higher.

MS. TOWNSHEND: Right. A minute for

description, and a minute for discussion for those that are 6.0 and higher, beginning with 10SCA26, Mrs. Rekha Shertukde, Stem Cell Graft Mapper Using Near Infrared Cameras for Imaging Stem Cell Migration and Differentiation. The institution is Diagnostic Devices. The peer review score is 8.0, and the peer review team is Goldhamer and Latham.

MS. HORN: And propriety information is claimed in this grant.

DR. LATHAM: This got its low peer review score, because of manifest lack of sophistication, at least on the surface of the application, about stem cells. Might be very useful to get this kind of imaging into the stem cell field, but there's not much detail at all about the application in stem cell context.

On the plus side, it's a Connecticut-based women-owned business, one of the few business applications we have, that all counts in favor of it, but it didn't have much detail about the application to stem cell.

MS. TOWNSHEND: Dr. Goldhamer?

DR. GOLDHAMER: I agree. No further comments.

MS. TOWNSHEND: Group discussion? Recommendation of the team? Is that the consensus of the

group? Thank you.

Next grant for consideration is 10SCA27, Erin Shull, Temporal Regulation of Neural Progenitor Cell Fate in the Developing Cerebral Cortex, Yale University is the institution, the peer review score is 7.4, and the consideration team is Goldhamer and Wallack.

DR. GOLDHAMER: Milt, should I go? So this is an application from a postdoctoral fellow at Yale. He has strong support from his mentor. So, very briefly, the investigator wants to do transcription profiling of different stages, different cell types during neurogenesis, neurogenic differentiation.

I won't go into any fine details, because of the score. I'll just tell you that the reviewers raised a number of technical issues that, to them, represented fundamental flaws, and I agreed with their concerns, and the overall enthusiasm of the review committee, as well as my own, was low, so I had voted a no on this.

MS. TOWNSHEND: Mr. Wallack? The recommendation of the peer review team is that this goes in the no category. Is that the consensus of the group? This grant moves to the no category.

Next grant for consideration is 10SCA37,

Sreyashi Basu, Response of Human Embryonic Stem Cells to Physiological Stresses, University of Connecticut Health Center is the institution, the score for peer review is 7.3, and the team for review is Arinzeh and Genel.

DR. TREENA ARINZEH: Okay. This proposal seeks to look at, stresses, in particular, temperature reactive oxygen species toxins on embryonic stem cells, IPS cells and non-stem cell controls.

Overall, the reviewers were not excited about it. They thought it had little significance or relevance to the development of techniques for culturing stem cells, and then they had a lot of criticism about some of the approaches, the experimental design mentioned here, and the investigators do not have embryonic stem cell experience, so they were pretty highly critical about this proposal, so I vote no for funding.

MS. TOWNSHEND: Dr. Genel?

DR. MYRON GENEL: No further comment. I agree.

MS. TOWNSHEND: The recommendation of the team is to place this in the no category. Is that the consensus of the group? So be it.

Next grant for consideration is 10SCA50, Anita Huttner, Modeling Pathogenesis of Temporal Lobe

Epilepsy, Yale University is the institution, the peer review score is 6.0, and the team for review is Arinzeh and Hiskes. No. My mistake. The team is Kiessling and Mandelkern.

MR. MANDELKERN: This is a seed grant proposal, which received a score of 6.7, which places it very low in the seed, which got 50 applications.

The peer review did not think very highly, inadequate approach, unlikely to accomplish aims, and I propose putting it in the no category.

MS. TOWNSHEND: Dr. Hiskes? Dr. Kiessling?

DR. KIESSLING: Right. I agree with that.

MS. TOWNSHEND: The recommendation of the team is to place this in the no category. Is that the consensus of the group? So moved.

Next grant for consideration is 10SCA17, Shangqin Guo, Engineering of Supportive Environment for Human Embryonic Stem Cell Differentiation, Yale University is the institution, 6.6 is the peer review score, Dees and Fishbone are the review team.

DR. RICHARD DEES: I can do this one. This project is an attempt to find the kind of right basis for stromal cells to maximize the differentiation of stem cells. The peer reviewers were not very enthusiastic

about it.

They didn't think their approach was likely to work, since there are many kinds of different environments that will be needed, and they didn't think that they had adequately thought about those kinds of issues, so this is a no grant, I think.

CHAIRPERSON GALVIN: Second reviewer?

DR. FISHBONE: I would agree with those comments. Many negative comments from the reviewers.

MS. TOWNSHEND: The recommendation of the peer review team, or of the team is that this be placed in the no category. Is that the consensus of the group? So moved.

Next grant for consideration is 10SCA08, Christopher Heinen, Converting Human Embryonic Stem Cells into Cancer Stem Cells, University of Connecticut Health Center is the institution, 6.3 is the peer review score, and the grant team for consideration, Dees and Pescatello.

DR. DEES: This grant is an attempt to understand how stem cells can become cancer cells -- role in DNA damage and the genesis of tumors. The peer reviewers argued that investigators did not really have the experience with stem cells to be able to pull off these experiments, especially since the experiments,

themselves, are not really that well defined. It's probably not worth funding at this time.

MS. TOWNSHEND: Second reviewer?

DR. PESCATELLO: Yeah. Poorly articulated, and I concur with the other comments.

MS. TOWNSHEND: The recommendation of the team is to place this in the no category. Is that the consensus of the group? So moved.

Next grant for consideration is 10SCA14, Professor Lynne Regan, Elucidating the Unique Features of Chromatin in Stem Cells, Yale University is the institution, 6.3 is the peer review score, and the team is Dees and Fishbone.

DR. FISHBONE: The hypothesis here was that the way that DNA is packaged in the nucleus is different in stem cells than in differentiated cells, and they seek to determine exactly what these differences are, and they hope to answer a lot of questions about them.

The reviewer said the project is interesting from a purely biophysical standpoint, but it seems quite preliminary, even for a seed grant. Direct evidence of their theory is limited. It's difficult to see how the methodology could ever be used in cells and not sure how it will directly answer questions about

pluripotency, so, overall, they were negative about it, and I would recommend that we do not fund it.

MS. TOWNSHEND: Second reviewer?

DR. DEES: Yeah. I'd agree with all that.

MS. TOWNSHEND: The team is recommending no. Is that the consensus of the group? So moved.

Next grant for consideration is 10SCA15, Deborah Eastman, Notch Signaling and Target Gene Expression in the Derivation of Neural Stem Cell Progenitors from Pluripotent Stem Cells, Connecticut College is the institution, 6.30 is the peer review score, and the reviewers are Dees and Genel.

DR. DEES: These experiments are intended to look at the differences between induced pluripotent cells and stem cells, embryonic stem cells and how they differentiate into neural cells in the notch pathway.

The reviewers didn't really find the study particularly innovative, and they're worried about whether this researcher in the context can really pull it off at her college.

There might be a case. I'll just say this one thing. This is a grant from one of the smaller colleges that doesn't have quite the resources of everyone else, and the question for the committee would be whether

it's worthwhile to think about, maybe helping out places where they don't have the kinds of resources. That would be my only, but I would still say probably not for this case.

MS. TOWNSHEND: Second reviewer?

DR. GENEL: Yeah. I have the same sense. I think, if this had gotten a somewhat better review, in terms of its theoretical aspects, I think I could be persuaded that it's worth funding, but the reviewers criticized not only the facilities there, but the basic underlying concept, and I think, from my perspective, with so many very good seed applications, in particular, I would not fund this.

MS. TOWNSHEND: The recommendation of the team is that this goes in the no category? Is that the consensus of the group?

DR. GENEL: With regret.

MS. TOWNSHEND: With regret. So noted. This grant is moved to the no category.

Next grant for consideration is 10SCA48, Role of Channel-Kinase, TRPM7 in Cardiaomyocytes, Differentiation from Human Embryonic Stem Cells, UCHC is the institution, 6.3 is the peer review score, the reviewers are Kiessling and Mandelkern.

MR. MANDELKERN: This review is -- this grant proposal is proposing to test whether a particular gene, I assume, will have an effect on differentiation of embryonic stem cells into heart muscle cells.

The preliminary data shows the way, but the peer review has many criticisms, in terms of not sufficient preliminary data and various other indications.

(Off the record)

MR. MANDELKERN: -- places it in the bottom 20 of 50 seed grant applications, I would propose no on this.

MS. TOWNSHEND: Dr. Kiessling?

DR. KIESSLING: Right. This is a grant application that was missing part of the application. The bio-sketches weren't there, and I asked if they'd actually been submitted, and I think somebody got back to me and said, no, they didn't show up, so this grant was missing about six pages of its submission.

MS. TOWNSHEND: So the recommendation of the team is to place this in the no category?

DR. KIESSLING: Right.

MS. TOWNSHEND: Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCA11,

Bing Su, Control Human Embryonic Stem Cell Self Renew by the Stress Regulated Protein Kinase Cascades, Yale University is the institution, 6.1 is the peer review score, and the reviewers are Arinzeh and Fishbone.

DR. ARINZEH: Okay. This proposal seeks to look at, again, it's actually another proposal that I'm reviewing about cellular stress, so the effect of stress on cells and how that might impose accelerated aging. The reviewers were, again, not excited about this proposal, because there's little evidence to show that embryonic stem cells actually undergo aging processes, and they really didn't develop that hypothesis well with preliminary data of any kind to indicate that they might have this potential there, so they saw this as a significant flaw, so they gave it a poor score, so funding recommendation would be no.

MS. TOWNSHEND: Second reviewer?

DR. FISHBONE: I would agree, and they said, basically, there is no preliminary data, and that the project would collapse if they find there's either no response or the human embryonic stem cells simply die, so, in other words, you'd give them $200,000, and they would have no basis for proceeding with the project.

MS. TOWNSHEND: So the recommendation of

the team is no. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCA39, Winifred Krueger, Stem Cell Secretion in Self Renewal and Differentiation, UConn is the institution, 6.0 is the peer review score, and the reviewers are Dees and Genel.

DR. DEES: These experiments are designed to understand the self-regulatory environment of stem cells by looking at the factors they secrete to understand better the mechanisms of self-renewal and differentiation.

In this case, the link to eventual therapies is reasonably clear, but pretty remote, but the peer reviewers really thought the experimental design was pretty poor, and they weren't quite sure the results would actually be meaningful, even if they worked, so I would recommend not funding.

MS. TOWNSHEND: Dr. Genel?

DR. GENEL: Yeah. I observed that Dr. Krueger submitted two peer review grants, two seed grants for review. I think the second reviewer is fairly scathing, in terms of the application, as well as some of the investigator's qualifications.

Limited expertise in proteomics by PI, who has a very limited publication record, given the she

finished training in the mid 80s, so, for what that's worth, no.

MS. TOWNSHEND: The recommendation of the team is to place this in the no category. Is that the consensus of the group? This grant now is moved to the no category.

Next grant, we move into grants that are peer reviewed score 5.9 or lower, so discussion and consideration time will move to five minutes, rather than one minute.

Next grant is 10SCA33, Steven Levine is the potential grantee, Functional Properties of Neurons Derived from Autism and Angelman Syndrome Patients, UCHC is the institution, 5.7 is the peer review score, and the reviewers are Hart and Latham.

DR. LATHAM: This is a seed grant from Eric Levine from the Health Center, along with a new collaborator, Dr. Chamberlain, and it seeks to prepare induced pluripotent cells from patients with either a specific autistic phenotype and Angelman Syndrome and to determine electrophysiological properties of those cells.

The basic comment from the reviewers was that it was a high-risk, high-potential project, but they judged it unlikely to be fruitful, and one of the key

questions at the end of the review was how will this affect the study of Angelman Syndrome, and that was one of the dots that really wasn't connected here.

My scale of judging these things, I did find that this was an appropriate seed for a senior investigator, though it was using non-embryonic stem cells, which are not a high priority for us, and it is federally eligible, and it was not heavily, not clearly tied to human health and disease, so, therefore, I did not give it more of an uptake on my scoring, so I recommend a no.

MS. TOWNSHEND: Second reviewer?

DR. HART: I was impressed by some of the comments of the reviewers characterizing this as a fishing expedition, which is their way of putting it the high riskness of it. They could find something important, but they could end up finding nothing at all, and, for that reason, I would also say no.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCA07, Choukri Ben Mamoun, Derivation of Hepatocytes from

Embryonic Stem Cells to Study the Initial Steps of Malaria Pathogenesis, Yale University is the institution, 5.6 is the peer review score, and the grant team is Dees and Pescatello.

DR. PESCATELLO: So this had a score of 5.6, and the reviewers had a couple of concerns. I guess I would categorize them as that models already exist for this type of work, and, also, there's a mention of the Gates Foundation already being very involved in this, so I guess I would be interested in what others think.

It's not a great score. There's some issue with the protocols that are going to be used. I guess I'm in a maybe category, because the comment about the Gates Foundation, and I know a little bit about the Gates Foundation work on malaria, and I would, if anything, I would say that having another funder, other funders, besides just the Gates Foundation involved in malaria research, is a good thing.

And if the scoring was better, I would be in the pro category, but I'm in a maybe right now.

DR. DEES: Yeah. I guess I took to heart a bit more what the peer reviewers were saying. They said that the model doesn't really offer anything for how the disease is going to work in their body, so they thought it

was really unlikely to have the kind of therapeutic uptake that we might hope, so it might have some clinically important stuff, but I really thought they thought, I'm a layperson here, so I wouldn't judge this, they thought the science really wasn't that good.

I would actually put it in a no category.

MS. TOWNSHEND: Paul?

DR. PESCATELLO: Okay.

MS. TOWNSHEND: The recommendation of the team is to place this in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCA41, Betty Lawton is the potential grantee, Development of Feeder-free Culture System for the Directed Differentiation of Human Embryonic Stem Cells to Myoblasts, UConn is the institution, 5.5 is the peer review score, and the team is Hart and Latham.

DR. HART: This was a proposal from a postdoctoral fellow that seeks to generate myoblasts from human ES cells, and it clearly would be a valuable application if it were successful.

The reviewers were very mixed. They found that there was several challenges in the project, and the

proposal appears very risky overall, however, they do point out that, if successful, the project would be incredibly innovative.

I found the topic of this very exciting for my own interests, but, overall, this was a study that used, again, a federally eligible embryonic stem cell line, and the health benefits were not directly made clear in the way the grant was written, even though it seemed kind of obvious as you were reading it. I guess, overall, with the score by the reviewers, I'd recommend no.

MS. TOWNSHEND: Dr. Latham?

DR. LATHAM: I agree with that.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCA10, Emre Seli, Functional Characterization of Embryonic Stem Cell-Specific Miro RNAs, Yale University is the institution, 5.3 is the peer review score, Arinzeh and Fishbone.

DR. FISHBONE: The investigator wants to gain insight into micro RNA control of the maternal to zygotic transition that is an important regulatory

parameter of development and, also, in the control of pluripotency.

There is a high probability -- all of the preliminary data is from zebrafish and the xenopus. I'm not sure what that is. While there's a high probability that similar mechanisms operate in mammalian development, additional preliminary data would reinforce the feasibility and the anticipated outcome.

The concern is that the applicants are only one tool to work with, and this is a big problem in their aims one and two, and aim three didn't seem to be so strong either, so I would recommend that this not be funded.

MS. TOWNSHEND: Second? Dr. Arinzeh?

DR. ARINZEH: Same recommendation. No.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group? This grant is moved to the no category.

Next grant for consideration is 10SCA19, Umit A. Kayisli, In Vitro Differentiation of Human Endometrial Mesenchymal Stem Cells to Neuron-Like Cells, Implications for Endometriosis Related Pain and Inflammation, Yale University is the institution, 5.2 is

the peer review score, the reviewers are Goldhamer and Pescatello.

DR. GOLDHAMER: All right, so, this applicant is an associate research scientist at Yale. It wasn't clear whether this is an independent position. There was no letter from a mentor, although the Chief of OB-GYN wrote a short letter, so the idea here is that there are cells in the endometrium, called endometrial stromal cells, which are apparently multi-potent cells, and it's known that patients with endometriosis have excessive innervation in the functional layer of the endometrium, and, so, the hypothesis is that these cells, these multi-potent cells, are excessively differentiating into neurons that then cause pain.

So the reviewers thought that this was a really important problem, and they saw that as the major strength of the proposal. The reviewers did point out a few weaknesses, and I'll just read what they said.

They said there are weaknesses that include the basis on which the hypothesis, hypotheses are founded, the actual veracity of the experimental design, and the overall presentation of the studies, which undermine its potential.

So given these weaknesses, enthusiasm was

low by the reviewers, and I agree with their assessment, so I had placed this in the no category.

MS. TOWNSHEND: Second reviewer?

DR. PESCATELLO: I agree with that.

MS. TOWNSHEND: A correction on the title. It is Mesenchymal. Thank you. The recommendation of the team is to place this in the no category. Is that the consensus of the group? This grant is moved to the no category.

Next grant for consideration is 10SCA09, Jae Eun Kwak, The Regulation of miRNA Expression in Polyuridylation in Controlling the Human Stem Cell Fate, Yale University is the institution, 5.0 is the peer review score, the reviewers are Fishbone and Pescatello.

DR. FISHBONE: The investigator seeks to determine whether a certain nucleotidyltransferase plays a role in regulating human embryonic stem cell behavior. Unfortunately, the end points for maintenance and differentiation are only superficially described.

Essentially, it involved demonstrating whether similar phenomena exists in humans and in mice, and they say support would be increased if a specific micro RNA had been identified, and, apparently, it had not, so that they didn’t seem to feel this was worthy of

support, and I agreed.

MS. TOWNSHEND: Second reviewer?

DR. PESCATELLO: Yeah, I concur with that. There's a lack of depth, I think, to the proposal.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCA20, Emre Seli, Metabolic Profiling of Human Embryonic Stem Cells, Yale University is the institution, 5.0 is the peer review score, and the team is Goldhamer and Pescatello.

CHAIRPERSON GALVIN: I note that this investigator is also originated grant to number 20.

DR. GOLDHAMER: All right, so, this grant, the purpose of this project is to characterize the metabolic phenotype of human ES cells, with the goal being to improve human ES cell cultures.

So the idea is that the investigator will analyze culture media under various growth conditions and do some sort of metabolic profiling. The investigator provides very little idea of what actually will be done, and there is no connection between the data that will be collected and how that relates to the health of the cells.

The reviewers had very significant concerns, and they agree that the research plan lacked detail, and I personally found the research plan to be really wholly underdeveloped, and, so, I had placed this in the no category.

MS. TOWNSHEND: Paul?

DR. PESCATELLO: I do, as well.

MS. TOWNSHEND: The proposal by the team is to place this grant in the no category. Is that the consensus of the group? This grant is moved to the no category.

Next grant for consideration is 10SCA40, Winifred Krueger, The Lamin Interactome During Stem Cell Differentiation, UConn is the institution, 5.0 is the peer review score, and the reviewers are Genel and Latham.

DR. GENEL: This is the second seed grant application from Dr. Krueger, and here it seems to me that the score probably underrates. It does not fit with the peer review. Reading the peer review, which seems to be generally rather favorable, the five seems like a very low score for what I read.

What she proposes is to study in human embryonic stem cells the Lamin gene, which is related to premature aging and the progeria and so forth, and the

peer reviewers indicate that this is an important proposal, not just for the purpose of understanding human HGPS, but also increasing our knowledge of the interactions in a number of genetic diseases result from Lamin mutations. A successful outcome would be very useful.

I think, from a conceptual point of view, I think this is precisely what we intended seed grants to do, and that is to provide small amounts of funding for innovative projects, so not withstanding the peer review score, I'd like to put this in the maybe category for the time being.

MS. TOWNSHEND: Dr. Latham?

DR. LATHAM: My inclination was the same for much the same reason. As you read through the peer review scores, you couldn't really understand where the five came from.

There were some concerns about whether the second beam of the study could be done within the two-year window, and there were some other concerns about inexperience with using human embryonic stem cells, but then there's a note that Dr. Rassmusen is also part of this grant, although not with a huge amount of time, but that should alleviate some of the concerns about

experience with embryonic stem cells, so I'd be inclined to put this in the maybe, as well.

MS. TOWNSHEND: The recommendation of the team is to place this in the maybe category. Is there further discussion? Is that the consensus of the group? This grant is placed in the maybe category.

Next grant for consideration is 10SCA34, Mei Wei, Induced Pluripotent Stem Cell Seeded Novel Scaffolds for Improved Bone Repair In Vivo, UConn is the institution, 4.8 is the peer review score, Hart and Wallack are the review team.

DR. HART: This is a project from Dr. Wei, who is an Associate Professor at UConn, along with a collaborator at the Health Center. The proposal is to work on biomaterials and, specifically, the three dimensional structure of bio materials for bone and connective tissue development.

Medically, very useful and very relevant. The reviewers found this as strikingly impressive approach and a very experienced team in tissue engineering and bio materials.

There was a number of structural deficits in the review. They found some of the parts of the proposal very unclear, details lacking, some things hard

to follow, and, so, therefore kind of downgraded it I think a great deal, based on grantsmanship.

I really vacillated on this back and forth quite a few times. I wrote in my notes maybe, crossed that out and wrote no once or twice, so I'm a little in between on this. It really sounds from the review like a no. It reads as though, again, like the last grant, it sounds like exactly the sort of thing we're looking for, in terms of innovative ideas.

I should point out that the PI has had a section of a group grant in the past of a different but similar concept, which makes it a little strange for this to be a seed grant, but, again, I think the kind of direct relevance, even though it wasn't terribly well developed in the project, the direct relevance to human health and disease helps it quite a bit, so I guess I'd end up saying maybe.

MS. TOWNSHEND: Second reviewer?

DR. HART: Subject to being argued with.

MS. TOWNSHEND: Second reviewer?

DR. WALLACK: I had a similar kind of response as I read it. I thought that it was an interesting proposal that had fairly significant potential importance. It's by an experienced investigative team.

I also went back and forth, but I came down on the side of no for a few reasons. One of them is that when we discussed seed grants, or when we initiated the concept of seed grants in Connecticut at least, it was with the idea that it would be for people, young investigators, who were entering the field, or senior investigators for that matter, who were not in the stem cell field yet, but that hoped to move laterally over to the stem cell field.

I think that it's inappropriate for us to be considering this from this team, which is basically a senior investigator team, they've been associated, I believe, with the Dr. Row(phonetic) group grant in '07, and there is this ambivalence in how it was written up.

I would not have anticipated, because of their experience, the craftsmanship problem if they were very, very involved and serious with the grant, and, also, there's a relatively very limited amount of time that they are proposing to spend with this grant.

So, again, I think you can sense the somewhat ambivalent feeling as Ron had, but I would come down on the no side for the reasons that I've indicated.

DR. HART: Yeah. I definitely don't disagree with what you've brought out as the negatives,

and let me add my other negatives that I withheld earlier, that, essentially, it's not an embryonic stem cell project, which should be one of our higher priorities. It is federally eligible, and, again, the issue of whether this embodies the spirit of what we believe a seed grant should be is a very valid point, so I can be convinced to be no very easily.

MS. TOWNSHEND: So the recommendation of the team is?

DR. WALLACK: No.

DR. HART: I'd say no.

MS. TOWNSHEND: No. Is that the consensus of the group? This grant is moved to the no category. Just a note. We will be breaking in about 10 minutes, around 10:00.

Next grant for consideration is 10SCA46, Yun He, Cerebral Cavernous Malformation 3 (CCM3) in Hemangioblast. Is that right? Differentiation and EC Maturation, Yale University is the institution, 4.7 is the peer review score, and the team is Kiessling and Mandelkern.

MR. MANDELKERN: This is a grant, again, that proposes to examine the role of a gene and how it relates to vascular disease and blood differentiations in,

blood cell differentiations in human embryonic stem cells and in a mouse model. It's important, because vascular disease are important in our population.

The peer review is very ambiguous. They say first good things that they propose to do on published data, and then they say negative things, like it's highly dependant on aim one, leading to aim two, and they go back and forth between the positive and the negative on this peer review.

It is not clear how success in this aim moves the field beyond what is shown in the data, a nice proposal, however, it lacks some data and so on. It's a very difficult one to assess from the written report, but the score of 4.7 places it very low in the 50 applications for seed grants, so I would propose a no on this, and we'll hear what Dr. Kiessling has to say.

DR. KIESSLING: Now this is basically a developmental biology team that is seeking to apply human embryonic stem cells to their research, and it's kind of a stretch, so I would like to see these applicants kind of come up with something that indicates the hES cells are going to do what they think, and I would place this in the no category.

MS. TOWNSHEND: The recommendation of the

team is to place this grant in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCA03, Madhav Dhodapkar, Harnessing Immunity to Pluripotency Genes in Humans, Yale University is the institution, the score is 4.6, and the team is Arinzeh and Hiskes.

DR. ARINZEH: Okay. I have Hiskes' comments. Do you want me to, or do you want me just to say her recommendations?

MS. TOWNSHEND: If you'd like to read those, it's your choice.

DR. ARINZEH: I can just give a recommendation. Okay, so, this proposal aims to better understand the properties of immunity to the pluripotency gene or antigen, OCT-4, on embryonic stem cells, so they're going to characterize T cell response against OCT-4, evaluate the ability of dendritic cells to activate these responses.

So the reviewers thought it was an interesting proposal, but the weaknesses, however, and thought the investigator was very strong in immune cell biology background, but the weaknesses were in the specifics of the approach, not really clear, as to whether

cells that do differentiate will lose this OCT-4 antigen, and, so, there's just some uncertainty there, so that they would like to have seen more preliminary data there to demonstrate. Some of their claims are, again, hypotheses.

They also were concerned about an overlap with the PI's current R01 funding through the NIH, so the recommendation here would be no, and then Hiskes also had the recommendation of no, no funding.

MS. TOWNSHEND: The recommendation of the review team is to place this grant in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCA32, Ivo Kalajzic, Bone Regeneration Potential of Mesenchymal Cells Derived from ES Cells versus Adult Mesenchymal Stem Cells, UCHC is the institution, 4.6 is the peer review score, Hart and Latham are the reviewers.

DR. LATHAM: This is a proposal to compare the osteogenic potential of mouse adult mesenchymal stem cells and embryonic stem cell generated mesenchymal stem cells, and then, also, to do the same with human cells and to test them both in vitro and in vivo in mice.

The peer reviewers were I think more enthusiastic than the score seems to indicate, and I would

put this in the maybe category.

MS. TOWNSHEND: Second reviewer?

DR. HART: Yes. The PI is a junior faculty member at the Health Center and has had just limited PI funding in the past, so, when I first read this, I really felt it wasn't quite in the spirit of a seed grant, but I think, realistically, as a pre-tenured sister professor, that probably makes sense.

This person did play a role on another, a larger project in the past that was funded by this group. I guess the only complaint I had, again, was that it was back to NIH fundable material. As a seed grant towards future NIH funding, this might make some sense.

You were right, that the reviews sounded much more positive than the score. I agree on maybe.

MS. TOWNSHEND: The team is recommending that this grant be placed in the maybe category. Is there discussion?

CHAIRPERSON GALVIN: Let me just say one generic comment. I think, when we put these in maybe, we have to have some sort of thought about what possibly would move them from a maybe to a yes, and a good idea, you know, what I've heard so far is good idea, poorly written up, good idea, based on a shaky concept, etcetera,

so, as we put these there, I don't think there's much point putting them there if we can't think of something that would move them from that over to a yes, but that's just an editorial comment.

MS. TOWNSHEND: Other discussion? The recommendation of the team is to place this in the maybe category. Is that the consensus of the group? This grant is placed in the maybe category.

Next grant for consideration is 10SCA02, Stephanie Halene, Generation and Functional Study of Induced Pluripotent Stem Cells from Primary Bone Marrow Hematopoietic Stem Cells from Patients with -- all right, somebody else say that one.

DR. ARINZEH: I think it's Myelodysplastic Syndrome.

MS. TOWNSHEND: Myelodysplastic Syndromes. Thank you.

DR. ARINZEH: Okay.

MS. TOWNSHEND: Yale University is the institution, 4.3 is the peer review score, the reviewers are Arinzeh and Hiskes.

DR. ARINZEH: Yeah, I had to get that right myself. Okay, so, yes, so this project aims to develop disease models and basically is going to be generating IPS

cells from patients who have this condition, MDS, and, so, this is a condition where there's a loss of, well, there's a lowering hematopoietic stem cells, and, so, you get low blood cell counts.

Again, it seems like an interesting project. The reviewers commented on that. It would be significant if it could work, but there are, again, just some fatal flaws, is that the investigator wants to generate these IPS cells from the MDS' patients bone marrow, and their bone marrow, again, what population of cells you're going to get from there if they're not growing well? How successful will be your ability to transfer those cells into IPS, so that was just a major fatal flaw in this proposal.

So they thought that they should be looking at other cells maybe from this patient, skin cells, something to convert them over. And then there's some other minor stuff about some of the experimental design, things like that.

So the recommendation would be no. Hiskes also is in agreement with the recommendation of no.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group? This grant is moved to the no

category. It is now 9:58, and we will take a 15-minute break and be back here at 10:13.

CHAIRPERSON GALVIN: Please remember that you should not be discussing things that have occurred here or are going to occur here, because you will be overheard, and it is not a private cafeteria.

Many times I'm sitting there, and I have no idea who is sitting directly behind me, and I recognize most of the players, but there are a lot of players and lobbyists and other folks like that here. Be careful of what you discuss.

(Off the record)

CHAIRPERSON GALVIN: While we're winding up, I thought that Dr. Arinzeh said something very potent when she spoke about fatal flaws, and, as I look at these grants, some of them have built in flaws, or very shaky parts, and I think fatal is probably the best word to describe those.

I think, as we see those, there's no sense in putting something over into a maybe that has something in there that's illogical, or multi-step-based just isn't going to work.

My personal feelings are some of the grants that we see I think are very good ideas, but they're not

presented in a very complete or cogent fashion, and I think some of it has to do with writing abilities rather than scientific potential and acumen, and I think some of those rightly belong over in the maybe category.

I've seen them in the Department. We get very good grants that are theoretically very good, and they're given to somebody to write up, and the write-ups are incomprehensible, or else they veer off so far from the stated purpose that they don't make any sense.

I think, as we look through, maybe we can identify some of the ones that are really very sound, but just not very well presented, and perhaps go back to them if we have the time.

MS. TOWNSHEND: Next grant for consideration is 10SCA04, Dr. Yong Wang, Artificial Extracellular Matrices for Controlled Differentiation of Human Pluripotent Stem Cells, UConn is the institution, 4.3 is the peer review score, the reviewers are Arinzeh and Latham.

DR. LATHAM: Sorry. I'm having a hard time following the order that we're following, but I'll be ready in just a second. All right. Treena, go first.

DR. ARINZEH: Okay, so, this proposal is looking at a novel biomaterial, basically a hydrogel to

deliver growth factors, in particular, transforming growth factor beta and BMPs for the differentiation of embryonic stem cells into cartilage cells, chondrocytes, so the novelty here is looking at the use of this hydrogel, and they're using these novel opti-meters(phonetic) for giving kind of controlled delivery of these growth factors, so there is a lot of novelty and interest here with this biomaterial hydrogel system on the reviewer's comment on that.

But there are some weaknesses looking at I guess the overall rationale, as to why you're using embryonic stem cells, but they thought that was a weakness, and they also thought the PI's background with embryonic stem cells was lacking, so the cultures looked -- the preliminary data of the cultures were not very good.

And there was also some concern about the formulation of the hydrogel and how that might affect the cells, but there was some enthusiasm, though, for it, so I thought the score might have been a little bit, maybe a little bit better. So my recommendation would be no for the funding.

MS. TOWNSHEND: Steve?

DR. LATHAM: Yeah. I've now found my place. My recommendation was also no. This is they're

trying to develop a synthetic mechanism for the care and feeding of cells in three dimensions better to approximate what happens in vivo, and the question is whether the testing they're doing of that extra cellular matrix needs to be done with human embryonic stem cells.

And this is a group, whose human embryonic stem cell experience doesn't seem to be that great, and the underlying reason why this should be done with embryonic cells, as opposed to others, why the testing of the gel should be done in that way is lacking, so I would also say no.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCA01, Julie Ann Sosa, Stem Cells for Cell Therapy of Hypoparathyroidism, Yale University is the institution, 4.2 is the peer review score.

MS. HORN: Proprietary information is claimed in this grant.

MS. TOWNSHEND: And the team is Arinzeh and Hiskes.

DR. ARINZEH: Okay. This proposal is

looking at approaches to the treatment of hypoparathyroidism, looking at the development, then, of embryonic stem cells that will turn into parathyroid cells, and then they would investigate these differentiated cells in an animal model by implanting them to muscle and then looking for whether or not physiological levels, calcium levels and other factors would be returned.

So the reviewers thought this was an interesting proposal, but, again, the reviewers were looking at certain weaknesses, in terms of the background of the PI. There's a limited background in cell molecular biology.

Also, there's no establishment of the protocol for differentiation of embryonic stem cells into parathyroid cells, so, because of that lack of preliminary data, then also the experimental design, in terms of what sorts of markers they would be looking for, is lacking or weak.

So my recommendation would be no for funding on this. Hiskes also had the same recommendation.

MS. TOWNSHEND: The recommendation of the team is to move this grant to the no category. Is that the consensus of the group? This grant is moved to the no

category.

Next grant for consideration is 10SCA23, Arvind Chhabra, To Develop Efficient Methodologies to Generate Customized Anti-Tumor Effecter T Cells from Human Embryonic Stem Cells and Induced Pluripotent Stem Cells by TCREngineering Approach, UCHC is the institution, 4.0 is the peer review score, Genel and Kiessling are the reviewers.

DR. GENEL: Ann, do you want me to start?

DR. KIESSLING: Yeah.

DR. GENEL: This is a resubmission of a seed grant that I gather was submitted last year, I presume, and did not make the cutoff last year. The reviewers indicate that it's substantially improved.

Basically, it's a concept to try and develop specific immune effecter T cells by utilizing the T cell receptor and developing specific T cells using both human embryo and induced stem cells.

The major criticism of the reviewer seems to be too ambitious, and they question whether or not it can be carried out in a two-year seed grant. On the other hand, the reviewers point out that this work could be very significant if it comes together, and a seed award is meant to encourage development of new areas of expertise,

so I mean I think that balances off, frankly, the criticism, and I would think we ought to put this in a maybe category for the present time.

DR. KIESSLING: Yeah, I agree with that, because I remember now the enthusiasm of the reviewers for this grant is much higher than a score of 4.0, because, although it's risky, they thought exactly that, that this is what seed grants are for. This person has a very strong background in T cell biology, weak background in embryonic stem cells, has gotten people that's going to show him how to do that, and I think it should be definitely a maybe.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the maybe category. Is there a discussion? Is it the consensus of the group to move this to the maybe category? This grant is moved to the maybe category.

Next grant for consideration is 10SCA25, Jun Lu, Computational Modeling of Molecular Regulators in hESC Differentiation, Yale University is the institution, 4.0 is the peer review score, the reviewers are Goldhamer and Wallack.

DR. WALLACK: I'll start. Can I ask you a question? There was a similar grant that Lu submitted,

SCA45. Would you want to go out of the rotation and possibly have -- you can't do that? Is that the ruling?

MS. HORN: We're proceeding by peer review score, so we'll just listen carefully to what you're saying now and remember that when we come to the next grant, but we'd like to stay within the ranking of the peer review.

DR. WALLACK: Thank you. All right, so, this is a seed grant request, but it's by a senior investigator. As a matter of fact, in 2009, he was awarded from Connecticut dollars an established investigator grant in a relatively similar field as we're talking about in this particular grant.

The investigator only proposes to spend about 10 percent of his time on the project. There were some questions about the budgeting and whether or not the fees and the costs are over estimated.

The material, the proposal does have some areas where it could be applicable and maybe some benefits coming from it, but my question is, if it's really in light of other research being done, really critical, and does it follow in the spirit of what we anticipate seed grants to represent, and with the 4.0 rating and my own reservations, I would vote no.

CHAIRPERSON GALVIN: If I might interject, I think there's a question here that probably deserves a little bit of an airing out. If you're an established investigator, can you get a seed grant, too?

DR. WALLACK: Well my understanding, Bob, and certainly you have your team here that can probably comment in a much more definitive manner, is, as I recall, there was no problem in having senior investigators request seed grants if the senior investigator was not already working in the stem cell field and wanted entree to that field, and that would be a method for him to be able to do that, so, again, that's different than somebody already being designated an established investigator and having already been awarded a significant established investigator grant by the state funding process.

CHAIRPERSON GALVIN: My notes indicate developing new research directions may apply for a seed grant, but I believe your question is is this an extension of the original work, and, if so, I have a question for my attorney friends, is should this be disqualified, because it doesn't fit within the framework of what we've asked people to do for consideration, and I don't know what we should do.

MS. HORN: Yeah. I think it's probably a

nuance to answer to that, but we certainly did allow for established investigators who were new to stem cell research to apply, or they were developing new research directions within stem cell research, so I'm not clear how that would come out in this case, but it sounds to me like he's going on maybe an established direction with this grant, not a new direction, and he's not new to stem cell research.

DR. WALLACK: That was my determination.

DR. GOLDHAMER: So I was the second reviewer on this. Let me just comment on these issues raised. I mean I haven't been present on this committee throughout, but I've been part of some of the deliberations on this question.

I thought the committee had kind of agreed or decided that even a senior stem cell researcher, who wants to go in new directions, is, can apply and will get full consideration.

To me, that makes a lot of sense. There aren't many venues for one to get funds to try new ideas and go in new directions. You can't really apply for at least most NIH mechanisms, there a couple of exceptions, for ideas where you don't have any background or any preliminary data, so, to me, getting a senior researcher

trying a new idea that maybe then could be leveraged into a large grant at the federal level is a good use of funds.

I can't specifically address whether this is a continuation of work he's already been doing. It's a little nuanced. It's not my direct area, the computational biology aspect of this, so I think there's two issues there.

But let me now, Milt, if I could just say a couple of comments about the merits of this particular proposal, in terms of the science? I also had a no for this application, and my concern -- so, in aim one, this applicant is hoping to identify, using computational methods, new regulators of embryonic stem cell differentiation.

I think where the grant fell down was in aim two, where they wanted to functionally test the new regulators that they identify, and the reason it fell down is there is essentially no information on how this is going to proceed.

Aim two is significantly underdeveloped and, to me, the greatest weakness of this proposal, so despite, you know, these other issues, or in addition to these other issues, I didn't think this grant was meritorious enough to warrant further consideration.

CHAIRPERSON GALVIN: Then we can put the other issues aside and maybe make that a topic for further discussion or guidelines for next year's grant and go ahead with the consensus.

DR. WALLACK: I agree. No.

MS. TOWNSHEND: The recommendation of the group is to move this grant to the no category. Is that the consensus of the group? This grant is moved to the no category.

Next grant for consideration is 10SCA43, Qin Yan, Epigenetic Regulation of Stem Cell Fate by Histone Demethylase RBP2, Yale University, 4.0 is the peer review score, Hiskes and Wallack the peer reviewers.

MS. HORN: And there is proprietary information claimed in this application.

DR. WALLACK: So Ann and I discussed this yesterday, and we questioned the relevancy, if it had application. The researcher proposes to spend a very limited amount of time. We both agree that we would not recommend funding.

MS. TOWNSHEND: The recommendation of the peer review, of the team is to place this grant in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCA28, Dasaradhi Palakodeti, Study the Role of Cytoplasmic RNA Binding Protein in Human Embryonic Stem Cells and During Neural Differentiation, UCHC is the institution, 3.8 is the peer review score, and the team is Kiessling and Mandelkern.

DR. KIESSLING: I have this listed under Gravely(phonetic). Sorry. I need to look at my notes on this. I'm sorry.

MS. TOWNSHEND: We'll go on to the next one, 10SCA36, Rosa M. Guzzo, Generation of a Novel Source of iPS Cells for the Treatment of Osteoarthritis, UCHC is the institution, 3.7 is the peer review score, the team is Genel and Hart.

DR. HART: Okay. This is from Dr. Guzzo, a postdoc in the DeRisi Lab at the Health Center. The idea is to generate new sources of inducible pluripotent cells to repair cartilage damage with the hypothesis that human cartilage cells harvested from joints will be better than iPS cells developed from skin.

The reviewers were somewhat mixed on the results. They complained about little preliminary data, although they did say that this would be novel and useful if it were true. There's a concern that the epigenetic

memory of the tissues, the cartilage tissues, may include the disease that generated the problem in the first place.

The underlying hypothesis, that the connective tissue source would generate a better source of repair tissues, the reviewers claim there was limited evidence that this was really true, and, so, they were a little skeptical of that claim.

This was a little bit of an in between for me. It's kind of the ideal seed grant. It's a postdoc in an active lab. It's got an interesting and potentially useful health related problem, directly health related problem.

It does not use embryonic stem cells. It certainly is eligible for federal support, but, again, it's a seed project, which would be more appropriate here than for the federal level.

So I was actually very back and forth, and I ended up coming down the side of maybe for this one on the idea that the science is sound, there's some limitations in background, but it's a postdoc beginning researcher. I give them extra kind of points for that point.

MS. TOWNSHEND: Dr. Genel?

DR. GENEL: Yeah, I agree. I think I was

more no than maybe, but I mean I think, for purposes of discussion, I would just assume leave this in the maybe category.

MS. TOWNSHEND: Discussion? The team is recommending that this grant be placed in the maybe category. Is that the consensus of the group? This grant is placed in the maybe category.

Are we ready to go back, Dr. Kiessling?

DR. KIESSLING: Yeah.

MS. TOWNSHEND: All right. We are going back to 10SCA28, Dasaradhi Palakodeti, Study the Role of Cytoplasmic RNA Binding Protein in Human Embryonic Stem Cells and During Neural Differentiation, UCHC, 3.8 is the peer review, Dr. Kiessling, Mr. Mandelkern.

DR. KIESSLING: Yeah. This is actually also a reasonable application from a young investigator for a seed grant. The problem with it is that they're going to try to apply, and this has actually got to be a confusing part, they're going to try to use invertebrate techniques on human embryonic stem cells, and there's some pilot data, but it's not terribly convincing, but it's such a good application from the standpoint of it being a seed grant for a young investigator.

I'd like to leave this in the maybe for the

moment.

CHAIRPERSON GALVIN: I don't understand what they mean by using invertebrate.

DR. KIESSLING: They're looking at RNA binding molecules and proteins, and that's a new field, hasn't been done very much in embryonic stem cells, but they've been doing it a lot in whatever their invertebrate system is, which I can't find my note on that.

So they're going to try to use those same techniques in cultured cells. It isn't clear if they're going to have enough material. The biggest problem with this application is it's really ambitious, even for a seed grant.

They're going to look not only at undifferentiated cells, but cells as they differentiate into neurons, so it's got lots of parts, and it's probably overreaching. That was a major criticism of the peer reviewers.

CHAIRPERSON GALVIN: What would change it to make it a yes? Why would you make it a yes?

DR. KIESSLING: I would make it a yes if -- it depends -- I don't know.

CHAIRPERSON GALVIN: Okay. I have a hard time following the logic.

DR. KIESSLING: That's a good question.

CHAIRPERSON GALVIN: After all these years, I've learned to speak stem cell-ease reasonably, but haltingly.

DR. KIESSLING: I mean, like a number of the applications in this pile, we're not funding a lot of grants, but I think these Connecticut investigators are to be congratulated on coming up with really good ideas, so this is a really good idea. It's just a little before its time.

CHAIRPERSON GALVIN: Like one of those wines?

MR. MANDELKERN: Dr. Galvin? As the other reporter on this grant, I find it reasonable. He's doing a lot of investigating on binding proteins, and it is ambitious, but I think that's what we're supposed to do with seed grants, fund ambitious investigators to see the results.

I don't find too much negative, except that he's an ambitious investigator, and he can do the work, so I would certainly keep it in the maybe, unless, Ann, we want to put it into the yes.

CHAIRPERSON GALVIN: Okay, well, there's nobody on this list that isn't ambitious or capable of

doing the work. I think you ought to look at logical inconsistencies and bridges too far and things.

If somebody has got a great idea and it gets funded and it just doesn't work out, that's okay. If it gets funded and it doesn't look like they're going to be able to go from one to two to three to four to five, then I think we have to look at it very closely.

DR. HART: Can I just comment one moment on one of your criticisms? The issue of using genes and proteins from other species here, these are highly conserved proteins that should not really be a problem, and the issue of doing RNA binding protein, followed by sequencing, which I assume, I did not read the grant, I assume that's what they're doing, is totally doable.

I mean my lab does that and we publish that, as well, in stem cells.

DR. KIESSLING: Their leap is from Dersafala(phonetic). That should work.

CHAIRPERSON GALVIN: Okay. Thank you for your comment. That puts a different light on it.

DR. FISHBONE: Can I just make an observation? I think we're getting now into the range where it's a little difficult to decide what should or shouldn't be. This is about the cutoff level that I would

have anticipated.

DR. KIESSLING: Right.

DR. FISHBONE: And I think, you know, especially in somebody who is beginning their career as a true seed, whereas a lot of the people we're looking at are established investigators, I think we ought to give this a little bit more credence and support than we might ordinarily, because it is around the cutoff point, and I don't think we should say no.

DR. KIESSLING: I would like to be able to compare this when we get a final group together, so that's why I would like to keep it a maybe.

CHAIRPERSON GALVIN: I think that's great, and I think that Dr. Hart's explanation makes it a little clearer. What I've tried to say a couple of times this morning, if something is totally illogical and strictly theoretical, I think we need to look at it in a different way, rather than somebody who wants to use good principles and apply a new method. That's what we're talking about, you know, two different kinds of things.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the maybe category. Is that the consensus of the group? This grant is moved to the maybe category.

DR. FISHBONE: Can I ask a question about the maybe group? My understanding, possibly incorrect, was that if somebody wanted it in the maybe group, it wasn't really up for other people's opinions. In other words, if somebody wants it, then it goes to the maybe group. Is that correct?

MS. TOWNSHEND: Yes, that is correct.

CHAIRPERSON GALVIN: Well, in that case, if the first reviewer says maybe, put it in maybe, and we'll go back and review them all over again. There's no point in having a discussion.

MS. TOWNSHEND: Next grant for consideration is 10SCA44, Paul Epstein, Targeting Phosphodiesterases to Induce -- thank you. I tried to do it. Right here.

CHAIRPERSON GALVIN: Targeting Phosphodiesterases to Induce Apoptosis of Leukemic Stem Cells.

MS. TOWNSHEND: What he said. Peer review score, or the institution is UCHC, the peer review score is 3.6, the reviewers are Hart and Wallack.

DR. HART: I guess I'll go first. This is from a fairly senior investigator and Associate Professor at the Health Center, Dr. Epstein, and the project is to

find ways to induce apoptosis in leukemic stem cells by targeting nuclear phosphodiesterases to prevent relapses in human leukemias.

It really reads like and is reviewed like a classic kind of cancer grant, and I looked for where to connect this to a stem cell program. The reviewers I think mistakenly attributed past funding to this committee when actually it had previous funding from a different state program it's my understanding, has had several -- let me get this out here.

Several recent projects funded from foundations and state programs, but I see no recent federal support listed, and the reviewers do complain about recent lack of productivity.

The overall criticism is not very harsh. The significance is listed as very high if the hypothesis is correct and the researchers can achieve their goals, but I was less convinced that this was really appropriate for this committee, both on the fact that it's listed as a seed grant, where the researcher had previously funded a very similar project on a different cell type and now is coming to us with the same concepts where the leukemic stem cells in my mind was not very well justified as a stem cell topic, so I came down on the side of saying no.

DR. WALLACK: So I agree. When I first read it, I had in my vote maybe. As I went through it and re-read it, there were a few issues that I had, building issues, as I went along in trying to understand it, and the bottom line, also, for me is that I don't believe there would be anything that would convince me later on in the day or tomorrow to put this in the yes category.

While I had some thoughts, ambivalence at the beginning, I'm clearly on the side of no at this particular point.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group? This grant is moved to the no category.

Next grant for consideration is 10SCA47, Carolyn Drazinic, Discovering Treatments to Prevent Neurodegeneration in Huntington's Disease using hESCs and Patient-Derived iPSCs, UCHC is the institution, 3.6 is the peer review score, Kiessling and Mandelkern are the reviewers.

DR. KIESSLING: This is, I think, an ideal, almost an ideal seed grant application by an Assistant Professor, who is an MD, Ph.D. and is actually in charge of the Huntington Disease Program at the Health Center.

The peer review score, what they say is much higher than a score of 3.6, and I would actually in lots of ways recommend that this application be put in the yes category. I would certainly not want it put in the no category, but I would live with the maybe, but I would like to see this funded.

This is a nicely thought out. They're going to make induced pluripotent stem cells from people with Huntington's Disease and then differentiate them into neurons and try to understand Huntington Disease failures.

MR. MANDELKERN: I agree with Ann, that the peer review is more enthusiastic than the score, and if we were to just look at the score, we would not possibly put it where I think it should go, in the maybe, because, as a 3.6, it's in the lower part of the first 20 seed applications, so I think we have to put it in the maybe to look at it and see how many others we have that might be more worthy, so I suggest a maybe.

DR. KIESSLING: Okay. The peer reviewers about this say the significance is very high and very important, innovation is very high, and the investigator has very great potential, so it isn't clear why they gave it a 3.6.

CHAIRPERSON GALVIN: What else do you want?

We're going to end up discussing the same grants two or three different times for your consideration.

DR. KIESSLING: Well I think the concern that Mr. Mandelkern has is the problem is that if we put it with the 3.6 into a yes category, it kind of jumps it way ahead of some others, and it probably needs to be compared with some other really good grants, but 3.6 is certainly minimalistic for this.

The peer reviewers were quite enthusiastic about it, so I'm surprised it got higher than a three.

DR. FISHBONE: I agree with all of that, but we have not set thresholds, as to how much we're going to fund for seed grants and how much we're going to fund for the established investigators, and I think those that, for one reason or another, whether artificially or not, are in a borderline zone.

I think we ought to just hold off before we make a definitive decision.

DR. KIESSLING: I'll go with that.

DR. FISHBONE: That's the only reason. I agree with everything you say.

DR. KIESSLING: That's fine. It can be a maybe.

MS. TOWNSHEND: Steve, did you have a

question?

DR. LATHAM: I did, but if we're going to discuss it as a maybe, I could ask it later, but it had to do with the role of human embryonic stem cells, as opposed to iPS in this grant.

MS. TOWNSHEND: This is going in the maybe category, so did you want to hold that question until that time?

DR. LATHAM: We can talk about it later.

MS. TOWNSHEND: All right, great. So this grant is now moved to the maybe category.

Next grant for consideration is 10SCA13, Ee-Chun Cheng, The Role of Epigenetic Factor-HP1 in Regulating Human Embryonic Stem Cell Pluripotency and Differentiation, Yale University is the institution, 3.5 is the peer review score, Arinzeh and Mandelkern are the reviewers.

MR. MANDELKERN: This is a proposal, again, to figure out I think it's a gene in regulating embryonic stem cell pluripotency and differentiation, the fundamental questions of stem cell research.

The peer reviewers were quite enthusiastic, a highly ambitious project, and the role of proteins, again, in embryonic stem cell renewal. They want support

for the role of investigating HP1, the gene involved, and it's the summation of the peer review says this is science, which stands to add to our understanding of gene regulation in the pluripotent state and cells differentiate.

I think it's a very worthy project. It has a 3.5, which, again, is in that nebulous range. Again, I don't think we should say yes, because there may be other more worthy among 20 above it in score, so necessity it has to go into maybe in cause of the way we're reviewing them, from worst to best, so if we put too many yeses, we might eliminate some coming up later with much better potential.

So necessity, the way it was structured, not that I'm being critical, this is a good way to do it, but we have to put -- I suggest a maybe.

MS. TOWNSHEND: Second reviewer?

DR. ARINZEH: Okay. Yeah, I agree with the recommendation. I think maybe is probably appropriate, because I was borderline between yes and maybe, based on the comments of the reviewer and looking at the proposal.

They do think it's ambitious, somewhat ambitious in the aims where they're looking at. They're doing some mapping, and they're going to be generating

tons of data. How are they going to analyze that data, make sense of that data, I guess was some of the concerns by the reviewer, so I'd put a maybe, but I think this is an interesting seed grant, appropriate seed grant.

It's a postdoc, who is in a lab that is by an investigator, who is well established in the field, so it's an appropriate seed grant.

MS. TOWNSHEND: The recommendation is maybe.

DR. ARINZEH: Maybe.

MS. TOWNSHEND: Did you have a comment?

DR. FISHBONE: Yes. Taking a note from President Clinton's date book, what is the meaning of the word yes in this situation? In other words, does yes mean that this is something that is worthy of funding?

I mean, at the end, there will be a list of grants that we're saying are worthy of funding, some of which will get funded and some will not, so what I'm wondering is whether by saying yes now I'm assuming that does not mean that that grant will necessarily be funded, but it will place it in a pool from which, you know, when the money runs out, that's the bottom of the pool.

So, in other words, I'm wondering if some of these that it seems have a lot of support would it be

wrong to put them in the yes category, and then, at the end, when we've got like 14 or 15, of which we can only fund 10, let's say, then we would discuss their relative merits.

CHAIRPERSON GALVIN: Very thoughtful suggestion.

MR. MANDELKERN: In that case, I would add to my comments, taking into account what Dr. Fishbone said, that we are putting actually into yes things that we may reconsider, because we'll have oversubscribed yes.

Dr. Arinzeh and I originally had agreed on a yes recommendation for this proposal, but because of the nature of floundering here, we went back to the maybe, so I would go back to our original, Treena, proposal and put this in the yes, considering that if we oversubscribe yes, we will have to consider them again.

MS. TOWNSHEND: Just one note of caution. There was a situation last year, where a grant was put in the yes category, the potential grantee was present, and the grant was later not funded, so I just wanted to raise that awareness, and I want to make sure that people are aware that there were some -- there was some confusion, and that the final vote is the final vote, and that is the deciding vote with regard to anything that is funded.

CHAIRPERSON GALVIN: Okay and in regards to Treena speaking about this grant, I have a little problem with that word “ambitious” that keeps popping up. I see it, or hear it used, and you know what I hear?

I hear probably impractical, or possibly impractical, so when I hear about a lot of data, a lot of analysis to do within $200,000 and then I hear, well, that’s pretty ambitious, that term usually means you’re probably not going to be able to do, in my experience, you’re probably not going to be able to do what you set out to do, and we need to be careful about that, the interpretation of what that means.

MS. TOWNSHEND: So the team is one yes and one maybe at the moment. It goes in the maybe category. It goes in the maybe category.

Next grant for consideration is 10SCA16, Erik M. Shapiro, In Vivo Evaluation of Human ES, IPS and Adult Brain Derived Neural Progenitor Cell Transplantation and Migration Using MRI, Yale University is the institution, 3.5 is the peer review score, Dees and Fishbone the reviewers.

DR. DEES: The goal of this study is to understand whether progenitor cells derive either straight from the brain, or by induced pluripotent route, or by

human embryonic stem cells will work most effectively, both in the lab and in animals, so the specific aims are to find the means to propagate, differentiate and arrest each kind of cell to see if they are similar, and then to graft them into rat brains and study their migration in the animals.

This is a grant from an Assistant Professor, Assistant Professor since 2005, so pretty junior. The reviewers like the study design. They've had previous grants, and they were a little bit worried about the lack of publications from the previous grants, but how useful this will be for future therapies is really pretty clear, and, so, I would say a pretty -- I guess I want to say yes, but given where we've been going, I'll make it a tentative yes.

MS. TOWNSHEND: Dr. Fishbone?

DR. FISHBONE: Well I would have said strongly yes, because he seems to be one of the few people in the field who are working in this idea of MRI-based cell tracking, and I think that's going to be a very useful technology for many different aspects of stem cells.

One of the major difficulties, I think, in stem cell research is knowing where do the stem cells go,

and are we putting them in the right place and so on, so I think the technique is a very important one to support further investigation with it.

MS. TOWNSHEND: The recommendation is maybe?

DR. DEES: I think you got a yes on that.

MS. TOWNSHEND: Two yeses? Is it the consensus of the group that this be placed in the yes category?

DR. KIESSLING: The score on this is a 3.5?

MS. TOWNSHEND: Yes, it’s a 3.5 peer review score. Again, is it the consensus of the group that this be put in the yes category?

CHAIRPERSON GALVIN: Hang on here. I think Ann may have a comment.

DR. KIESSLING: Just seems risky.

CHAIRPERSON GALVIN: I haven’t looked at this grant, in particular, but it seems like an awful lot of work for a couple of hundred thousand bucks, particularly when you’re doing a lot of MRI stuff.

DR. DEES: But, oddly, this was not a grant in which the reviewer said it’s overly ambitious.

CHAIRPERSON GALVIN: No.

DR. FISHBONE: By the way, the kind of MRI

is different from the MRI that we're used to. This is on a special animal MRI. It's a lot cheaper than humans.

Humans seem to have a much greater value when it comes to the cost of examining them, so I think, you know, he addresses that, and it's just a question of whether you think that it's worth supporting research using this kind of methodology, you know, because I think it's going to have significance in the future of stem cell work.

CHAIRPERSON GALVIN: You okay with that, Dr. K.?

DR. LATHAM: Can I get a just a summary count either from Chelsey, or from Lynn, or someone else who is keeping track? How many stem -- how many seeds have we looked at, and how many are left with higher scores than what we've looked at so far?

MS. TOWNSHEND: We've looked at 38, if I'm reading this correctly.

DR. LATHAM: And there are 15 with higher scores than the one we're looking at now.

MS. TOWNSHEND: At this point --

(Off the record)

DR. HART: I understand from last year that even if we're oversubscribed in the yes category, that we

still do come back and visit the maybes. Is that true?

MS. TOWNSHEND: Yes, that's correct.

DR. HART: Okay.

MS. TOWNSHEND: There are 16, Mr. Mandelkern? Sixteen still to consider. At this point, the recommendation is yes. Is that the consensus of the group? Sir?

DR. FISHBONE: Can I maybe move that to a maybe, only in the sense that there are a lot more grants to look at, and we don't want to have the same problem that you described earlier.

MS. TOWNSHEND: Maybe, it is, unless I hear otherwise from the group. This grant is placed in the maybe category.

Next grant for consideration is 10SCA12, Yingqun Huang, Analysis of the Biological Function of Lin28 in Human Embryonic Stem Cells using a Novel RNA Interference Method, Yale University is the Institution, 3.3 is the peer review score, Arinzeh and Fishbone are the reviewers.

DR. FISHBONE: Dr. Huang wants to test the hypothesis that knockdown of Lin28 may decrease proliferation and induced differentiation of human embryonic stem cells and induced pluripotential cells.

He's basically probing the basic biology of pluripotent cells, and it's an important undertaking to better understand what pluripotency differentiation in cell programming are.

One weakness is it doesn't appear to articulate much of a project beyond performing the knockdown experiment. It's more of a hypothesis generating than hypothesis driven project.

Also, they have concerns regarding the specificity of the Lin28 knockdown and, also, some concern about overlap with already funded research, so while they feel this is an important area to look at, they're not quite sure what he's going to do with it and whether what he finds will be very specific and may already have funding for this project or for some of this project overlap.

MS. TOWNSHEND: Second reviewer?

DR. ARINZEH: Just a comment that while the reviewers did comment how highly significant the work is, so they thought it was a very, you know, interesting proposal and could have significant impact, but, yeah, there is this concern about overlap with I guess a proposal that was funded last year with a similar title, Molecular Function of Lin28 in Human Embryonic Stem Cells,

so that would be my concern.

MS. TOWNSHEND: The recommendation of the team is?

DR. ARINZEH: I say maybe.

DR. FISHBONE: I would say maybe.

MS. TOWNSHEND: It goes in the maybe category.

DR. FISHBONE: Because I'm a little concerned. When you're getting down to this number, do the recipients of the grants have any idea what the numbers are of their rating?

MS. TOWNSHEND: I believe they have had access to that, yes.

CHAIRPERSON GALVIN: Yeah. It's posted.

DR. FISHBONE: So you have the -- you may have, as you say, the inconsistency of a grant with a better number not getting funded.

MS. TOWNSHEND: That's correct.

DR. FISHBONE: Than having to justify that, which may be difficult for you.

MS. TOWNSHEND: Go ahead, Warren.

MR. WARREN WOLLSCHLAGER: If I could just respond to that? If we're simply going by peer review, then we should just go by peer review. I mean, there's a

lot of other factors that should be considered besides just a peer review score, and, really, I'm not a scientist, but I'm not sure I understand the significance between a 3.3 and 3.2, so I don't think we need to be overly concerned about the minutias of the peer review scores.

MS. TOWNSHEND: Yes, sir?

DR. WALLACK: I totally agree. I mean I think that we're here, to the best of our ability, to deliberate. I've given up two days. People have traveled from out of state, and I think that we have to make our own judgments.

Sure, we use the guidance, and it's an important aspect of what we do, but we have to be able to invest ourselves in this process.

CHAIRPERSON GALVIN: Well I think what you say makes good sense to me, Milt, and I think we're making our own decisions, and we need not to be concerned whether some cases, well, you know, Wollschlager got funded and he had a 3.2, and I didn't and I had a 2.9. That's not right.

We're looking at what we think is appropriate for a statewide program, and the folks who look at it internationally are looking at different kinds

of things, and they have different associations with various universities and individuals, so I think we need to make up our own mind.

And if the consensus of this board is we don't think it's a very good project for us to invest our effort into, then we need to move on to another one.

MS. TOWNSHEND: It sounds like this grant is going into the maybe category, so if we're ready to move on, the grant that we're considering next is 10SCA22, Matthew S. Rodeheffer, Identification and Characterization of Multipotent Cell Populations from Human Adipose Tissue for Application in Regenerative Therapies, Yale University is the institution, 3.3 is the peer review score, Goldhamer and Pescatello are the reviewers.

DR. GOLDHAMER: Okay, so, this is a grant from a new Assistant Professor, who started in 2009. It's a resubmission of a seed grant from last year. The grant is essentially identical to what was submitted last year, with just a bit of additional preliminary data.

The purpose of the grant is to identify and characterize populations of cells from human adipose tissue that will provide a superior starting material for use in tissue engineering and regenerative medicine. That's kind of the stated goals.

Both the reviewers and I were a little concerned of the lack of clarity in defining the significance. The major emphasis here is on the production of fat, and I think the applicant could have done a better job in explaining to us the great need for additional fat in regenerative medicine.

I'm being a little glib, but I am serious in saying that I think it's the responsibility of the investigator to really tell us more about why this is an important project.

Now there are strengths, a number of strengths in this proposal. This investigator has published and published prominent work in the characterization of what he calls an adipose derived multipotent stem cell, ASC for short, from mouse tissue, and, essentially, this is a relatively straightforward proposal, where he wants to apply what he has learned in the mouse and identify and characterize similar cell types from human fat.

So, in aim one, he wants to test a panel of markers on human tissues to try to purify a comparable population and test whether they can differentiate down multiple lineages, fat being one of them, but, also, cartilage, bone and muscle, and, in aim two, he wants to

test these cells in vivo by injecting them into immunodeficient fatless mice.

So, again, the grant is straightforward. The investigator probably will be successful, although there are differences in marker profiles between mouse and humans. This is an experienced person, who can figure this out, I think.

The question is whether or not -- how significant is this proposal for this funding mechanism, and that is where I had a little bit of trouble, and the reviewers also weren't -- they were enthusiastic, but not as enthusiastic as a number of other grants that I read, and they were concerned about significance, as I've already stated.

One thing that I also want to mention is that he did include human embryonic stem cells in this grant by merely saying that he could use human ESCs if he cannot identify these multipotent cells from human fat, but he said nothing else about human ESCs. It's almost like he needed to add the word to the proposal to make it applicable to this funding mechanism, so that wasn't great.

So because of these concerns, concerns about the significance, and the fact that this type of

project is certainly fundable by a number of other mechanisms, despite a solid score of 3.3, I had put it in the no category.

MS. TOWNSHEND: Paul?

DR. PESCATELLO: I put it in the maybe category, because I thought on two fronts. There's sort of a basic research aspect to it, learn more about fat cells, and, also, the mouse to human also has a nice translational aspect to it, so I thought, because the score was pretty good, but I agree with David on the flaws that he pointed out.

Given the other things we've discussed, I would put it in the maybe at this point.

DR. GOLDHAMER: I mean I would be okay with maybe. I was trying to make a definitive determination and try to get a few grants off the table. My actual recommendation was maybe, leaning towards no, and I convinced myself as I was talking that I was comfortable with the no.

DR. PESCATELLO: The reviewers talk about a large amount of preliminary research that's been done, which is good, but that backs up this proposal and cause an overall very strong application for seed and junior faculty. That's what seed grants are all about, so I

would say maybe.

MS. TOWNSHEND: This grant would be placed in the maybe category.

CHAIRPERSON GALVIN: Okay. That's seven out of the last eight that are in maybe, so I'm not sure whether we can or should skip ahead to the top rated grants, because everything else I think is going to end up as a maybe.

MS. TOWNSHEND: Discussion?

DR. FISHBONE: Could I just ask one general question? When we didn't fund somebody like him last year, what happened to that researcher? Did he do any of this work under another grant, or did he completely take a different turn?

In other words, there's a year that's unaccounted for, in terms of --

DR. GOLDHAMER: Well I can't answer that in its entirety, but I do know that he did add a little bit more preliminary data to this. He started the cell sorting analysis to try to identify this cell type in humans.

He did find a population that had some characteristics of what he was looking for. It wasn't exactly what he was looking for, but he has made some

progress. He doesn't have external funding. He has a large startup package from Yale. He started last year, so that's, as far as I know, what he's been doing.

DR. LATHAM: As to the Commissioner's suggestion, that we skip ahead, I know we probably can't, and, in any case, I'm going to recommend no on one that's coming up.

MS. TOWNSHEND: But is your partner?

DR. DEES: Just about that grant, I actually had a small ethical concern. I mean they're getting these fat tissues from people from basically discarded fat tissue.

I mean I don't know whether legally they need to get permission and stuff, but there was nothing about getting any permission for these kinds of materials, and it struck me as at least a question to be raised about this grant.

MS. HORN: It's certainly something this committee can weigh in on. It also must be approved by the institution's ESCRO committee before it gets funded.

DR. DEES: Yeah. I mean they were talking about they got HIPAA waivers, which I was a little confused why even HIPAA waivers were even relevant here, though maybe I don't understand something here, but

nothing about even looking for human subject approvals and stuff.

MS. HORN: They do need to have all of that before we would fund it.

MS. TOWNSHEND: So this grant is going into the -- yes, sir?

DR. WALLACK: So, picking up on David's thought process, we're going to have to be going back over these grants, and this one, in particular, I've heard a lot of concern. It's going to be hard for me to imagine how all of those concerns are going to be able to be overcome in a second discussion.

I'm wondering if we, therefore, can't put it into -- have a reconsideration of the maybe to a no, especially since it's not like this is the first time. Last year, we went through the same thing with this investigator, and it wasn't funded.

Now we have another sequence, so I'm wondering why we just can't go to the no right now, especially when it says the significance of the proposal is still not clearly defined.

MS. TOWNSHEND: As outlined earlier, because there is a maybe, it would go in the maybe category.

DR. WALLACK: I understand that, but I'm wondering if the maybes might want to reconsider.

DR. PESCATELLO: Let me ask David a question, the scientist.

MR. MANDELKERN: Well I would put it into a maybe, because I think this is a very important area of research and is certainly getting a lot of commercial attention, the question of white and brown cells. I think we have to put it into the maybe. It has sufficient strength not to put it away now.

DR. PESCATELLO: Let me ask David a question, as I said, the scientist. So, if I understood the proposal correctly, one of the things he's trying to do is to create adipose tissue, but, also, in and of itself, for transplantation, but I thought, also, that he was trying to find multipotency in the adipose tissue for use, for differentiation into other types of tissue, so I didn't understand the reviewer saying you're just talking about fat.

I thought he was talking about finding things in fat to be able to make other types, like cartilage and heart muscle, and, so, that didn't jive with their -- and that's another reason why I put it in the maybe category.

DR. GOLDHAMER: You're right. He does mention that he's looking for a multipotent cell that can adopt these other lineages, as well. I mean it is partly a matter of grantsmanship that he chose to focus on fat for most of the grant, but he mentions in a couple of places that he wants to assay these cells for their ability to make muscle and bone and cartilage.

So, clearly, he's thinking about a cell that has a greater capacity than just making fat. He didn't get that across or emphasize that enough, but you're right. And, so, why fat?

Many tissues have stem cells that a lot of groups are trying to isolate. Fat, as he mentions, has the advantage of it is relatively easy to get, unfortunately, and it's easy to dissociate, so, apparently, yields of stem cells from fat may be higher than in some other tissues.

MS. TOWNSHEND: We are already well past the time of five minutes and five minutes. This grant is going into the maybe category.

CHAIRPERSON GALVIN: I'm going to make myself obnoxious by, once again, or more obnoxious, by, once again, saying that I find it very difficult to understand that, with the kind of exceptions that were

raised, how is this all is going to move from one area to the other?

I'm beginning to feel with this morning's group that we're sort of trying to figure I wonder what he really is trying to do, and how can I -- I think he's trying to do this, or she's trying to do that. I don't think that's our point.

I think, when we have distinguished scientists that say it's flawed here, it's flawed there, I think you said something about adding something at the end, or adding a word, or a phrase, just to make it work, that bothers me.

DR. GOLDHAMER: I mean that's my interpretation, but, yes, I think the grant has nothing to do with embryonic stem cells, but he uses that language, I think, because it's more palatable.

CHAIRPERSON GALVIN: The grant has nothing to do with embryonic stem cells. We'll put it into a maybe.

DR. PESCATELLO: Dr. Galvin, just as to your frustration about all the maybes, I guess I would just come back and say that I think it's very hard to know how we're going to come out, until we see the whole group, and then all sorts of other considerations at that point,

both the amount of money, you know, as to your comment about the overly ambitious, I would say there's a lot of criticism from the lay community of academics that are very conservative, maybe too conservative, too incremental, and, so, I see overly ambitious and I think, hum, let's fund something that's, you know, from the outside looking in to academia, I'd say let's push them a little bit.

So I think those types of considerations at that point, when we see the whole group of things, of maybes, I would be surprised, too. I would just say, as we get the higher scores, that we don't say this is definitely a yes.

CHAIRPERSON GALVIN: I think your comments are well taken, but when I hear that this is not really applicable to stem cell, and I'm Chairman of the Connecticut Stem Cell Committee, and we're trying to dispense 10 million dollars for stem cells, I had a little trouble. There's a logical disconnect there for me.

DR. PESCATELLO: I think that's good to hear from the scientists if there's a very little stem cell nexus. As a layperson, I would say I'm impressed by the translational aspect of it, too, which is also a charge of our group.

DR. GOLDHAMER: Well let me clarify. There's little human embryonic stem cell connection. I mean these may be stem cells, or progenitor cells, multipotent cells, is what he's looking for, that can adopt different phenotypes, so it is potentially a stem cell grant, but not a human embryonic stem cell grant.

DR. FISHBONE: Can I ask you a question? It's my impression that last year we expanded what we would consider funding to include induced pluripotential cells, so that although it's not a human embryonic stem cell project, I thought we had -- we are funding, I think, some things that are induced pluripotential, and I think a lot of people are looking at fat, because it could be a very important source of pluripotent stem cells.

MR. MANDELKERN: I think we've spent a lot of time, and we're all anxious to see the grants that this has to be compared to, so I think of necessity it has to be a maybe.

MS. TOWNSHEND: With all due respect, I would recommend that we move on to the next grant for consideration.

Next grant for consideration is 10SCA38, Chunsheng Dong, Efficient Gene Targeting in Human Embryonic Stem Cell via Recombineering Based Long Arm

Targeting Vector, the institution is Yale University, the peer review score is 3.3, and the reviewers are Hart and Mandelkern.

DR. HART: This is a seed application from a postdoctoral associate or recent Ph.D., 2006 Ph.D. joined Yale Stem Cell Center in 2009. Excellent training facility.

The project is potentially valuable. It's to learn how to take advantage of some recombineering techniques in yeast and bacteria to apply them to do homologous recombination in human stem cells, which would give us the advantage of making knockouts, knock-ins and so on that's always been lacking in human stem cells.

So, overall -- oh, I should say the advisor, Che Hung Sho(phonetic), wrote a very strong support letter, as well. The reviewers had what I consider to be quite minor scientific complaints, one about the choice of which gene to use to validate the technology.

I think that, realistically, any competent scientist, such as this postdoc's advisor, would see the writing on the wall when they saw the review, if not, before, and there was comments about the serum-free, feeder-free differentiation conditions, which, again, I

think, in this environment, are relatively minor.

Dr. Dong has strong training in virology and molecular biology, which is appropriate for this type of a grant. I guess, when it comes down to this, I look at the idea of the seed grant and the criteria for what this committee is intending to be funding.

This is embryonic. This is relatively useful, in terms of the science of stem cells. It's a beginning investigator and an outstanding training environment, and, so, I'd like to try to be decisive on this one and come down and say yes, even though I have some that I'm very much less enthusiastic about coming up in the higher scores.

MR. MANDELKERN: As the other reviewer, I concur with Dr. Hart. I would come down on a yes. It's very worthwhile science, and the credentials are outstanding with publications and other work that he or she, the reviewer didn't know whether it was a man or a woman --

I would also say propose a yes for this grant.

MS. TOWNSHEND: The recommendation of the team is to put this grant in the yes category. Is there any discussion, or is that the consensus of the group?

This grant is placed in the yes category.

Next grant for consideration is 10SCA45, Jun Lu, Establishing Gene-Expression-Based High-Throughput Assays for hESC Differentiation, Yale University is the institution, 3.3 is the peer review score, Hiskes and Wallack are the reviewers.

DR. WALLACK: So Ann and I discussed this yesterday. Ann initially was probably on the side of wanting to fund this. We had an extended conversation, and she also, at this particular point, similar to my own consideration, feel that it's a grant that we probably would not, at this point, want to fund.

It's a continuation of some similar work. In our estimation, it's similar to a previous grant that we've already considered earlier this morning, and it's a grant by an established investigator, who is working on a grant that was awarded last year as a four-year duration to 2013, so it's our considered opinion that we would say no to this grant.

MS. TOWNSHEND: The recommendation of the review team is to move this grant to the no category. Is that the consensus of the group? This grant is moved to the no category.

Next grant for consideration is 10SCA30,

Efrat Oron is the potential grantee, Molecular Mechanisms of Germ Layer Induction in Human Embryonic Stem Cells, Yale University is the institution, 3.2 is the peer review score, Goldhamer and Wallack are the reviewers.

MS. HORN: And there is proprietary information that is claimed in this grant.

DR. WALLACK: You want me to start? I thought that this grant was a very well thought out, potentially very important avenue of research. It's by a young investigator fitting the kind of consideration that Ron just talked about, actually, that the person is quite accomplished. There's a very, very good team around this particular individual, and I think that this particular grant should, in fact, be funded. I would give it an enthusiastic yes.

DR. GOLDHAMER: Okay and I will just temper that enthusiasm a little bit with a couple -- my enthusiasm is tempered a little bit, and I'll tell you why. So one reviewer thought that this absolutely should be funded, that this was a promising young investigator and a good lab.

The other reviewer had very serious concerns about one of the approaches, and, so, I'll just give you a little bit of detail. So one thing that this

group wants to, or this postdoc wants to do is to do transcription profiling of embryonic stem cells as they differentiate into EBs, embryoid bodies.

Now the reviewer was concerned that getting a transcription profile of an EB doesn't give you that much information, because the embryoid body is made up of many, many cell types from all three layers, and there's doubt in my mind, as well as in the reviewer's mind, how much useful information will come out of that kind of analysis.

The other concern was that they then plan on doing functional analyses with up to 100 of these genes that they identify as potentially significant. It's not entirely clear how they'll come up with that list, but 100 genes analyzed from the seed grant to me seems should I say overly ambitious?

So just for the record, overly ambitious is code for unrealistic, or any other lack of focus, so, anyway, so it's a new promising investigator. I'd like to support the work. I just had issues with, you know, technical issues, so if someone else would like to weigh in on this and whether or not they agree or disagree, I'd appreciate it.

DR. WALLACK: So I understand, David, how

you temper your feelings on it, and I'll come back and indicate, though, that it does seem, from my reading of it and, more importantly, maybe the peer review group, that it is thought to be a very, very well-written grant.

There's significant support, letters of support for the grant, and there is significant enthusiasm for the studies that are proposed. The people who he'd be working with and the labs that he'll be involved with are very, very strong people, and, again, it's my sense that while -- if this was an established investigator grant and some of the aspects that David rightly presents was part of that, I would probably have more hesitation.

I don't have that hesitation with this particular grant, being a seed grant, being a young investigator, being somebody who already has a track record and is fortunate to be able to work under the mentorship of a strong group. I don't have that same concern, and I think that I would want to give this particular individual, for all the reasons that I've stated and the peer review people have stated, the opportunity, and that's why I would vote yes.

DR. GOLDHAMER: So I agree with that analysis. I still do have concerns about what is actually being done, and, so, I would vote a maybe.

MS. TOWNSHEND: This grant goes in the maybe category.

Next grant for consideration is 10SCA18, David G. Wells, Control of mRNA Translation in Neuronal Differentiation from hESC, Yale University is the institution, 3.0 is the peer review score, Fishbone and Goldhamer are the reviewers.

DR. FISHBONE: He proposes to study, or his studies use state of the art molecular approaches to gain insight into the contribution of, here we go, cytoplasmic polyadenylation element binding protein, otherwise known as CPEB, in the control of mRNA stability and translation in human embryonic stem cells and in differentiation to neuronal phenotypes.

So he’s using state of the art approaches to look at the contribution of this protein to the control of mRNA stability and translation. The strengths include fundamental biological and clinical relevance, experience of the applicant, preliminary data pointing to the key role of CPEB proteins in biological control, and potential value as a therapeutic target.

The weaknesses are the requirement to further define contributions of culture conditions to mRNA metabolism and a -- of preliminary data and discussion of

the potential pitfalls, as well as the alternative approaches.

It doesn't sound like a fatal flaw, but I'd like to hear what David has to say about it.

DR. GOLDHAMER: So a couple of issues I wanted to bring up. So it's an interesting proposal. It is risky, in the sense that this factor that they want to study, CPEB, and its role in neurogenesis and embryonic stem cells has not been investigated, so it might be interesting, it might not be interesting, but there's no preliminary data to suggest that it is interesting or involved in neurogenesis in this system, so that is a concern.

Then the other technical issue that I had with aim two, I won't go into a lot of details here, but what they want to do is to transfect embryonic stem cells with an inhibitory form of CPEB and look to see what effect that has on neuronal differentiation.

Now they say that, again, without going into too much detail, their transfection efficiency could be as low as 10 percent and up to 50 percent, but if you're transfecting an inhibitory molecule into a population of cells and you only have a 10 percent transfection rate, you're not going to see the affect.

So that is a significant flaw in that aspect of that aim. Now that's not the only aspect of that aim, which, if it was, I would say there's no way, but they aren't going to do some single cell analysis, and they do have a way of identifying those individual cells that have picked up this inhibitory molecule, so it's not all done on a population level, so I don't consider that one flaw to be a fatal flaw for that entire aim.

So, anyway, its translational control is emerging as very important, as known to be a very important biological control. This molecule maybe is interesting in some context. It's unknown in ES cells, and then I have concerns, technical concerns, so this grant score was seventh best, 3.0.

Jerry, since you led, do you want to give your recommendation first?

DR. FISHBONE: I think I went from a yes to a maybe, given all of your concerns.

DR. GOLDHAMER: I just wanted you to say maybe first.

MS. TOWNSHEND: That's a maybe. Next grant for consideration is 10SCA31, Anton M. Bennett, Dual-Specificity Phosphatases and Muscle Stem Cell Regulation, Yale University, 3.0 is the peer review score, Hart and

Wallack are the reviewers.

DR. HART: I'll give you the quickie, then. The project is to determine how phosphatases regulate muscle stem cell renewal in skeletal muscle regrowth and regeneration, and, so, in this project, our definition of stem cell is the underlying cells that help muscles to regrow and regenerate after injury or disease, otherwise known as satellite cells in most cases.

So this researcher is a fairly senior person, Associate Professor at Yale Med and Pharmacology. The reviewers find this to be a well-written, well-thought-out grant, which one would expect from such a productive and senior researcher for a seed proposal.

Point out that he has been very productive with recent papers in highly competitive journals, so we should have, you know, strong respect for the science and the grant application.

I'll point out, programmatically, that the topic of this proposal is extremely similar sounding, just from the title, to a recently expired RO1 grant from NIH, Myogenesis by Protein Tyrosine Phosphatases, is the title, and that should have expired the end of March.

He has another RO1 that's still in effect, which sounds actually quite different. The reviewers --

one complaint is the question about why he chose MAP kinase phosphatase 5 with apparently limited preliminary data, although it's clear that, again, this researcher is highly expert on this topic and I think would do well no matter what you handed him.

So my real -- you know, it's an excellent grant. It's an excellent proposal. My two strikes here in my mind are, one, is that I'm not sure it really qualifies as a true seed grant. It's not a terribly new direction of research for an established investigator. That's why I say that.

And, two, is that it's only in the most limited definition of the term a stem cell grant. You could argue that a tissue stem cell is a stem cell, but I think, for the priorities of this grant, one wouldn't put this in the highest priorities for this program.

So I'm very torn. I feel as though it's a strong science. I'm just not sure this is the right place for it.

DR. WALLACK: So I'll pick up. I'm not sure what distinguishes this proposal. Seems my observations were that it seems as though it follows other work that he's already been doing, and it seems as though, Ron, I'm not quite sure you might be able to talk to this

more than I can, this led me actually to come down on the side of not funding it, is that it seemed as though this is a project that could easily be funded from other sources and that could more appropriately, in fact, be and should be funded from other sources.

I'm also not sure of the commitment time wise of the researcher. Very little time is being spent by the researcher, and it almost appears as though, in reading the proposal, that he's acting as a PI for other young investigators. All of these reasons I would come down on not funding it.

DR. HART: Yeah and, in fact, if this, for example, if this had been a proposal for a postdoctoral fellow in this person's laboratory as a seed project, I'd be much more enthusiastic about it, but as it came in, the way it's outlined, I'd like to be decisive and say no, as well.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group?

DR. KIESSLING: This is CA31?

MS. TOWNSHEND: Yes. This grant is moved to the no category.

Next grant for consideration is 10SCA42,

Xin-Ming Ma, Exploring the Roles of Kalirin in Human Neural Stem Cells, UCHC is the institution, 3.0 is the peer review score, Hart and Latham are the reviewers.

DR. LATHAM: While we're being decisive, I also want to put this in the no category. I was absolutely mystified, as to how it got the 3.0. If I can read from the reviewer's statement?

The applicants propose to study the role of kalirin in neural fate specification in a human developmental model. Unfortunately, there is little preliminary data to suggest that this protein should play such a role. Their own data suggests that it's not involved at all in this process.

A little further down, the overriding problem with this proposal is the issue of preliminary data in their own models, etcetera. Basically, for the first two-thirds of the review, they say that this is not based on good preliminary data, and then you realized that review is a committee process, and you get a little bit further down and someone else, evidentially, says, based on their -- oh, I have to find it.

Their strong preliminary data, they're complimented by what is evidentially a different peer reviewer on preliminary data, but that reviewer goes on to

say, to criticize the design overall of the proposal and its ability to reach a conclusive endpoint.

So how those things together ended up with a 3.0 I don't understand, and I would recommend against funding.

DR. HART: The comment that I have written at the bottom of the review form I have is review sounds worse than the score, and I think that's absolutely true. I was trying to look at it in the best possible light. Again, this is an Assistant Professor, but a professor that's been on board since 2005 and has been at the Health Center since 2000.

I don't give this as much, then, leeway as I would a beginning postdoctoral fellow, is why I bring that up, so, again, to give it its due, because it's based on fundamentally sound science, Roe(phonetic) wanting exchange factors are very exciting in stem cell differentiation and so forth, but I think the reviewers are correct, that they were unable to come up with sufficient preliminary data to raise our enthusiasm to the point it should, so I guess I'd agree with a decisive no, then.

COURT REPORTER: One moment, please.

MS. TOWNSHEND: The recommendation of the

team is to move this grant to the --

DR. HART: Let me just finish by saying that the size of no's to make sure there is room for other maybes we've had that really do have much more sound science.

MS. TOWNSHEND: Thank you. The recommendation of the team is to move this grant to the no category. Is that the consensus of the group? This grant is moved to the no category.

Next grant is 10SCA21, Xiaofang Wang, Regulating Caspase Activity to Enhance Differentiation Efficiency of Human Embryonic Stem Cells, UCHC is the institution, 2.7 is the peer review score, Genel and Pescatello are the reviewers.

DR. GENEL: Well this is a very strongly positively reviewed grant from a postdoc fellow working in Ren Xu's lab. Basically, involves the role of caspase in differentiating cell differentiation in human embryonic stem cells. It's highly reviewed.

I think it's an appropriate seed grant. I would say it ought to be funded.

DR. KIESSLING: Dr. Pescatello had to leave for a conference call, but he did leave his review and indicated that he was interested in putting it into the

yes column, as well. Into the yes column, yes.

MS. TOWNSHEND: The recommendation of the team is to move this grant to the yes category. Is that the consensus of the group? This grant is moved to the yes category.

Next grant for consideration is 10SCA24, Li Yang, Novel Roles of Long Non-Coding RNAs in Human Embryonic Stem Cells, UCHC is the institution, 2.7 is the peer review score, Genel and Kiessling are the reviewers.

DR. GENEL: Well I'll defer, or are you deferring?

DR. KIESSLING: Let me just find my notes.

DR. GENEL: Well I'll have it up here in a minute. I thought I had it up here.

DR. WALLACK: Point of order, please?

CHAIRPERSON GALVIN: Yes?

DR. WALLACK: Point of order. On SCA21, Wang's proposal, that we just voted into the yes category?

CHAIRPERSON GALVIN: Yes.

DR. WALLACK: Can someone explain to me the first sentence, this seed grant application is proposed by Dr. Dong?

DR. GENEL: That was a typo.

DR. WALLACK: Was that a typo? Okay.

DR. GENEL: That's what I assumed.

DR. WALLACK: Okay. Okay, thank you.

DR. GENEL: Well the proposal by Dr. Yang is from an extraordinarily well-trained postdoc, who did a postdoc first in Sid Altman's lab at Yale and then moved on to the immunology group at UConn. The proposal is to look at the role of non-coding long RNAs in stem cell maturation and development. It got very, very strong review, and I think he's an ideal sort of investigator, a postdoc, with a well-established background.

I would say this ought to be in the funding category. Ann, do you agree?

DR. KIESSLING: Right. Yes. This is essentially an ideal seed grant. I'm looking now, but I think this person is a postdoc.

DR. GENEL: Yes.

DR. KIESSLING: So this is actually a postdoc application from a lab that has a good background in looking at interfering RNAs, and they've now established themselves in the last two or three years with another grant application in human embryonic stem cells, so, yes, I actually thought this was a really obvious one for us to fund.

MS. TOWNSHEND: The recommendation of the

team is to move this to the yes category. Is that the consensus of the group? This grant is moved to the yes category.

Next grant for consideration, 10SCA06, Brian J. Aneskievich, Nuclear Receptor Control of the Human Epidermal Stem Cells, UConn is the institution, 2.5 is the peer review score, Dees and Pescatello are the reviewers.

DR. DEES: I guess that means I'm on. This study is designed to quicken the rate at which skin cells can be reproduced, so they can aid in wound repair. The specific names are determined to what stage to the differentiation factors that increase cell replication or work and how it works.

This is from a more senior investigator. He's an Associate Professor. The reviewers think this work is important and is novel and can be improved. Perhaps by looking at genetic means confirm these results, but they were pretty enthusiastic on the whole.

For me, I thought that the link to human health and therapy is pretty clear, and that makes the project pretty attractive, so I was inclined to say yes.

MS. HORN: And Dr. Pescatello did leave his recommendation, which was yes.

MS. TOWNSHEND: The recommendation of the team is to move this grant to the yes category. Is that the consensus of the group? This grant is moved to the yes category.

Next grant for consideration is 10SCA29, Radmila Filipovic, Generation of Layer V Pyramidal Neurons from Human Embryonic Stem Cells, UConn is the institution, 2.3 is the peer review score, Kiessling and Mandelkern. Mr. Mandelkern has left the room.

DR. KIESSLING: Do you want me to go ahead?

MS. TOWNSHEND: Go ahead.

DR. KIESSLING: Yeah. This was one of the best grants in my stack. This is from an investigator, who has kind of an unusual appointment I think in the laboratory that she's in, and this would be her first independently funded grant.

She has been at UConn for awhile, I'm looking now for her CV, but she took her Ph.D. from Serbia while she was at UConn, so I'm not too sure exactly how that worked, then she was a postdoc, and now she's a research associate in this lab.

She's developed a system for differentiating what she calls layer V neurons from human embryonic stem cells. According to the letter of support,

she developed that technology in the lab, and now she's using that technology to study whether or not these can actually integrate into a rat brain.

Now I looked in this application for some kind of ESCRO review. I didn't see it, so this is a hot topic ESCRO issue, but it's really good science, and it's from an investigator who has actually spent some time working in this, and it's in a good laboratory, so I recommend that this be funded. I would like to put this in the yes category.

MS. TOWNSHEND: We'll have to come back to this once we hear from Mr. Mandelkern.

Next grant consideration is 10SCA05, XinQuan Ge, The Role of Dormant Replication Origins in Ensuring Genome Integrity in Human Embryonic Stem Cells, Yale University is the institution, 2.2 is the peer review score, and the review team is Dees and Hiskes.

DR. DEES: So this grant is concerned mostly with the mechanisms by which stem cells work. DNA begins replications at many sites, most of which are ordinarily dormant, but some will become active when problems occur to ensure that replication can occur accurately, so studying these dormant sites they think helps us to understand how the genetic integrity is

maintained.

So the specific aims here are to look at where replication starts and how dormant sites are used in stem cells and pluripotent cells, induced pluripotent cells in neural stem cells and blood stem cells, second, to determine the importance of these dormant sites for stability and, third, to determine what is needed for the dormant sites to become active.

So the peer reviewers are impressed with the experimental design and with the researcher. The only worry is that perhaps that deadly word, it might be too ambitious, and practical I guess is the word we should be using.

From my point of view, the connections to therapies here is pretty remote, but this seems like pretty fundamental research that’s going to help us understand a lot about how stem cells can be used and how they can be used reliably, so my conclusion was a yes.

Comments I got from Dr. Hiskes was this project proposes to study DNA replication in human stem cells, investigating the role of dormant replication. The reviewers regard the proposed project to study an important and understudied phenomenon.

They described the project as innovative

and their experiments as well-designed, logical and feasible. They're extreme enthusiastic, describing the project as groundbreaking, so the science is of high quality, and there are no other kinds of concerns, so she also voted yes.

MS. TOWNSHEND: The recommendation of the group is to move this, or the team, is to move this grant to the yes category. Is that the consensus of the group? This grant is moved to the yes category.

Let's go back to 10SCA29 and hear from the other half of that team that was considering that grant, Mr. Mandelkern.

DR. KIESSLING: Bob, I recommended that it go into the yes category.

MR. MANDELKERN: And I discussed this, and we both enthusiastically had agreed that it should go into the yes category.

MS. TOWNSHEND: The recommendation of that team is to place grant 10SCA29 into the yes category. Is that the consensus of the group? This grant is placed in the yes category.

And, finally, the last one in the seed grants, 10SCA35, the proposal comes from Lee, Maturation of Human Embryonic Stem Cell-Derived Cardiomyocytes In

Vitro Using 3D Engineered Tissue Model System, Yale University is the institution, 2.1 is the peer review score, and the reviewers are Goldhamer and Hiskes.

DR. GOLDHAMER: Okay, so, this is a very strong application from a postdoc in Laura Niklason's lab, and the PI of the grant will use 75 percent effort on this grant.

So this is a person, who is going to study cardiac muscle differentiation in vitro, and one of the -- although embryonic stem cells tend to like to differentiate into cardiac muscle, it is immature in nature when produced under normal conditions, and, so, they want to try to use mechanical methods, mechanical stretching methods that cardiac muscle during development usually is imposed on cardiac muscle during development to try to elicit this maturation process, with the idea being that the cardiac muscle has to be more mature in order to be used therapeutically.

So this was considered to be an innovative, exciting grant, with high significance. The applicant has great training for this. The applicant received a Ph.D. in biomedical engineering from Columbia and also worked with the top cardiac muscle researcher at Hartford, Kim Chen(phonetic), for her postdoc, so she's really well-

suited for this project, it's timely, and it was overall a very strong proposal, so I had voted yes, and Ann Hiskes concurred on that.

MS. TOWNSHEND: The recommendation from the team is to place this grant in the yes category. Is that the consensus of the group? This grant is placed in the yes category, just in time for lunch.

It is now just three minutes before the hour. Could you tell I was in radio once? We're going to take a 45-minute break for lunch, and we will be back here at 12:45. Thank you so much.

By the way, we will pick up with the established investigator grants after lunch.

(Lunch recess)

MS. TOWNSHEND: We are going to begin the next portion of our meeting, and we're going to start with the established investigator grants.

Again, this is ranked by peer review score, and we will begin with number 10SCB32, Hemchandra Shertukde, Near Infrared Imaging Using State of the Art Cameras and Wavelet Transform Tracker for Embryonic Stem Cell Identification, University of Hartford is the institution, the peer review score is 8.0, and this would be Goldhamer and Mandelkern.

MS. HORN: And there's proprietary information marked in this grant.

MR. MANDELKERN: I would just make one comment about this grant, which I would recommend for no, but this investigator is very much interested in working in embryonic stem cells, and she put in two grant proposals this time and last year, also, and it is the only one we get from the University of Hartford, so I think, in some way, if it's possible, the committee should recognize her enthusiasm, her interest, and ask her to raise her standards a little bit.

MS. TOWNSHEND: Second reviewer?

DR. GOLDHAMER: I concur with the no. It's not a competitive grant.

MS. TOWNSHEND: The recommendation is that this grant be placed in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCB27, Anthony van den Pol, Stem Cells in Treatment of Human Brain Cancer, Yale University, 7.0 is the peer review score, Hiskes and Mandelkern.

MR. MANDELKERN: I discussed this with Dr. Hiskes before she left for somewhere, I don't even

remember where, and we both agreed this was a grant that was not worth funding. It didn't have the scientific content, and we both agreed to place it in the no category.

MS. TOWNSHEND: The recommendation of the team is that this grant be placed in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCB14, Hector Leonardo Aguila, Characterization and Isolation of Stem Cell Intermediates from Human Pluripotent Stem Cells for Efficient Regenerative Therapies, UCHC is the institution, 5.5 is the peer review score, Dees and Pescatello.

DR. DEES: Dr. Aguila -- the studies will try to improve the differentiation of stem cells, so that they can be used in therapies. Its specific aims are to improve the methods of differentiating cells in different intermediaries and the supporting materials for each of those lines to identify and characterize the cell markers to verify the differentiation and to graft these into animals to assess for transplant potentials.

The reviewers think much of the project is ill defined, and, so, its potential impact is really

unknown. I would argue that a kind of key working hypothesis, that intermediate progenitors are really necessary, is -- I mean I can't see how you could possibly prove that by any kind of experiment. It seems like it's too broad, but my conclusion would be no.

MS. HORN: And Dr. Pescatello is still on his conference call, and I have no feedback on this from him.

DR. WALLACK: If there's a recommendation of no and there's a consensus of no, I mean why can't it go through as no?

MS. HORN: I was just commenting. It can go through as no.

DR. WALLACK: I would recommend no.

MS. HORN: Warren?

MR. WOLLSCHLAGER: If the secondary comes up with a maybe recommendation, that automatically puts it into the maybe category.

MS. TOWNSHEND: We can hold off and consider the next grant. We can come back to it.

Our next grant for consideration is 10SCB13, Zhiwei Hu, Targeting Cancer Stem Cells for Novel Ovarian Cancer Therapies, Yale University is the institution, 5.3 is the peer review score, this is Dees

and Fishbone.

DR. FISHBONE: The investigator wants to explore the use of a novel anti-tumor therapy in ovarian cancer, namely, a photo-activated antibody to tissue factor, known as TF. The weaknesses are numerous. Nowhere does the applicant state that TF is expressed on CD 133 cells, which are the cancer stem cells.

Preliminary data is from a single ovarian cancer line of unknown origin, does not actually show that cancer stem cell causes cancer in mice. Stem cell-specific focus of application is dilute. I guess that means not very good.

The system has been -- he's using the same targeted immunotherapy for lung cancer and breast cancer, and they're saying the impact of this study is likely to be low, as the only novelty is that he's using in another organ system.

I could go on, but I think that's probably enough weaknesses.

DR. DEES: Yeah. I don't have anything really to add to that. The reviewers didn't really see that there was much new in this, except we're doing the same thing we've done to a new organ system, so no.

MS. TOWNSHEND: The recommendation of the

team is to put this in the no category. Is that the consensus of the group? This grant will be placed in the no category.

Next grant for consideration is 10SCB34, Mark G. Carter, Biological Relevance and Functional Consequences of Heterogeneous Expression Patterns in hES Cells, UConn is the institution, 5.3 is the peer review score, this would be Hart and Wallack.

DR. WALLACK: Ron, if you want me to start, I'll start.

DR. DEES: I have it as on my list.

DR. WALLACK: I'll start.

MS. TOWNSHEND: Dees and Wallack. Sorry.

DR. WALLACK: What did I say, Mark? No. Anyway, to go on, so my feeling about the grant is I'm not sure that this grant really advances stem cell science much beyond where this investigator has already gone, or others have also similarly gone.

Secondly, I'm not sure of the relevancy of the application, and the applicant, I believe, doesn't clearly indicate how the results will be achieved. The PRs point out that the grant is, in fact, highly dependent on the use of the postdocs.

I'm not sure, bottom line, of the overall

value of the proposal, and I would recommend not funding.

DR. DEES: I don't have much to add to that. The peer reviewers didn't really think the work is -- it wasn't clear that it was that important, and they were really actually worried whether this lab could really perform the work they're proposing and had some worries about some of the budget items, but that's not that important, so no, as well.

MS. TOWNSHEND: The recommendation of the team is to put this grant in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration is 10SCB04, John D. Elsworth, Biochemical and Morphological Characterization of Candidates for Cell-Based Therapy of Parkinson's Disease, Yale University is the institution, 5.0 is the peer review score, and this is Arinzeh and Hiskes.

DR. ARINZEH: Okay. This proposal is looking at the use of embryonic stem cells, neural stem cells and IPS at several stages of development towards dopamine forming neurons for treatment of Parkinson's Disease.

Yeah, so, this proposal actually is with

collaborators currently in California at CIRM, so a portion of this project is being funded in California, but I guess, due to their funding restrictions at CIRM, they are not able to support Connecticut investigators and I guess that arm of the project, so they are looking for funding here to support that arm of the project.

With that said, so they did receive support from California for some of this, however, the reviewers thought, at least this arm in Connecticut, it's not very good. There are several weaknesses in looking at the various cell populations that they're proposing. They're just poorly defined.

There really is not a whole lot described about the various populations that they plan to use. The proposal, itself, is not written well. The justification for certain experimental plans is not laid out clearly, so there are just several flaws here with this proposal, so the recommendation would be not to fund. Hiskes also had the same recommendation.

MS. TOWNSHEND: The recommendation from the team is that this grant would go into the no category. Is that the consensus of the group? That grant is -- yes, sir?

DR. FISHBONE: Could I ask a question?

MS. TOWNSHEND: Yes.

DR. FISHBONE: I'm not quite sure how this all integrates with the grant that we funded for Dr. Redmond in previous years. They're obviously working in collaboration. Do we know if this has any impact on the grant that we funded for Dr. Redmond?

MS. TOWNSHEND: I don't know.

DR. FISHBONE: I'm wondering if the reviewers --

DR. ARINZEH: The reviewers didn't mention any of that. They have Redmond as a collaborator, but they didn't talk.

DR. WALLACK: My sense, also, is that this was part of the same island part of it, but that it was an additional component that would not adversely affect Redmond's grant at all.

MS. TOWNSHEND: Is it the consensus of the group, then, that this be placed in the no category? This grant is placed in the no category.

Next grant for consideration, 10SCB31, Marcus Bosenberg, The Role of miRNAs in Melanoma Cancer, Yale University, 5.0 is the peer review score, this would be Goldhamer and Hiskes.

DR. GOLDHAMER: Okay, so, this work kind of

builds on the investigator's prior discoveries, or accomplishments of being able to purify single melanoma cancer stem cells in mouse models, and, apparently, he can do that to homogeneity, which makes this project doable, so what he would like to do is to determine the role of micro RNAs in the establishment differentiation and function of cancer stem cells.

So the reviewers considered the qualifications of the PI and the innovative aspects of this proposal to be clear strengths, however, they had considerable reservations, which then dictated the score of 5.0, and the reservations were that the reviewers, and I agree, considered the grant to be exploratory in nature, and there was no preliminary data provided that micro RNAs are involved in this particular biological process, so it's a similar concern as some other grants that we've had, where everything is basically contingent on aim one, and, without positive data in aim one, the other aims won't be doable.

So the reviewers considered this to be, I'm paraphrasing, but to be premature for this type of a grant, based on the lack of preliminary data, so I agree with that assessment, and I had put this in the no category, and Ann Hiskes had agreed with that and placed

it in no, as well.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group? That grant is in the no category.

Next grant, 10SCB11, Erica Herzog, Cigarette Smoke, Anti-viral Immunity or Vial Immunity? Viral? Thank you. And Lung Epithelial Stem Cells, Yale University is the institution, 4.7 is the peer review score, Fishbone and Goldhamer.

DR. FISHBONE: The proposed studies have been designed to experimentally address the contribution of cigarette smoke and anti-viral immune responsiveness to the viability of epithelial stem cells.

The strengths are that the investigator's translational relevance, use of both animal and human models and the preliminary data, so it has a lot of strengths.

The concerns are potential confounding components of the animal model and regulatory -- that can be experimentally dissected. I don't quite understand, but it sounds they're not happy with the animal model.

And they say the approach could be enhanced by further pursuit of mechanics that can serve as a

roadmap to restoration of stem cells in COPD patients, so I don't quite see any connection to what we're -- this is obviously an important area, but there's nothing that I see about embryonic stem cells or even induced pluripotent cells that would make it come into our category of funding.

DR. GOLDHAMER: Yeah, so, just a couple of comments. So this cell type that they're studying in the lung apparently has certain stem cell-like properties, which is why I think it was submitted.

The reviews were okay. They weren't terrific. There was some criticisms, but they were overall fairly positive, and it wound up at a score of 4.7, so I think that's kind of an, from my reading of the reviews and looking at the grant, it seems like an accurate reflection of the reviewer's opinion, so, at that score, with no mitigating circumstances, I had put that in the no category.

MS. TOWNSHEND: The recommendation of team is to place this grant in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant for consideration, 10SCB09, Yingqun Huang, Role of Pluripotency Factors in a

Subpopulation of Stem Cell-like Cells in Ovarian Cancer, Yale University is the Institution, 4.6 is the peer review score, Fishbone and Goldhamer.

DR. GOLDHAMER: Do you want me to start with this one?

DR. FISHBONE: Doesn't matter.

DR. GOLDHAMER: Okay, so, this is a grant that looks at two pluripotent seed genes, Lin28 and OCT-4 in epithelial ovarian cancer, or EOC. They're interested in understanding the roles of these two pluripotency factors in cancer stem cells.

The problem is that they haven't shown that Lin28 and OCT-4 expression actually identify cancer stem cells, and, so, the reviewers were very concerned that, you know, that this really wasn't a stem cell grant.

They said it's a very good cancer grant, but there was no indication that it was a stem cell grant, and, on that basis, I have to agree with that recommendation, that it was a good and interesting grant, and there's evidence that Lin28 and OCT-4 are important in this system, but it's a cancer grant, not a stem cell grant until proven otherwise, so, because of that, I agreed with the reviewers and placed this in the no category.

DR. FISHBONE: I would agree with that completely.

MS. TOWNSHEND: The recommendation is to place this grant in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant is 10SCB15, Tian Chi, Transgenerational Epigenetic Memory in Mouse ES Cells, Yale University is the institution, 4.6 is the peer review score, Fishbone and Goldhamer.

DR. GOLDHAMER: Looks like it’s your turn, Gerry.

DR. FISHBONE: These studies focus on the molecular parameters of epigenetic memory with emphasis on the mechanisms that mediate epimutations with the objective of providing a basis to develop mechanisms to repair epigenetic mutations, so, basically, they’re saying that you can have mutations in the epigenetic aspects of disease, and they feel that epigenetic memory is an important part of it.

The strength is that they’re highly qualified combining in vivo and in vitro good preliminary data. The concern is that they are not discussing DNA methylation, which is an important epigenetic factor, that

maybe that makes the project more realistic in its scope.

It is unclear whether this phenomenon is specific to the locus, or transgene, or the human embryonic stem cell state. They gave it a 4.6, which indicates that they didn't feel this was, you know, should be highly rated, and I would recommend it for non-approval.

DR. GOLDHAMER: I agree with that.

MS. TOWNSHEND: The recommendation of the team is to move this grant into the no category. Is that the consensus of the group? This grant is moved to the no category.

Next grant for consideration is 10SCB20, Dr. Choudhary, Identification and Characterization of Potential Human Embryonic Stem Cell Derived Mesenchymal Progenitors for Differentiation in Trabecular Meshwork-like Cells, UCHC is the institution, 4.6 is the peer review score, Hart and Mandelkern.

DR. HART: Dr. Choudhary is an Assistant Professor in the Department of Surgery at UCHC. His project is to develop differentiation protocols that generate precursors of the tribecular meshwork-like cells for treating various eye diseases.

The project follows on the heels of an

earlier stem cell grant, and I think that the main criticism of the reviewers and my criticism are tightly linked, that there were no publications from the prior seed grant, and the reviewers point out that there are no data to support that cells express combinations and markers that are basically central to the entire project are actually expressed in this particular cell type.

I really felt as though there was a fundamental shortcoming in the productivity and a somewhat serious flaw in the science, so I vote no.

MR. MANDELKERN: This is an interesting grant, because it deals with a problem that is widespread in the community, inter-ocular pressure and leading to glaucoma problems, and it does one thing that we were looking for.

It builds upon a seed grant that was completed, however, the peer reviewers say that there's not enough experience, even with the seed grant completion, does not appear to have much experience with pluripotent differentiation, as their approaches seem naive in the field, therefore, we regretfully have to agree and put it in the no category.

MS. TOWNSHEND: The recommendation from the team is to place this grant in the no category. Is that

the consensus of the group? This grant is moved to the no category.

Next grant for consideration, 10SCB28, Weimin Zhong, Mechanisms for Balancing Stem Cell Self-Renewal and Differentiation During Human Neurogenesis, Yale University is the institution, 4.6 is the peer review score, Arinzeh and Wallack.

DR. WALLACK: This is an extension of previous work, which the researchers have been involved with. It, however, may not be very novel, from what I can tell. It appears as though the grant is structured in a way that there will be a great utilization of the PI's postdocs.

Somehow or other, it gives me the feel of maybe it should have been a seed grant. The value is unclear to me, and I would vote no on this one.

DR. ARINZEH: Just to add a little bit more about the weakness of the project, is that, well, the PI has a lot of experience in specifically these proteins, the num(phonetic) proteins, and, so, he's basically trying to extend some of his work that he's been doing for about 10 years with these proteins, now going into the embryonic stem cell area.

And, so, I think the weakness the reviewers

were stressing a little bit was that they, you know, found that he had a limited expertise in embryonic stem cells, and he's just trying to extend his current focus area into that field, so my vote is no, as well.

MS. TOWNSHEND: The recommendation of the team is to move this grant into the no category. Is that the consensus of the group? That grant is moved to the no category.

Next grant for consideration is 10SCB10, Urs Boelsterli, Stem Cell Approaches for Defining Patient-specific Predisposition to Idiosyncratic Drug-induced Liver Injury, UConn is the institution, 4.5 is the peer review score, and this would be Genel and Kiessling.

DR. KIESSLING: This is an application from a new recruit, a new full professor at UConn, who is heading up the toxicology division, I believe, and this person has come from Europe somewhere.

The biggest problem with this application, which the peer reviewers picked up on and which I agree with, is that they're looking to use hepatocytes derived from stem cells to study liver injury.

The problem is nobody has really been able to derive reliably hepatocytes from stem cells, and these investigators haven't shown that they can do that either.

The efficiency is really low. How the hepatocyte-type stem cells are is not clear, so this is very premature follow-up for cell lines that they're not even sure they can get.

The peer reviewers pointed out that this would be a great application for seed grant for this new faculty person, but, as it stands now, there's just everything depends on being able to do something that nobody has reported being able to do, so I'm afraid that this very nice application really should not get funded by this group.

DR. GENEL: I agree.

MS. TOWNSHEND: The recommendation of the team is that this grant be placed in the no category. Is that the consensus of the group? This grant is placed in the no category.

Next grant up for consideration is 10SCB18, Tai-Hsi Fan, Developing a Microscale Artificial Stem Cell Niche, UConn is the institution, 4.3 is the peer review score, Hart and Latham.

DR. LATHAM: This project wants to develop, further develop a microchip that allows you to control different conditions in the culturing of mouse, human and IPS cells, particularly to direct their differentiation on

the surface of this chip down neuronal lineages.

The reviewers don't have any problem with the core science of the review. It's nice that this was developed originally with some seed grant money from us and they're now following up, moving from having successfully adapted this chip to control the development of mouse embryonic stem cells toward human.

The reviewers think there won't be any problem with moving it in that direction. One thing I like about this proposal is something we haven't talked much about at this committee, but I actually see the potential for intellectual property rights flowing from this, because if they develop a good chip that really allows you to control neuronal differentiation in that chip by controlling more features than competitive biochips can control, that could potentially sell to researchers around the world, and that could give Connecticut a little bit of ROI.

On the other hand, the difficulty is partly that the two lead researchers are going to put a very small amount of time. They're down for .3 of a summer month each in year one and again in year two.

It's also not very specific to human embryonic stem cells. This is development of a chip

that's designed to be for murine models and for human cells and for IPS cells, so it's not clear that it's a high priority project for us to fund if we're trying to focus specifically on human embryonic stem cells.

While I think it looks like a really nice, neat project, and it's already been proven pretty well, and they've done well with the seed funding that they had before, and it's nice, also, that it's a joint venture with engineers, I'm afraid it's not a top priority for us, and I also don't see the time being spent on it by the PIs.

DR. HART: Well I actually was hoping that we should spend just a little bit of time on this, because this might be one of those unusual ones. The review, itself, really does not sound as bad as a 4.3 score in general.

I think that you reflected that correctly in your statement. Would you agree with that statement?

DR. LATHAM: Yes.

DR. HART: Okay. The biggest flaw scientifically, I thought, and what the reviewers pointed out was that, let's see, they didn't talk much about extra cellular matrix, which makes a lot of sense, but that, to me, is the biggest problem they came up with.

The major criticisms of the grant were more about grantsmanship, and I think that for a junior faculty member, we might give them a little bit of a free ride on that one.

This particular person is the Assistant Professor in the Department of Mechanical Engineering, has had one publication from seed project in the past, and if you look at current supports, is at or just after the end of several major projects, including NSF, this organization and others.

And, so, actually, you know, I'd almost like to go as far as to say yes for this one, but I don't think that's quite right and fair to the other projects, but I would like to make sure it's in the maybe population.

Oh, and, lastly, among our selection criteria there is AF benefits, including financial benefits to the State of Connecticut, and, so, for IP that would make sense.

DR. LATHAM: Yeah. The IP aspect of this really leapt out at me.

MS. TOWNSHEND: It sounds like the recommendation from this team is to place this grant in the maybe category?

DR. LATHAM: Yes.

MS. TOWNSHEND: Is that the consensus of the group?

COURT REPORTER: One moment, please.

MS. TOWNSHEND: This grant is placed in the maybe category.

Next grant is 10SCB24, Dr. Mina Mina, Derivation of Neural Crest Cells Capable of Forming Skeletal and Dental Tissue of the Craniofacial Region from Human Embryonic Stem Cells, UCHC is the institution, 4.3 is the peer review score, Dees and Pescatello, and since Dr. Pescatello is not yet back, we will hear from Dr. Dees, and then we will move on.

DR. DEES: Do you think it’s worth hearing from me now, or should we just wait for Dr. Pescatello?

MS. TOWNSHEND: Go ahead.

DR. DEES: Okay. The studies that are intended here are intended to direct stem cells into neural crest cells and into cranial facial bone structures, so their specific aims are to characterize the path by which stem cells, embryonic stem cells become neural crest-like cells and then characterize the cells that they’ve been formed, and, second, to show that these in vitro cells have the same properties as neural crest

cells in vivo in animals by transplanting them into chick embryos.

So the reviewers found these experiments really well-designed and novel in really kind of an explored area. They really worry about the differences in the mouse models that they're using as the basis for the experiments in the human ones and about really the practical problems of using chicks, which is somewhat unusual, especially since the environment of chicks, embryo chicks is really very different from humans.

In some ways, this is a project worth funding, but I think the science is weak enough that I'll lean towards a no.

MS. TOWNSHEND: We'll hold off with categorizing this until Dr. Pescatello returns.

Next grant for consideration is 10SCB33, Alex Lichtler, Gene Targeting of Mutations in iPS cells from Osteogenesis Imperfecta Patients using Zn Finger Nucleases, UCHC is the institution, 4.3 is the peer review score, Wallack and Arinzeh.

DR. ARINZEH: This grant proposal is looking at the use of zinc finger nuclease-directed homologous recombination as a method to correct genetic defects in iPS cells derived from OI patients, so

osteogenesis imperfecta patients, so the idea is to correct, then, this collagen mutation, collagen type one.

So this would be an interesting, very interesting proposal. The reviewers commented on the fact that this would be a very nice proposal as a seed grant, but as an established investigator grant, there's a lot of preliminary data that's lacking to establish that they can actually pull this off.

They would be getting the vectors from Sigma, and, basically, Sigma would be designing these vectors, and, so, there's concern there by the reviewers, you know, they should, in theory, already have these vectors produced, so it would have been nice to have shown in the grant proposal.

And then the PI also lacks familiarity with the zinc finger system, and, so, there's a concern there, as well, so these were the two major weaknesses they presented, so my vote would be no for this.

DR. WALLACK: I would agree, and I would add that the project may also better be suited for another grant source, such as NIH, and I agree with the no vote.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group? This grant is placed in the

no category.

Paul, we have a couple of grants in established investigator on which you were part of the team, that if you could give your recommendation, and I will give you the numbers, if you're ready.

The first one is 10SCB14. That is Hector Leonardo Aguila.

DR. PESCATELLO: You already discussed this?

MS. TOWNSHEND: We've already discussed this, and the recommendation that came from your partner was no.

DR. PESCATELLO: Not to fund.

MS. TOWNSHEND: The recommendation on this grant is to place it in the no category. Is that the consensus of the group? This grant is placed in the no category.

10SCB24, also, Dr. Pescatello, that would be Dr. Mina Mina. We've heard from Dr. Dees.

DR. PESCATELLO: Not to fund.

MS. TOWNSHEND: Not to fund.

DR. KIESSLING: Is this application a resubmission?

MS. TOWNSHEND: I don't know. Does anyone

know? Oh, Chelsey is nodding her head.

MS. CHELSEY SARNECKY: I believe it is, but I can take a look through the files.

MS. TOWNSHEND: The recommendation of the team is that this grant be placed in the no category. Is that the consensus of the group? This grant is placed in the no category.

And you're all caught up, except now you're part of one of the next grants, which is 10SCB25, Craig Nelson, Derivation of Human Mesendoderm and Mesectoderm Progenitors for Regenerative Therapy, UConn is the institution, 4.0 is the peer review score, Dees and Pescatello.

DR. PESCATELLO: Let me just look at my notes here. So, in this grant, the reviewers had several issues, problems, including the cost. This is also an ambitious project. I had a hard time making sense of the peer review, in that there were some pretty highly recommended components of it, but they had issues with the -- it builds on another grant. I'm sorry. I'm just getting my notes together here. It builds on a previous grant, which is good.

It's a high-classed, almost a million dollars, and I guess, in terms of my own consideration of

this grant and the cost benefit analysis, which I don't know if we want to talk about now as a group, it seemed like a lot of money, and it was buying a lot of equipment, that the peer reviewers mentioned, also, this equipment didn't already exist and was available on the campus. My colleague?

DR. DEES: Yeah. I mean what they're trying to do here is they're developing some techniques for differentiating stem cells into like heart muscle cells, blood and vascular tissue cells and skeletal connected tissues, so, in some ways, it's a nice project, in that it's really essential work for future kinds of therapies, but they did think that a lot of the work here was not, while it was important work, it wasn't particularly unique to this lab, it wasn't something that had to be done here, and that was kind of the baseline, was that they sort of thought not for this amount of money. It's a good project, but not for this amount of money.

DR. PESCATELLO: That's a good bottom line.

MS. TOWNSHEND: So the recommendation of the team is no?

DR. PESCATELLO: No.

MS. TOWNSHEND: The recommendation of --

yes, sir?

DR. WALLACK: So I understand the cost factor, but the reviewers also indicate that it's quite an impressive proposal, with significant amounts of preliminary data to support the experimental plan.

They go on and talk about the significance of the project as being quite high, so what I guess I'm wondering about, and we've done this before, maybe we might want to consider putting it in the maybe category and coming back and recommending our own adjustment and this precedent to us doing this, our own adjustment to their budget.

So we can discuss this if it becomes a maybe, and that's why, with the peer review's comments, I would suggest that we keep it on the table.

MS. TOWNSHEND: We have a maybe, so this would go into the maybe category. Go ahead, Paul. I'm sorry.

DR. PESCATELLO: I mean if those are our rules of procedure. I think, too, if you look at the type of equipment that's being purchased under this grant, like the PCR hoods, that's something that must be available. I mean you could commonsensical could say is otherwise available and why we would be funding this, why this

specialized pot of money for stem cell research would be funding some very standard equipment.

I don't know if it's the highest and best use of that, of our funds.

DR. WALLACK: Question?

MS. TOWNSHEND: It goes in the maybe category.

DR. WALLACK: Okay.

DR. DEES: Unless we convince you otherwise. I mean I think there are lots of many, many better grants than this one ahead of us, and there's only a fairly small pool of money for million-dollar grants.

DR. PESCATELLO: Yeah. That's the issue. For a million bucks.

DR. WALLACK: I think that's a very good point, Richard, and I probably can withdraw my maybe, then.

MS. TOWNSHEND: So your maybe is now a no? And the team is recommending no, and is it the consensus of the group that this would be no? This grant is placed in the no category. Next grant for consideration is 10SCB26, Craig Nelson, Chromatin Control of Sporadic Gene Expression in Human Embryonic Stem Cells, UConn is the institution, 3.9 is the peer review score, Dees and

Latham.

CHAIRPERSON GALVIN: How is it that Dr. Nelson's two grants have exactly to the dollar same amount of money? I find that odd.

DR. LATHAM: All right. I can go first. This has got a really sort of neat background biological idea, which is that noisy or sporadic gene expression in human embryonic stem cells actually might have a biological purpose, and the idea of this study is to start trying to track down in some specific cases the effects and the reasons for sporadic gene expression.

So the aims are to screen for sporadic genes and assess chromatin state of 10 percent of the genome in an undifferentiated human embryonic stem cell and cells exiting pluripotency and initiating differentiation, and then to examine the expression, status and chromatin state of sporadic genes in human embryonic stem cell lines and determine the role of chromatin and controlling sporadic expression.

I'm shortening. The peer reviewers of this very much liked the idea and saw some significance in the general background idea, but were disappointed with the clarity and framing of the proposal.

They also note that the PI's time -- it's

not clear how the PI's time is going to be spent on this, and they also think that there's an awful lot in that first aim that's taking on an awful lot for the limited amount of time that they'll have under the grant.

So, basically, the reviewers' overall take seemed to be that there's some really terrific ideas, which were incidentally developed in an earlier seed grant, which did get a publication, but which at least one of the reviewers has said has not proceeded very far, so, with those warnings, basically, they think there's some really great background ideas here, but that the execution is not clearly laid out in the proposal, so I would recommend no.

DR. DEES: I largely agree with that. I mean the reviewers really thought -- they used that word ambitious again, by which they mean impractical, so there were really worries about that, and they had a number of problems with what the general applicability of the results would be, even if the whole thing works, even though they think it has some pretty cool ideas in it, so I'd say no, as well.

MS. TOWNSHEND: The recommendation of the team is to move this grant to the no category. Is that the consensus? Yes, sir?

DR. GENEL: I agree with the categorization, but just to make an observation and a point, is that I think, when we see applications that come through from previous seed grant observations, and I think it's something we ought to take note of, and I've noticed several of them here.

If the purpose of seed grants is to provide preliminary data that would provide the basis for substantive larger applications, then I think this is something -- it's a very, very positive sign, but doesn't necessarily mean it has to be funded by Connecticut.

The notion would be, if you generate those ideas, those ideas ought to be substance for a grant to other funding agencies, and I would hope that the review that would be available to the investigator of these two grants would be helpful, in terms of how to reframe those for other applications, but, yes, I agree with the no funding. I just wanted an opportunity to make that observation.

MS. TOWNSHEND: Thank you for your comments. Anyone else? If we're in agreement, this grant will be moved to the no category. Is that the consensus of the group? This grant is --

DR. KIESSLING: Is this also a

resubmission?

MS. TOWNSHEND: Chelsey, do you know?

DR. KIESSLING: Are either one of Dr. Nelson's grants a resubmission?

DR. LATHAM: I think the one we just talked about, it may sound like a resubmission, because it's based on a seed that we considered in the past.

DR. KIESSLING: Okay, because I think a number of these are resubmissions, and I'm just wondering how many times we're going to have them resubmit.

MS. TOWNSHEND: This grant is moved to the no category.

DR. GENEL: More relevant, are we consistent when they come up the second and third time?

MS. TOWNSHEND: Good point.

DR. GENEL: Maybe that's why they come back.

MS. TOWNSHEND: The next grant for consideration is 10SCB08, Jonathan Covault is the potential grantee, Investigation of Molecular Adaptations to Alcohol in iPS Cell Derived Neural Cultures from Alcohol Dependant and Control Subjects, UCHC is the institution, 3.8 is the peer review score, Genel and Kiessling.

DR. GENEL: Well I'll defer to Ann on the science of this. I mean this is an attempt to -- it's a fishing expedition, basically to try and generate cells from individuals who have substance abuse, or alcohol dependency and those who don't, and to try and define what the specific epigenetic abnormalities are in this, and I think the reviewers point out I think that it's a very interesting and intriguing idea, but they don't have any data to support it.

This would have been a perfect seed grant, from my perspective, had it been put in that format, but, as an established investigator grant, I don't think it's competitive.

DR. KIESSLING: This was actually a very hard -- I spent a lot of time thinking about this grant, because this is a really difficult area of research.

It's very hard to come up with some kind of model to study alcoholism, and the score of 3.8 I think actually reflects one of the opinions of one of the reviewers, who simply doesn't feel that iPS cells are going to be very useful, so one of our peer reviewers we need to keep in mind doesn't think iPS cells as a science is going to be terribly useful.

On the other hand, I really agree with what

Dr. Genel just said. There's just so -- first of all, this group has quite a bit of money now, so they're going to be able to get some pilot stuff done. This is a well-funded and active mental health group. He's a psychiatrist, an MD, a Ph.D. psychiatrist, and they're studying drug abuse and alcoholism, and I agree.

I mean if they had any even one or two iPS lines to put in here, his background data would be much more compelling to fund them, but I think I'm going to have to say no to this one.

MS. TOWNSHEND: The recommendation of the team is to move this grant to the no category. Is that the consensus of the group? This grant is moved to the no category.

Next up is 10SCB23, Laura B. Grabel, Directing Differentiation of Embryonic Stem Cells to Epiblast, Wesleyan is the institution, 3.8 is the peer review score, Goldhamer and Latham.

DR. DEES: Actually, I'm taking this one for Dr. Goldhamer.

MS. TOWNSHEND: Okay. Dees and Latham. Thank you.

DR. DEES: There's conflict of interest with the collaborators.

MS. TOWNSHEND: Got it.

DR. DEES: All right, so, the goal of this grant is to understand how stem cells begin to lose their pluripotency by looking at the transition from cells that can produce extra embryonic tissues to epiblast stage, in which the cells can only produce embryonic ones using both mouse and human cells.

Specifically, they're aiming to characterize the markers for the epiblast stage and to isolate cells in the epiblast stage and determine their developmental potentials, and, third, to identify the signals that lead to development of the epiblast.

This work is really important for basic stem cell biology. Its relevance the therapy is a bit remote, especially since, as some of the reviewers note, the understanding of the particular transition may not be particularly necessary for actual use of therapeutic stem cells.

On the whole, the reviewer -- mostly favorable, noting the really long and productive record of the PI and that this grant is really well-written and well-conceived, however, they do think the work is not especially innovative and would not reveal some other things that they think are important to know, so this is

one of those ones where in some ways it's a worthy grant.

My feeling is that there are a lot more worthier grants to come, and, so, I'm more inclined just to say no at this point.

DR. LATHAM: I'm afraid. I mean I have the greatest respect for the PI in this grant, but the virtue of this grant is also its vice, which is that it's really basic biological cell biological research and very far away from the kind of translational priorities that we're supposed to be pursuing, so I'm afraid I would also say no.

MS. TOWNSHEND: Discussion? Sir?

DR. GENEL: Well I will grant everything that's been said, but I think part of our role is to insure that there's diversity of the funding. I think this is the only one outside of Yale and UConn that is even potentially fundable by an established investigator, so I would not reject this out of hand.

I think we ought to put it into a maybe category and then consider it, because I think that's the role of this advisory committee, is, in fact, to make those types of judgments.

DR. KIESSLING: I would agree with that.

MS. TOWNSHEND: This grant is placed in the

maybe category.

Next grant for consideration is 10SCB06, Zihai Li, Stem Cell Vaccine Against Cancer, UCHC is the institution, 3.7 is the peer review score, Genel and Kiessling.

MS. HORN: And this grant has marked proprietary information in it.

DR. KIESSLING: I just ask, actually, if this is a resubmission, but I remember now this was actually a seed grant last year.

This is an investigator, who is interested in developing and using stem cells to develop targets against cancer. It's a really intriguing proposal, and they've made some progress on when they were funded before.

What they're hoping to do is essentially teach stem cells to target cancer and destroy cancers, and they're doing this by some interesting cell tricks that might work.

They have enough background information. My concern about this application is that it's a big budget for what they're trying to do, and I would like to put this in the maybe category and then revisit how much money we've got and see how much of this work we can actually

fund, because this is a follow-up to a seed grant.

It's a really interesting idea. The reviewers liked it. It's got some problems, because it's not a slam dunk that it's going to work, but if it did work, it would be really, really useful, so I'd like to put this as a maybe.

MS. TOWNSHEND: This grant goes in the maybe category. Sir? Did you want to comment? You're the other reviewer, after all.

DR. GENEL: Well my notes pretty much mirror what Ann says, except I would be inclined to put it in the no category, in part because of the competition up above.

The notes I wrote down is that he already has a four-year grant, apparently, so that this is not --

DR. KIESSLING: This is the second --

DR. GENEL: -- essential to do this work, and the peer reviewers point out it's high risk, so I would say, well, you know, I think, at some point, we've got to make some tough decisions. I'd move this one over into the no.

DR. KIESSLING: So, Mike, is this second to a seed grant, or does he have another four-year grant? I was just actually going to try to pull up his budget page.

How much money do they have right now?

DR. WALLACK: Ann, I think this was a continuation from a seed, Ann. Seed.

DR. KIESSLING: So they don't have another?

DR. GENEL: It's a continuation from a seed. My apologies.

DR. KIESSLING: Okay.

MR. DANIEL WAGNER: This investigator has an established grant, established investigator grant last year.

DR. KIESSLING: I'm sorry. Say again, Dan? So it was a seed grant and an established? No.

MR. WAGNER: Last year, they received an established investigator award of half a million dollars for -- let me count.

DR. WALLACK: Was it the same subject, Dan, because --

MR. WAGNER: Similar.

DR. KIESSLING: It's similar.

MR. WAGNER: Similar, but not the same title. I mean that's with the work they're doing, obviously.

DR. GENEL: Well, I'm sorry, I can't find explicitly where I found it, and I stand corrected if I'm

wrong.

DR. KIESSLING: Well it's a well-funded group.

MR. WAGNER: It's a three-year grant.

DR. KIESSLING: They've got two NIH grants.

DR. GENEL: Page 21. I think it's the --

DR. KIESSLING: They had a seed grant from '07 to '09.

DR. GENEL: Yeah.

DR. KIESSLING: Right.

DR. FISHBONE: There is a comment in the review about the preliminary results from a 2006 stem cell research program from us.

DR. KIESSLING: Right, so, that was funded from '07 to '09.

DR. GENEL: Yeah, and I see, also, an active grant. It says Therapeutic Differentiation of Regulatory T Cells from iPS and hES Cells for Immune Tolerance, DPH. Is that the biochemical? That's the other funding?

MR. WOLLSCHLAGER: My understanding, Dan, is it originally started off with a seed grant, then parlayed that into an established investigator grant last year.

DR. GENEL: Last year, so we're already --

MR. WOLLSCHLAGER: We're into year two of an existing three-year established investigator grant.

DR. KIESSLING: Where is that listed, Dan, because if you look on their budget page, they only talk about the seed grant? They've got two NIH grants. I don't see the other. The established investigator funding from us, I can't find it in this application.

MS. TOWNSHEND: Did we want to pass on this and move on to other grants?

DR. KIESSLING: And look at the budget. Maybe we should.

MS. TOWNSHEND: It's already in a maybe category. Did you want to leave it there, Ann?

DR. KIESSLING: Yeah, and we'll look at the budget.

MS. TOWNSHEND: Okay. Next grant for consideration is 10SCB07, Caroline N. Dealy, Use of the hESC and iPSC-derived Skeletal Progenitors for Mammalian Limb and Digit Regeneration, UCHC is the institution, 3.7 is the peer review score, and, again, Genel and Kiessling.

MS. HORN: And, again, proprietary information is indicated in this grant.

DR. GENEL: This is an interesting

application to try and generate cells that would be able to replace excised limbs in an experimental animal model. I can't recall what the model is here. I was looking for it.

DR. KIESSLING: It's a rodent.

DR. GENEL: A mouse, yeah. It was well-reviewed. If anything, I think the score is a little bit high, if you will. High, in the sense that it's a higher number than the text of the review, which is more enthusiastic. I would put this in the maybe category until we see what we have available.

DR. KIESSLING: I actually love this grant, and I would put it in the yes category.

DR. GENEL: I won't argue with that.

DR. KIESSLING: Partly because this is like I think exactly what part of our mission is. They're using human embryonic stem cells to regenerate limbs, or damaged limbs, or joints, and they've come up with some proprietary information, I mean some IP that could actually, you know, lead to translation in a pretty quick manner.

This is a good group. This is absolutely what they're going to do here is going to lead to some answers. They've included both the pros and the cons and

what problems they might have in the grant. I was very enthusiastic about this.

I don't know why it only got a score of 3.7. And the reviewers were enthusiastic about it, too, so I don't understand where the score of 3.7 came from. I would have thought it would have been at least a three.

DR. GENEL: I think only because I felt it ought to have a better score that I put it in a maybe category, rather than in the highest category. It's also based on information derived from a seed grant --

DR. KIESSLING: A seed grant.

DR. GENEL: -- that we funded.

DR. KIESSLING: Right.

DR. GENEL: Which is another reason I think.

DR. KIESSLING: Right.

MR. MANDELKERN: I would like to see this put over into the maybe to see the relationship between this grant and the group grant at the same institution with Dr. Row, which we funded in the millions, not one million. And it seems to me that it's --

DR. KIESSLING: There might be some overlap?

MR. MANDELKERN: -- that it's the same area

of investigation, that limb development through the use of stem cells, so if we're funding the same thing with a group and now with an EI, I don't know if that's the best use of our dollars, so I'd like to put this in the maybe to see how it all rolls out.

DR. KIESSLING: How it overlaps. That's all right.

DR. GENEL: Okay.

MS. TOWNSHEND: Any other comment?

DR. WALLACK: Comment. I think, I could be wrong, but Dr. Row's grant is probably coming to an end now. Is that right? Or one year from now?

DR. KIESSLING: I don't know. Maybe a program can tell us.

DR. GOLDHAMER: The grant has ended. The Row grant ended in April.

DR. WALLACK: That's what I thought, so I don't know if the consideration that we just placed on the table would be a hindrance to this, and, if anything, I would think that would be an inducement, from my perspective, at least, to go forward, also recognizing the fact that institutionally there's been hopefully a built-in expertise that could aid in the movement forward of this particular research project.

I heard some yeses, and I would endorse the yeses and hopefully make a definitive decision about this one at this point.

MS. TOWNSHEND: The recommendation of the team is yes, and we do have a maybe from Mr. Mandelkern, so this would go into the maybe category.

DR. WALLACK: Unless he withdrew his maybe.

MS. TOWNSHEND: Maybe we'll go on to the next grant. Next grant is 10SCB35, Ren-He Xu, Do Various Culture Conditions Matter to Differentiation Ability of Human Embryonic Stem Cells, UCHC is the institution, 3.6 is the peer review score, and this would be Hart and Wallack.

DR. HART: So this is a proposal from Dr. Xu, who has managed, of course, the main cores to identify differences in at least three major methods of culturing embryonic stem cells and judge them based on both gene expression and proteomics-based assays.

The reviewers, again, it's one of these things where the score and the tone of the review doesn't quite match up. I thought the tone of the review sounded a little bit worse than the score in this case.

They were very critical of some of the lack of preliminary data and especially that the interpretation

of some of the preliminary data, as well.

One of them, for example, is he's studying phosphorylation of proteins and does not demonstrate that this has any effect on differentiation capacity, so it's not clear how meaningful some of this interpretation is.

Furthermore, there's a question about one of the markers that's chosen for an early hematopoietic cell type not being specific enough and that the percentage of cells that are CD34 positive may not be sufficient to get some of the results they're hoping for.

So, you know, overall, you almost hate to take a proposal from such a productive researcher like this and such a helpful researcher and say no to it, but it really sounds like that's what the scientist's review is telling us to do.

Lastly, I noticed that in the support section what's listed is essentially 100 percent, three different Connecticut Stem Cell Research Fund programs and no NIH funding, and I think, with a project proposed like this, with a little bit more preliminary data, it's time to go to NIH. Reluctantly, I'm recommending no.

DR. WALLACK: I would agree with the no on this particular project, with regret, because I think that what Ron said is absolutely on the mark. This is an

excellent researcher, who has contributed tremendously not only to what's going on in the State of Connecticut, but around the nation, and we're all very, very appreciative of that.

I'm not sure, however, that this particular project is the kind of project that has to be funded. It's a project that is going to be done mostly by postdocs, and it's the only one that I read that is also going to be worked on by graduate students, as well.

If I saw it coming across as a seed grant, I might feel, I would feel entirely different. So, with great reluctance, I have to agree and say no.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the no category. Is that the consensus of the group? Hearing no objection, this grant will be moved to the no category.

Next grant for consideration -- yes, sir?

CHAIRPERSON GALVIN: I'm just going to interject a comment. I know that several of the members have said that, have observed some things about the scoring, and one of the things that you'll notice is that everybody has their own way of scoring things, and some people think that a really good grant is a four and a half, and a superb grant is a 2.6, and if you have two

people of the three who think that a good grant is a three and a third person thinks that a good grant is a 4.2, that drags your score down by almost half a point.

So when you get into that sub four and a half to maybe 2.8, you're going to see things where just, if you get all people who are characteristically high raters, I did a lot of this work in a different venue in the past, and I was a characteristically a high rater, but if you get two high raters or three low raters, it's very hard to figure that out, particularly when you're looking at small differences.

But the thing that I think we all notice consistently is some people attach relatively poor write-ups to relatively good ratings, which makes it sort of like why did you rate this so low and write it up badly, but that's sort of characteristic.

The only way you can get around that is run a profile on the raters, so that every time you put up -- let's just say Paul Pescatello, and then you have how many times out of, you know, statistically has he ever given a two, no, has he ever given a three, once, so what Paul would consider a really good grant is 3.2 or a 3.4, and there are other people who never give anything higher than six, and you can do that, but that's kind of cumbersome.

What we used to do in the military is they would stamp your rater profile on top of your rating, and then you could make some sense out of, you know, okay, Pescatello thinks a solid B is a good grade, Galvin thinks an A- is a good grade.

DR. FISHBONE: Could I ask you question about that? With the reviews, which are a mixture of obviously more than one reviewer, it looks like, if it were one reviewer, they have split personalities, because the first half is often good, the second half is not, and then we get an average grant.

And it would make a difference to me if a three was two people giving him three, or if it was one person giving him six, and the other one giving him one, because you might, then, get a better idea of where the dichotomy is and, as you say, people's way of rating would be a little more apparent, so I'm just wondering if that has an impact on, as you were saying, on what the average grant is.

It's like, if your head is hot and your feet are cold, in the middle you're just about right.

CHAIRPERSON GALVIN: Well I think there's a lot to say with that, particularly that, if I were unfortunate had a pretty decent grant and I was

unfortunate enough to get three low raters or two very low raters and an average rater and then I got people who wrote the things up in a way that wasn't consistent with the rating, then I might lose a very large grant, unless the people considering it.

Of course, we're able to leaven those things here a bit, but we might want to consider in the future getting a profile on the people that do them. Do they consistently give people high ratings and low write-ups? What are they like for our internal purposes?

DR. DEES: But you can do something short of that, which is, I mean, we don't have what individual peer reviewers gave. All we have are the average, and it might make a difference to me whether, you know, this has a low score, because one person thought it was really bad, but the other two thought it was really great. It might make a difference to how I think about it, where if they all agree on it, it might sway me a different way, and that would be, I presume, pretty easy to do, wouldn't it?

MR. WOLLSCHLAGER: Well we have all the scores. I mean I have the scores from the individuals available. I will say that in the case where there were three reviewers -- well, if I could back up, the primary narrative that you see represents the write-up of the

primary reviewer, so to the extent you see something that seems a little disjointed, that means a secondary or tertiary reviewer is added, as well, but if there's only a single narrative, that's from the primary reviewer, so sometimes that's a disconnect between the narrative and the overall averaged out score.

Scores are averaged when they are within a couple of points, so you're not going to take a 6.0 and a 2.0 and come up with a 4.0. That's not the process they follow. That requires a reconciliation process.

In the four cases this year, where there was a significant discrepancy between the two reviewers and the third, they actually brought in a fourth reviewer, so it's not simply a case of taking a two, a four and a six and coming up with a score of a four.

DR. DEES: Thank you. That's very helpful.

MS. TOWNSHEND: Any further discussion? That's why DJs only go for four hours.

(Off the record)

MS. TOWNSHEND: What did we do with that? 35 I had as the team recommending no? Is that the consensus of the group? All right, then, we're ready to go on to 10S -- yes, ma'am? No, I was just about to announce that one.

10SCB01, Wang Min, Regulation of VEGFR2 Signaling in Hemangioblast: Mechanism and Therapeutics, Yale University, 3.5 peer review score, Arinzeh and Hiskes.

DR. ARINZEH: Okay. This grant proposal is about understanding the role of this intercellular protein Epsin, which is a modulator of VEGF, which appears to regulate hemangioblast differentiation from embryonic stem cells, so they are going to be looking, then, very closely at this VEGF regulation or expression of the VEGF and then using this and, also, looking at Epsin.

And, again, the hemangioblast is the cell, precursor that gives rise to endothelial cells, smooth muscle cells and blood cells, so they think that this is the most favorable cell to use for cardiovascular treatments and therapies over, say, current treatments or potential treatments looking at endothelial progenitor cells.

This is a resubmission. They were able to address the majority of the reviewers' comments, and, so, the reviewers were favorable with this resubmission. They thought the proposal was feasible, and they thought it had important clinical implications for, again, cardiovascular disease.

They call this a major weakness, although the way it's reading and the way the reviewer posed it seems like it's a minor weakness, but they said it's a major weakness, in that the aim one may not -- you know, again, there might be a disconnect. If aim one is not successful, then you can't do aim two, but they established a lot of preliminary data to show that they could actually get hemangioblast differentiation.

So I see this as a minor weakness, because they actually were able to accomplish that in preliminary data, and then they had another little minor weakness, so, overall the PI is well-established.

He or she, I'm not sure if it's a she, has significant amount of NIH funding in cardiovascular area, very distinct projects, so very well-established investigator. So I would go for voting yes for funding for this. Hiskes also voted yes.

MS. TOWNSHEND: The recommendation from the team is to place this grant in the yes category. Is there any -- is that the consensus of the group, or is there discussion on this grant?

DR. KIESSLING: I mean this is a lot of money. Are we definitely just going to put this in the yes category?

MS. TOWNSHEND: Just remember that even a yes could change over to a no. There's no final decision until that final vote is taken. Yes, sir?

DR. LATHAM: As a practical matter, putting something in the yes insulates it to bid from discussion, because we're going to talk about the maybes with the total yes amount in mind and all that.

DR. FISHBONE: There is a comment that the budget needs some improvement in the reviews.

DR. KIESSLING: Up regulated, or down regulated? What kind of improvement?

DR. ARINZEH: I was borderline maybe. I was maybe/yes, okay? I was going back and forth. I'm willing to change it to a maybe, if you feel like there needs to be more discussion on it.

MS. TOWNSHEND: What does the group wish to do? Right now, the recommendation is yes, with a possible move to maybe.

DR. GENEL: Well I think what's troubling all of us is that we really don't have parameters of how much money is going to be available for this category.

DR. KIESSLING: Right. I mean it's equal to five seed grants.

DR. GENEL: I'm looking at about seven or

eight million dollars higher than this at this point, at least by peer review scores, so I think, you know, we're going to have to set some sort of parameters and then determine what the funding is.

MS. TOWNSHEND: Are you recommending a maybe?

DR. ARINZEH: Okay.

DR. GENEL: Maybe is what I'd recommend.

MS. TOWNSHEND: Is that the consensus of the group? Well I guess, actually, it just goes into maybe.

Next grant for consideration is 10SCB21, Dashzeveg Bayarsaihan, The Epigenetics of Wolf-Hirschhorn Syndrome, A Stem Cell Approach, UCHC is the institution, 3.3 is the peer review score, Hart and Latham.

DR. HART: I got the waive there. Okay, so, this is from an Assistant Professor at UCHC, and he proposes to generate induced pluripotent cells from a disease, known as Wolf-Hirschhorn Syndrome, to investigate gene expression, epigenetic abnormalities in tissues, such as neural crest bone derived tissues and neural lineages.

The reviewers were reasonably positive and pointed out that there's some lack of adequate discussion of possible pitfalls and alternative strategies. The

preliminary data, more preliminary data would be helpful, and this person is apparently one year into a previous award from us.

There's a very interesting and exciting component to it, where there's a histone methylation regulator that comes into an epigenetic type of approach to this. That makes it very interesting, as well.

The grant is not an embryonic stem cell. It could be appropriate for NIH. It's relatively basic science, even though it is disease related. It's at the early stages of finding out what might be the phenotype cellular level of the disease.

There is some -- let's see. Let me go to the back page here. This PI does have NIH support for a different project involved in creating cranial facial development and, also, carries a career development award from NIH associated with that RO1 project, and, as I said, started in '09 a project on William's Syndrome associated TF21 factor and epigenetic marking in hESC and iPS cells.

I could not tell, just by looking at the title, how much independence of overlap there was in the projects, but they do sound a little similar.

I guess I'd put this in the solid maybe category in my book.

CHAIRPERSON GALVIN: What is the incidence of this disease in the general population?

DR. HART: I saw that. I have to pull that out.

MS. TOWNSHEND: Wolf-Hirschhorn Syndrome.

CHAIRPERSON GALVIN: Because I've never heard of it before today.

DR. HART: Here it is. About one in 120,000 babies in the U.S. -- no. That's total birth defects. I'm sorry. I'm sorry. I thought I saw that when I was reading this, and I've lost where I saw it.

MS. TOWNSHEND: Wolf-Hirschhorn Syndrome is known as deletion 4p and 4p syndrome. Most common abnormalities are seen include profound mental retardation, seizures, poor muscle tone, cleft lip, or cleft pallet. Thank you, Wikipedia.

DR. HART: We don't see incidence, though.

DR. FISHBONE: If I could ask a question? If something that is that uncommon, would that give it a high priority? I mean is it important to understand how that disease works, in terms of us funding?

DR. HART: Well why don't we hear from the second reviewer first and actually come back to that?

DR. LATHAM: I just found something from

NIH, so it's actually a reasonably authoritative website that says Wolf-Hirschhorn Syndrome is estimated to occur in one in 50,000 births, but that may be an underestimate, because some affected individuals are never diagnosed.

I was inclined more toward no than toward maybe, only because it's an iPS project and, therefore, eligible for funding elsewhere, and when I looked down the list, I see many higher ranked human embryonic stem cell projects, and, so, I was just inclined to not fund it for that, mainly for that reason.

DR. HART: I'm not disagreeing with your interpretation, but remember that most of the embryonic stem cell projects we've read are eligible for NIH funding. Very few of them are not.

DR. LATHAM: Yeah. I guess I was just muddling the question of eligibility for NIH funding, which of course has changed, and the stated priorities of this body, which are in the area of human embryonic stem cell research.

MS. TOWNSHEND: We do have a maybe on the table, so barring any further discussion, this would -- Dr. Hart?

DR. HART: Yeah. Ideally, this would be near the bottom of the maybe, so we could consider it.

MS. TOWNSHEND: Okay, so, this grant will go into the maybe category.

Next grant for consideration is 10SCB17, M. Hicham Drissi, Development of Novel Translational Approaches for the Repair of Human Osteoarthritic Cartilage Explants Using Embryonic Stem Cell-derived Chondrocytes, UCHC is the institution, 3.2 is the peer review score, Hart and Latham.

DR. HART: Your turn.

DR. LATHAM: The idea here is to turn the CT2 embryonic stem cell line into articular-like chondrocytes and implant them into human cartilage defect in an organ culture using discarded articular joints.

This was pretty well received by the reviewers. It has both in vitro and in vivo tests built into the plan. I think it’s also attractively closer to clinical application, and it’s also attractively multi-disciplinary, and it’s in the researchers who are cooperating in it.

The reviewers rated it as highly innovative, and they very much liked the cooperation between UCHC and the New England Musculoskeletal Institute.

I do have a question about the physical

location of the New England Musculoskeletal Institute, which do we have that before us? Because that speaks to the Connecticutness of the grant. Oh, I see.

MS. TOWNSHEND: It's part of the UConn Health Center.

DR. LATHAM: Okay. All right. In that case, my inclination is pretty favorable. I would be inclined to say yes, because of the reviewers of it and because of its closeness to translational opportunity.

DR. HART: Yeah, I think that's exactly right. It's kind of high enough in a scientific review score to make it eligible for automatic yes, and the positives that build on that are the use of, at this point, non-federally approved embryonic stem cell lines so far, and the close association was kind of pre-translational studies, so I agree. Yes.

MS. TOWNSHEND: Comments?

DR. KIESSLING: I thought this was a great application, for what it's worth.

DR. FISHBONE: I'd like to ask one question about the reviews. It says insufficient information was provided why they chose the CT2 human ES cell line, and they cultured human embryonic cells in their laboratories.

Lack of required experience with human ES

cells is less critical to a seed grant, but is a serious concern for a four-year, one-million-dollar grant. My understanding is that the established investigator status refers to their status in stem cell research, not just the years or ranks of an investigator in overall research.

DR. HART: Sounds a little unfriendly, but they are claiming in the resources access to the stem cell core, and I would assume, without having read this, that the choice of the cell line was based on their experience or those of their collaborators. That would be the only reason for doing that.

MR. MANDELKERN: Again, I would like to know how this fits with the large Row grant work that was done in the same area. Is this replication? Is this new? Where does it fit with what was just finished, and what sort of results came from the large grant that was given to Row in the several million-dollar group grant?

DR. HART: I wasn't around for that, so I can't answer.

MR. MANDELKERN: Does anybody have any answers to that, because we've gotten several EI million-dollar requests for funding in the same area? I'm not knocking, but I'd like to know where it stands.

MS. TOWNSHEND: Dr. Lalande?

CHAIRPERSON GALVIN: Marc, would you care to comment?

DR. MARC LALANDE: No.

MS. TOWNSHEND: But he will anyway.

CHAIRPERSON GALVIN: In English, please, not French.

DR. LALANDE: I will. I will endeavor to do that, Commissioner. Dr. Drissi was not part. Dr. Drissi is a relatively recent rival I think within the last two years. He was not part of the original group grant. Started his own lab down in a separate building down the hill, so he was not part of the original group grant, and that's all I can say.

He was not part of that group, and he's basically started this work on his own. He comes from a different background, works in transcription factors related to osteogenesis, and actually has a translational component down with the docs down there, so it's a more translational environment than the previous group. I don't know if that's helpful, but that's all I can say.

CHAIRPERSON GALVIN: Thank you.

MS. TOWNSHEND: Thank you.

DR. HART: There is no mention of that other grant under research support, so that concurs.

MS. TOWNSHEND: The recommendation of the team I understand is yes, to place this in the yes category. Is that the consensus of the group? This grant is placed in the yes category.

Next grant for consideration is 10SCB22, Andrew Xiao, Epigenetic Mechanisms During Cellular Reprogramming, Yale University is the institution, 3.2 peer review score. This would be Dees and Pescatello.

DR. DEES: I think it's my turn. These experiments try to understand the basics of cell reprogramming that are the key to characterizing induced pluripotent cells. They will look at the pathways by which DNA and chromatins are reset by looking at the role of a particular histone and the enzyme that seems to play an important role.

The plan is to look at the role of the system and the enzyme during reprogramming and see how it regulates chromatin domain structure. This is from a new assistant. He's an Assistant Professor, so a fairly young researcher.

This work is really important for understanding the processes involved in induced pluripotent cell reprogramming, though it's really a pretty far distance from what we've just been talking

about, translational kind of research. It's pretty distant from therapy.

The reviewers were really pretty impressed with the design and with the thorough methods that are being used, but they point to a few significant problems, whether this particular histone is as critical as they think, for example, and whether some of the experiments are, in fact, feasible. Those sound like fairly significant problems to me, so I wasn't quite sure why it got as good a score as it did, but I was willing to defer a bit to them.

My original inclination was to say yes, but I guess I'm more inclined to say maybe now.

MS. TOWNSHEND: Second reviewer?

DR. PESCATELLO: I guess I would just start by saying that our charge is for translational. That's an emphasis, but it's also basic research. I mean it's not just translational, and I think basic research done in Connecticut and good basic research is really important.

And I thought, as far as I could tell, that this was such a project that it was very important basic research, being done by a highly credentialed sort of new person, relatively new person to the field, which is something we should encourage.

I have to say that -- so I'll just read. Under the significance, the summary, it says the study examined some of the important features in cell reprogramming, however, the outcome might be that this histone variant has a role in determining cell survival or proliferation rather than a direct impact on reprogramming, per se.

I see this as that's what it's all about, is to understand that, and the reviewer seems to be having a problem with the outcome, and this is all about the research, so I was a yes.

MS. TOWNSHEND: We have a maybe and a yes, so it would go into the maybe category. If there's other discussion? Ann?

DR. KIESSLING: The only problem I have with this is that we have another -- we've got two or three reprogramming grants, and, if we're not careful, we're going to be spending three million dollars on reprogramming grants, and this is a lot of money to ask this question.

It isn't going to cost a million dollars to answer the question of this histone factor. That was my concern about this application.

MS. TOWNSHEND: Is it the consensus of the

group -- well it goes into maybe. Okay.

Next grant for consideration is 10SCB16, Natalia Ivanova, Transcriptional Control of Pluripotency in Human Embryonic Stem Cells, Yale University is the institution, 3.1 the peer review score, Fishbone and Goldhamer.

DR. GOLDHAMER: All right, so, this is a grant that builds on the PI's previous work in mouse embryonic stem cells, in which he's identified a number of pluripotency genes that are distinct from the ones that we all know about, OCT-4, SOX2 and Nanog.

And, so, she has had, I think has perhaps just ended a seed grant, and she's now applying for an established grant, based on the results from the seed grant, so, in her seed grant, she was able to identify seven genes that are implicated in pluripotency and differentiation, because when they're knocked down, when their function is eliminated, these cells rapidly leave the pluripotent state and differentiate.

And, so, what I liked about this grant are a few fold. First of all, she's a new Assistant Professor at Yale. She's been there two years. She's productive. She's accomplished. She has the technical know how, particularly with the team she's put forth, to do these

kinds of functional analyses and to handle the large volumes of data that will come out of her analysis, which will include various types of transcriptum analyses.

And I also liked the fact that, again, this is a theme that we're hearing today, that she had a seed grant, she was productive in the sense of generating data that she's now parlaying into this established grant, so, all-in-all, I was favorably impressed. It was a well-written grant. The reviews were positive. And I'll just tell you just a couple of lines about what the reviewer said.

They said the strength of the proposal lies in the applicant's strong in vitro data and collaboration with scientists in complimentary fields. She plans to build on very successful efforts in understanding mechanisms of self-renewal and differentiation from murine cells.

And they thought that the experiments were highly feasible, which is what I have tried to get across, because of her experience and past experimentation. I like the grant, I thought it was very solid, and I put it in the yes category.

DR. FISHBONE: I would agree with everything that David said, and she apparently is a very

strong researcher, highly regarded, and produced very good work, and I think we should support this.

MS. TOWNSHEND: Is it the consensus of the group this grant be moved to the yes category? This grant is moved to the yes category.

Next grant is 10SCB29, In-Hyun Park, Epigenetic Regulation of Reprogramming, Yale University, the score is 3.0, for those of you who are following the same sheet that I am. It had said something different, but it is 3.0, Kiessling and Mandelkern.

MS. HORN: And there is proprietary information in this grant marked.

DR. KIESSLING: This is an application from someone who has trained in George Davies lab at Harvard. He actually developed some of the methods for deriving iPS cells from fiberglass cells for disease-specific iPS cells in that lab.

And because he was in that lab, that’s quite a rich CV now for a young investigator, and he’s just been recruited to Yale. The basic problem with this application is it’s just not very innovative.

Lots of people have done -- much of what’s been done is being proposed in this grant. He’s simply going to look at a lot of epigenetic modifications of iPS

cells.

It's not nearly as innovative and strong as the grant that we just heard from, the Ivanova grant. It is more comparable to the grant above that, although, again, it's not quite as imaginative.

I don't know quite what to do about this grant, because I'm sure this investigator is going to do all this work. I don't know that we're going to get a million dollars' worth of information after he has done all this work, and one of my concerns about him is that, for some reason throughout this grant, he's expressed the opinion that if iPS cells are not exactly like hES cells, they may not have clinical value, and I don't think that's a generally held view.

I think we need to understand iPS cells and exactly what their limitations are, but I don't think the goal is to make them -- I don't think the general view is that they have to be exactly like hES cells to have therapeutic value.

So I'm wondering, if that's his overwhelming push here, if he's going to miss some really important information along the way, so I have concerns about this grant, because I think it's pretty routine. It's a lot of money for a young investigator. Bob?

MR. MANDELKERN: I'm the other reviewer on this grant, and it's strange. Two-odd years ago, all you heard was iPS cells taking over from hES cells. Every time I lifted my head, I was told that hES is passe and iPS is what's around.

Now here's a grant that tends to do a lot of work in the iPS field, with the comment is an excellent young investigator with an extensive record of publication in high-impact journals, and he's recently been recruited to our state to work in stem cell and the iPS field.

It seems to me that this is an area that once we've opened we can't turn our backs on iPS, because it's endemic. I would say that this should go in the yes area for the quality of the work that this investigator has done and for the quality of work he proposes to do and his publication record, so I would propose a yes.

MS. TOWNSHEND: Dr. Kiessling?

DR. KIESSLING: Well I would actually like to compare this with the -- I mean we're looking at three essentially reprogramming grants here, and I don't think we want to spend three million dollars on iPS cell reprogramming, so I would actually like to keep this in the maybe, and we'll compare it back to the other grants in the similar topic from the same institution, and I

think we're going to be able to use the money more judiciously that way.

MS. TOWNSHEND: This grant will be -- oh, Dr. Latham?

DR. LATHAM: No.

MS. TOWNSHEND: Okay. Your mike was on. Sorry. This grant will go into the maybe category.

Next grant for consideration is 10SCB12, Laijun Lai, Generation of Hematopoietic Stem Cells and T-cell Progenitors from Human ESCs, UCHC is the institution, 3.0 is the peer review score, Genel and Wallack.

DR. WALLACK: I found this grant to be a clear, well-written proposal. It's, again, something that we've mentioned a few times. It's an extension of work that has created documentation. He started with a seed grant.

In reading the grant, if successful, could be a major breakthrough. He's working in an area that I think that could, in fact, be on the cusp of translational work. I would fund this.

In this instance, my own reading of his proposal was that my rating of it would be, in fact, better than the PR's 3.0, so I would endorse going forward and funding this particular project.

MS. TOWNSHEND: Dr. Genel?

DR. GENEL: Yes, I agree. If you look at the review scores, they write up exciting preliminary data from a seed grant. The only caveat is the concern that this may be more ambitious than they can carry out, but I'm not deterred by that. I agree. I think I would put this in the yes category.

MS. TOWNSHEND: Discussion? Is it the will of the group, or the consensus of the group to --

DR. GENEL: Tentatively, until we determine how much money we have.

MS. TOWNSHEND: Tentatively, yes? Would that be maybe? Tentatively, it's yes.

DR. GENEL: At some point, we're going to have to decide how much money we have.

MS. TOWNSHEND: So the question is is there a consensus among the group that this go in the yes category?

DR. GENEL: Move yes.

MS. TOWNSHEND: This grant is placed in the yes category. We have six more grants to go before you get a break, so I'm just letting you know.

10SCB19, Caihong Qiu, Regulations of Lin28 in Human Embryonic Stem Cell Self-renewal and

Differentiation, Yale University is the institution, 2.8 the peer review score, Hart and Pescatello.

MS. HORN: And there's proprietary information marked in this grant.

DR. HART: Okay. This is a grant from an established investigator at Yale, part of the stem cell core there. The proposal will look at Lin28 and how it regulates OCT-4 expression at a translational level and the molecular circuitry involving Lin28.

The review was very nice. It says it was a well-written and straightforward proposal, moderately innovative, but significant. It investigates specific elements involved in stem cell renewal and differentiation.

The most negative thing we could really find in the review is the question about how valuable the science was at a million-dollar price tag and that this proposal is a highly ambitious line, which is, you know, either a concern about the focus of the proposal, or the scope of what's involved in the time allotted.

The one other point that came up during reading this was that, literally, as I was reviewing this grant, popped up on my screen was a publication from George Daily's lab that published a Lin28 knockout mouse,

which should provide a lot of the science that's being proposed here, but not in a human stem cell situation. It's just kind of interesting.

Both shows the competitiveness of the idea, and the fact that things are changing so rapidly we almost can't judge the grant, based on what's proposed today.

However, the project is human stem cell associated. It's, at this point, with the cell lines being proposed, not NIH fundable. It has kind of indirect health medical related application, and the only real negative that I've got is that this should be an NIH grant at this point, or this should be very close to an NIH grant at this point.

This laboratory has listed four Connecticut stem cell grants active right now and one completed. It seems to me that this group it's time for them to go to NIH, but, with that said, I'm going to mark it yes, with a little bit of reluctance, just based on -- I wish they'd shoot a little higher.

MS. TOWNSHEND: Paul?

DR. PESCATELLO: I think that's a good summary and good comments. I think we're going to have to have a little talk about reprogramming. I think that's a good way, actually, to judge the remaining one, when we

have all of our maybes and yeses and categorize all the reprogramming and have a discussion about that, but I would vote yes, knowing we're going to do that. That's a yes.

MS. TOWNSHEND: The recommendation of the peer reviewers, or the reviewers is placing this in the yes category. Is that the consensus of the group? Yes, sir?

DR. FISHBONE: One of the things that is concerning me about several of the grants is that the same quotation has come up. This is interesting work, but it's not worth a million dollars, or is it worth a million dollars?

And I know that last year we increased our funding for established grants to a million. I'm just wondering, you know, maybe David could comment on that, because I know he has feelings about this, but it's interesting how many times that observation has been made that it's a good project, but is it worth a million dollars to get that information?

MS. TOWNSHEND: Any further comment?

CHAIRPERSON GALVIN: Yeah, I have a comment. What my understanding is, on the last four of the six, with this grant we've just allocated four million

dollars out of a total of 9.8, and we've already allocated 14,494,360, 15 million, and we only have 9.8 million to spend.

Certainly, on these smaller grants, you can't go back and take a $200,000 grant and cut it in half. It ain't going to work, and there's only a minimal amount on even these million-dollar ones.

If you cut them too far, they're impractical, so I guess what we're going to do is continue to go on and approve and then go back and somehow trim all these back?

DR. WALLACK: Bob, can I just comment on that? As I'm sitting here, as I've done for the last four years now, I think that's exactly what we're going to have to look at doing.

It's interesting. Just because we have put out there a million-dollar budget for a particular grant, it's very interesting to me how they all come in exactly at a million dollars, for the most part. There's the exceptions, of course.

CHAIRPERSON GALVIN: Are you surprised?

DR. WALLACK: But that's my point, and my point, also, is the fact that it's impossible four years down the road to know what supplies and other costs will

be. There are other weak spots in it. There's travel expenses in it. There's all kinds of things in it, and, as we've done before, and I had no problem with doing this, I'm anticipating that if we really think that a particular grant is worthwhile, we may like it even more at, say, 50 percent of the requested amount, so, yeah, I think we have to come back either later today or tomorrow ready to cut some of those grants, the larger grants.

DR. GOLDHAMER: Can I make a couple of comments? I mean I'm not in favor of an across-the-board cut, but I think we have heard today that there's a number of grants where the million-dollar price tag isn't justified, and those should get special scrutiny.

I also want to say so I was a proponent of increasing the budget per grant this year, so a million-dollar grant that's an $800,000 direct cost grant, and for an established investigator over a four-year period to fund, you know, a couple of postdocs with salaries and fringes and 10 percent, let's say, of a PI's salary, or maybe sometimes I'm looking at one that's about 20 percent, the money goes fast.

And, so, you know, if someone asks for a million dollars, I wouldn't certainly out of hand say that that's excessive and they just shot for that maximum

value.

And I think, in a number of cases, probably the majority of that can be justified, but I agree that we need to look at this on a case-by-case basis and be very ready to cut those where there was hints that the million dollars can't be justified.

CHAIRPERSON GALVIN: I have trouble, although I agree with what you just said, but I have trouble. It's not much when you spread it over four years, but if you cut the million dollars back to 600,000, then is that just foolishness, or are we better to pick the very best ones we can and fund them in a reasonable fashion?

I mean anybody -- if we said, look here, Pescatello. You asked for a million bucks, and we think you got a hell of a lot of nerve, but we're going to give you 500,000, what are you going to say?

DR. PESCATELLO: I'll take the five now, Bob.

CHAIRPERSON GALVIN: I'll take the five, yeah. And I just wonder how handicapped -- I think we need a philosophy for that.

DR. PESCATELLO: I just want to point out my sense is that when the reviewers and when we say

something is not -- we question whether it's worth a million dollars, we mean if the investigator finds what they say they want to find, is it really worth it to the world, four million dollars?

CHAIRPERSON GALVIN: Sure.

DR. PESCATELLO: They're not saying that they're ripping us off, that there's excess, there's fat in the budget. There may be, but I think there are occasions where they pointed that out, where we either have seen that, or the peer reviewers have said do you really want to fund PCR hoods?

I'm going under the assumption that the peer reviewers and we, in going over the budgets, would identify fat in the budget, but, again, I think that value thing is the value for the outcome of the research.

CHAIRPERSON GALVIN: Ron?

DR. HART: I think what we're really after here is value for science, of course, both the quality and quantity, in terms of the value, and, so, we've had grants in this category, where there's a million-dollar max where they're spent a $500,000 budget, and, in my mind, that was a plus, in terms of maybe it was a little more a chancy project, but we weren't vetting as much money on it, of the taxpayers' money on it either.

So it's a better value for what we're trying to accomplish here, however, if we do come back and feel as though there is a benefit to funding some more projects with less money, in my mind, the best way to do that is to say let's ask the PI to take it as a three-year or a two-year project at the same per year rate and reduce the number of aims proposed to match.

CHAIRPERSON GALVIN: We've done that before.

MR. MANDELKERN: I would like to make a comment, that the two reviewers on this grant both propose yes, so far as I understood, and then the question of are these grants worth a million dollars was raised in a generic sense, so I think it's kind of an inequity to stop in the middle of this grant, which had yes, and raise the question of what it's worth.

I think we should go ahead. So far, my calculations show we've said yes to four established and seven seeds. That's five and a half million dollars that we've said yes to, all subject to review, so we're not in deep trouble with the dollars.

I think this yes should go forward, and one, two, three, four, five more reviews should be done, and we're at a point, is the way I see it, not to stop in

the middle and suddenly put the burden of the whole question on one particular grant. It's unfair.

MS. TOWNSHEND: Dr. Fishbone?

DR. FISHBONE: Bob, the only reason I asked the question at this point was it says these are all valuable science, but a million dollars is quite a high price tag for the potential results. That's in their review. It's in their review of this grant.

MS. TOWNSHEND: The recommendation of the team is yes. Is there a consensus within the group that we move this to the yes category?

DR. FISHBONE: Yes.

MS. TOWNSHEND: Yes. Thank you.

CHAIRPERSON GALVIN: Five to go, and we'll take a break.

MS. TOWNSHEND: Next grant is 10SCB02, Lawrence J. Rizzolo, Co-differentiation of the hESC-derived Retinal and Retinal Pigment Epithelial Progenitors, Yale University is the institution, 2.5 the peer review score, Arinzeh and Hiskes.

MS. HORN: And there's proprietary information indicated in this grant.

DR. ARINZEH: Okay. This proposal investigates the use of embryonic stem cells as a source

of retinal pigment epithelium in retinal cells and to promote their maturation and culture as a way of improving success for transplants.

This, again, is for age-related macular degeneration, and, currently, these are PE or retinal pigment epithelium do not fully differentiate, so that's the problem, so they would like to use ES cells as a transplant if they can get them to mature.

So the reviewers were very excited and had a lot of enthusiasm for this proposal. They felt that the investigator had a really good sense of knowledge about the limitations of the various specifies, mouse genetics versus human. They explained that very well in the proposal.

They're looking at various embryonic stem cell lines, and then they plan to do the various molecular and biochemistry level assessment of differentiation. They're also going to be doing co-culturing with other cell types to get this maturity.

So the reviewers were very favorable. There was a minor weakness, in that they would hope they were looking for a progression to in vivo validation of the cells. That would make the application stronger, but they felt that that was a minor weakness.

They still felt that the application was very strong. Experimental data, preliminary data it was very solid, and they used the term “compelling,” so the recommendation would be yes, and Hiskes also had the recommendation of yes.

MS. TOWNSHEND: The recommendation from the team is yes. Is that the consensus of the group? This grant moves into the yes category.

Next up is 10SCB03, Diane Krause, Use of Human Embryonic Stem Cells and Inducible Pluripotent Stem Cells to Study Megakaryoblastic Leukemia, Yale University is the institution, 2.5 the peer review score, and that is also Arinzeh and Hiskes.

MS. HORN: And it also has proprietary information indicated.

DR. ARINZEH: Okay. The PI’s goals here are to determine how infantile leukemia develops, so they would like to modulate blood progenitors in order to determine how they develop, so they’re basically going to be developing these progenitors from murine liver, as well as human embryonic stem cells.

So they will focus on this, again, infantile, this acute megakaryoblastic leukemia. Let’s just see. Okay, so, the reviewers, again, were

enthusiastic. We felt this was a very well-written proposal, with a lot of preliminary data. The investigators are highly qualified to perform the studies. They thought it had a multi-faceted approach, and, again, likelihood of success, because they're looking at different cell lines and species. They thought some of the -- were a little risky, but, again, those were minor issues, because the investigator laid out alternative approaches.

So, overall, the reviewers weren't enthusiastic. Very little to say about any weaknesses at all with this proposal, so the recommendation would be, again, yes. Hiskes also said yes.

MS. TOWNSHEND: The recommendation of the team is to move this grant into the yes category. Is that the consensus of the group? This grant moves to the yes category.

Next up, 10SCB05, Angelique Bordey, Mechanical Control of Neural Stem Cell Fate, Yale University, 2.5 is the peer review score, Arinzeh and Hiskes.

DR. ARINZEH: Okay. All right, so, the proposal here is to look at, the hypothesis here, I guess, is local mechanical cues on epigenetic factors controlling

neural stem cell proliferation and fate.

And, so, the novelty really in this proposal the reviewers were going at was that they have a neat way of doing this kind of in vivo labeling.

COURT REPORTER: One moment.

DR. ARINZEH: So, yeah, the novelty here is we'll oversee some of the neat things that they're able to accomplish, is that they are able to do this live labeling of a subpopulation of these neural stem cells, again, these characteristics of neural stem cells.

So they're going to use this technique to really understand, then, kind of this presence of these cells, the distribution of these cells. They're also going to look at mechanical cues, how these control neural stem cell proliferation and fate.

The local mechanical cues work they're doing in vitro, and they're using parameters that they believe would occur in vivo. I thought that was -- personally, I thought that was some weakness there in the aim, but the reviewers didn't really seem to pick up on that so much, but they do comment that that's a controversial issue about the physical cues on cell differentiation, so they thought that was a bit of an issue.

But, overall, the reviewers were enthusiastic, it's a solid grant proposal, so my recommendation would be yes, and Hiskes is also yes.

MS. TOWNSHEND: The recommendation of the team is to place this grant in the yes category. Is that the consensus of the group? This grant moves to the yes category.

Next up, 10SCB30, James Yuanhao Li, Modeling Parkinson's Disease using Human Embryonic Stem Cells and Patient-derived Induced Pluripotent stem cells, UCHC is the institution, 2.5 the peer review score, Genel and Mandelkern.

DR. GENEL: This is an application that got very well scored to develop specific cell lines for Parkinson's Disease by inserting some newly discovered familial genes for very rare types of Parkinson's Disease and use that to develop a cellular model of Parkinson's Disease to study.

This was well reviewed, as per the score. The only caveat is the comment by at least one of the reviewers, that dopaminergic neurons have already been derived from Parkinson's Disease by several groups and that the grant application was not particularly innovative.

That aside, the other reviewer seems to be quite positive, so I would put this in the yes category for the present time.

MR. MANDELKERN: I'm the other reviewer for this grant, and I spoke to counsel about it, and while there's no legal proscription from my participating, we felt, for my own protection and the protection of the committee, that I should recuse myself in case any ethical or other issue would be raised that would hurt the committee, so I recuse myself from reporting or commenting on this grant.

MS. TOWNSHEND: Thank you. The recommendation from part of the team is that we place this grant in the yes category. Is that the consensus of the group?

CHAIRPERSON GALVIN: Let me make a -- I'm a little concerned about that the dopaminergic cells have already been derived from other sources, and this appears to be an attempt -- the word very rare forms of Parkinson's Disease.

DR. GENEL: Well, no. I think it's an attempt to take advantage of the discovery of rare types to learn more about Parkinson's Disease, rather than to learn something specifically.

The notion is that you can create a cellular model of Parkinson's Disease by utilizing these genetic factors that have been uncovered in a few families, so I think it's more opportunistic in that sense than it is an attempt to study a rare form of Parkinson's Disease, and the first reviewer does say that this is an innovative and feasible proposal.

This might be a grant that would fall into the category of funding, but not at the level requested. One would wonder if they've already, in fact, generated these lines. The application was submitted several months ago, and, if it was feasible then, it was -- now is feasible, then I would wonder if they already have generated the cells.

But I don't think it's an attempt to study a rare form of disease, rather to --

CHAIRPERSON GALVIN: I heard it as very rare, and maybe it's medium rare.

DR. GENEL: No, no, no, no, no. The genetic disorder is rare, but Parkinson's Disease is certainly not rare.

CHAIRPERSON GALVIN: I know that. I have a relative with it, but the very rare bothered me.

MS. TOWNSHEND: Is the consensus of the

group that we move this to the yes category? This grant is moved to the yes category.

And, finally, 10SCB36, Richard A. Flavell, Reconstitution of Human Hematopoietic System by HSCs Derived from Human Embryonic Stem Cells in Humanized Mice, Yale University is the institution, 1.8 the peer review score, Kiessling and Mandelkern.

CHAIRPERSON GALVIN: What kind of mice?

MS. TOWNSHEND: Humanized.

CHAIRPERSON GALVIN: Like Mickey?

MS. TOWNSHEND: Sort of.

MR. MANDELKERN: No, like Mini. It is my extreme pleasure to report on this grant, which received the highest peer review score of 89 grant proposals. It is an innovative proposal to study embryonic stem cells, in terms of humanizing immune deficient mice and represents significant advance of some mice characterizations that have been done by this group.

It’s true that they have money from other sources, but with a 1.8 score and the highest among 90, I feel, and the science is sound, that I recommend a yes proposal.

DR. KIESSLING: This, actually, I think is going to be a really good topic of discussion, because

this is a tough decision, I think, for us to make. This grant actually has the same criticism as the liver grant that I reviewed before.

The peer review actually says the same thing. This is a senior investigator. He has no experience deriving human hematopoietic stem cells. Deriving human hematopoietic stem cells is not a cookbook operation quite yet. He's got some people involved in this work.

This is an extremely well-funded investigator. He definitely -- he isn't even asking for any of his own salary, so I just -- we were going to really have to, even though this is the top score, it's a beautifully written application, he has a lot of really good people on it, and it's another use of this wonderful mouse model that this immunologist has come with.

So the concept of a humanized mouse is that you can put human cells into this animal, and they don't get rejected as foreign right away. Sometimes, they do. So it's a beautiful system, he's a wonderful scientist, he has a ton of money, and he has exactly the same criticism as the other senior investigator that I reviewed.

There's no experience, absolutely no preliminary data that they know how to derive human

hematopoietic stem cells, but the reviewers didn't criticize this application for that, whereas they did criticize the other application on the liver grant.

So even though this is the top score in our pot, I think we really need to decide if we want to give this very well-funded investigator another million dollars.

CHAIRPERSON GALVIN: Yeah. If I can summarize, he's very well-funded, he's a very nice guy, they write very well, and he's got very nice people that work for him. That's terrific.

DR. KIESSLING: Well, no. It could be that this is really good use of Connecticut money. I mean this mouse model may solve the problem of why we can't derive human hematopoietic stem cells very easily.

CHAIRPERSON GALVIN: But don't you think it's the quality of the work that can be done, rather than the individual, or whether he wears Botany suits, or has them custom made in Italy, or whatever.

DR. KIESSLING: They may be able to do it, but I thought it was interesting that the score is a 1.8 for this application, whereas for the other application on the liver grant it was a similar concern, a very well-established senior investigator, trying to do something

that they hadn't really done before in a good model system, but that one scored in the three somethings, and this one scored as a 1.8. So I think we're going to have to put a yes. This goes in the funding category, but I think we really should think about the best use of taxpayer dollars for the grants.

DR. FISHBONE: There is a line in the reviews that say that although he has not had experience in generating hematopoietic cells, he has active -- he has indicated active collaboration with others who have expertise in this area.

DR. KIESSLING: Well so did the other grant, right. I mean this is not that easy to do. This is almost exactly the same criticism as the liver grant.

MS. TOWNSHEND: Dr. Hart?

DR. HART: So I wanted to, first of all, point out, since he's using a form of humanized mouse, that this actually work would now be illegal in Arizona, for those of you that are concerned about (background noise).

DR. KIESSLING: It's a new law in Arizona?

MR. MANDELKERN: Since, fortunately, we're living in Connecticut --

DR. HART: -- specifically make illegal

human animal hybrids of any form.

MR. MANDELKERN: I would like to make the comment that the money that's being requested is for actually employing, as I saw it, mostly postdocs to involve them in this work.

What more do we want than a senior investigator, experienced in this humanized mouse model, now employing four postdocs in his well-reputed lab to go on with work that might be very, very productive, and then we might hit the jackpot?

MS. TOWNSHEND: I think we're at a point where this is -- Ann, correct me if I'm wrong. Would you put this in the yes category or maybe?

DR. KIESSLING: We have to put it in the yes category, but I think we just have to figure out exactly how we want to do this, because we've got somebody else with a senior investigator with a similar issue, but this grant was, you know, clearly swayed the peer reviewers, just because of its presentation.

MS. TOWNSHEND: Is that the consensus of the group, that we put this in the yes category? This goes in the yes category.

We're going to take a 15-minute break. We're going to let CI update us when we come back, as to

where we are, in terms of yeses and maybes, and we'll reconvene at 3:18.

DR. PESCATELLO: Is there any way the maybes and the yeses could be (mike shut off) by subject matter?

MS. TOWNSHEND: Chelsey? Categorized by subject matter?

DR. PESCATELLO: Yes. In other words, if we could look at all the reprogramming, if we could kind of, rather than just go in order of the score, group them.

MS. TOWNSHEND: We'll just have to be very conscious of that.

DR. PESCATELLO: If we could look at them as a whole, like five of them together, rather than --

CHAIRPERSON GALVIN: Yeah. I think what you're getting at, Paul, is we need a way to look at this rather voluminous amount of information in a relatively efficient fashion.

DR. PESCATELLO: Yes.

CHAIRPERSON GALVIN: Okay.

(Off the record)

MS. TOWNSHEND: Take your seats, please. Dan, Chelsey, could you give us an update, as to where we currently stand? For example, how many grants, in what

categories to which we said yes and maybe, and the amounts for those categories?

MS. SARNECKY: Okay. So far, Dan is going to add up how many we have for each type of grant, but we do have some totals. So far, with the yeses and the maybes, we have a little over 20 million dollars. The yeses come out to about 10 million dollars, and the maybes are -- I don't think that's right, Dan.

The maybes are a lot more than 10 million dollars.

MS. TOWNSHEND: That's not correct, is it?

MS. SARNECKY: No.

MS. TOWNSHEND: Okay.

MS. SARNECKY: Just one sec.

MS. TOWNSHEND: I think it's about the same, is it not, 10 million?

MR. WAGNER: So we have 37 total grants, 16 yeses, and we have it's split half and half, 10 million yeses, 10 million maybes, 10.1 in each case.

MS. TOWNSHEND: How many seed, established investigator and -- seven and nine?

MR. WAGNER: We have one group or core maybe, we have seven yeses in seed, 13 maybes in seed, and then about half and half in established.

A MALE VOICE: What is that number, the half and half?

MR. WAGNER: About nine. Nine each, yeses and nos, or yeses and maybes, so however you want to start.

CHAIRPERSON GALVIN: We will be adjourning at 4:00. Tomorrow, we will start at 8:30. It is my opinion that we need some sort of a mechanism to decide which of these grants we're going to fund and which of them we are going to, if we decide that, partially fund.

Now one of the easier solutions is, if not the easiest, is to just fund the yeses, and one would have to think of what would make me take a yes and make it a no? I don't know that on each individual grant.

I think that the group has to evolve some standards about how they're going to evolve these things and how we're going to make decisions. At the other end of the decision making tree, we can take all the grants that seem to have merit and give them, you know, $100,000 each, and then everybody will get a little bit of money, and nobody will go away empty-handed. That's the other extreme.

I think, when we consider what are we here for, we're here to make the best possible use of a skosh

under 10 million dollars. I believe, from what several of the members have said here today, our emphasis has, at this point, has been turning somewhat towards translational work, rather than original basic research. There is a lot of good work here, a lot of work that's very highly rated.

I would hope that, as these get discussed, we could avoid personalities and what we think this investigator might do or think. I don't think, if I were voting, I wouldn't want to vote on a postdoc just because he was somebody's postdoc, unless I knew a little bit more about the program.

Postdoc may be good, or he may be great, or he may be equal to his boss, but you need as a group to evolve what it is that you want to do. Do you want to go through and separate out the ones you absolutely think should be funded?

I do think that there's, with the larger grants, that if they're spread over several years, even if you cut a year off them, you begin to -- peeling them back more than 15 percent really kind of is just giving them a financial assist. I don't think some of the programs are able to scale down from $200,000 to 150.

They all can. Nobody is going to return

back the money if you give it to them, but if we're going to discuss these one-by-one, we'll probably have to come back next month and do it, so I would ask some of you, who are the more thoughtful and introspective members of the group, to decide how we're going to proceed from this point to apportion the 9.8 million.

MR. MANDELKERN: If I may?

CHAIRPERSON GALVIN: Yeah. I think Milt was first. Go ahead.

DR. WALLACK: Yeah, Bob, I've alluded to this before, and I'll say it again. I think that our intent, and I think it's a noble attempt, is to involve as many people in the process as we possibly can, and since I know that budgets are just that, they're estimates, I wouldn't have a problem in judiciously adjusting a budget. We've done it before. It seems to have worked.

Also, couple that with the idea of, and I'm looking at the first one, and we were just trying to find how many years that is, you know, maybe reducing a four-year to a three-year or some other formula, so I don't know if we have to go through every single grant and rediscuss it.

I'm comfortable with some formula that I just discussed.

CHAIRPERSON GALVIN: Well I have some problems with saying, okay, I'm going to take Dr. Wang's grant and cut him back, he or she back to $160,000, but I'm not going to touch Dr. Cheng's grant. How do I come to that conclusion about whose budget, and we've had this discussion before, and I think we ended up at the point where we said we'll cut everybody by 10 percent, or 15 percent, but that's not going to satisfy our needs.

We've got twice as much grant, people looking for grants as we have money, so what is going to be -- I'll be with you in just a moment, Bob. Be patient.

We have twice as much money as we have people looking for grants, so how do we decide on a fair scheme to do that, or do we pick and choose, or do we go back and reduce incrementally? I don't know how to do that, and if Bob knows how to do it, then --

MR. MANDELKERN: No, I don't know how to do it, and I have a fairly not introspective rational approach. I know we're scheduled to go another 40 minutes. I don't believe we can complete our work reasonably and justifiably in the next 40 minutes.

I would propose that we get an accurate count of the categories and that we adjourn and resume tomorrow morning when we can do justice to all the maybes

and the maybe/yeses and the yes/maybes. I, for one, cannot do it any longer tonight with justice to all the proposals.

CHAIRPERSON GALVIN: We're not looking at any proposals. We're just trying to figure out what sort of scheme we're going to use tomorrow to evaluate them, so we're not looking at anything, specifically, but we have to have some kind of idea than sit here and twiddle our thumbs in the morning and say a lot of good grants here, too many grants, not enough money.

DR. KIESSLING: One of the things that I think is sort of a side that we need to decide as a group is do we want to fund the core? The core is a maybe, and we talked about that earlier. Do we want to have it go into the category of like senior investigator, or what do we want to do with the core?

DR. PESCATELLO: Also, would it be helpful to scroll through the yeses and maybes amongst the whole group in the remaining 40 minutes and categorize them, attach one, or two, or three key words, labels to them, so that we could, then, tomorrow use those key words as a way to look at the different categories?

CHAIRPERSON GALVIN: It would have been a lot easier for us to do that instead of having to

reconstruct everybody's memory, but we could certainly start going --

DR. PESCATELLO: We could have the reviewers on the committee do it, give the key words.

CHAIRPERSON GALVIN: Yeah, we could do that.

DR. PESCATELLO: If that would be helpful.

DR. FISHBONE: I was wondering if one possibility would be to look at the maybes and decide, first of all, whether those are yeses or nos. Now that we've seen the whole package, we probably are better able to say about the maybes that maybe should be a yes or should be a no.

CHAIRPERSON GALVIN: I like Paul's idea. Why don't we just scroll through and put a couple of three words, so when we come back tomorrow, we get a good idea, a better idea? Does that work?

DR. LATHAM: I have a slightly different suggestion, at least with regard to the seeds this might work. It may work for the others, as well.

If we treat this as sort of a consent agenda and basically say we're going to have to say no to the maybes, because we've funded too much already on the yeses, unless someone, who is part of the reviewing team

or is particularly familiar, really wants to raise one of the maybes for discussion, so what we could then do is sort of dismiss the entire category of maybes for seed grants, except for whichever ones happen to have an advocate around the table, who really wants to raise them and say, no, this one should be a yes for some reason.

That way, I think we could get rid of probably quite a few in bulk and only hear from the ones that have a real advocate around the table.

CHAIRPERSON GALVIN: I think that's a good suggestion, and I think, from the point of, okay, if you take a maybe, you're going to have to knock a yes off, pretty much. Mike?

DR. GENEL: I support what Steve has proposed, but can you tell us how many of the seeds -- what have we approved in the seeds so far we've said we would fund? Seven? So we've said seven.

I think we should be able to fund many more seeds than that. I sort of arbitrarily had a three-million-dollar sort of, even four-million-dollar level in mind, because I think that's where we get the greatest bang for our buck, frankly, so I think we need to --

MR. WAGNER: If you fund all of them, it's 3.8, just under 3.8, all of the seeds.

DR. GENEL: All of the seeds are 3.8?

MR. WAGNER: Um-hum.

DR. GENEL: Oh. Seven? It's got to be more than seven.

MR. WAGNER: No. All the maybes and all the yeses.

DR. GENEL: Oh, including the maybes?

MR. WAGNER: Um-hum.

DR. GENEL: Well, if you think about that, that's 3.8. You know, I think maybe we ought to start looking at how we're going to proportion out the money here and then determine how much time to spend on various categories.

I'm not uncomfortable with 3.8, because that leaves us 6.2 million, six. That leaves us six. Well it leaves us six million.

CHAIRPERSON GALVIN: That's six of all those really good --

DR. GENEL: The sense I got was that none of the group funds were rated well enough to even make the maybe list, so that takes that off the list. The only question is whether or not to fund the core, and we don't have to fund it at the requested level, but it's not a heck of a lot of money to begin with.

DR. KIESSLING: They're not asking, right. They're not asking. It's two-year budget, really reasonable. We just have to decide if we want to do the core or if we want to do one of the senior investigator grants. That's what it's going to come down to.

DR. GENEL: Well I would vote for doing the core, frankly, but that's a decision. In any event, what I'm suggesting is, if we sort of come up with some rough parameters of how much money we want to put into each category, I think it will be a lot easier to make these determinations.

DR. WALLACK: Bob, I would second Steve's suggestion and move right to it right now, and, that way, at least we get that large group of requests out of the way. We can do that.

CHAIRPERSON GALVIN: Okay. The motion has been moved and seconded. Comments? Would you, Steve, put the motion on?

DR. LATHAM: All right. When I suggested it, I didn't actually mean to make it a motion, but all right, I will, if people are asking me to, which is that I move that we proceed, as follows, by treating the maybes in the seed grant category as one large group and that we not fund them, unless someone around the table wants to be

an advocate for one of them, and after discussion with regard to the one that someone has raised, we move it into the funding category.

And if no one wants to speak up and make an argument for why a maybe seed grant should become a yes seed grant, we should, in bulk, decide not to fund any of the remaining maybes.

DR. PESCATELLO: I would second we proceed with that immediately. That would mean 1.4 million?

DR. WALLACK: No. Paul, if somebody wants to from the maybes include that, that would be included.

DR. PESCATELLO: But if no one advocated for any maybes, how much money would it be? 1.4, okay.

CHAIRPERSON GALVIN: No. There's more money than that.

DR. WALLACK: No, no. It's only seven, so it would be 1.4.

DR. PESCATELLO: That's what led to Mike's comment, that it would be such a small group.

CHAIRPERSON GALVIN: Well there's probably going to be someone in the group who wants to advocate for one or the other of the maybes, and there's room for that.

MR. MANDELKERN: I would like to comment on the motion. We have spent five hours torturously

considering each grant whether it should be a yes/maybe, or a maybe/yes, or a no, and now, in one swoop, we're going to disregard all the efforts we made simply for the sake of expediency.

I think the wise thing is not to do this, but, in fairness to all the proposers, who put their guts into these proposals and the peer reviewers, that we sleep on it overnight and come back fresh, and then we can do justice to all of it.

I don't think it's logical that, in five minutes, we should put aside five hours of good work.

DR. WALLACK: Excuse me. Bob, if you want to advocate for a particular grant, you have the ability to do so, but if no one wants to do it, then their maybe suggestion has -- seen all the rest of them, so I don't see any problem with it at all. I would offer to call the question.

MR. MANDELKERN: Well was that a direct question to me?

DR. WALLACK: No, it's not a direct question. I call the question.

CHAIRPERSON GALVIN: There's a motion on the floor. The motion, basically, if I understand it, if I can paraphrase it correctly, is, of our seed grants, we

are going to, that are maybes, we're going to make them nos, with the exception of ones that may have particular merit, which can be articulated by one or more members of the group. Does that sound correct?

MS. HORN: I just would like to make one comment, in terms of process, that to have a way that we go through each one of the maybes, just raising it, calling out the number, and giving people the opportunity to advocate for it, rather than having that come sua sponte, so to speak, so that somebody may get left out or ignored. I think it's fairer to do it that way.

DR. WALLACK: That's very fair, and I think it takes care of Mr. Mandelkern's concern. I agree.

MR. MANDELKERN: It does not take care of my objection. I appreciate your concern, Dr. Wallack, but it does not take care of my objection.

CHAIRPERSON GALVIN: We need a motion for that, don't we?

MS. HORN: We can do it through a motion.

CHAIRPERSON GALVIN: Okay, then, I will let you propose a motion.

MS. HORN: I'm not on the committee, correct?

CHAIRPERSON GALVIN: You're my attorney.

MS. HORN: Adding the process to the motion that was made by Steve Latham, that we take each one of the maybe grants that's the seed grants and call out the number, and if anybody advocates for it to be moved into the yes column, that that be done by consensus, so there's no consensus that it be done by vote, and we just move through them that way, so that we know that we've addressed each one of the maybes fairly.

CHAIRPERSON GALVIN: Dan?

MR. WAGNER: And in the brevity of time here, I guess, you know, we have 20 minutes, and we're not going to get through all the seeds, the discussions for all of them. We're not going to finish.

DR. KIESSLING: We might.

MR. WAGNER: The maybes?

DR. KIESSLING: The maybes.

MR. WAGNER: We only have one core. I mean that might be one that you could actually come to a decision on today.

DR. KIESSLING: How many maybes are there in the seed grants, Dan?

MR. WAGNER: Thirteen.

DR. KIESSLING: You can get through 13.

CHAIRPERSON GALVIN: You could get through

13.

DR. KIESSLING: Yeah. Go for it, and then we'll know how much money we have for the core.

DR. FISHBONE: Call the question.

CHAIRPERSON GALVIN: Okay. Do we all understand?

DR. FISHBONE: Do we have some idea of the amount of money that we want to give out in seed grants?

DR. KIESSLING: No.

CHAIRPERSON GALVIN: No.

DR. FISHBONE: Should we have some idea?

DR. KIESSLING: No.

CHAIRPERSON GALVIN: No.

DR. FISHBONE: No? Okay.

CHAIRPERSON GALVIN: Okay. There's a motion. A little bit more discussion, then I'm going to call the question.

DR. GOLDHAMER: Are we doing this only for the seeds?

CHAIRPERSON GALVIN: Yes.

DR. GOLDHAMER: And why? I'd like to know the rationale for that.

DR. KIESSLING: We can get to the seed tomorrow.

DR. GOLDHAMER: Oh, I see. So, tomorrow, we would do the same thing with the --

DR. KIESSLING: Yes.

CHAIRPERSON GALVIN: Okay.

DR. DEES: Just one comment. I guess I sort of think we're doing this backwards. I'd rather actually do this with the investigators first, but maybe -- I could see other people shaking their heads, because it seems like there's a number of grants here that we might want to say maybe.

If we have the money for it, we'd say, oh, this is that much money, but I'll defer to others.

CHAIRPERSON GALVIN: Yeah, we've got 10 million dollars that we'd say yes to if we had another 10 million dollars, but we don't. There's a motion on the floor. It's been moved and seconded. All in favor? Does everybody understand what we're trying to do? All in favor?

VOICES: Aye.

CHAIRPERSON GALVIN: Opposed?

VOICES: Opposed.

CHAIRPERSON GALVIN: Okay. The ayes carry it. So want to start with that list?

MS. TOWNSHEND: We will start with the seed

grants. This is 10SCA40, Winifred Krueger, UConn, the score was 5.0, and are there any objections to moving this to the no category?

MR. WAGNER: Do you want to mention who the reviewers are, so they could --

MS. TOWNSHEND: The reviewers are -- oh, gosh. Goldhamer and Genel.

DR. LATHAM: I was one.

DR. GENEL: I was one. I think this was scored much too low for the grant, frankly, and I would fund it.

A MALE VOICE: There were two from Krueger.

DR. GENEL: Right. This is the higher one. This is the one that was funded at five. The other one was funded at six.

CHAIRPERSON GALVIN: Okay. What is the consensus on Dr. Krueger's grant?

DR. HART: My understanding the motion was that if someone wanted to fight for it, we'd leave it in as a yes.

DR. GENEL: I'd say leave it in.

DR. LATHAM: Actually, I thought the idea was that if someone wanted to fight for it, we would then vote about whether we left it in or not, we'd be voting on

each one as we go down the list.

The idea is that we would save time only in the circumstance in which no one was willing to fight for one of these to be moved.

DR. PESCATELLO: Now is the time for somebody to advocate for it. We have to be convinced.

MS. TOWNSHEND: So we should call -- unless there's further discussion on this one, we should call for a voice vote, Marianne?

MS. HORN: Yes.

CHAIRPERSON GALVIN: Because we have to vote on each grant individually anyway.

MS. HORN: At the end.

MS. TOWNSHEND: Right. I understand, but this is a vote for?

CHAIRPERSON GALVIN: Maybe to no.

MS. TOWNSHEND: This is a vote for maybe to no. All those in favor? All those in favor, say "aye."

VOICES: Aye.

MS. TOWNSHEND: All those in favor of moving this from maybe to no, please say "aye."

VOICES: Aye.

MS. TOWNSHEND: Opposed?

VOICES: Opposed.

MS. HORN: I think we have to go to a voice vote, I mean a roll call.

MS. TOWNSHEND: I don't have a roll.

A MALE VOICE: So it's got to be a roll call, excluding people with conflict.

MS. TOWNSHEND: Okay, so, this is 40?

COURT REPORTER: One moment, please.

CHAIRPERSON GALVIN: All right. This is going to get very mixed up. We should start again in the morning on the same agenda. Do you want to spend 15 minutes and discuss Dr. Antic's grant?

DR. FISHBONE: Yes. I think that's a good idea, and leave everything else.

CHAIRPERSON GALVIN: And leave the rest until the morning, when we're all bushy-faced and bright-eyed.

DR. FISHBONE: Yeah.

MS. HORN: Sounds good. Then we'll have our roll call.

CHAIRPERSON GALVIN: Okay? Now how about 10SCD01? That's a core grant. That's the core grant.

MS. HORN: Right now, it's a maybe.

MS. TOWNSHEND: So we're opening discussion on --

CHAIRPERSON GALVIN: The core grant.

MS. TOWNSHEND: -- whether or not it should be yes or no.

CHAIRPERSON GALVIN: Yes or no.

MS. TOWNSHEND: Dr. Hart?

DR. HART: My recollection of one of the key points of the discussion was whether this was going to translate to the entire community statewide.

The letters of support within the grant, from my recollection, were all from UCHC. Is that correct?

DR. KIESSLING: I was one of the reviewers. I thought there was somebody. Well the Connecticut core is also shared with Wesleyan, so I think that's a given. Whether there was any support there from somebody from Yale, I don't know.

MS. TOWNSHEND: Steve, you were the other reviewer?

DR. LATHAM: Yeah. Certainly, the intent is stated in the proposal to share the facility with everyone around the state. I don't remember if there are support letters from other universities, but one of the concerns raised by the peer review group was whether they had made realistic plans for sharing the capacity beyond

the local facility.

MS. TOWNSHEND: Further discussion?

CHAIRPERSON GALVIN: What would make us move this grant into a yes?

DR. LATHAM: Well I think everyone looked at it and thought it was a really good idea for a core. It's a kind of facility that we don't have in the state right now and would be of great deal of use for people doing neuronal.

DR. KIESSLING: Yeah. Physically, it's going to fund this investigator's lab, except for one function, which was going to be in some other space, as I remember. I don't know. I'm sort of on the fence about this, because this would be a really unique resource.

There's a lot of need for this kind of resource for people doing neuronal derivation. He's got a table in his grant that I think he lists about 14 or 15 Connecticut-funded neuronal stem cell labs that would be able to -- that need this core now. On the other hand, it's $600,000.

CHAIRPERSON GALVIN: But you can't be on the fence anymore. Yes or no?

DR. LATHAM: There are no letters of support from other universities. I've just been looking

down the list.

DR. KIESSLING: Okay.

CHAIRPERSON GALVIN: Okay? Yes?

MR. MANDELKERN: I would like to speak in support of this grant. In view of the fact that of 90 applications the peer reviewers saw fit to give it the second highest rank, it obviously fills a need we do not have in Connecticut.

It's a new core that will be used widely, I believe, by all stem cell researchers, and it's a very modest cost of $600,000 over three or four years. I don't know how long the funding period is.

DR. KIESSLING: Two.

MR. MANDELKERN: What's that?

DR. KIESSLING: It's a two-year budget.

MR. MANDELKERN: It's a win/win situation, I believe. Considering the dollars and the purpose and the peer review and the enthusiasm, I think it's a win/win situation for us.

CHAIRPERSON GALVIN: In regards to the peer review, we agreed that this would not be our priority. It's an impressive peer review, but what is it that will push it? I think the group needs to be convinced of what pushes it from maybe to yes. What do you think, Ann?

DR. KIESSLING: Well I'd actually like to look at the budget again and see if it needs $600,000. I think that's reasonable to do. That's what we've done with all the cores. We've carefully looked at their budgets and decided if they really needed, because our first cores needed five million each, remember?

I would be happy to look the budget over tonight and decide if that's how much it needs.

CHAIRPERSON GALVIN: Okay. That's enough for one day.

MS. TOWNSHEND: If I may? I just whispered to the Commissioner. He suggested that I ask the group to do this. If you would each this evening, when you have some down time, look at the yeses and the maybes and come back fresh in the morning with ideas, considerations, questions, so that we can have or you can have a discussion.

DR. GENEL: That's fine. Can I ask if the list be e-mailed to us, because I have certainly not kept a running total of them.

MS. SARNECKY: I was just going to say I can e-mail this around to the group now.

MS. TOWNSHEND: That would be wonderful. Thank you.

MS. SARNECKY: You're welcome.

DR. FISHBONE: Could I ask that the person who put it into the maybe be prepared to speak a little about why it's in the maybe?

MS. TOWNSHEND: Did we keep track of actually who decided, because it was mainly a consensus of who decided. Often, it was the recommendation of the two reviewers, so it may be up to the two reviewers.

MS. SARNECKY: I think, if we just ask the reviewers tomorrow morning to open up with their comments, that would probably be a good process.

CHAIRPERSON GALVIN: Good idea.

MS. TOWNSHEND: We're not officially done, so we don't need a motion to dismiss, just a reminder not to talk amongst yourselves about any of the grants.

DR. LATHAM: I have something to say, which is that, as I notified the staff about two months ago, I'm not able to come tomorrow, and this, therefore, is the end of my last meeting with this august body, because, as you know, I've submitted my resignation, so I will miss you all.

If there's anything that I can do to facilitate tomorrow, in terms of sending you an e-mail or something like that, I can work more tonight to get that

done. I understand that there's not a quorum problem with my being absent tomorrow on the UConn side of the vote. So thank you, all.

MS. TOWNSHEND: Thank you. Your service is much appreciated. (Applause)

CHAIRPERSON GALVIN: Good luck to you, and you'll be missed. I will personally miss you a great deal. I don't usually say that.

MS. TOWNSHEND: We will gather again at 8:30 tomorrow morning. Those of you who need a ride back to the hotel, I will be leaving at 4:00.

(Whereupon, the meeting adjourned at 3:50 p.m.)