VERBATIM PROCEEDINGS

STEM CELL RESEARCH ADVISORY COMMITTEE MEETING

ROBERT GALVIN, CHAIRMAN

JULIUS LANDWIRTH, CHAIRMAN

MARCH 31, 2008

HARTFORD HILTON
315 TRUMBULL STREET
HARTFORD, CONNECTICUT

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

. . .Verbatim Proceedings of a meeting of The Stem Cell Research Advisory Committee held on March 31, 2008 at 8:10 a.m. at the Hartford Hilton, 315 Trumbull Street, Hartford, Connecticut. . .

MS. LYNN TOWNSHEND: Good morning everyone. And welcome to the Stem Cell Research Advisory Committee for March 31, 2008. My name is Lynn Townshend and for opening remarks I turn this over to the Chairman of the Committee, Commissioner Robert Galvin.

DR. ROBERT GALVIN: Good morning and thank you for being here friends old and new. I know that all of you have come some distance but all of you have come a distance from very, very busy days and very, very busy lives. And I appreciate that and take great cognizance of -- particularly of our friends who are here from Boston and New Jersey and don’t live just around the corner as I do.

We had a very successful year last year with our grant determining process and I know we’re going to repeat that this year. Hopefully, it will not use all

of two days. I want those of you who haven't heard me discuss this topic before to understand my reason why I don't want to have it as one long session that, perhaps, went into the evening or even the late evening hours and finish up in a day. But I think the ideation behind that is that I want to give everyone the proper opportunity to have their grants properly understood and properly adjudicated. I do not wish to repeat this process on the basis of someone feeling or getting the impressions that we rushed through their grant and did not give it the proper attention. Therefore, I'm going to take more of your time than I'm sure a lot of you would like, but we want to do the job correctly and do it right the first time.

I think that it's very noteworthy that we have lots of -- a lot more grants this year than last year but we have half the money. We have somewhere short of $10 million to disburse this year.

I do think we should take particular notice of the grants from new investigators and tabulate those at the end of the cycle of grants this year. It would be very interesting for me and for members of the Committee to take note that there are, perhaps, some grants that show a great deal of promise but they could not be

successfully funded this time around and, perhaps, we need to look more closely at them for funding and the like over the next several years of this Committee meeting.

With that, I welcome you all. You have my heartfelt appreciation for being here. I once again would like to say that I don't take anybody's time here lightly. And this program has been extremely successfully nationally and internationally. That has to do a lot with the great minds that are sitting here at the table and also with Wollschlager, Attorney Horn and Denise Lakemere and all -- all the folks who have contributed to moving this forward.

With that, are you ready to proceed Mr. Wollschlager?

Mr. WARREN WOLLSCHLAGER: Yes, I think we're all set to -- to move forward. If you want to move forward with maybe a roll call just to make sure that we have everything straight who's here and who's not. Marianne, do you have the -- or I guess Lynn, do -- do you have the list of Committee members?

MS. TOWNSHEND: Can you hear me?

COURT REPORTER: Yes.

MS. TOWNSHEND: Thank you. First of all, for those who are wishing wireless access we do now have

your code. Your conference code is (left out intentionally). Again that's (left out intentionally).

I guess we will actually proceed with the attendance followed by the opening remarks and outline of the meeting as it is to go for the remainder of the two days. Dr. Galvin?

DR. GALVIN: Here.

MS. TOWNSHEND: Dr. Lorenza?

DR. LORENZA: Here.

MS. TOWNSHEND: Dr. Canalis?

DR. ERNESTO CANALIS: Here.

MS. TOWNSHEND: Dr. Fishbone?

DR. GERALD FISHBONE: Here.

MS. TOWNSHEND: Dr. Genel?

DR. MYRON GENEL: Here.

MS. TOWNSHEND: Dr. Huang?

DR. PAUL HUANG: Here.

MS. TOWNSHEND: Dr. Jennings?

DR. CHARLES JENNINGS: Yep.

MS. TOWNSHEND: Dr. Kiessling?

DR. ANN KIESSLING: Here.

MS. TOWNSHEND: Dr. Landwirth?

DR. JULIUS LANDWIRTH: Here.

MS. TOWNSHEND: Dr. Latham?

DR. STEPHEN LATHAM: Here.

MS. TOWNSHEND: Mr. Mandelkern?

MR. ROBERT MANDELKERN: Here.

MS. TOWNSHEND: Dr. Wagers?

DR. AMY WAGERS: Here.

MS. TOWNSHEND: Dr. Wallack?

DR. MILTON WALLACK: Here.

MS. TOWNSHEND: Thirteen members of the Committee in attendance. I have opening remarks for the Committee which will, again, outline what is going to transpire over the following days.

The Committee will first consider the seed grant category for those grant applications peer review scored at 2.5 or above on the 5 point scale. We will receive a description and discussion period of one minute after which Commissioner Galvin will ask if there are any objections to placing the grant application in a particular category, the categories being yes, no or maybe as determined by group consensus.

If you have an objection and wish to see the grant application placed in a category other than that of the consensus of the group, please make your objections known immediately. That objection automatically places the grant application under the maybe category so that

your objection can be considered during the second phase of seed grant considerations. Seed grant applications peer review scored below 2.5 will receive four minutes description and discussion after which they will also be categorized based on group consensus of yes, no or maybe. After all of the seed grants have been considered, the maybe and yes category grants will again be discussed again with a four minute time frame. The no grant applications will be eliminated.

The remaining categories will similarly be considered as outlined on the agenda today with the following time limits. Core and group proposals, each will receive 14 minutes description and discussion no matter their peer review score. Established investigative grant proposals scoring 2.5 or above will receive a one minute description and discussion and established investigative grant proposals scoring below 2.5 will receive five minutes description and discussion.

We ask that you respect time limits agreed to by the Committee and, again, please express your objections and opinions according to the process in place.

Full funding considerations will be held until the end of the consideration of all grant categories. 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 amongst themselves with others such as audience members or potential grantees and, particularly the media during breaks, lunch or off hours tonight or tomorrow should a second day become necessary.

There may be a need for the Committee to adjourn to executive session to consider a grant proposal where propriety information contained in the proposal is pertinent to the decision-making. During that time, the audience will be asked to leave the room.

Two 15 minute breaks and a one hour lunch have been planned during the course of this meeting. Lunch will be provided to all Committee members and designated support staff in a separate room which is out these doors and to the left where a continental breakfast was this morning at approximately twelve noon. Your adherence to these limits is certainly appreciated.

Finally, the possibility exists that a second day will be required so that all of these grant proposals may be considered in full. Arrangements have been made to have those Committee members who stayed over last evening to remain in their same rooms this evening as well with additional rooms set aside for those members who

previously expressed a need to stay should this meeting run long. A decision will be made on that prior to 3:00 p.m. today.

To the audience, thank you for being here today. As you've heard, there are 87 grant proposals to be considered and a great deal of work to be completed by our Committee members. We respectfully ask that conversation within the audience be kept to a minimum. You are welcome to continue any conversation in the foyer 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 or between days of this meeting.

Should it become necessary for the Committee to move into executive session, a period of two minutes will be allotted for audience members to move into the foyer. You will be notified when executive session has ended. Audience members will then be welcomed to re-enter in the room.

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 when we will gladly recognize you to speak.

And for everyone, a little bit of housekeeping. The bathrooms, should you need them, are out the door, through the foyer, past the elevators on the left. And we do ask that you silence at this time your cell phones, your blackberries, your pagers and your laptops. Thank you.

DR. GALVIN: And I will have a brief -- a brief add on. These proceedings are public. As you can see, the doors are open. People may come and go who are generally interested or representative of one or the other of the print board, visual or audio -- audio media. We have always done that with the stem cells here in Connecticut.

I would advise any of the new members that we need to keep our conversations civil. Occasionally, we've gotten into some heated discussions and we kind of prefer that that doesn't happen. If it happens, it happens. But we need to be cognizant of the fact that there are folks in the audience who are listening and we want this to be understandable to them and the process to be smooth.

Attorney Henry Salton is here right down to the left of Attorney Horn. Although I jokingly refer to him as judge, he really is here in the same capacity as a

magistrate would be to rule on the fairness of -- of our procedures and are our procedures staying within the limits of what is acceptable practice in the state of Connecticut and to make sure that we adhere to the original legislative intent and the -- the add-on legislation that has happened over the -- the last couple of years. So he'll be making some rulings and suggestions as to what it is that we can or can't do particularly in reference to our particular legislative imperative to the state of Connecticut.

And, with that, I will get the proceedings started unless there's something else. If at any time things are unclear, please -- for our new members, please feel free to ask the question. As we all know, several of us here have connections with one or the other or sometimes both of the major universities -- Connecticut -- Yale and the University of Connecticut. And there are certain projects and grants that we will have to recuse ourselves from voting on because of our connections with those institutions. And with that, we'll move on.

MR. WOLLSCHLAGER: I just -- two points before we turn it over to our colleagues at CI. First, I want to note for the record that peer review members were unanimous in citing the quality of the applications. They

understand that there's less money available this year but they wanted it noted that they were impressed with the quality of the work that was submitted for their review.

And just finally, I think we tried to introduce you to everybody but for those of you who haven't met in person our colleague from New Jersey, Dr. Treena Arinzeh has joined us in person. She's been on the phone the last couple of meetings. And so I want to welcome you to Connecticut and thank you for joining us doctor.

DR. ARINZEH: Thank you.

MS. TOWNSHEND: And away we go. We are starting with the seed grant category. And what I will do is announce the number of the seed grant, the principal investigator, the score and I will ask the two people on the Committee who were to consider that, one of them to speak out with regard to whether or not they recommend that this be funded.

And starting with 08-SCA-UCHC-012. The principal investigator is Chandawarkar for the amount of $200,000, peer review scored at 4.5. Huang and Genel?

MS. HORN: I would note for the record that there has been propriety information claimed on this grant. If you get into the technical details of the

grant, we will need to go into executive session.

VOICE: We're having a problem with sound. It's very difficult with the hum and everything. So somehow those who are chairing the meeting --

MS. TOWNSHEND: We need to get right up on the microphone like this? Is that better?

VOICE: That's better.

MS. TOWNSHEND: Alrighty, thank you. CI.

VOICE: Yep, there is.

MS. TOWNSHEND: Starting at the bottom of the seed grant categories.

DR. JENNINGS: Could -- could that be circulated so that we could be organizing our --

MR. WOLLSCHLAGER: If I -- if I could just point out, and some of you don't I know, that were sent to you, basically, they're going in order from the scored -- from the seed grants that were scored closest to 5. That is the lowest ranking score in order up to the highest ranking score. What you have in your materials is a listing that shows it the other way around, from the ones down to the fives. So if you look at your materials, you -- you do have those to follow along.

MS. TOWNSHEND: Yes, Amy? Unfortunately,

the lights are at their peak. I apologize for that.

DR. JENNINGS: I have a question.

MS. TOWNSHEND: Yes, sir?

DR. JENNINGS: Are there some to spare --

COURT REPORTER: You need to speak into the microphone, sir, into the microphone.

DR. JENNINGS: I'm sorry. I just thought there might be some spare paper copies of specific grants if any of us feel the need to examine something more closely.

MS. TOWNSHEND: I would have to turn to CI. Chelsey?

MS. CHELSEY SARNECKY: There's two copies of each grant over here --

DR. JENNINGS: Okay.

MS. SARNECKY: -- if you need.

DR. JENNINGS: Probably won't need it for this initial session, but it's available, right? Two -- you said two additional copies --

MS. SARNECKY: Yes.

DR. JENNINGS: -- so they would have to be passed around.

MS. SARNECKY: Yes.

DR. JENNINGS: Thank you.

MS. TOWNSHEND: Do we also have those on disc and jump drive?

MS. SARNECKY: Yes.

MS. TOWNSHEND: Thank you. I know that those with computers may be able to access that on jump drive and disc.

DR. JENNINGS: And I have another question.

MS. TOWNSHEND: Yes, sir?

DR. JENNINGS: Could you repeat for us the entry -- the user IDs and codes so --

MS. TOWNSHEND: Oh, I apologize.

DR. JENNINGS: -- that we can access the grants on the CI website? I filed that away somewhere.

MS. TOWNSHEND: A conference code? Is that what you're looking for?

DR. JENNINGS: No, if we wanted to look at the PDFs of the grants which can only be accessed through the CI website?

MS. TOWNSHEND: I don't have that. CI would have to provide that.

MS. SARNECKY: The user name is --

DR. JENNINGS: Can we just go more slowly. Can we start with --

MS. TOWNSHEND: I can't hear you speaking. Can you use the microphone there?

DR. JENNINGS: I assume a lot of people want this as far as people wanting to be able to look online at grants that they don't have in front of them, is that right?

MS. SARNECKY: Let me write it on the board. I'll write it.

DR. JENNINGS: Yeah, that would be.

A VOICE: Then the word stem cell, all lowercase.

DR. JENNINGS: What's the URL that's connected to CT Innovations first, right?

MS. TOWNSHEND: Ladies and gentleman, with regard to microphones. Although Dr. Galvin and I and the head tables seem to have the direct microphones that you can see, they're also the flat microphones on the table, which it would be helpful if when you are speaking you could speak directly into those flat microphones, I know the transcriptionist would appreciate it as well as your fellow committee members so that we can hear the full debate. Are we ready to proceed or are we still organizing?

DR. JENNINGS: I at least -- can somebody

spell out the URL that we go to to use the password? I got as far as Connecticut Innovations but I don't see the --

MS. SARNECKY: Connecticut Innovations dot com. Bracket --

DR. JENNINGS: Yeah, I got that.

MS. SARNECKY: I'm sorry, but is there a microphone there?

MS. TOWNSHEND: Connecticut Innovations dot com slash?

MS. SARNECKY: Slash stem cell.

MS. TOWNSHEND: Slash stem cell.

DR. JENNINGS: Okay. And then authentication required?

MS. TOWNSHEND: Authentication code is there?

DR. JENNINGS: And that's what's written up on --

MR. DAN WAGNER: CG and then smaller case stem cell, okay? And then the password is stem08review capital S.

DR. JENNINGS: And that's not confidential information from the public is it? Not anymore.

MR. WAGNER: Not anymore. Does everyone

have it?

DR. JENNINGS: I'm sorry what's it? C-T uppercase stem cell singular lower case and then 08.

MR. WOLLSCHLAGER: And Henry, maybe you have a suggestion that it is confidential information that's now out there.

MR. SALTON: Has anybody successfully gone into it? What is it -- (intentionally redacted)

MS. HORN: We would ask to have that redacted from the transcript. Thank you. That is confidential information.

MS. TOWNSHEND: Are we ready to proceed? We are at stem cell seed grant 08-SCA-UCHC-012 Chandawarker peer review ranked at 4.5 and the Committee members who are cognizant are Huang and Genel. One minute.

DR. HUANG: Okay. If I may proceed, Dr. Genel? So this is a grant that deals with the hypothesis that diabetic wounds can be healed by culturing the -- by the super date instead of growing from stem cells grown in the presence of the diabetic cells. The idea is that if the stem cells produce factors that are important to healing then we can identify those factors and -- and use those to improve diabetic healing.

There's various problems with this, the most important of which, according to the peer review, is that there is no specific evidence that when one co-cultures diabetic tissues with human stem cells that there will be vectors produced. There's no preliminary data. There's no rationale for this and that's the major weakness. This was scored at the 4.5 and I would recommend that it be put in the no category.

MS. TOWNSHEND: Is there group consensus with regard to that suggestion?

DR. HUANG: Dr. Genel is -- is the other reviewer.

DR. GENEL: I'm not sure I would've scored it quite that low.

COURT REPORTER: I'm sorry. You need a microphone.

DR. GENEL: I said I'm not sure I would have scored it quite that low. I mean there's --

COURT REPORTER: You need to speak into that microphone. Thank you.

VOICE: No, the other.

DR. GENEL: I think there's Some attractive things in having clinicians actually work on some of these issues but the peer review is scathing so,

yes, I would rate it no.

MS. TOWNSHEND: The group consensus agree or disagree?

VOICES: Agreed.

MS. TOWNSHEND: Agreed? This grant is -- grant application is placed in the no category. I would remind the Committee that we are at one minute with review to anything that is 2.5 or above and we hope to stay within that time frame.

The next grant for consideration is 08-SCA-UCHC-007. The principal investigator is Das that is currently scored at 3.75 and the Committee members of cognizance are Arinzeh and Mandelkern.

MR. MANDELKERN: Dr. Arinzeh, I believe we decided that you would report on that.

MS. ARINZEH: Okay, is it working?

MS. TOWNSHEND: Yes.

MS. ARINZEH: This proposal was to look -- the objective of this work was to look at Redox, well the title is Redox Signaling & Stem Cell Mobilization for Cardiac Repair. And the objectives were to look at signaling effects -- Redox signaling effects, homing and survival of stem cells that travel from bone marrow -- bone marrow to heart so this is myocardial infarction.

The PI established investigator with a good record of publication and the overall external approach. The problems with -- the reviewers problems with it is that the overall experimental approach is not well justified and the model only enables for short term assessment of the fate of bracken cells and survival of the cells.

MS. TOWNSHEND: Recommendation?

MS. ARINZEH: Recommendation is no.

MS. TOWNSHEND: Group consensus? Do we agree?

VOICE: Yes.

MS. TOWNSHEND: That is placed in the no category. Thank you. Next up for consideration is 08-SCA-UCON-038. The principal investigator is Ma. The peer review score is 3.75 and the Committee members of cognizance are Kiessling and Landwirth.

DR. KIESSLING: Is this microphone working? Is this microphone working?

MS. TOWNSHEND: Yes.

DR. KIESSLING: Okay. This is an application for essentially a senior post-doc in the Center for Regenerative Medicine. And it’s an interesting application. It’s very superficial and this is one of the biggest reasons it scored so poorly. It’s going to use

mouse model and T cell some lines it's derived. There is discussion of using human cells but actually no description of any experiments that would be done. So this is an area that's of real strength in the Center for Regenerative Medicine but this is a very poor application as it's presented. This investigator also serves as the PI on a number of Chinese grants. So I have a feeling that this was just maybe simply overextended. It scored 3.75 for -- on the peer review and I would agree with that. So my recommendation is that it be placed in the no funding category.

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

VOICE: Right.

MS. TOWNSHEND: Please move this to the no category. Thank you.

DR. GALVIN: Lynn, your mic is down.

MS. TOWNSHEND: I'll try to get even closer.

DR. GALVIN: Thank you.

MS. TOWNSHEND: Thank you. The next grant for -- grant application for consideration is 08-SCA-YALE-026 Kocer with a peer review score of 3.75 and the Committee members of cognizance being Canalis and Wallack.

DR. CANALIS: So in -- in this application Kocer proposes to induce Carotinocyte cell differentiation out of embryonic stem cells and then study conditions that would determine the fate and cell renewal of the cells.

The scientific review is not favorable. They consider the investigator did not have sufficient expertise, had limited publication and the science itself was somewhat superficial.

MS. TOWNSHEND: And your recommendation, sir?

DR. CANALIS: No.

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

VOICE: Yes.

MS. TOWNSHEND: This application is moved to the no category. Next application is 08-SCA-UCON-050. Xue is the principal investigator and it is peer review scored at 3.5 and the Committee members are Wagers and Latham.

DR. WAGERS: So this is a grant that is aimed at differentiating coelomocytes from human embryonic stem cells by Xue. The -- the peer review Committee found the proposal lacking evidence of unique approaches or expertise. In general, it was too diffuse and lacked a

rationale for the experiments. And, so for these reasons, I would put it in the no category.

MS. TOWNSHEND: Is that the consensus of the group? Thank you. Please move this application to the no category.

Our next consideration is 08-SCA-YALE-032 Henegariu. Peer review scored at 3.4 and the principal members of the Committee were Canalis and Wallack.

DR. CANALIS: Henegariu proposed this to use human embryonic stem cells to induce differentiation between pancreatic beta-cells so that these cells can be used for the treatment of diabetes mellitus. The peer review considered the proposal somewhat vague and ambitious and they considered that the investigator did not have the appropriate experience. He, indeed, has been an associate on the faculty for about 20 years after his degree. So my recommendation is no.

MS. TOWNSHEND: Is that the consensus of the group? Thank you. Please move this application to the no category.

DR. GALVIN: I'm going to interrupt for one session and I'll give you a very short lecture. But I'm going to ask you to try to speak up as loudly as you can. I can see that Bob Mandelkern, Bob and I are a

couple of old duffers and I'm having trouble -- some trouble hearing and I think Bob is further away.

But I will give you a lecture on a phenomenon known as masking. And masking is with hearing problems associated with noises that are in the same frequency as human speech which -- which tends to cancel out human speech. And the problem with this room is that the noise in the background sounds to me like somewhere around five or maybe 600 decibels or whatever or hertz. And it's canceling out some of the stuff so if you could all speak a little louder it would help Mr. Mandelkern and myself.

MR. MANDELKERN: Thank you, Dr. Galvin.

MS. TOWNSHEND: Thank you sir. We are moving on to grant application 08-SCA-UCHC-018. Zou is the principal investigator with a peer review score of 3.13. And the Committee members of cognizance are Jennings and Genel. And I believe this is possibly a proprietary grant. Is that correct? That's correct. Dr. Jennings, Dr. Genel?

DR. JENNINGS: Okay. I'm -- shall I --

MS. TOWNSHEND: Oh, I'm sorry.

DR. JENNINGS: I'm sorry. Ccan you hear me? So this -- this grant they're trying to find stem

cells for human ovarian cancer and the idea is this is an approach that's been used for a number of human cancers and will be a major advance if it was successful. And the referees have commented that it's an extremely ambitious proposal and -- and there's really not much in the office track records to suggest that they could actually accomplish this. And I think it's -- the scope of what is being proposed is far beyond what could be accomplished in a -- in a two-year seed grant. And that was certainly consistent with my own impression and I would recommend no.

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

VOICE: Yes.

MS. TOWNSHEND: Thank you. Please move this application to the no category.

Application 08-SCA-UCHC-017 Chhabra peer review scored at 3.0.

MR. MANDELKERN: I think we missed one. You skipped 039.

MS. TOWNSHEND: My apologies, Lieberman, Thank you, my apologies. 08-SCA-UCHC-039 Lieberman peer review scored at 3.0 and Committee members of cognizance are Kiessling and Landwirth. Dr. Kiessling? Dr.

Lanwirth? Oh, Dr. Kiessling, thank you.

DR. KIESSLING: This -- this is an application by an orthopedic surgeon who's interested in using embryonic stem cells for -- to repair -- particularly to repair bone conditions that have a large need, not -- not just somebody whose broken a bone but somebody with a large gap.

The major -- the reason that this scored so poorly by the peer review group, and I have to agree with it, is that there's no discussion in this application as to early differentiation of these cells before they're put into the bone. So there's no particular way to know -- they're just going to pop embryonic stem cells into the bone and then look to see if they differentiate in the bone. It's pretty poorly described. This is a research fellow as an orthopedic surgeon. He's had no experience with stem cells. This is a good -- I mean a good project to pursue. When I read this application, one of my questions is what -- what are we -- how much merit or how much weight are we to put as to whether this application could have been funded by the NIH or not.

So some of our applications that are a little bit weaker are not fundable by the NIH and some of the applications -- many of the -- most of the

applications could be funded by the NIH. So when I read this I wondered because this is an application that could definitely have been funded by the NIH.

MS. TOWNSHEND: And your recommendation?

DR. KIESSLING: Is that it be not funded by us.

MS. TOWNSHEND: Is that the consensus of the group? Please move the application to the no category.

And now we move on to 08-SCA-UCHC-017 Chhabra peer review scored at 3.0 with Huang and Mandelkern as the Committee members of cognizance. I would note that this application has claimed proprietary information.

MR. MANDELKERN: This is an application, excuse me. This is an application to consider generation of tumor specific affected T cells from human embryonic cells. It received a score of 3.0 from the peer review. And the comments of the peer review committee were that the project is interesting but could not be possibly completed within the time line. It also stresses that the investigator trivializes the development of specific blood cells from the human embryonic stem cell starting point.

And finally is that the applicant's

understanding and ability within the field of immunology are highly respectable but they have to be better applied to human embryonic stem cells involving systems which the applicant is still not experienced in. Therefore, the recommendation is that we do not fund this grant.

MS. TOWNSHEND: Is that the consensus of the group? Please move this grant application to the no category.

08-SCA-UCHC-042 Maulik is the principal investigator, peer review scored at 2.88, although I have it also listed at 2.9 -- a bit of an inconsistency here. Wagers and Landwirth are the Committee members of cognizance.

DR. WAGERS: This is an application from Maulik which is aiming to precondition Mesenchymal stem cells in order to facilitate their ability to generate blood vessel or endothelial cells. The peer review committee found several issues with this application with regard to the design of the experiments and how they would be interpreted. In addition, there was concern that there was a lack of demonstration of some sort of rationale or support for the hypothesis proposed or feasibility of the types of studies that -- that were going to be performed and no alternative strategy was given if the proposed

strategy didn't work out. And so for those reasons, I would put it in the no category.

MS. TOWNSHEND: Is that the consensus of the group? Thank you. Please move this application to the no category.

Our next application for consideration is 08-SCA-UCHC-013. Furneaux is the principal investigator, 2.75 the peer review score and the Committee members of cognizance are Huang and Genel.

COURT REPORTER: You need to be on a microphone.

DR. GENEL: The peer review score has a --

COURT REPORTER: I still can't hear you. I'm sorry.

DR. GENEL: The peer review score was 2.6.

MR. WOLLSCHLAGER: If I may? This was the application that -- this was the application discussed at the last meeting where the score was actually 2.75.

DR. GENEL: It is 2.75? Two very senior investigators who are moving to a more conventional appeal of stem cell research. And I think that critique notes that their lack of familiarity with the -- with the subject is a major incentive. I think with the score of the other grants that are much higher on the group is to

move this to the no the category.

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

VOICE: Yes.

MS. TOWNSHEND: Please move this application to the no category.

Our next application is 08-SCA-UCON-055. Yao is the principal investigator, 2.75 is the peer review score, Committee members of cognizance Arinzeh and Fishbone.

MS. ARINZEH: This proposal, the PI, Yao, is looking at a method for development of a quantitative analysis of protein phosphorylation in human ESC cells. There is importance in this work and they are inventing new analytical methods for quantitatively determining phosphorylated proteins in -- in these cells. And looking at relationships or having these changes in the protein phosphorylation may -- may affect the cells.

The reviewer just comments that this is an overlap with the PI's existing 2006 grant and that there also seems to be an overlap with this years core facility grant and the PI is a co-PI on that board facility grant. So the reviewer doesn't comment on the merit of the work which I thought that was a little strange. And this is

not my area so I couldn't comment on the merit of the work myself. But based on the reviewer's comments, I would say no.

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

DR. FISHBONE: Can I -- can I just make a --

MS. TOWNSHEND: Sure.

DR. FISHBONE: -- point?

MS. TOWNSHEND: Yes, sir.

DR. FISHBONE: It's a very technical ground. He points out that although they state there is no overlap with the other work and he's funded for several other projects in the same area, that the other funding will illustrate the level of feasibility of this project. So, you know, it's very technical and the question is whether one thinks it's worth investing in with all the other things he's doing.

MS. TOWNSHEND: Would we like to move this into the maybe category for consideration later? That sounds like what you're suggesting, sir.

DR. FISHBONE: I -- yeah, yeah.

MS. TOWNSHEND: Please move this grant to the maybe category for consideration at a later moment.

Our next consideration is 08-SCA-UCON-004. Wang is the principal investigator, peer review scored at 2.75 and Committee members of cognizance are Fishbone and Arinzeh.

MS. ARINZEH: I'll start again. Okay, the PI is Wang and the proposal is a polymeric membrane for safe and efficient culture of human ESC cells. So that they are developing a matrix to contain mass embryonic fiberglass and they will use these in co-culture with the embryonic stem cells.

And the reviewer says that there is significant weaknesses in the proposal and that they are -- when they are doing these co-cultures, they're only looking at one pathogen of a given molecular size and it happens to be a human pathogen. So they're not looking at these mouse pathogens.

MS. TOWNSHEND: And your recommendation is?

MS. ARINZEH: The recommendation would be no.

MS. TOWNSHEND: Is that the group consensus?

VOICE: Yes.

MS. TOWNSHEND: Thank you. Please move

this application to the no category.

COURT REPORTER: One moment, please.

(Off the record.)

MS. TOWNSHEND: Our next grant for consideration is 08-SCA-UCON-052. Amano is the principal investigator, 2.75 the peer review score, Committee members of cognizance Wagers and Wallack or Latham?

DR. LATHAM: Latham.

MS. TOWNSHEND: Latham.

DR. LATHAM: Is this -- is this working?

MS. TOWNSHEND: It is.

DR. LATHAM: Okay. This is -- the PI is Amano. The proposal is basically to produce offspring from infertile mice. They'll start with mice with the C-kit gene mutation or infertile, use SENT technology to generate cells from those mice, try to correct them in vitro and then derive genetically corrected cells and induce those by directed differentiation to become germ cells.

I found a disconnect between the -- the peer review discussion and the score. The peer review discussion is full of praise for the preliminary results and the qualifications of the people to be involved. But the score is only 2.75. I would favor putting it in the

maybe.

MS. TOWNSHEND: Please place that application in the maybe category.

Our next grant for consideration is 08-SCA-UCON-041. Nelson is the principal investigator, 2.75 the peer review score and the Committee members of cognizance are Kiessling and Landwirth.

DR. KIESSLING: We -- we have to ask that this be -- we come back to this grant because neither Julius nor I can find our notes on this application.

MS. TOWNSHEND: Fine, thank you. 08-SCA-UCHC is the next grant for consideration 020. Crocker is the principal investigator, 2.7 is the peer review score and the Committee members of cognizance are Jennings and Genel.

DR. GENEL: Charles, if I may?

COURT REPORTER: I think you need to direct that right in front of you.

DR. GENEL: Are you asking me to put my mouth on it?

COURT REPORTER: Practically.

DR. GENEL: The -- this is -- this is another one where I think the peer review comments and the score do -- do not match. The -- this is a young

investigator who, at the time of the application had just come to UCONN from Scripps. And the primary -- the primary criticism seems to be lack of -- lack of experience and specifics with the details. I would think that I would move this into a maybe because I think that this is the type of individual who seed grants that are attended to encourage. But, Charles, I'd be interested in your comments.

DR. JENNINGS: Yeah, I wouldn't disagree with that Mike. I also thought that it was -- the PI had quite a good track record for his relatively early career stage. I'm not sure that it's going to emerge as one of our front grants but it is I think stronger than its low score might have implied. So I certainly wouldn't object to a more careful discussion later on.

MS. TOWNSHEND: Please place that grant in the maybe category. Did we want to come back to you Dr. Kiessling, or?

DR. KIESSLING: No, we can't.

MS. TOWNSHEND: Okay.

DR. KIESSLING: We're going to have to come back to this after a break.

MS. TOWNSHEND: Alrighty, thank you. Our next grant for consideration is 08-SCA -- yes, sir?

DR. GALVIN: We -- we have a total of 12 nos, we have three maybes and one deferred. Does everybody agree with that?

DR. JENNINGS: Deferred at this point because they haven't --

DR. GALVIN: We all okay with that -- the nos? Because last year I remember we went -- I recall that we went back in and some of the maybes inadvertently got into the nos. But at this point everybody -- and I will do this from time to time today to make sure that we have -- the nos are nos -- we have 12 nos, three maybes and a deferred. Everybody alright with that? Okay, let's go.

MS. TOWNSHEND: Next grant for consideration is 08-SCA-UCHC-001. Mamoun is the principal investigator, 2.63 is the peer review score and the Committee members of cognizance are Arinzeh and Fishbone.

DR. FISHBONE: I can take that.

MS. TOWNSHEND: Go ahead.

DR. FISHBONE: This grant deals with erythrocytes derived from human embryonic stem cells can be effective in developing treatments for malaria which is a very important disease. The reviewers point out that to them it would make much more sense to use more abundant

easily differentiated cord blood derived erythroid cells in the study than human embryonic stem cells. The investigator continues to state that the amount of red blood cells obtained from cord blood are not sufficient to perform the required study.

So it's a question of whether you believe the reviewer or the investigator. And this is a resubmission from last year and they said last time no preliminary data has shown that erythrocyte derived from human embryonic stem cells can be obtained in the investigator's laboratory. So I don't think the reviewers were very high on this particular grant.

MS. TOWNSHEND: And your recommendation?

DR. FISHBONE: No.

MS. TOWNSHEND: Is that the consensus of the group? Please place this application in the no category.

Our next grant for consideration is 08-SCA-RECO-028. Sundaram is the principal investigator, 2.6 is the peer review score. Canalis and Wallack are the Committee members of cognizance.

DR. CANALIS: This application proposes to transform human embryonic stem cells to differentiate towards the -- towards the formation of neurons so that

they then will be able to use the cells for the treatment of Parkinson's. They'll use a number of animal models, a rodent, primates and then eventually humans.

The scientific review has a number of concerns regarding this application. In addition, the commitment of the PI is somewhat limited. Because of that I would favor not to fund the application.

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

VOICE: Yep.

MS. TOWNSHEND: Thank you. Please move this application to the no category.

Our next grant for consideration is 08-SCA-UCHC-024. Maye is the principal investigator, 2.6 the peer review score and the Committee members of cognizance are Jennings and Latham.

DR. JENNINGS: Should I take it?

DR. LATHAM: Yes.

DR. JENNINGS: Okay. So this is from a new faculty member at UCONN. And so the proposed aim of the proposal is to use herpes simplex virus based factors to introduce large pieces of DNA into human embryonic stem cells. So it's basically a technology development proposal. They will -- they -- I think it's a reasonable

goal.

The referee scored it some 2.6, I believe. The main concern is that the authors have not demonstrated with what efficiency the spirals will actually affect the human embryonic stem cells which is really an essential piece of information to evaluate the likelihood of success of this project. So I guess my own view would be not to support this. But I think it is a marginal case and if Stephen wanted to advocate for it, I wouldn't.

DR. LATHAM: I wouldn't support that, no.

MS. TOWNSHEND: It looks like the recommendation from both is no? Is that the consensus of the group? Please place this application in the no category.

Next application for consideration is 08-SCA-UCHC-016. Gu is the principal investigator. I may be saying it wrong, I apologize. 2.6 is the peer review score and the members of cognizance are Huang and Mandelkern.

MR. MANDELKERN: This is an application -- this is an application that ranked -- that scored 2.6 and among 50 seed grant applications, this ranked number 31. It's a proposal to track and employ cells from human embryonic cultures and relies on some reasons and

findings.

The problem is that peer review found it somewhat risky and that it was behind the reach of a post-doc that only recently joined the lab. The PI's mentor is also new to the work, has an extensive track record in HES and is funded already by an established investigators grant and core grant from our work last year. It does not seem to me that with a rank of 31 among 50 seed grants and being somewhat risky that we should consider funding it. Therefore, my recommendation is no with any addendum from my colleague, Dr. Huang, who understands the science slightly better than I do.

DR. HUANG: I agree with this being in the no category.

MS. TOWNSHEND: Is that the consensus of the group? Please move the application to the no category.

We are now moving into peer review score of 2.5 and below which means our time for discussion and description or description and discussion now moves to four minutes.

Our next grant application is 08-SCA-UCON-054. Srivastava is the principal investigator, 2.5 is the peer review score and the Committee members of cognizance

are Wagers and Genel.

DR. GENEL: I like this grant. It's, first of all, fairly low cost. It's primarily to pay for the PI who is an engineer to go to Wisconsin to -- to do some research on modeling of stem cell biology. And I think it's, again, I think this is the sort of thing that I thought the seed grant program was intended for. And it comes in under cost. It's $170,000 so we save $30,000 for another one. I would fund this.

DR. WAGERS: So I was actually on the other side. I thought my one concern which was that it requires that the PI travel to Wisconsin to acquire the technology and he's only planning to be there for three weeks. And it's not clear that he'll be able to transfer the technology adequately in that time and that the infrastructure will be set up.

It's also -- I also wasn't clear on how the -- the whole proposal is based around the idea of metabolic profiling of embryonic stem cells and mathematically modeling that but it wasn't clear on how that model would be created or what it would be useful for and what we would take that information -- how we would take that information and use it in moving forward to try to promote using these cells in some sort of therapy. So

those were the two reasons I was -- I was more negative about the application. But, perhaps, we should put it in the maybe category if we need to discuss it some more.

MS. TOWNSHEND: If placing this in the maybe category is the consensus of the group, we'll move forward with doing that. Please place this grant application in the maybe category. No, it's 2.5 and below.

Our next grant for consideration is 08-SCA-COGN-044. Hambor is the PI, the peer review is 2.5 and the Committee members of cognizance are Wagers and Latham.

DR. WAGERS: So this is a grant to study the functional geno-mix of human exanthema stem cells. And the proposal has five specific aims, each of which is designed to identify genes that promote different aspects of exanthema stem cell biology, their proliferation, their differentiation to bone cells, to cartilage cells to fat cells to heart and muscle cells. It's not -- the majority of this will be done by modulating gene expression using small hairpin RNAs that change -- that they're going to get from a company called Dharmacon.

And so there is multiple -- the major issue with the grant is that there are multiple ways that the data can be interpreted and it's not clear how the

different effects will be parsed. They rely in many cases on a single gene or a single phenotype to discern whether they're getting enhanced production of these different types of cells and this could be misleading. It's also very, very diffuse and there's a huge inter-dependence of the different readouts which makes it difficult to consolidate the information that will be coming from the study.

And so I think there are significant concerns with the way the experiments are designed and the way they will be interpreted in order to get the useful information at the end and so I would put this in the no category.

MS. TOWNSHEND: Is that the consensus of the group? Please move this application to the no category.

Our next consideration is 08-SCA-UCON-051. Kotha is the principal investigator, 2.5 the peer review score.

MR. MANDELKERN: I think we missed one. 021.

MS. TOWNSHEND: Oh, I'm not going to make the day, thank you. 08-SCA-UCHC-021. Epstein is the principal investigator, 2.5 is the peer review score,

Jennings and Genel are the Committee members of cognizance.

DR. JENNINGS: Okay, so this one the proposal is to look at mechanisms for cell death in cancer stem cells specifically AML and ALL and leukemias. And what they're planning to do is to examine -- is to isolate these cells and then look at the role of cyclic A and P signaling pathway and try to inhibit the various phosphordiasphorates as they regulate the activity of this pathway.

So the clinical potential is considerable. The idea of killing cancer cells with stem cells is very attractive and phosphordiasphorates is known to be a very drugable target. So, in principal, this is an important thing and it scored relatively poorly I think because the referees found that the specific plans were rather diffuse. It's -- there are a very large number of phosphordiasphorates and it's not clear which ones it would go after. It's also unclear whether the authors have the expertise to actually grow these cells. They have a very substantial track record in the -- cell signaling and phosphordiasphorates, much less so in cancer stem cells.

And so the referees' bottom line is

although this has great potential and needs to be focused and narrowed and there needs to be some indication that they can actually isolate and grow these cells -- that these investigators can actually do that. So I would recommend that we don't -- that we don't fund this one.

MS. TOWNSHEND: Is that the consensus of the group? Please place this in the no category.

Our next application, I believe, is 008-SCA-UCON-051. Kotha is the principal investigator, 2.5 is the peer review score and the Committee members cognizance are Wagers and Latham.

DR. WAGERS: So this is an interesting -- and interesting idea that I think suffered from a lack of demonstration that there was a real feasibility behind the experiment. So the idea is that the PI will generate a method for encapsulating RNA that encodes a factor that the PI believes will drive human embryonic stem cells to differentiate into bone cells. So he's going to encapsulate that in a bead, figure out a way to inject those beads into ES cells and have those beads slowly release the RNA into the cells and drive them into -- into bone.

So the issues are there's no demonstration that this factor actually will drive those cells into

bone. It's not clear that ES cells will survive this procedure in having beads injected into them and it's not clear that the RNA will actually survive this encapsulation procedure.

So, and then with all of those caveats, other potential approaches to being able to generate bone cells from ES cells aren't adequately discussed. And so I think with a little bit more support data that this isn't an approach that would be feasible that this proposal would have scored better. But as it is, I think I would place it in the no category and maybe encourage them to come back after they've demonstrated a little bit more how the system will actually work.

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

VOICE: Yes.

MS. TOWNSHEND: Please move this application to the no category.

Our next application for consideration is 08SCA-UCON-030. Peczuh is the principal investigator, 2.5 is the peer review score and Jennings and Latham are the Committee members of cognizance.

DR. JENNINGS: Okay. Alright, here we go. Okay, so the idea of this proposal is to convert human

embryonic stem cells into dopamine neurons which, of course, could then be used for treating Parkinson's disease. And what the author is planning to do is to manipulate growth factor signaling and the way they're going to do that is by synthesizing small peptides that mimic the effects of growth factors and also testing a class of molecules known as spirocyclates which are apparently said to interact with growth factor receptors and they're going to use those alone and in combination -- in combination with various other known small -- small molecule regulators of cell signaling to look for ability to manipulate differentiation in an actually therapeutically useful way.

And the referees had a number of concerns and they commented that the authors have made some -- made some misstatements or confusion between mouse and human embryonic stem cells. And I think one factor that -- that I would put some weight on is that they haven't significantly considered the, if you like, the combinatory explosion -- the number of possibilities that could be tried here is extremely large and they really don't -- they haven't given any thought to the scale up or the number of conditions that one would need to try or get a meaningful result out of this.

The first author is -- has a background in Chemistry. I'm certainly not a chemist. But he's been -- he has a productive track record. However, he doesn't have a strong track record in biology I don't think and I think the referees are finding some naivety in this proposal and I would certainly share that view. So my thought would be not to go with this one.

MS. TOWNSHEND: Is that the consensus of the group? Please place -- place this application in the no category.

Next application is 08-SCA-UCHC-029. Drazinic is the principal investigator, 2.5 peer review score and the Committee members of cognizance are Jennings and Latham.

DR. LATHAM: Once again, Charles, please.

DR. JENNINGS: Okay, sure. Just one second if I may to find my notes. Here we go. Okay. So the idea of this proposal is to study the -- the genetic factors that may underlie schizophrenia or bipolar disease. So these are two major psychiatric disorders that have a strong rather complex genetic etiology and there is certainly a need to develop new systems for studying the basic knowledge of these diseases.

What these authors are planning to do is to

take blood cells -- white blood cells from the patients and fuse them with stem cells -- with human embryonic stem cells and then generate some kind of cell that could be differentiated into neurons and could be used to study -- look for abnormalities in those derived from the patients.

I'm hunting for the referees' comments, but to me -- let me just have a look. This to me seems almost fantastical. Yes, the reason I'm having a hard time is the referees' comments are not terribly articulate. So the butt of my conclusion is, best written grant, important project but not productive. And it would be more -- it raised some questions about the use of EBV. I confess I cannot see the benefit from the use of EBV. I guess I have a concern with this which I thought the referees' comments weren't clearly focused on the content of the application and the major problems. I personally think that this is a deeply flawed application and I would see it as a non-starter but I'm concerned that I may be overstepping my role as an advisory committee member here. So I wonder whether this needs to go back for further discussion. And Steve, do you want to comment?

MS. TOWNSHEND: Your recommendation is?

DR. JENNINGS: I guess I kind of look to

the group for advice. My recommendation wearing my scientific hat is that this is a non-starter. My recommendation from a procedural perspective, it may need more -- more examination. So, perhaps, we should go with the procedural.

MS. TOWNSHEND: I'm sorry. I didn't hear. With the --

DR. JENNINGS: I said, perhaps, we should go with the procedural perspective and say that we should discuss it further.

MS. TOWNSHEND: So we'll put this in the maybe category for later discussion?

DR. JENNINGS: The maybe category.

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

MR. SALTON: Well, I think at this point it's either a maybe, yes or a no. That's the process that we followed. Under the eight factors that we have for evaluation by the Committee, every application has a scientific merit so, clearly, that is something that you can -- any Committee member can express or utilize that viewpoint. And one of the reasons why many of the people on this Committee who have scientific background is because that's contemplated as part of the contribution to

the Committee.

So, if you want further discussion then I think you're -- you would have to call for a maybe on it. If you don't -- if you feel it can stand on your --

DR. JENNINGS: I feel sufficiently confident you can vote on me to recommend rejection. I would be happy to defend that if we decide we need further discussion. This is a percentage so that proposal is to fuse white blood cells from psychiatric patients with human embryonic stem cells to generate hybrid cells which could then be used to study the underlying abnormalities in psychiatric cases.

MR. SALTON: If any member of the Committee wishes to call for a maybe at this point, it will move to the maybe category.

DR. GALVIN: I'm a different kind of scientist from everybody else sitting at the table. But I thought I heard Charles use the term fantastical. This doesn't sound reasonable to me. Perhaps, you could, I mean I don't -- how are you going to do this? How could somebody? I don't know.

DR. JENNINGS: There is -- so little is known about the property of these fused cells. What we know about psychiatric disease is that these are not

connected to simple diseases. There are a very large number of genes that affect the risk of psychiatric disease. Each gene is individually likely to have only a very small effect. I think that's pretty well established from the genetics. The likelihood that you could pick up or interpret or make sense of these subtle effects in a cell culture system that is so poorly characterized, that is a fusion between a lymphocyte and a human embryonic stem cell when you don't know what -- you don't know what kind of cell you're trying to turn it into, what specific type of neuron, you don't know what kinds of things you should be looking at. The only reason for using blood cells is that you can't just take the brains out of psychiatric patients and experiment on them as a practical matter.

DR. GALVIN: That is a practical matter.

DR. JENNINGS: That is a practical matter and alternatives that have been proposed by others would be to take -- you can do nuclear transfer and make a cell line that is purely derived from the genetic material of the patient. I think that even that, that's a very challenging project.

DR. GALVIN: What kind of schizophrenic? Schizo-affective? Schizoid personality? Paranoid

schizophrenics? That's a clinical diagnosis which is fairly subjective.

DR. JENNINGS: I wouldn't -- I wouldn't shoot it on those grounds because I think those -- those diagnostic categories it is not well known how those map on to biological patterns. So if they didn't have an answer to that question I wouldn't mind so much and my concern is more with the cell and molecular biological methods are there.

DR. GALVIN: Thank you.

MS. TOWNSHEND: So where do we stand, maybe or?

DR. JENNINGS: I continue to recommend rejection but to the Committee too.

MS. TOWNSHEND: I'm seeing --

VOICE: No.

MS. TOWNSHEND: So this application will go into the no category. Thank you.

Next application for consideration is 08-SCA-UCHC-014. Chamberlain is the principal investigator, 2.5 is the peer review score and the Committee members of cognizance are Huang and Genel.

DR. HUANG: Okay. This is a proposal that deals with PRC2 which is Polycomb Repressives Complex 2.

It's a -- it's a chromatin binding protein complex that modifies crest stems. And the hypothesis is that PRC2 is involved in genes -- the transcription and expression of genes involved in development versus plura-potency.

The PI of this proposal has done mouse work showing that when you knock out some of the equivalent genes in mice that you have changes in the plura-potency of the cells and proposes now to do work in humans using RNAi and then to check for potency.

Even though this is scored at a 2.5, the review actually was relatively positive about the fact that the PI has had previous experience in the same system in mouse. That the -- this work is likely to have value in -- in determining the factors that are important in the expression of different -- differentiation versus plura-potency genes.

There was some discussion about whether the ES cells would be truly plura-potent if they changed the kinds of cells they could differentiate into. But it appears that this to me is more of a semantic point that if the cells are no longer podi-potent that they may still be plura-potent and able to turn into various different kinds of cells even though they're not -- it would turn equally into all kinds of cells.

So I would say that I would put this in the maybe category.

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

VOICE: Yes.

MS. TOWNSHEND: Please move this application to the maybe category.

Next we have for consideration is U -- I'm sorry, 08-SCA-UCON-003. Wang is the principal investigator, 2.5 in the peer review score, Arinzeh and Fishbone are the Committee members of cognizance.

DR. FISHBONE: This project is to develop rapid real time and in-situ MRMA detection in living embryonic stem cells with nanoprobes. And so they want to apply nanoprobes for the detection of these particular proteins in embryonic stem cells.

The reviewer says the project could in theory provide a means by which to analyze the state of embryonic stem cells without having to destroy them. But there are a number of questions about it. It's not clear why he hasn't explored the same research in mice and in other human cell types in order to find out what he has to use in the way of probes.

And I think he -- the reviewer felt that --

he's not convinced that the technology has been developed enough to the point of applying it to human embryonic stem cells by this investigator. So I think he likes the idea but feels that it should be worked out in mice embryonic stem cells before it's applied to human embryonic. So my -- my feeling would be no.

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

DR. KIESSLING: Well, I have a question about that. Why -- why --

COURT REPORTER: You need to be on the microphone.

DR. KIESSLING: I didn't read this application but I thought our purpose was to study human embryonic stem cells. There doesn't seem to be any in vivo work suggested here so I'm not too sure of why that would be a criticism. I think -- I guess maybe I think there's actually just way too much mouse work going on. I'd give it a maybe.

DR. FISHBONE: If I can answer that? I think they're not saying do it in mouse cells because, you know, we're not ready to do it in human cells. But I think what he's saying is you've got to work out the techniques. But Ann makes a very good point. You could

work them out I guess in human embryonic stem cells so maybe it should be a maybe.

MS. TOWNSHEND: Do we wish to place this application in the maybe category? Can we hear from the other reviewer, please?

MS. ARINZEH: Yeah. I didn't hear exactly what the question was down there, but.

MS. TOWNSHEND: I believe it had to do with --

DR. KIESSLING: My question was why would you want to do a tissue culture study in mice embryonic stem cells instead of human embryonic stem cells?

MS. ARINZEH: Well, I think they do want to do human embryonic stem cells. I think it was just the fact the preliminary data wasn't convincing enough to demonstrate the investigator at this point with that technology could go to human ES cells.

DR. GALVIN: I think Dr. Kiessling brings up a very valid and important point about as we get further along in our process and as we have gone from a $20 million dollar aliquot of funds to $10 million, I think we may need to focus a little better on exactly which direction we're -- we're taking. And I think that she -- I think that Ann has a very valid -- valid point.

And I think in particular if sometime in the future that we want to approach the General Assembly for additional funding, if that should be our decision, that we're going to have to cull this down a little further and concentrate on what they asked us to do which is human embryonic stem cell. But I think that what Ann says and what I've just said and part of what Bob Mandelkern says is part of the evolving philosophy of the Committee about just where -- where are we going with this stuff. Thank you.

MR. SALTON: So you're recommendation is no?

MS. TOWNSHEND: Do we wish to place this in the maybe category?

VOICE: My recommendation is for maybe.

MS. TOWNSHEND: Please place this application in the maybe category.

Our next grant for consideration is 08-SCA-UCHC-008. Hurley is the principal investigator, 2.5 the peer review score, excuse me. And the principal members of cognizance are Arinzeh and Madelkern.

MS. ARINZEH: Okay. This -- this proposal looks at -- it's from an established investigator that will look at different FGF fibroblast growth factor

isoforms and their potential role in human embryonic stem cell renewal. So overall they would look at -- they were characterizing the relationship between the mouse embryonic fiberglass and freshly isolated human embryonic stem cells in the context of this FGF2 production and FGF receptors. They will look at whether mice expressing these different FGF isoforms have the ability to support embryonic stem cell renewal, whether this FGF plays a critical role in cell renewal.

The reviewers comment on the fact that -- there isn't -- there isn't a large amount of effort being demonstrated here by the personnel on the project and so -- and this is established in the -- in the budget. And there also is a lack of embryonic stem cell experience of the PI so this may slow down the progress.

MS. TOWNSHEND: Your recommendation?

MS. ARINZEH: So the recommendation is no.

MS. TOWNSHEND: Is that the consensus of the group? Please move this application to the no category. Our next grant?

DR. GALVIN: Once again, I would like to call your attention to the no category. I presume that everyone has glanced at that and there are no items over there that we wish to discuss any further. There are

what, a total of 22 over there? Are we all comfortable with that they are all nos? If there's somebody who thinks there's a maybe over there or something is misplaced, speak up, otherwise we'll consider those 22 are all solid nos, six maybes and one for further discussion.

MS. TOWNSHEND: Our next grant for consideration is 08-SCA-YALE-034. Mishra is the principal investigator, 2.5 the peer review score. I will note that this application does contain proprietary information and --

VOICE: Lynn, you missed 035. Did you get any more?

MS. TOWNSHEND: I missed 035. I'm just getting ahead of myself. I apologize.

08-SCA-YSME-035. Massaro is the principal investigator, 2.5 the peer review score and Kiessling and Wallack are the members of the Committee of cognizance.

DR. KIESSLING: This is an application actually from a fellow in -- at Yale who is a hematology fellow. And this is a very interesting application in that it starts out very strong and then there's actually no experimental details. So I think that the score on this is more reflective of the mentor on this project than it is this project itself. I would have scored this

project much lower. This is an individual who has had a lot of post-doctoral experience and she's not published one paper.

So this is an interesting project. It's coming out of a very strong laboratory but this investigator needs to really develop exactly what she's going to do rather than simply describe the literature. This is a literature review.

DR. GALVIN: Ann, if I -- if I understand you correctly, earlier -- a little earlier in your conversation you indicated that perhaps the grant score was based on the mentor rather than the person who's going to do the grant?

DR. KIESSLING: Yes, this is coming from a very strong laboratory but this is not a strong application.

DR. GALVIN: Okay. Do you have something --

DR. HUANG: You meant lower?

DR. KIESSLING: Yes, I would rank -- I would actually move to not fund this. I think the score on this is more reflective of the mentor than the application itself.

DR. GALVIN: You would then give it a

higher numerical score?

DR. KIESSLING: Yes, a higher numerical.

DR. GALVIN: A higher numerical score puts the grant down lower. As you approach 5, you approach the --

VOICE: Lower is better.

DR. KIESSLING: So I would move this from a maybe category to a no.

DR. GALVIN: Okay. Do we have another reviewer?

DR. WALLACK: Yeah, I would -- I think that the strength of the lab is impressive to me. I think that the -- the review -- the reviewer of this application felt there was some value to it. I think in the translational area it has merit in the area of potential of treating leukemia. So I would put it in the maybe myself.

DR. GALVIN: With respect, I think we're -- that's reading between the lines Milt. I think we have to look at what's being presented and how it's being presented. After all, this is a qualitative and -- a quantitative, not qualitative, this is a quantitative and scientific discussion. And I think when we allow issues of the quality of the facility where the work is being

produced and the quality of the mentor rather than the quality of the grant and the -- and the grant recipient, I think we're, in my opinion, this is not a direction that I want to head and I think that Dr. Kiessling said it correctly. And once again, I don't think we can prognosticate from looking at -- at the description about, nor should we, in my opinion. I think we need to stick to generally recognized scientific and quantitative principals.

COURT REPORTER: One moment, please.

(Off the record.)

DR. KIESSLING: I wouldn't be opposed to we can discuss this again. You can put it in the maybe category if you want. It is a human ESO grant but the -- considering everything else that we have to fund, I think this is a pretty low -- low priority.

MS. TOWNSHEND: Let's place this in the maybe category. Is that the consensus of the group?

DR. KIESSLING: That's fine.

VOICE: Maybe.

MS. TOWNSHEND: Let's place this application in the maybe category. Now, if I'm tracking myself correctly, Charles, did you have something?

DR. JENNINGS: Just sort of a quick

comment. I have the dim recollection that we funded Diane Krause's lab last year. And we definitely funded them last year and I have a dim recollection that it was a somewhat related project. So I just wanted to raise that as a general issue. Are we looking at these well-known labs that are already funded by -- through last year's grants? Are we looking at overlap between projects? I don't need a response to that now but maybe when you come back to the discussion, we should look at that question. I may have just remembered the details of Diane Krause's last -- last run. But it's a general issue we should be looking at.

MS. TOWNSHEND: Now, if I'm in the right -- oh, sorry. If I'm in the right place, we're looking at 08-SCA-YALE-034. The principal investigator is Mishra, 2.4 the peer review score. Please note that there may be the consideration of proprietary information with regard to this application and Canalis and Wallack are the Committee members of cognizance.

DR. CANALIS: Do you want me to go? Mishra is going to culture human embryonic stem cell lines and --

MS. TOWNSHEND: Dr. Canalis, can you get a little bit closer to the microphone? Thank you.

DR. CANALIS: My pleasure. So Mishra is going to culture human stem cell lines which apparently are available through NIH and may be an issue of consideration. And basically she is going to or he is going to identify markers of cell differentiation, basically is going to use -- transpose on the pay system to tag proteins in these cells. And using -- using this -- these markers it then will develop ways to induce cell differentiation, once they identify specific markers that appear during differentiation.

The peer review or scientific review of the application is not recommended as a positive. Fundamentally, they question the fact that the grant is not hypothesis-driven but basically is a fishing expedition trying to identify what markers appear during the differentiation of these cell lines which are already established.

MS. TOWNSHEND: Your recommendation?

DR. CANALIS: To me they’re no. The score is 2.4.

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

VOICE: Yes.

MS. TOWNSHEND: Please move this

application to the no category.

Our next consideration is 08-SCA-UCON-053. Amano is the principal investigator, 2.35 is the peer review score and the Committee members of cognizance are Wagers and Wallack.

DR. WAGERS: Okay. So this is a grant to basically perform some proof and principal experiments in mouse cells looking at whether therapeutic cloning would be useful for the treatment of cardiovascular disease. The principal investigator is the same principal investigator as UCON-052 and large chunks of the application are exactly the same basically where they've replaced differentiation of these nuclear transfer generated cells into germ cells, now they're going to differentiate them into heart cells. They're going to use a model of LDL receptor knocked out mice and they're basically going to generate nuclear transfer ES cells from these knocked out mice, correct the deficiency in the mouse embryonic stem cells and then differentiate the repaired cells into hepatocytes.

So concerns about this are, first of all, that there's no data on how robust it will be for them to generate hepatocytes from these -- from these nuclear transferred ES cells. And interestingly and the peer

reviewer noted this, they don't propose to do any transplantation studies which one would expect would be the ultimate goal of generating a corrected line.

One issue that I had is that really this is kind of setting up a system, you know, that's amenable. They created genetic deletion and then they correct it and this is a proven concept experiment that has done before but doing it again in mice, it's not clear to me how that moves us forward where we want to go which is to correct cells generated from humans and use those. So I think that I was less enthusiastic about this grant because of that so I would put it in the no category.

MS. TOWNSHEND: Is that the consensus of the group? Please move this application to the no category.

Our next application for consideration is 08-SCA-UCHC-006. Heinen is the principal investigator, 2.25 is the peer review score, excuse me. And the Committee members of cognizance are Arinzeh and Mandelkern.

MS. ARINZEH: Okay. The investigator is going to examine effective DNA damage on human embryonic stem cells and so this has -- this has significant importance in relation to the maintenance of genetic

stability of ES cells. The post-studies will measure cell death and cell cycle pertibations following treatment with DNA damaging agents such as gamma radiation, UV radiation and acylating agents and then examine expression -- examine expression of post-translational modification and looking at cell cycle checkpoints and DNA repair proteins. And the same cells will be carried out on differentiating cells and void bodies.

So the reviewers comment on though that there was -- they had less enthusiasm for the proposal because the study design may not be informative. The long term objectives of the study were not -- were not clear.

MS. TOWNSHEND: Do you have a recommendation?

MS. ARINZEH: The recommendation would be no based on this score.

MS. TOWNSHEND: Is that the consensus of the group. Mr. Mandelkern? Is it alright to put this in the no category? I thought you had something to say. Is that the consensus of the group to place this in the no category?

DR. WAGERS: Is this 053?

VOICE: No. UCH --

MS. TOWNSHEND: This is 006 Heinan, 2.25.

DR. JENNINGS: 006 Heinan.

MS. TOWNSHEND: Are we moving this to the no category? Ann, are you all set? Okay. Please move this application to the no category.

Our next application for consideration is 08-SCA-UCHC-043. Gryk is the principal investigator, 2.25 is the peer review score and the Committee members of cognizance are Wagers and Landwirth.

DR. WAGERS: Okay. So this is a grant that is focused largely on bioinformatic analysis of existing data about the expression of receptors on embryonic stem cells. So what the investigators are going to do is to take existing databases that are already available, compile them into a Connecticut stem cell database website that they will provide to investigators and then they'll teach a number of seminars and training workshops around the state in order to help people use that database.

So the reviewers commented that this could be a useful thing, although it is not an innovative proposal. An issue that I don't think it was well discussed is exactly how conflicts in the data will be dealt with in that if you take a large number of expression data sets from a large number of different

investigators, you will likely find areas that don't agree and what data quality filters would be put in there, how you would resolve such conflicts in the data, how the complex biology of the embryonic stem cells would be reflected in a way that made this a useful compendium.

It's also a concern that oftentimes the expression of MRNAs does not correlate well with the expression of proteins or with their activity. And so there is in some ways a limited amount of information that one can gain from this -- this kind of profiling. It's really a hypothesis generating a type of resource that then would have to be -- would only be useful in as far as people could mine it easily and effectively and then utilize that.

And so it's not fair, especially with the seed grant mechanism, the longevity of such a database, you know, once the funding would end, how would this be sustained. And so, so I think it -- while it is an interesting idea, there are some concerns with the strategy for setting it up and also for -- for maintaining it and how well it would be utilized. So I would -- I would put it in the no category.

MR. MANDELKERN: Can I comment to that?

MS. TOWNSHEND: Yes, sir.

MR. MANDELKERN: I'd put -- at least put it in the maybe category. It seems to me -- I'm not able to comment on the technical aspects of the database but it seems to me that the reviewers gave it pretty high -- pretty high marks in terms of the -- the qualification of the investigators and the importance in the design of the project. They did have something to say something about the budget which they thought was excessive and that brings up the question of whether we have the flexibility to deal with budget negotiations on the second round of discussions. I'd make a determination on the merit at this round.

MS. TOWNSHEND: So is it the will of the group to move this to the maybe category? Please move this application to the maybe category.

Our next grant for consideration -- grant application for consideration is 08-SCA-UCHC-037. Li is the principal investigator, 2.2 is the peer review score, Kiessling and Landwirth are the Committee members of cognizance.

DR. KIESSLING: This is -- oops, I'm sorry. This is an interesting application from an investigator who is actually already well -- pretty well funded by this program who wants to move from their area

of expertise into cancer stem cells. And the -- I've agreed with the criticisms of the reviewers on this application in that the biggest problem was they show very little experience or understanding of the nuances of cancer stem cells.

It isn't clear why they want to move in that direction. I can't decide whether they're simply trying to broaden their base, but they're pretty well funded already and this application shows a lot of holes in terms of what they understand about cancer stem cells. So I would actually move to at least leave this in the maybe, if not, move it to the no.

DR. LANDWIRTH: Why would you, excuse me. Why would you want to consider something that has holes in the science?

DR. KIESSLING: Because it's a human embryonic stem cell application.

DR. LANDWIRTH: Okay, but I -- if I had my eyes closed and was looking the other way and I heard what you just said, I'd deep six it, as they say. But --

DR. KIESSLING: There is some -- I mean there is some strong points in this application and it is a human embryonic stem cell application, so if anybody else wanted to -- to consider this further later on, I

would be happy to do that.

DR. GALVIN: Let me ask you if you think this is a question of not properly presenting the grant or is it a deficit in basic knowledge?

DR. KIESSLING: It's a question -- it's a question of an investigator moving into a new field and, of course, that's what seed grants are for. This investigator has expertise in another field. They want to move into cancer stem cells. So -- so their cancer stem cell review here is just a -- when they discuss it, it's a bunch of review articles. They've not had any real experience. They would be advised to get someone with experience and expertise in that area to help them. But that's what the seed grant mechanism is for. This is an established investigator trying to move into a new area. So I mean it's worthy of more consideration if anybody else liked this grant --

DR. GALVIN: I understand.

DR. KIESSLING: -- better than I did.

DR. GALVIN: Maybe?

DR. KIESSLING: This could go in a maybe.

DR. GALVIN: Okay.

MS. TOWNSHEND: Please move this grant application to the maybe category.

Our next grant for consideration is 08-SCA-UCHC-015. Martins-Taylor is the principal investigator, 2.2 is the peer review score and the Committee members of cognizance are Huang and Mandelkern.

DR. HUANG: Okay. This is a proposal that deals with DNA methylation and there's two -- two specific aims. The first is to look at the sub-cellular localization of DNA methylation factors. And the second is to do Chromatin immunoprecipitation on ChIP assays to systematically look through many different human promoters and look at DNA methylation.

So this was scored at a 2.2. Even though the project is of significance, it is somewhat exploratory in the sense that there is a systematic categorization of the Chromatin immunoprecipitation. And there was also concerns that the preliminary data showing that the sub-cellular localization studies could be done in a high enough resolution was not presented.

So I would recommend that this go into the no category.

MS. TOWNSHEND: Is that the consensus of the group? Please move this grant application to the no category.

The next application up for consideration

is 08-SCA-UCHC-033. Choudhary is the principal investigator, 2.1 is the peer review score and the Committee members of cognizance are Kiessling and Landwirth.

DR. KIESSLING: This is actually an interesting -- let me -- let me look at my notes here for just a minute but I think this is one of the grants I really liked. This is an interesting application to study an eye disease, which we don't -- this is a very disease-specific application. And they're proposing to use various methods to derive -- to tease embryonic stem cells into what they call tribecular -- I actually learned a lot reading this grant so maybe that's why I was impressed by it. But it's a glaucoma-related application and it's very well written.

The reviewers liked it. I'm surprised the reviewers didn't give it a slightly higher score. They had some technical -- some problems with technique. But this is a very well thought out application by a young investigator and I think that this should go if not in the maybe, in the yes category.

MS. TOWNSHEND: I'm actually looking for guidance from the group. Should this go in the yes category or the maybe category?

MR. MANDELKERN: If I may?

MS. TOWNSHEND: Yes, sir.

MR. MANDELKERN: I think it should go into the maybe category.

COURT REPORTER: I'm sorry, you --

MS. TOWNSHEND: Mr. Mandelkern, could you speak right into the mic? Thank you.

MR. MANDELKERN: If I might put my comment, not on the science but on the mechanics that we should possibly put this in the maybe because there are a series of reviews -- of applications, I beg your pardon, with lower scores and better ranks that might possibly first go into the yes. So if you might accept the recommendation to put this into the maybe so as not to eliminate many lower ranking -- there are at least ten seed grant applications which score 2 to 1.5. So my recommendation is maybe.

DR. KIESSLING: That -- that's fine.

MS. TOWNSHEND: Is it the consensus of the group to move this to the maybe category?

DR. JENNINGS: Mr. Chairman, if I may ask it? Could you just remind the group the approximate number of seed grants that we expect to pass because I think it might be helpful even at this early stage?

DR. GALVIN: We could fund up to $2 million.

DR. JENNINGS: That would be up to ten -- up to ten grants of $200,000.

MR. WOLLSCHLAGER: But if I may, Mr. Chair, it's by the amount of money, not by the numbers because we do have some capacity to -- to partially fund. The total amount of money is up to $2 million.

DR. JENNINGS: I wasn't looking for an absolute number but just a ballpark.

DR. GALVIN: So ten would be a reasonable but we may want to -- if we have 12 that are really outstanding, we may want to do something with the dollar amounts. But I think that's a very good working hypothesis that we're going to fund roughly ten give -- give or take another two. Yes, Mr. Mandelkern?

MR. MANDELKERN: Dr. Galvin, Dr. Jennings, I think as Henry would probably point out to us momentarily, the RFP says specifically that we will fund at least ten percent of the funds which means that there is a floor on seed grants at ten percent which is $1 million or five, but there is no ceiling. I think Dr. Galvin -- Dr. Galvin, my pill box, excuse me, Dr. Galvin has put forward a reasonable hypothesis but we should pay

attention to RFP which specifically says there is a floor but no ceiling on seed grants.

DR. GALVIN: I think that's a well taken --

COURT REPORTER: Mr. Chairman, if you would please bring that -- yeah, bring that up.

DR. GALVIN: I think that's a well taken comment and I think that what you're speaking about is there going to be an evolution on how we do these grants and disburse these funds once the cores have been and the larger grants that have been established and what is the relationship between funding seed grants and bringing people into Connecticut etc., etc.

So as we discuss some of the maybes, we will probably be moving at what -- what is our policy and is our policy just to do human embryonic cells, mouse cells and the like. So in addition to doing the grants, we're also evolving the -- the process of what it is that we're looking for and what it is we're concentrating on. And that will give me a better understanding of what to communicate to the elected -- the popularly elected officials who will make decisions on -- eventually at some point in time on where this program will go or not go. Thank you.

MR. SALTON: If -- if I may, Commissioner? Mr. Mandelkern is correct that the RFP only puts a floor of ten percent of at $10 million, or slightly less than $10 million dollars. I just want the record to be clear that there is no $2 million dollar cap and the Committee should not be guided by or make decisions at this point in time on the basis that there's a $2 million cap on funds. That -- that's not a rule that applies in this process.

Now, it may be that at some point in time the Committee as part of its deliberations needs to sort among the categories that are valid funding categories and decide where you want to allocate money overall. But that's a process we haven't reached yet.

DR. GALVIN: I think that Henry says it very well. I think that once again we are evolving what we're going to -- what we're going to do and we certainly don't want to be locked into, you know, ten of these, three of these and four and a half of those. But that part of our discussion will -- will be part of our evolution as a Committee and as a scientifically based organization.

At this time, unless there are any further comments that need to be made, I think it would be a good time to take a break I believe.

MS. TOWNSHEND: We do need to clarify that application 08-SCA-UCHC-033 is going into the maybe category. Is that the consensus of the --

DR. KIESSLING: We're fine, that's fine.

MS. TOWNSHEND: Please move that to the maybe category and we will now take a 15 minute break. Thank you.

(Off the record.)

VOICE: So what do we do with?

MS. TOWNSHEND: Which one sir?

VOICE: 020 Crocker, 2.7.

VOICE: That's a maybe.

VOICE: That's a maybe?

MS. TOWNSHEND: I would have to look up there. I've only been checking them off as I've called them.

The next application is 08-SCA-YALE 031. Qiu is -- oh, Qiu is the principal investigator, 2.1 is the peer review score. This does contain proprietary information in the event we need to have the Committee go into executive session. And our Committee members of cognizance are Canalis and Wallack.

DR. CANALIS: You really want me to go? I'll go, but. So basically Qiu is going to induce the

differentiation of the embryonic stem cells towards the hematolytic lineage and he's going to optimize ways to induce the cell differentiation and selection procedure. So that is probably one of the -- that is -- that is the strength of the -- of the grant proposal.

The second aim is to determine whether or not two signals are activated. One is the Notch signaling pathway and the other one is the WNT signaling pathway. And the assumption is that Notch is activated during this hematolytic cell differentiation and that WNT is not. And he's going to use conventional methods to determine -- to determine the involvement of these two signals.

The peer -- the scientific review is non-committal. They don't say much pro or against the application. I had minor concerns regarding the way that the investigator is going to approach the Notch signaling pathway. He's going to use one of the Notch logins which is jagged but he's going to use it in a soluble form. And in that form usually jagged inhibits the not induced Notch. But other than that, you know, I thought that the proposal had a degree of interest.

MS. TOWNSHEND: Your recommendation?

DR. CANALIS: Maybe.

MS. TOWNSHEND: Is that the consensus of

the group? Please move this application to the maybe category.

Our next grant for consideration is 08-SCA-YSME-011. Sasaki, 2.1 is the peer review score and the Committee members of cognizance are Huang and Mandelkern.

DR. HUANG: This is a proposal that deals with the issue of spinal cord injury. And the idea is to use neurospheres which are derived from human embryonic stem cells and then to put the neurospheres into the spinal cord and to assess the function of the brain upstream from that innovation.

The peer review thought that this was a strong proposal, that the clinical relevance is very, very high and the principal investigator is a qualified physician and scientist. However, there was some -- also concerns about lack of experience with human ES cells and potential complications of the animal model with the human cells.

Overall, I think we would put this in the -- Mr. Mandelkern and I would put this in the maybe category.

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

VOICE: Yes.

MS. TOWNSHEND: Please place this application in the maybe category.

DR. JENNINGS: Mr. Chairman, if -- if I may? I can see that we're on course to generate a rather large maybe category in which we're pooling those things that are maybe and probably quite promising and things that are maybe that are almost certainly not. And I just wonder if there's some way that we can separate them into the more or less promising maybes, I think that might reduce our work later on. I see we already have a shelf. I just offer that as a possible procedural suggestion.

DR. GALVIN: I'm having a little difficulty myself. Everything is ending up over in maybe and I'm not sure whether we maybe we should have started with the low numbers and worked to the high numbers, but. Charles, what was your -- what was your proposition?

DR. JENNINGS: My specific proposition is to subdivide the maybes into a serious -- not serious contenders, but the high maybes and the low maybes. Because most of the early maybes, I think, we're likely nos, but I'm starting to see some that might be serious contenders.

DR. GALVIN: Yes, Bob?

MR. MANDELKERN: Dr. Jennings, I'd like to

call to your attention that we are at the point where we have 12 seed grant proposals out of 50 to consider. I don't think we should at this moment go back and reconsider maybes. Let us proceed with the next 12 because I think the next 12 might clarify a great deal of our work. I think to divert now to do a discrimination on the maybes would cost us a great deal of time.

DR. GALVIN: You can't -- you can't do that. We'd have to go back and start all over again.

DR. JENNINGS: I withdraw the --

DR. GALVIN: It's a good idea for next time but you know --

DR. JENNINGS: Yeah.

DR. GALVIN: -- we're -- we're sort of getting into a grading process here. You know this is kind of like taking pass/fail to high pass, low/fail, fail/fail and sort of pass.

DR. JENNINGS: Right.

DR. GALVIN: And we need to figure out how we're going to do this procedurally or else we'll be doing AA, A minus, B plus, B and we'll have a --

DR. JENNINGS: Mr. Chairman, I'll withdraw the suggestion. I can see how it would --

MS. TOWNSHEND: So 011 is in the maybe

category.

The next grant for consideration is 08-SCA-UCON-002. Wang is the principal investigator, 2.1 is the peer review score and the Committee members of cognizance are Arinzeh and Fishbone.

MS. ARINZEH: Okay. The -- the investigator's plan to develop a hybrid of peptide and SIRNA to allow efficient knockdown of gene expression in the cytoplasm as well as in the nucleus of human embryonic stem cells. So it's a novel method of trying to get transvection. And let me just see, okay.

So overall the reviewers thought it was a good proposal and that it was novel work. The concerns were however that there weren't appropriate comparisons with traditional methods such as your standard vital vector method. And the peptide -- I would say more concerning is that the peptide approach was not investigated or is not planned to be investigated long term to determine if it's effective. And when I looked through the proposal I did not see any preliminary data establishing that they could actually do this other than just synthesis of this -- of the peptide hybrid construct.

So it's novel work, but I can see the score was valid so obviously no.

DR. GALVIN: Second reviewer?

DR. FISHBONE: Yes, it seemed like it was an interesting proposal that the reviewers liked with a couple of caveats that were mentioned. My one concern, and I'm not sure if it's appropriate to bring it up but I'll do it, Dr. Wang has three applications in. Each have identical budgets, you know, to the penny. And I am wondering whether he will be able, you know, whether this is an attempt to put in three in order to get some or will he be able to do the work on three simultaneous but different subjects.

DR. GALVIN: Are we quite sure that this is the same Wang --

DR. FISHBONE: Yes, they're the same bio in each three. There is another Wang who is much lower down in the list who is at Yale. I am pretty certain this is the same Dr. Wang at UCONN.

DR. GALVIN: The question being that if your estimates tell you that 25 percent of your grants will be funded and you only submit 25, and you'll get six. Does that mean if you submit 100, you'll get 25? And that's an interesting question to -- to consider. I wonder if any of the other members have. I think, Gerry, what I understand you're saying is this is one individual

applying for three distinct and unrelated grants?

DR. FISHBONE: Yes, they are distinctive and unrelated.

DR. GALVIN: Okay, so we -- so maybe it's one individual who has three wonderful ideas or one wonderful idea split into three. But at any rate, I think we have to consider them on -- on an individual basis. But I do share your -- your comments and I am concerned about if it's a proportion -- if you consider a proportion of your requests are going to be funded, are you not better off to have a larger pool to draw the proportion from? I don't think that's really correct. That's just me. Any further comments on this particular -- particular grant? I hear that there is some difficulties with the -- it seems to be with the intent and with the science.

MS. ARINZEH: Yeah, I think there's some criticism of the science.

DR. GALVIN: Thank you. Well, we have -- I believe that you're recommending we not fund it?

MS. ARINZEH: I recommend we not fund it.

DR. GALVIN: Okay. And --

MR. MANDELKERN: What's the recommendation?

DR. GALVIN: No. The original

recommendation is no. Gerry?

DR. FISHBONE: I -- I would say no.

DR. GALVIN: Okay, is that the feeling and the consensus of the group? If so, we will remove UCON grant is that O -- I can't quite -- 002 and that's going -- everybody understands where that's going? That's going from been discussed, it's going over into the nos. You alright with that? Okay?

Next grant is 023-UCHC and I can't quite make out the name of the -- Witola. Who are the reviewers? Charles?

DR. JENNINGS: I'm one of them and I'm happy to summarize.

DR. GALVIN: Okay, would you summarize, please?

DR. JENNINGS: Could we just clarify? My understanding is that Witola who is the original PI is leaving UCONN. Can we clarify that this is still on the table and Mamoun is now the P -- the new PI, is that correct?

VOICE: That is correct.

DR. JENNINGS: Thanks. So the aim here is to --

DR. GALVIN: Excuse me, Charles. We all

understand that the name on the grant is not the name of the individual who is the potential grantee. But, okay? Here we go.

DR. JENNINGS: So I quite liked this. They are studying malaria and the idea here since the malaria parasite after it is injected into your bloodstream by the mosquito it goes to the liver and it -- it's life cycle is in the hepatacytes. And so they are proposing to turn human embryonic stem cells into hepatacytes in order to have a good culture system for this particular phase of the malaria parasitic life cycle which apparently is something that doesn't currently exist. And that seemed like quite a reasonable suggestion to me and I think also to the reviewers. And the comment here is overall this is the bottom line comment is overall this is an ideal project for a committed post-doctoral fellow who has a bright future in scientific research.

Now, Witola himself had a good track record I thought. His track record is now completely moot since he's not going to be the PI on this -- this grant. So I think it will come down to whether somebody else in Dr. Mamoun's lab is going to take the lead on this. And the conversion of human embryonic stem cells into hepatacytes is a major door for many different groups for many

different reasons, toxicology models, for example. So whether -- whether they can do it, I think we don't know and I don't believe they provided preliminary data on -- on how to do it. But there are so many groups working towards that goal it seems likely that it will be -- will become feasible. And I've never heard of anybody else making hepatocytes from ES cells specifically in order to study malaria.

They'd then have some specific hypothesis -- and what are they doing here? They wanted to look at something to do with the role of (indiscernible). They have a specific hypothesis about the mechanism of entry of the parasite into hepatocytes which -- which all seemed reasonable.

So I was very favorable to this. I think I'm echoing the reviewers and I would -- if you have the top of a maybe category, I would put -- put it there and what we have in the yes category, those two and nothing yet and we might want to comment on that.

DR. GALVIN: We had some -- Ms. Hartley had some additional information on the replacement individual who would be the primary investigator.

MS. PAMELA HARTLEY: Well, I think -- I think that what you stated was accurate. We received

correspondence from the sponsor, Choukri Ben Mamoun indicating that on March 30th the PI, Witola, I guess that was yesterday, left UCONN Health Center. And in the correspondence memo it indicates that he would like to suggest a new post-doctoral fellow. However, I don't believe that has happened. So he will be assuming the role of PI -- Dr. Mamoun.

DR. JENNINGS: My enthusiasm for it will be reduced if we -- if we don't have an identified person who's going to take the lead on the project and who's biography we can examine. We're going to just look again at the budget. The budget calls for 100 percent contribution from Witola who is no longer here. It doesn't -- as far as I can see, it does not have any specific component for Dr. Mamoun. So what we're talking about here is a revised proposal in which 100 percent of the effort is coming from an unidentified individual and zero percent is coming from the person who -- who is now the PI in the absence of an identified individual. So I'm not very comfortable with that. But others may feel differently. Or it may be that they have somebody that -- you said that they've not --

MS. HARTLEY: Our understanding is that Mamoun would serve as PI.

DR. JENNINGS: But it's not -- I don't believe that. In a sense, I don't believe that Mamoun will be putting 100 percent effort onto this project. He may be the PI but he will not be the person doing the work and we don't know who is going to be doing the work and the original plan was 100 percent of the work will be done by somebody who's no longer -- no longer there.

DR. GALVIN: I think your points are very well taken. The -- I really don't want to get down the path of funding an institution rather than an individual particularly on a seed grant. And no matter how good the institution's track record is -- who is your second reviewer on this case, Charles?

DR. GENEL: I wouldn't fund this. I mean the --

DR. GALVIN: Would or would not?

DR. GENEL: I would not. The peer review says this is an ideal project for a committed post-doctoral fellow who has a bright future in scientific research and we don't know who that is at the moment. We have a lot of competition -- a lot of good competition. I wouldn't fund this.

DR. GALVIN: Amy?

DR. WAGERS: I was just going to say is I

have -- I'm uncomfortable with going forward with this application if the PI of the application is no longer going to be the PI of the application. So just -- it seems to me, it should be withdrawn and resubmitted next year with the person who is going to do the work.

Presumably, Witola wrote this application, developed the ideas, and then to give that over to someone else, it just -- I'm uncomfortable with that when we don't know who that person is.

DR. GALVIN: Once again, that would mean we'd be funding the institution on a -- on a guesstimate on who might be the primary investigator.

DR. JENNINGS: So, Mr. Chairman, I'm going to recommend that we not consider this and as a side comment that we invite them to come back next year if they have a post-doctorate that's going to take the lead on it.

DR. GALVIN: That's reasonable. And certainly things with malaria are very important. More people die from malaria in the world than of any other infectious disease. Is it the will of the group that we take -- put this in a no and with some suggestion of a reconsideration in 20 -- 2009?

Move it -- that's grant number 023 and that goes from -- goes into the no category. Does everybody

understand what we're doing?

VOICES: Yes.

COURT REPORTER: One moment, please.

(Off the record.)

MS. TOWNSHEND: Moving onward, consideration of grant 08-SCA-YALE-019. Ivanova is the principal investigator, 1.9 is the peer review score and the Committee members of cognizance are Canalis and Fishbone.

DR. CANALIS: Alright, so what the investigator is going to do is he's going to extend prior experience into human stem cell research. And basically she is going to take undifferentiated stem cells, she's going to induce cell differentiation and is going to do gene profiling. And then what she's going to do in the second set of experiments, she's going to silence genes that are expressed early on in the differentiation stage of the cells using a lentavirus approach. So by knocking down the virus -- by knocking down the genes, she is going to induce cell maturation. And she's going to use the gene knock down at various stages of cell differentiation so she'll be able to identify what genes have cell differentiation at various stages.

The application, you know, had very good

scientific review and it is someone who is currently an Assistant Professor at Yale and has the appropriate experience to conduct the work. I really found I would be very much in favor of supporting this application.

DR. GALVIN: Thank you, Dr. Canalis. A second reviewer?

DR. FISHBONE: That's me and I would agree.

DR. GALVIN: Okay.

MS. TOWNSHEND: Are we moving this to?

DR. GALVIN: Wait a minute, whoa, whoa. Comments from the group? Are you all comfortable in moving it from where it is to a yes?

VOICES: Yes.

VOICE: It is very well done.

MS. TOWNSHEND: Next application for consideration is 08-SCA-UCON-040. Carter is the principal investigator, peer review score 1.85 and the Committee members of cognizance are Kiessling and Landwirth.

DR. KIESSLING: This -- this -- I really liked this grant.

MS. TOWNSHEND: Do you have a microphone? Thank you.

DR. KIESSLING: Sorry. I really liked

this grant application. This is a really good example of a young investigator moving from the mouse to human ES cells. He's got extensive experience with gene re-analysis and gene analysis and they now want to look in human embryonic stem cells for a number of transcription factors that might play the same role. He's particularly focused on one level of development of mouse embryos. He has described self-transcription factors that are stage-specific and they are also expressed spuriously in mouse cells and he now wants to apply that technology to human embryonic stem cells.

So he has a very good track record. He came -- he's really well trained with the National Institute of Aging, that whole group that developed all the mouse genoming. So this is an excellent seed application from a young investigator. It's just a beautifully written grant. So I would definitely like to put this in the yes category.

DR. GALVIN: Second reviewer concur?

DR. LANDWIRTH: Just the comment that the reviewers felt similarly. They gave it very high ratings.

DR. GALVIN: Committee, comments?

DR. GENEL: My question is -- I didn't read the grants closely, but the one just above that is

the same investigator. It also has a laudable -- a laudable review. Are we going to fund two?

DR. GALVIN: We don't know.

DR. KIESSLING: Let -- if this is --

DR. GALVIN: We're taking -- we're taking them one at a time on -- on the merits. I believe conceivably we could fund ten from one individual but we have to consider this one on the merits.

DR. FISHBONE: Could I ask a point of information? Is this the same gentleman who became the PI on Dr. Yang's grant from last year?

DR. GALVIN: Yes.

DR. KIESSLING: Yes.

MR. SALTON: Commissioner, one of the factors for the Committee to consider is the ability to perform the research. And so if you have an applicant who has said I'm going to put in 75 percent of my full time FTE on one project and 75 percent FTE on a second project and 75 percent on a third project, then that would weigh in on the individual application. At some point the Committee has to say we're not assuming someone's working 100 hours a week. So an ability to perform is an individual factor for each individual application.

So I don't know, for example, if Professor

Carter, Dr. Carter is saying this is something I'm going to work on half time and my second project I'm going to work on half time so I can cover both projects. That's something -- I don't have the knowledge of the individual applications but that the Committee should consider.

DR. GALVIN: That -- that being said, I think we need to consider them one -- one at a time. I don't know how I could -- could we possibly sort -- are we going to start sorting out everything by investigator and deciding how much he or she can do? I think we need to look at one grant and then make a consideration. Certainly the point raised is very valid that -- how -- how thin can one person stretch his talents. But I don't know how I would evaluate it to take two or three grants from the same individual and try to figure out which one I should fund and which one I shouldn't.

So my point was I think we should take them one at a time. That's a very Russian point of view. Americans like to link things, Russian's don't -- a very Soviet Russian.

DR. JENNINGS: A European compromise would be when we come back to re-review them maybe we should look at the ones from the same investigator in consecutive order so that we have them all in our minds this way.

DR. GALVIN: I think now -- are you saying we need -- we need to put that in a maybe or put it into a yes and then potentially move it back into a maybe?

DR. JENNINGS: I guess I would say whichever category it goes into both of them should travel together so they're both examined together since, on the face of it, they look like they may be related and --

DR. GALVIN: Well, I think that would mean you'd have to put them into a maybe.

MR. MANDELKERN: What's the recommendation from the -- the Committee?

COURT REPORTER: Mr. Mandelkern, do you have a microphone?

DR. KIESSLING: My recommendation is yes but I doubt if we're going to fund all the yeses.

DR. GALVIN: Alright, where -- where would you like to put this?

DR. KIESSLING: I would like to put this in a yes category. This is an excellent grant.

DR. GALVIN: Put it in the yes category.

VOICE: We can always through it out --

DR. GALVIN: Next grant is --

MS. TOWNSHEND: Next grant for consideration is 08-SCA-UCON-056. Carter is the principal

investigator, peer review scored at 1.75 and the Committee members of cognizance are Wagers and Wallack.

DR. WAGERS: So as we already discussed, this is a second grant application from the same PI as the previous application. Unlike -- I didn't read the previous application, but this one at least was not as compelling. It aims to do global epigenetic profiling from mouse embryos and human embryonic stem cells and then compare them. But the description of the project is -- is very superficial. It's very unclear how he will assess conservation of epigenetic modifications, what kind of statistical analysis will be used, how he's going to compile this information and exactly which markers he's going to examine.

And so it really, perhaps, because he was putting a lot of effort into the other proposal, it wasn't a well developed idea. It wasn't really clear what the deliverables were going to be out of this. So actually I would -- I would put this in the no category which may clear up some of our other issues as well.

DR. GALVIN: Second reviewer? Second reviewer? Is that you Dr. Wallack?

DR. WALLACK: Yes, I really wouldn't substantially disagree with Amy except that, and I don't

know the science part of it, the peer reviewers did give it a 1.75.

DR. GALVIN: I can see some logical inconsistencies with the way that Dr. Wagers has described it.

DR. WALLACK: Which I wouldn't disagree with. I'm not sure if I would just throw it out yet. I think I might be more comfortable putting it in the maybe for now. But I certainly wouldn't be strongly opposed to somebody saying well, I want to put it in the no.

DR. GALVIN: How much of Dr. Carter's -- is it Dr. Carter who's this? How much of his time is to be devoted to this particular project? Do we know that?

DR. KIESSLING: Over 2.4 calendar months a year.

DR. GALVIN: Okay, so that's a quarter of his time would we agree?

DR. JENNINGS: No, it's 20 percent.

DR. WALLACK: So.

DR. GALVIN: Okay, so twenty percent of his time on this grant. Okay. Do you want to move it over to -- there is a difference of opinion as to whether this should be a no or a maybe.

DR. KIESSLING: I -- I haven't read this

as thoroughly but I sort of agree with Amy. This looks like a -- more like a fishing expedition than his other grant in which he was focused on really specific genes. This is just -- what he's doing here is just something he knows how to do because he's done it a lot.

DR. GALVIN: I think that's certainly a valid comment. It dovetails with what Dr. Wagers says. So what is the opinion of the group?

VOICE: No.

DR. GALVIN: No? Any demurs? That grant it -- it goes to the no category. It's UCON-056.

MS. TOWNSHEND: Next grant for consideration is 08-SCA-YALE-036. Wang is the principal investigator, 1.75 is the peer review score. Please note that this does contain proprietary information if during consideration there needs to be executive session. And the members of cognizance of Kiessling and Wallack.

DR. GALVIN: Would you care to comment, Dr. Wallack?

DR. WALLACK: I'm going to defer to Ann.

DR. KIESSLING: I have to find my notes, sorry. Do you want to go on to the next grant?

DR. GALVIN: We'll move on to the next grant.

MS. TOWNSHEND: Okay, 08-SCA-YALE-022. Breunig is the principal investigator, 1.75 is the peer review score and the Committee members of cognizance are Canalis and Fishbone.

DR. CANALIS: Shall I take it, Gerry?

DR. FISHBONE: Yeah, I just have to get to where --

COURT REPORTER: Are you on a microphone? I'm sorry, sir, you need to be on a microphone. Could you pass that down to him?

DR. GALVIN: Do we have enough information to consider the grant that's off to the left side there? Yes, no?

DR. CANALIS: Do you want me to run?

DR. GALVIN: Okay, go ahead. Which review Dr. Canalis? I've confused things. I will allow you in your great wisdom and charm to straighten it out.

DR. CANALIS: If Dr. Fishbone wants to -- prefers to wait.

DR. FISHBONE: Yes. Oh.

DR. CANALIS: You prefer to wait? That's --

DR. FISHBONE: No, I have it. I have it here now.

MS. TOWNSHEND: And this is --

DR. CANALIS: Do you want me to go ahead or?

MS. TOWNSHEND: -- 036 or 022?

DR. CANALIS: 022 Breunig.

MS. TOWNSHEND: Thank you.

DR. GALVIN: Okay, Pamela, would you mind putting that grant off to the left so we all know which one we're talking about. This is the one we're talking about now, is that correct, Dr. Wang's grant?

MS. TOWNSHEND: No, Dr. Breunig's.

DR. GALVIN: We're talking about Breunig's -- about Breunig's grant and the number is 022 and it's a Yale grant.

MS. TOWNSHEND: Correct.

DR. GALVIN: Okay.

DR. FISHBONE: This is a study of a substance called Notch which is known to be able to maintain the neuronal stem or progenerative cells by blocking their differentiation so it maintains their state in -- their stem cell state or genitive state.

In this proposal, she is testing a hypothesis whether Notch is able to promote a conversion of human embryonic stem cells into neural stem or

progenerative cells achieving the goal of robust induction of neuronal-producing cells from stem cells. And the reviewers say that if this goal can be achieved, it will provide an insight into induction of embryonic stem cell differentiation and the impact on clinical treatment of neuronal degenerative diseases would be very important.

So I think they liked this project. A very bright young scientist dedicated to translation of basic research into clinical treatment of human neuronal diseases. He's one of the pioneers in improving the culture condition of mouse neuronal cells by manipulation of Notch. So he's in a very good lab, a very good researcher and they really like this. So my recommendation would be to fund this.

DR. GALVIN: Okay, I -- I lost a point there. I didn't quite see how this substance relates to human embryonic stem cells.

DR. FISHBONE: Good question. Let me just.

DR. JENNINGS: It's a suspected regulatory differentiation.

DR. CANALIS: I do not quite fully agree, sir. Do you want to wait for your -- my comments on the grant or?

DR. GALVIN: Okay, so go ahead.

DR. CANALIS: The Notch is a trans-membrane receptor and the fundamental problem I have is that the impact of Notch and Notch target genes such as this on neuronal cell differentiation have been examined by various Japanese groups including Kaliyama so. The fundamental issue I have is the novelty of the grant is -- is modest.

The -- the other issue that I also have is that this is a first year post-doctoral fellow. So I think we need to look at also, you know, whether first year post-docs should -- should qualify for this type of grant.

From a scientific point of view, the approach -- it's -- probably the better approach is to -- to look at Notch impact. He's looking, he/she, whatever is looking at Notch intercellular domain expression for -- for gain of function which is appropriate. But for loss of function, they're using dominant negative mastermind and the Notch receptors can be cloned and probably flox Notch receptors exist. There are probably other ways that you could delete Notch instead of using a dominant negative approach through the vector that is probably short-lived.

And I mean I think I would settle for a maybe. I think Notch is a very interesting signal. My major concern is that much of the work has been done, you know, and it is not quoted in the application.

But --

DR. GALVIN: Say that again, please.

DR. CANALIS: Much of the work on Notch and neuronal cell differentiation has been done and it is not quoted in the application.

DR. GALVIN: That makes me uncomfortable, Dr. Canalis.

DR. CANALIS: But that is okay. It may be lack of knowledge, you know. I don't want to be totally negative but a yes was a little bit too enthusiastic for me.

DR. GALVIN: I have some questions.

DR. CANALIS: Yep.

DR. GALVIN: I'm -- I'm -- if this money were coming out of my pocket --

DR. CANALIS: Please.

DR. GALVIN: -- I wouldn't be too happy with a lack of knowledge, but that's just me.

MR. MANDELKERN: There seems to be a slight difference of opinion between the two

collaborators.

DR. GALVIN: It's a maybe.

MR. MANDELKERN: I would like to support Dr. Fishbone's position because in looking at this proposal, it ranks -- with a score of 1.75 it ranks fifth among 50 grant proposals. And I don't think we should be in the position of redoing the scientific work of peer review.

VOICE: That's not what I'm doing.

MR. MANDELKERN: I think in applying the Connecticut standards to this proposal, it is outstanding because of the objectives that we want to do to encourage human embryonic stem research across collaboration and talking that it might move forward quite quickly to a higher level of investigation. So I would support Dr. Fishbone in his recommendation for a yes on this proposal.

DR. GALVIN: I'm going to move it to a maybe.

DR. CANALIS: One comment? I'm not trying to do the science again but I think -- I don't think it would be a service to this Committee if you know that the work has been carried out not to mention it.

DR. GALVIN: The work's been done.

DR. CANALIS: That is not doing the

science, again, is knowing the science. In the future if you prefer me not to make the comments if I'm aware about scientific advances already being made, in that case, we need to make that rule and we will not make those comments.

DR. GALVIN: I need -- I need to hear those comments.

DR. CANALIS: I need guidance here.

DR. GALVIN: This is supposed to be seed grants, not grants to do work that's already been done before. And if the group would like to put it in maybe, go ahead.

DR. CANALIS: I would vote for a maybe.

DR. FISHBONE: I would like to agree with Dr. Canalis because I do not have any personal knowledge of Notch. I'm just going on what the reviewers said. That he clearly has knowledge of the subject and I would absolutely defer my recommendation to his.

DR. GALVIN: Well, both our reviewers at present have said put it in the maybe. Put it in the maybe.

VOICE: Put in the maybe.

MS. TOWNSHEND: Are we going back to consider YALE-036? Are we ready for that? The

application is 08-SCA-YALE-036. Wang is the principal investigator, 1.75 is the peer review score. And I believe this is also one that does contain proprietary information. The members of cognizance are Kiessling and Wallack.

DR. KIESSLING: This is -- this is an interesting application. This is actually a very exciting new field, an application on something called piRNA which are very tiny, tiny RNAs that have their own special protein binding. And this investigator actually is -- did a Ph.D. at UCONN and I don't know if it's a he or a she but they stayed on there and did a post-doc. And they've now recently just been recruited to Dr. Lindsley at the laboratory at Yale to the stem cell laboratory.

So one of the big -- this is -- this is very exciting science. There's two big concerns I have about this. One is the work -- the budget is only going to pay for one person to do all of this work so it's got to pay for this person's salary and supplies, that's it. It's a very ambitious grant and for one person to think that you could -- how much you could get this done in two years is a lot.

And, secondly, one of their -- one of the aims depends entirely upon being able to develop a new

antibody with no particular information about whether that's going to work or not. So this is a really overly ambitious project for a single investigator to do. On the other hand, it's a very exciting field. They're going to do it in human embryonic stem cells and they are pioneers in this particular area of investigation. So in some ways it's perfect. It's a perfect grant application for a seed grant. But I'd like to put it in a maybe because I think this -- we should come back to this grant and see if we actually think this is feasible.

DR. GALVIN: Okay, this is a one person grant?

DR. KIESSLING: Yes.

DR. GALVIN: Okay, so that's one person working all their time on the grant?

DR. KIESSLING: Yes.

DR. GALVIN: Okay. Is that person the same person as the one who's over in that maybe? Is that the same Dr. Wang?

DR. KIESSLING: No, this is --

DR. GALVIN: It's a different one?

DR. KIESSLING: This is the Yale Wang.

DR. GALVIN: Okay, alright. So that individual has no other grants before us?

VOICE: No.

DR. GALVIN: Okay. Everybody alright with maybe?

MS. TOWNSHEND: Next grant for consideration is 08-SCA-UCHC-009. Lai is the principal investigator, 1.75 is the peer review score and the -- I apologize. The members of cognizance are Huang and Genel.

DR. HUANG: This is a proposal from an immunologist and a junior faculty member who wants to look at on turning human embryonic stem cells into transplantable hematopoietic stem cells in vitro, so similar to the kinds of stem cells that are in bone marrow that you can transfer to other recipients and have turn into different blood types.

So Dr. Lai has shown that a hybrid cytokine which has part of Il-7 and part of hepatocyte growth factor data is able to do this in mice under certain conditions and now proposes to do this in both mice and humans.

This proposal received a 1.75 score from the peer review but the peer review was only three sentences. And looking through the tone of the comments as well as looking through the application, it’s not clear that this is necessarily any better or in the definite yes

category than many of the maybes so I would propose to put it in the maybe category just by that score.

DR. GALVIN: Paul, is this part of an overall hepatocyte studies program at the institution?

DR. HUANG: No, I don't believe so. This is --

DR. GALVIN: This is unrelated to the earlier --

DR. HUANG: Right.

DR. GALVIN: -- discussion we had about hepatocytes and malaria?

DR. HUANG: Right.

DR. JENNINGS: But this is not hepatocytes, right?

DR. HUANG: Right. This is hematopoietic.

DR. GALVIN: I'm sorry, I didn't --

DR. HUANG: This is hepatocyte growth factor in the area of transplant.

DR. GALVIN: Okay. And I hear you'd like to put that into the maybe category?

DR. HUANG: Correct.

DR. GALVIN: Any further comments from the second reviewer or others? If not, we'll put that grant into -- I can't see Dr. Jennings. Oh, there he is.

VOICE: Are you obliged to --

DR. GALVIN: I have lots of those.

MS. TOWNSHEND: I think it's probably. I'm sorry. I'll sit back. That will be placed in the maybe category.

Our next grant for consideration is 08-SCA-YALE-005. Cantley is the principal investigator, 1.65 is the peer review score and the members of cognizance are Arinzeh and Mandelkern.

MR. MANDELKERN: I'm happy to report on this grant proposal. It received a score of 1.65. It is third ranked out of 50 grant proposals that we received. It is submitted by an established investigator very skilled in cell biology I guess you would say and particularly his area of expertise is kidney research. He's published many papers that have been peer reviewed in journals.

His interest now is to use human embryonic stem cells to see what he can learn about the development of undifferentiated human embryonic stem cells towards the specialized kidney cell. He's done some genetic modification already of embryonic stem cell or kidney development cells. He's very experienced and he's at the peek of his career. He intends to spend only a small part

of his time on the project. Most of it will be done by a post-doc but he will guide the work.

And I think this is exactly what we are looking for because this could have tremendous application for the treatment of kidney disease which is becoming more and more prevalent as the population ages and the problems are more difficult with an aging population.

So I would propose that we consider strongly funding this proposal as it exactly is the work of attracting new investigators inside Connecticut and from outside Connecticut to work in human embryonic stem cells in an area of disease that certainly needs investigation and progress.

From the other criteria applying to Connecticut, there is strong commitment from the institution. There is potential for collaboration and the benefit to Connecticut if some patient-specific therapies do come from this work are very, very important and could really put Connecticut in the forefront of the international seed if it’s achievable.

So with the agreement of my fellow reviewer, Dr. Arinzeh, we propose funding this grant request.

DR. GALVIN: This certainly sounds like a

good project. I think we're fairly far away, however, from curing renal failure, particular that of glomerular sclerosis and the type of stuff that is associated with getting old. But it looks like a good project and I wonder if Treena had something to say?

MS. ARINZEH: Okay. So what makes this proposal really interesting is the fact that they have come up with an elegant viral vector, a very novel viral vector for being able to track these cells in vivo during the differentiation process. And so it could be potentially applicable, at least that strategy could be applicable to other lineages or what have you.

So I think it's worthwhile in terms of that aspect, that it's just kind of new, a new vector that they're establishing. In terms of, if you wanted specifics of the vector, but I don't know if you want to know all that, but. So that's really where the enthusiasm is. It's not even so much that it's even for the kidney, I think anyway, but it's this viral factor that they are able to establish.

DR. GALVIN: Thank you. Are there any further comments?

DR. FISHBONE: I got the impression just from reading the reviewer's remarks that he needs to do

all this work in mice -- in mice embryonic cells before turning to human. Will he within the time frame of the two years will he be doing any work in human embryonic stem cells?

MS. ARINZEH: So that -- maybe that's a concern then for the Committee to -- to look at. But, yeah, he is doing all this in the area of the mouse embryonic stem cells because for him to look at a differentiation in an animal model, he has to do it in the mouse -- use the mouse embryonic and then look at differentiation in a mouse model. And so the plan is to move in -- what he has written there -- is the plan is to move into humans after two years of establishing this in a mouse model. And he would do that by, again, submitting another proposal receiving funding for that.

DR. GALVIN: But that's very clear. Do we have a consensus that this is a yes? Now, while that's happening, I would invite all of you to address your attention when you can to the nos and make sure that somehow something is not in the nos that you thought was in the maybes.

Okay. Our next grant is also a grant where the principal investigator is not going to be present and a second individual will be doing that.

MS. TOWNSHEND: That grant application is 08-SCA-UCHC-025. Havens initially was the principal investigator?

DR. GALVIN: There were -- there were two. I think the co-investigator -- I'm sorry.

MS. TOWNSHEND: Co-principal investigators and Mina is the second principal investigator as part of the application, is that correct?

VOICE: Yes.

MS. TOWNSHEND: That is correct. Peer reviewed at 1.6 and the Committee members of cognizance are Jennings and Latham.

MS. HARTLEY: I'll just clarify. This is Pam. We had received correspondence from UCONN Health Center indicating that Havens was -- had either left or was in the process of leaving and, if approved, the award would be transferred to Dr. Mina who is currently the co-PI.

DR. JENNINGS: Okay, shall I?

DR. GALVIN: Go right ahead.

DR. JENNINGS: So the authors are interested in the ultimate therapeutic goal of bone transplantation bone grafts and their expertise is in the development of chick -- specifically chick mandibles as a

-- as a model system. So and what they're planning to do here is there is prior evidence that grafts that are derived from crest derived bone are more -- are better source of transplant material than those from this derived bone. And so what they want to do is to turn human embryonic stem cells and chick mandibles here -- turn human embryonic stem cells into crest cells and try grafting them into chick mandibles to explore their capacity for differentiation.

And the referees comment -- they scored it a 1.6. They comment it's unclear whether they can make human crest cells from human embryonic stem cells. But I vote it would be extremely interesting if they could pull it off. And I was slightly less enthusiastic about this one than the referees and I feel that it's not, it's not obviously, stronger than some of the others that are scoring just marginally below where -- where this one is. I think Dr. Havens' track record is now moot because he's not going to be on the project. Dr. Mina has a long track record in studying chick -- chick mandible development and chick development generally but I believe no prior track record with human embryonic stem cells. And the whole question of whether you can convert -- whether you will be successful in converting human embryonic stem cells into

crest cells which are not an absolute prerequisite for the project but I think it is unclear in the view of the referees. And it seems to me that this is a very long way from a -- from a therapeutic application at this point and I would be lukewarm about it and I would recommend that we put it in the maybe category.

DR. GALVIN: Second reviewer do you concur?

DR. LATHAM: I don't know enough about the science to -- to vary from what Charles said. I have a different point to make about it which is that as a control for the -- the crest implantations into the chick eggs, they were planning to put undifferentiated human embryonic stem cells in to compare and that would result in the creation of a human animal hybrid chimera. And one of the reviewers raised an issue whether we had any problems with the ethics of creating such a thing. I personally don't but I thought it was worthwhile bringing to the Committee's attention that that -- that part of the plan in this -- in this proposal was to create human animal hybrids as a control group for the crest comparison.

DR. JENNINGS: The referee also comments that that's not a particularly important experiment in the

context of the project. So if anybody raises ethical concerns, it could be dropped without an end because that was my take as well, but thank you for raising that.

DR. GALVIN: I'm not sure that that sort of combination fits with our charter and would be considered appropriate by the citizenry who fund us. The Koreans had a good deal of problems with that when they were working on their combining different types of DNA with a different species and I'm not sure where that's going to take us. Yes?

DR. JENNINGS: Mr. Chairman, if I can just clarify the Korean -- I think it's probably misleading to compare them to the Koreans but who knows a whole raft of problems that I don't think apply here. What we're looking at here is a cellular chimera. This is not nuclear transfer. But in any case, I think --

DR. GALVIN: Is this not though what the Koreans got in trouble -- one of the things that they were.

DR. JENNINGS: For making cellular chimeras?

DR. GALVIN: That's what I thought but I did not read that in great detail.

DR. JENNINGS: Yeah, I'm not -- I think

this is probably distinct. But in any case, I think the reviewers have pointed out that's probably not an essential experiment. If it turns out to be an experiment -- essential experiments -- I would defer to the escrow on whether it's -- whether it has been justified. I personally have no problem with that, so.

DR. KIESSLING: Can I ask a question about whose going to do this work now?

DR. JENNINGS: That -- that was unclear all along. So the budget call for -- let me make sure I give you accurate information --

DR. KIESSLING: Dr. Havens was only on at ten percent.

DR. JENNINGS: Yeah, he was ten percent. Dr. Mina was two percent and so the remaining whatever it is percent, 70 percent, it doesn't add up -- but whatever is an unidentified post-doctoral fellow.

In general, I am more enthusiastic about grants in which the person who is going -- the post doctoral student that actually is going to do the work is identified and we can evaluate that track record and talents and energies and that's not the case here. And I think that's one criteria among many that -- that would be a weakness in my view. So only -- only two percent of the

effort is from a known person at this point.

DR. GALVIN: I was just having a conversation with my administrative assistant and I think that this -- why don't you just say it? You said it very well. I don't need to quote you.

MS. TOWNSHEND: I think when we are looking at the citizenry of Connecticut they do not understand the science the way that you as experienced scientists and ethicists understand it. And I'm not sure that they would be able to differentiate between the nuclear transfer and the chimera as you described it Dr. Jennings. I think what they would see is, oh, my goodness, a hybrid of humans and animals and would not -- certainly not be popular. It's just my opinion.

DR. GALVIN: That would be my impression that the citizenry would not be happy with this and see this as, you know, some sort of -- I understand what you're saying. And -- but I think the guy on the street who's paying the State income tax may not see it the same way and see it as the beginning of a -- of a very slippery slope of combining different types of --

DR. JENNINGS: I think it's an extremely important distinction and it's one that goes to the heart of what one is going to do with human embryonic stem cells

and the need for experimental animal model systems in order to evaluate the potential of those stem cells before they're put into human subjects. So I would say it's -- it is so important to give more rationale to stem cell therapy. But it's -- if we feel that there's not public understanding, it is incumbent upon us to communicate to the citizenry those important distinctions. They have been extensively discussed by the bio-ethics community and the National Academy of Science has written extensively on them. It's really a core issue that I think we can't just -- we cannot simply allow that distinction to be confused and I think it's our obligation to clarify where the distinctions lie and what they mean. I think that --

DR. GALVIN: That is what I'm -- I'm saying is that I understand it and that everybody sitting around here, all of whom are doctoral levels or have more than one doctorate understand it but there's about three million four hundred thousand -- four hundred eighty thousand people who would -- in Connecticut who probably don't understand it very well would see it the wrong way unless we, as you say very wisely, unless we -- we indicate exactly what we mean.

Do we have a recommendation? Yes? No? Maybe?

DR. KIESSLING: I think the biggest problem with the application is that there's nobody to do the work -- that the only person we know about is going to devote two percent effort. There's nobody to do this work right now.

DR. GALVIN: Mr. Wollschlager, do you have a comment, sir?

MR. WOLLSCHLAGER: Just a comment to reference a previous application that we put into the no pile just for the point that Dr. Kiessling has raised and Dr. Jennings has raised, is that you made the comment about not funding institutions -- funding individuals. In this case, you don't know who you're funding.

COURT REPORTER: One moment, please.

DR. GALVIN: We do have a co-PI on this one but I think that in these discussions we're coming to a very interesting point that if you come up with a pretty decent grant and you lose your primary investigator you're in deep trouble or could be.

COURT REPORTER: One moment, please.

(Off the record.)

COURT REPORTER: Okay.

DR. WAGERS: Okay.

VOICE: I know.

DR. WAGERS: Okay, yeah, I guess I just -- since I had brought up the concern about the previous grant, I actually make a distinction with this grant in the sense that the person who will be taking the lead PI position was listed as a co-PI on the grant initially and so they were always intended to direct the project together.

I guess my question and that's what I'm -- I was trying to look at here, but I haven't really found the information yet, is sort of the -- the co-PI, who will be taking lead of the project, what her -- is it her?

VOICE: It's a her.

DR. WAGERS: It's a her. Her specific expertise is in running it. And then secondly, to Ann's point about we don't know who will do the -- the science. Are you referring to what post-doctoral fellow they will hire? Because I think in that case it's totally reasonable for a PI to recruit a fellow to -- to do the work in the lab and that happens quite often that you have a to be named person that will actually do the work, as long as the scientific input is coming from the PI.

DR. KIESSLING: Yeah, I -- that I think would be -- that logic applies to something like an R-01,

but this is a seed grant application. And so the -- the spirit behind seed grants is that you're funding either a seasoned investigator to do something new or a young investigator to get launched. And we don't know who this investigator is going to be and the laboratory doesn't actually need this money.

DR. WAGERS: So, sorry, just to -- to clarify. So your concern is that Dr. Mina's lab doesn't need the money?

DR. KIESSLING: I don't think Dr. Mina needs a seed grant.

DR. JENNINGS: And full -- I mean if we're getting from -- to Havens was putting in -- I want to make sure we have the right -- ten percent effort. Dr. Mina was putting in two percent effort of the -- you're talking about a six fold increase in Mina's commitment to this -- this project is what we'd be looking for plus an unknown post-doc. I mean I think there's a seriousness of it.

DR. GALVIN: Okay, let me -- let me recapitulate. We have raised some -- some issues that -- that have an ethical basis and our emphasis have -- have -- and other members have made decisions about that and I think we've decided that we need to keep the public

educated.

There's also an -- two other issues have been -- have been raised, but we're not quite sure whose doing the grant and that perhaps the institution may have other sources of funding to do this kind of grant. So I think we can take the -- the issue of the chimera -- chimera issue and that seems to have been -- have been decided.

Now, are we going to base our decision on being not quite sure whose going to do the grant or what is the basis of making our decision is where --

DR. JENNINGS: Mr. Chairman, if I can just make one more point? This grant depends on the ability to manipulate human embryonic stem cells and turn them into crest cells.

Dr. Mina, as far as I can determine from this record, does not have a background in human embryonic stem cells or even mal syndromic stem cells. That Dr. Havens, who is not on the project, did. So it's -- it's unclear who will bring even the critical expertise that is needed to make this work.

DR. GALVIN: Dr. Genel and --

DR. GENEL: I think -- I think we're spending an inordinate amount of time on this.

DR. GALVIN: We are.

DR. GENEL: I would say very simply, we have a lot of competition for a small pot of seed grants and when the -- the PI of a seed grant is no longer available, I think we ought to just move them over and get on with it. Irrespective of that -- I quite agree with Ann, I think the purpose of the seed grant is to encourage young investigators or mature investigators and we switch them over to another topic. It isn't whether or not the work can be done.

DR. WAGERS: So --

DR. GALVIN: Dr. Wagers.

DR. WAGERS: I just wanted to address something that actually, I think, comes to both points that were made and that is, first of all, regarding Dr. Mina's expertise in this area with human embryonic stem cells and that is that as I spoke to here, I noticed that she is the project leader of Project Six in a grant that we funded to UCONN with the head PI being Dr. Rowe and the title of that project is Salutogenic Differentiation from Human Embryonic Stem Cell Derived Neural Crest Regenerator Cells. So it does seem as though she's working in this area already, if she's the head PI of that grant.

It does also raise another issue of -- of overlap, I would guess, although she said there is no overlap with the current proposal. I think it speaks to her involvement in this area, her expertise in this area, her relevance as a PI, but maybe also gets at what Ann was talking about as to whether we're -- we're ending up funding a -- a very similar project as a seed grant that's already been funded as a project under another mechanism.

DR. GALVIN: I would also -- thank you. I would like to -- to make a comment that perhaps when we solicit our next bunch of grants, we ask that the grant requestors indicate to us whether or not the person they're indicating as primary investigator is going to be there.

My impression is, and you can tell me I'm wrong, that most of these people leave at the conclusion of the academic year. I don't think they give two weeks notice and go out the door. So I -- I would presume that the fact that investigator A or B is going to leave is probably known well before the grant gets in. Now, maybe some of this is unavoidable, but I'd like not to have to discuss this next year. But in concern and consideration of this request, what is the pleasure, yes, no, maybe?

MR. MANDELKERN: Sir.

DR. GALVIN: Yes.

MR. MANDELKERN: With the purpose of moving forward, I would recommend we put it with the other 15 maybes, making 16 maybes and proceed to the last of the seed grant proposals that we have. We are now at the last one for first consideration. So my proposal is to put this into maybe and to move forward.

DR. GALVIN: I think we've discussed this very thoroughly. I'm going to call for a meeting -- a roll call of the members to see where they want this grant to go. Saying yes, means yes, saying maybe, means maybe, and saying no, means no.

MS. HORA: I think we need to be careful that -- that -- in terms of taking the roll call --

COURT REPORTER: I'm sorry, but I can't hear you.

MS. HORA: Only the people who do not have a conflict on this grant, which I believe is a UCONN grant, should be voting.

MS. TOWNSHEND: I have that list. I have that list. Eligible reviewers. Just to clarify, no is --

COURT REPORTER: Bring that microphone up

please.

MS. TOWNSHEND: No means it goes into the no category, yes means it goes into the yes category, maybe means it goes into the maybe category. Yes, Warren.

MR. WOLLSCHLAGER: Just to clarify it means not -- it goes into a new category of final dispositions, it's been voted on, right? If we vote now, then we don't need to vote later whereas we're deciding those in a vote later.

MS. TOWNSHEND: Is that correct? Warren, yes.

DR. GALVIN: No.

MS. TOWNSHEND: No?

DR. JENNINGS: No, not correct.

DR. GALVIN: Once they're in no, they're --

DR. JENNINGS: Nos.

MS. TOWNSHEND: Once they're a no, they're a no.

DR. JENNINGS: If we have a roll call, it's in a unique category of --

DR. GALVIN: Yeah, that's why I keep asking you to look at the nos, because we got into this

last year with people saying I really didn't want it to go there. I wasn't paying attention or I was out of the room.

So, once again, look at the nos and if there's one -- if there's something there you think should be a maybe, please let's move it, because I don't want to have to go back later on and go through every single one of those to make sure that the -- I don't care if you have a legitimate concern, but -- but my concern is please pay attention to what's over there.

MR. WOLLSCHLAGER: Yes.

DR. GALVIN: Yes, Warren.

MR. WOLLSCHLAGER: Just before you take the roll call, procedurally, I thought the process was a single maybe from the entire committee sends it to maybe.

DR. GALVIN: Put it in maybe.

MR. WOLLSCHLAGER: It doesn't need a consensus.

DR. GALVIN: Put it in maybe.

VOICE: One person can raise an objection.

MS. TOWNSHEND: Finally, for consideration, 08-SCA-YALE-010, Reinke is the principal investigator, 1.5 the peer review score, and the members of cognizance are Canalis and Fishbone, four minutes.

DR. CANALIS: Obviously these -- that is currently on behalf of the group and basically what the investigator is going to do is going to look at p53, the function of the human embryonic stem cells. She has discovered a kinase which may be an inhibitor of p53. So the proposal basically is going to look at the interactions between p53 and the inhibitor and kinase. So it is going to determine -- and it is going to determine whether silencing of this kinase rescues p53 activity.

As earlier with the best score, she's done this previous work in seed elegance and now she wants to carry this into a million cells. As an experienced -- experienced investigator, I'm basically the justification of this type of work as she is changing fields. I would favor a yes.

DR. GALVIN: Second reviewer?

DR. FISHBONE: Yes, I -- I thought this was without -- without, you know -- I thought this was a very good grant and a very important subject, because P -- you know, one of the problems with embryonic stem cells is that when there's any DNA damage, they might form tumors and it's one of the things that most concerns using them in humans.

And I guess it's a well-known fact that p53 is a tumor suppressive protein, which in most cells causes the cell to die if there is DNA damage, but doesn't in undifferentiated embryonic stem cells.

So the knowledge of how that works and, you know, whether you have a substance that she's discovered in -- in seed elegance that will allow p53 activity to occur I think would be a very important basic concept to see if there is a way to stop embryonic stem cells from forming tumors and so it seems to me this is an important subject and I thought that the reviewers felt the same way by giving it the highest rating of all the grants that we have.

So in the absence of scientific knowledge that says it's been done or whatever, I would recommend it being approved.

DR. GALVIN: I hear both reviewers are in favor of this. Is there any further comment from the members? If not, we will move that grant into the yes column.

Now, we're going to go back to UCONN Grant 041, which we were -- decided to put to one side until we could get some more information. Ann, are you ready to discuss that grant?

DR. KIESSLING: Well --

DR. JENNINGS: We're going back to a no?

DR. GALVIN: No, it's one that we didn't --

DR. KIESSLING: No, we -- we -- Nelson, we skipped because neither one of us could find our notes. And now that we've looked at it, we have two applications from the University of Connecticut to develop a stem cell database and this is one of them. So -- the other one didn't do very well. It seems to me like what we want to do is put both of the -- we want to put this grant back into the maybe category.

We need a stem cell database. Amy was concerned about the other application, because it wasn't clear how it was going to get extended and how it was going to happen. One of these applications is coming from the Health Center, the other one is coming from Storrs, and so somehow these people need to get together and develop a database. The ideas in both of these are really good.

So I don't know exactly how this Committee is going to shake this out, but a database is definitely needed. These are slightly different approaches to doing it. The University of Connecticut doesn't need two,

certainly Connecticut doesn't need two, but I don't know exactly how to play this out. So I would actually like to look at these two database proposals side by side when we get down and see how much money we have.

DR. JENNINGS: How much money are they asking for?

DR. KIESSLING: They're each asking for $200,000. And one of the criticisms is that that seemed to be a lot. I have a hard time deciding that. One of them is more a Bioinformatics person than the other -- Nelson is a Bioinformatics person, the other person is more of a biologist. I don't know. I mean I think we really need to look at these two grants side by side. It's a really good idea to develop a database.

DR. GALVIN: The only focus I have for you is -- on that is that the new President Mike Hogan, the new UCONN President, wants to have a single combined Dean of all research and I think that -- that when that happens -- I don't think anyone has been designated for that position, but I think when that happens that will consolidate things.

What Mike Hogan -- Dr. Hogan has said -- President Hogan has said is that he wants to have a single person in charge of all research and I think some

of this -- two -- two grants that seem to be doing the same thing will be remedied at that time. When that's going to happen, I'm not privy to.

VOICE: Can I make a suggestion.

COURT REPORTER: No, I'm sorry, your microphone please. Microphone.

VOICE: Can we award the grant to Mike Hogan?

DR. GALVIN: I think that would be a great idea.

DR. FISHBONE: Could I ask a question about this whole subject? Is there any work being done nationally, so that each state doesn't have to come up with its own database of what's available? I mean it's -- I'm just wondering if it's a Connecticut issue or a national issue.

DR. GALVIN: Well, I think Warren, having put together or having worked with genomics and with cord blood and -- and genetic banking, DNA banking, can probably tell you about difficulties from state to state and give you sort of a one minute projection on having a national network.

MR. WOLLSCHLAGER: Well, thank you, Commissioner. I -- it's actually the kind of issue that

we have been talking about with the Interstate Alliance and you -- you look at efforts -- what's already happened in Wisconsin, where there's federally designated repository, the bank, and they have the same type of effort going on to develop banking activities in Massachusetts right now and, you know, and the state dollars being dedicated to that.

To the same extent, to what extent do we want a bunch of parochial databases being developed? This would be the type of thing you would think that perhaps would be handled at the federal level.

DR. KIESSLING: These -- these applications are not simply for banking. These are databases we're going to look at.

MR. WOLLSCHLAGER: No, I understand.

DR. GALVIN: But we're talking about databases in general.

MR. WOLLSCHLAGER: Right.

DR. GALVIN: And what we're seeing is that everybody's got their own database and no one has quite yet pulled a lot of things together into a coherent database --

MR. WOLLSCHLAGER: Right.

DR. GALVIN: -- where we can exchange stem

cell information with say Wisconsin or California or any of -- any of the states. And our comments were across the board that as we develop these new research and development issues that we -- we're beginning to see that everything is -- is done on a statewide basis and -- and therefore, is -- what is it that we want to do? Develop a separate statewide data system and is that going to -- to dovetail with New York's and with Maryland's and whoever else's?

MR. MANDELKERN: I'm confused. Have we reached a conclusion on --

MS. TOWNSHEND: Mr. Mandelkern, do you have a microphone?

MR. MANDELKERN: -- the UCONN 041 principal investigator Nelson? Have we reached a conclusion on that?

DR. KIESSLING: I suggested it be put into maybe. I would like it -- I --

DR. GALVIN: I think that's a reasonable suggestion, then perhaps we can compare the two similar grants to each other and consider it when we're talking to one University entity.

DR. JENNINGS: I think we've agreed that goes into maybe.

DR. GALVIN: Maybes, yeah. Alright, alright, we have four yeses for a total of $800,000. We are -- we are going to devote at least 20 percent of our slightly less than $10 million to seed grants, but we're not -- not limited to that figure.

I presume that everybody has eyeballed the nos and is agreeable to the fact that they're there and we're not going to -- we're not going to discuss them later this afternoon. And if that's -- if everyone understands that, we'll proceed.

MS. HARTLEY: Excuse me. Can I just add -- I just wanted to read one more excerpt from an email that pertains to the Witola grant. I don't know if this will make a difference or not, but --

DR. GALVIN: Which -- give me a number on the grant.

MS. HARTLEY: It's let's see -- 08-SCA-UCHC-023.

DR. GALVIN: Okay. Everybody know what we're talking about?

DR. JENNINGS: This is the Malaria firm hematocytes.

DR. GALVIN: Yep, okay. Go ahead.

MS. HARTLEY: Yes, it's currently a no.

So this is from an email from Mamoun, who is supposed to be taking over as the PI. It says -- he's referring to two different grants. But he says both ideas to generate normal and transgenic erythrocytes and hematocytes to study Malaria infection are mine and I share the concept and design with William Witola during his tenure in my laboratory.

DR. GALVIN: Okay, when did that email come in?

MS. HARTLEY: This came in March 20th.

DR. GALVIN: Okay, have we -- Attorney Salton, have we considered information like this after the end point of the grant submission and is this an appropriate bit of information to consider?

MR. SALTON: The answer to both questions is yes.

DR. GALVIN: Okay. So I need you to read that again.

MS. HARTLEY: Okay.

DR. GALVIN: I got lost in the verbiage.

MS. HARTLEY: Sure. Okay, hopefully my -- I'm pronouncing everything correctly. Both ideas to generate normal and transgenic erythrocytes and hematocytes to study Malaria infection are mine and I

share the concept and design with William Witola during his tenure in my laboratory.

DR. GALVIN: Now, this is -- this is a grant that we rejected because the primary investigator moved on and it is in the nos right now. Do we want to put it in the maybes or leave it in the nos, put it in the yeses, what is your pleasure? Charles.

DR. JENNINGS: Mr. Chairman, as the primary reviewer, I don't feel that that fundamentally changes the issue which is the 100 percent of the effort according to the budget will be done by somebody unidentified. I think it goes without saying that the eyes in the labs contribute substantially to the --

DR. GALVIN: And does everybody understand that -- that the -- the person who is going to do all the investigation, although the person who -- is not the person who wrote the email, authored the email, if I may say.

MS. HARTLEY: Well -- well that person --

DR. GALVIN: Is that correct?

MS. HARTLEY: That person is supposed to be the PI at this point.

DR. GALVIN: Okay. So we have a difference here. My understanding is that someone that

we don't know is going to do all the investigating and I think that was the reason for the rejection. Does that communication change that for anybody?

DR. KIESSLING: What percent effort? Do we have a percent effort? Do we have a new budget?

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

DR. JENNINGS: Do we have a new budget?

MS. HARTLEY: A new what?

DR. JENNINGS: Did -- did they send a revised budget along with that additional email?

MS. HARTLEY: No, no, they did not send a revised budget.

DR. GALVIN: Okay. Does the information that we received -- now, does everybody know which grant we're talking about?

DR. KIESSLING: Yes.

DR. GALVIN: Warren, can you pull that out of the -- yeah, well, just so somebody doesn't say to me, I didn't understand that's what you were talking about. Okay, this is what we're talking about, that's the Malaria Investigative Grant or with the application --

MR. MANDELKERN: And I'm sorry, the number again was?

MR. WOLLSCHLAGER: 023.

DR. GALVIN: 023. Please make sure we're -- we're all on the -- as they say, on the same piece of paper.

DR. WAGERS: Can I ask a clarification?

DR. GALVIN: Go ahead.

DR. WAGERS: Oh, so the person that you just read the email from is the PI of the lab?

DR. JENNINGS: Is Mamoun, yes.

DR. WAGERS: And that person will now be the PI of this grant?

MS. HARTLEY: He was the sponsor when Witola was the PI, but now he's going to be the PI since Witola has left.

DR. WAGERS: So we do know who the PI of the grant is?

MS. HARTLEY: Right.

DR. WAGERS: Okay. So that's different than what I think a lot of us had thought.

MS. HARTLEY: There's also in this note he said this is as of March 20th, I would like to suggest a new post-doctoral fellow. So I don't know I guess you could assume that he's going to be PI until perhaps he may want to name a post-doctoral fellow, but --

DR. GALVIN: Charles, I'll get to you. I do not like this communication and I think that it -- what it suggests to me is that we will then be receiving little missives and epistles and maybe a gospel or two as -- as we're developing probably a hundred grants or we're looking at a hundred grants next year and then trying to forward all this stuff. I -- I'm personally not happy with this procedurally. Charles.

DR. JENNINGS: No, I'm going to continue to recommend no.

DR. GALVIN: Okay. Now does everybody -- does everybody understand the issue or issues here? And I think the -- if I'm going paraphrase Charles, but if he -- if he -- certainly, if I don't correctly paraphrase you, let me know.

I think the issue has been that -- that the individual whose name is posted on the grant is not there any longer. Someone else has said that they are going to be the principal investigator and a third party yet to be determined is going to do the work, 100 percent of the work and -- and we did receive a long email etc., etc.

And I think Charles has indicated that he still maintains his negativity about the grant and I

think I would have to say properly so. But what -- what is the sense or direction of the group?

MR. MANDELKERN: My sense is that we stay with the recommendation of no on this grant for the reasons stated.

DR. GALVIN: Okay. Put it back. Thank you, Warren.

MR. WOLLSCHLAGER: You're welcome.

DR. GALVIN: This seems to be an ideal time to take our -- our luncheon break. Once again, as -- on your way out of the room, take a look at that group of nos and if there's something there that gives you agita or heartburn or acid reflux depending on your orientation, let us know about it.

I have been requested to attend the gubernatorial cabinet meeting. Dr. Landwirth has agreed very graciously to chair at least a portion of the afternoon --

DR. LANDWIRTH: Yeah, of course.

DR. GALVIN: -- while I attend that meeting.

DR. LANDWIRTH: Sure.

DR. GALVIN: Thank you.

MR. MANDELKERN: Dr. Galvin.

DR. GALVIN: Yes.

MR. MANDELKERN: One point. I would appeal to the administration to find some way to upgrade this sound. During the break, I spoke to members on the other side of the table and they said they couldn't hear us and I know that I cannot hear them. So something should be done during the lunch break to upgrade the sounds.

We are considering very serious matters and it would be good if we could understand -- and hear and understand each other on a higher level. Thank you.

DR. GALVIN: Yeah, Bob, I think the good deal of the problem is with the background hum.

MR. MANDELKERN: Can we switch it --

DR. GALVIN: You might be able to shut that down or off, if there's some way of doing that.

MR. MANDELKERN: Well, what -- I'm just suggesting something be done. The few people I spoke to said they couldn't hear me and I know I can't hear them. And I think the same is true --

DR. GALVIN: It's a point well taken. This is not an ideal facility for doing this kind of work. Charles, did you have a comment?

DR. JENNINGS: Two alternate suggestions.

One is we ask the hotel to switch off the fans at least intermittently, so that we can hear. The alternative would be to rearrange the tables, so that we're not quite as far away from each other.

DR. GALVIN: That's a thinking man's way of doing things.

DR. JENNINGS: I'm willing if the -- does the group vote to do so.

(Off the record.)

MR. WOLLSCHLAGER: Just a couple of quick announcements. If you have not already done so, please give us a copy of your parking ticket and we will get that validated for you at the next break.

The next thing is that we have requested that the blower be turned off. They did turn off one blower, but they turned on another blower, so we're working on that still. Hopefully, with some folks moving a little bit closer together in the interim though it will be a little bit better.

VOICE: Can Mandelkern hear us on this side now?

MR. MANDELKERN: Yep.

DR. HUANG: Yes, we can hear you.

VOICE: I'm not worried about you Paul,

I'm worried about --

MR. MANDELKERN: Yeah, well, if you -- I think if you just project and hit this, I can hear you.

MR. WOLLSCHLAGER: Okay. And again, we're still working on the Dean, he's our contact here, our AV guy, he is trying to fix it. You'll see now that the Chair's seat is being occupied by Dr. Landwirth at the request of Commissioner Galvin who has been called to a mandatory meeting with the Governor beginning at 1:00 today. He is hoping to be back here before the end of the day, but he's asked that Dr. Landwirth move the meeting along in the interim.

And let me see, also, finally, Lynn Townshend has also had to leave for an emergency today. She will not be coming back, so that's why I'm sitting here.

Just to review where we're at there, Dr. Landwirth, the next step in the process then was to review the maybes and make the determination should they go into the no or into the yes category. The process is lined out -- laid out by Lynn was that each of the grants would be discussed again, again with the four-minute time limit, no more than four minutes. No grants will be eliminated, yes grants will be considered later. We're

not going to make funding decisions until all the categories are considered.

And I believe our colleagues at CI have -- have prioritized -- have rank ordered the outstanding maybes either from low -- lowest to highest or highest to lowest, I can't quite see it here, but I think it was the Chair's desire to consider the maybes in the reverse order that we did last time. So we'd start with the highest ranks maybe.

DR. LANDWIRTH: Very good.

MS. SARNECKY: The best.

MR. WOLLSCHLAGER: The best of the best.

MS. SARNECKY: Yes.

MR. WOLLSCHLAGER: I'm sorry, I know we used -- good -- best --

MS. SARNECKY: Yes, the best is on the top and it's from left to right.

MR. WOLLSCHLAGER: So Havens, if I'm looking at it correctly, Havens would be the best peer reviewed out of the remaining maybes.

MS. SARNECKY: Yes.

MR. WOLLSCHLAGER: Okay. So Havens is 025 and Mr. Chair, I think you were going to direct the two original reviewers to remind us -- give us an overview.

MR. MANDELKERN: Can you give -- repeat the number of the grant?

MR. WOLLSCHLAGER: Yes, it's -- yes, the number is 08-SCA-UCHC-025, the PI is Havens, and the title is on another sheet. The title is --

VOICE: Novo in vivo --

MR. WOLLSCHLAGER: Novo In Vivo Model of, thank you, of Human Neuro Crest Differentiation. So we all know which one we're on?

VOICE: Whoever discussed it last time should take over.

DR. LANDWIRTH: I'd like to suggest that we start it as discussion of each of the -- each proposals with the individual who reviewed it last time, just giving us a quick two sentence summary of the nature of the project and the -- and how it got into the maybe column.

DR. LATHAM: I was one of the two original reviewers on it. I would now put it in the no, because this is the grant where the original PI has been removed and co-PI substituted. It's not clear who's going to do the work and the co-PI is not an appropriate candidate for a seed grant.

DR. JENNINGS: Right. I was -- I was the

other reviewer and I would agree with that. So I vote no.

DR. LANDWIRTH: Okay, so there's a recommendation on second review is that that particular project be moved from the maybe to the no column. Any general discussion or --

DR. JENNINGS: That's correct.

DR. LANDWIRTH: Agreement about that, done. Please move it.

MR. WOLLSCHLAGER: Okay. Okay.

DR. LANDWIRTH: Alright, there's one further question on the first one, I've been advised to also ask you if there was any disagreement about moving it from the maybe to the no column? None.

We're going on to the next one. I'll just read the last three digits are 009. It's a UCONN project. The PI is Li. The title of the project is --

DR. HUANG: This is Cytokine-induced Production of Transplantable Hematopoietic Stem Cells from Human ES Cells.

DR. LANDWIRTH: Yes, please -- would -- go ahead.

DR. HUANG: This is the proposal by an immunologist who wants to use a hybrid cytokine that in

mice can turn ES cells in to hematopoietic stems cells and is proposing now to study the equivalent process both in mice and in man. It was ranked at a 1.75.

The reason it's in the maybe is because the review by the peer review committee was on the short side. There were no glaring problems with it and I think it still is an excellent grant. So I would propose that it go in the yes category.

DR. LANDWIRTH: Let me understand. The reason it became maybe because the review was brief?

DR. HUANG: The review was brief, it was three sentences.

DR. LANDWIRTH: It was brief because it was --

MR. MANDELKERN: Uninformative.

DR. HUANG: It was -- it was short. Basically, it's novel and interesting. They made one recommendation for how it could be stronger, but it wasn't as detailed as many of the reviews that we've seen.

DR. LANDWIRTH: Okay.

MR. MANDELKERN: So you're now suggesting that it be moved --

DR. HUANG: Right. So that's why without

seeing all the other grants that were in the yes category, I did not feel comfortable automatically putting it to yes for its score.

MR. MANDELKERN: At this time you're suggesting that's what we do?

DR. HUANG: Now, that we've gone through all the grants, yes.

MR. MANDELKERN: It's also, if I may point out --

DR. LANDWIRTH: Yes.

MR. MANDELKERN: In the ranking, it's the fourth highest among the 50 grants that were scored.

DR. LANDWIRTH: Thank you. Any other discussion about that particular project? All agreed that we move that into the yes column and is there any disagreement about that? Thank you.

DR. HUANG: Right.

DR. LANDWIRTH: Our next one is --

MR. WOLLSCHLAGER: Regulation of Embryonic Stem Cell --

DR. LANDWIRTH: It's Yale 022. The PI is Breunig and the title is Regulation of Human Embryonic Stem Cell-derived Neural Stem Cells by Notch Signaling.

Can I have a couple of comments from the

original reviewers, please? Just give us a bit of a background -- a review of what the subject was and how it got to be a maybe and what your current recommendation is. That's the format. Anybody?

VOICE: I believe it was Dr. Canalis and Dr. Fishbone.

COURT REPORTER: You need to be on a microphone.

DR. CANALIS: Yeah, it goes to the maybe for two reasons. One was that this the initial year of post-doctoral training of the PI. He has a limited track record and the fact that the impact of knowledge and its target genes in neuronal cell differentiation has been examined, so that's why it became a maybe. On the other hand, it does have a 1.75 score and Dr. Fishbone was much more enthusiastic than I was. So that's what we got.

DR. LANDWIRTH: Okay. Dr. Fishbone, any further comment?

DR. FISHBONE: Yeah, in my ignorance about publications, I thought this was a very good grant and what I liked particularly was that they thought that Joshua Breuing was a very bright young scientist and this part interested me, he was dedicated to translation of basic research in the clinical treatment for neuronal

diseases. So it was a translational person, very bright, and it looked very impressive.

But as Dr. Canalis pointed out, I think you said that a lot of this stuff had been done before or that he wasn't aware of all the publications.

DR. CANALIS: I mean he's since six or nine months --

DR. FISHBONE: You said at the prior --

DR. CANALIS: -- from a degree. Frankly, he's six to nine months from his degree.

MR. SALTON: I think they're asking about the prior publications in this area.

DR. CANALIS: I'm not an expert in neuronal cell differentiation. My understanding is various Japanese groups have looked at the impact of not neuronal cell differentiation. That is, you know, if you're in the element, that is one of the reasons why Notch deletions are lethal. I mean and I know the field peripherally. If you guys like it, you know, it's a 1.75, I don't have an objection. I -- I was lukewarm about it.

MR. WOLLSCHLAGER: I would move that we put it in yes.

VOICE: Mr. Chairman --

DR. LANDWIRTH: Can I -- can we first get the updated recommendation from the primary reviewer, see if any one is --

DR. CANALIS: That's a yes, Gerry?

DR. FISHBONE: It's still under discussion.

DR. LANDWIRTH: Dr. Fishbone.

DR. FISHBONE: I'm sorry.

DR. LANDWIRTH: Are you -- do you have an opinion about where this ought to go at this point?

DR. FISHBONE: My feeling was we should fund it.

DR. LANDWIRTH: Okay.

DR. FISHBONE: But, you know, I'm willing to bow to more scientific expertise in the area than I have.

DR. LANDWIRTH: Okay.

DR. CANALIS: It is not my job to do a scientific review.

DR. LANDWIRTH: Right.

DR. CANALIS: So if -- you know if you feel that this should be funded and we have discussed the problems with the grants, you know, the grant, I don't have a problem with a yes.

DR. LANDWIRTH: Okay. We have another suggestion that it be funded.

DR. WALLACK: From the philosophical standpoint, Juli, I have a positive attitude about the fact that he is a younger researcher. My attitude about that is that I want to attract as many of those kinds of people who are bright, who are involved in their subject and who have the support of their lab.

And obviously, as described in the report, the environment that he'll be working on it seems to be a very supportive environment. I would, on the basis of what Dr. Fishbone has talked about and with Ernie not having any major reservation, I would be comfortable voting.

DR. LANDWIRTH: So we have a -- I'm sorry, Charles.

DR. JENNINGS: No, I'm sorry. I would just like to second what Milt -- Milton said.

DR. LANDWIRTH: Okay.

DR. JENNINGS: I think I'm uncomfortable with rejecting it grounds -- on the grounds that the post-doctoral is relatively junior. But the reviewer specifically flagged the fact that he's very accomplished. (indiscernible) lab is one of the world's

top developmental neurobiology labs, so, you know, I think there's a high chance that this will lead to something good. I'm very supportive of that based on --

DR. LANDWIRTH: Okay. So we now need to take a vote about what -- we have a motion that this be moved to the yes column. And all in favor of that?

VOICE: Yes.

DR. LANDWIRTH: Take a voice vote.

VOICE: Yes.

DR. LANDWIRTH: Any opposed? Thank you. We'll move it over to yes.

MR. WOLLSCHLAGER: I'm just double checking procedurally Henry, I'm trying to remember -- I know we've been trying to reach consensus on this stuff, if we don't have consensus, do we vote? And if we are voting, then we can only vote based on who is eligible to vote, right?

MR. SALTON: That's correct.

MR. WOLLSCHLAGER: So I guess rather -- because we just had a vote and I'm not sure everyone that voted was eligible to vote.

MR. SALTON: I think that --

MR. WOLLSCHLAGER: So is there a consensus to move this --

MR. SALTON: I think there was a consensus, Warren.

DR. LANDWIRTH: And let me just ask a question if there are any -- any naysayers or any votes no on the suggestion that that be moved to the yes column? Thank you.

MR. WOLLSCHLAGER: Okay. And I think that's probably the easiest process which is just to say the recommendation of the reviewers is blank and does anyone disagree. If no one disagrees, then you have a consensus and move it from maybe to whatever you want to do.

DR. LANDWIRTH: Next project is SCA-YALE-036, the PI is Wang and the title of that one is The Role of the piRNA Pathway in Epigenetic Regulation of Human Embryonic Stem Cells.

DR. WALLACK: I'll comment.

DR. LANDWIRTH: Please.

DR. WALLACK: I'm on the grant --

DR. LANDWIRTH: Proprietary information involved with this one, so what does that mean?

MS. HORA: That just means we cannot discuss the information that's been indicated by the proprietor.

DR. LANDWIRTH: Okay. So we'll need to be respectful of that information which has been dubbed proprietary.

DR. WALLACK: I'll stick with non-proprietary information, but I will speak to the issue that the subject matter, I think, is a very important subject. I think it is a young -- again, a young researcher, a very energetic and accomplished researcher, who is published extensively and also the individual has strong support in the letters of recommendation and so forth and support of her -- of her lab.

I would think that on all of those basis as well as the ranking on the scientific side of 1.75, I would endorse the funding of this grant.

DR. LANDWIRTH: Would you remind us please why we made it -- why we made it a maybe?

DR. WALLACK: Yes, the maybe had to do with the fact that it may have been an ambitious project for -- for her to accomplish within the two-year period, but I will point out that she is specifically devoting 100 percent of her time to the project and her lab support also states that in the event there is additional support that is needed for her to accomplish what she's trying to accomplish that her support people are there

and available to try to help her to make it work.

So I don't have quite the reservation based upon all of that information that we would ordinarily have by the scope of the project.

DR. LANDWIRTH: Comments from the other reviewer?

MS. HORA: That was Ann.

DR. LANDWIRTH: Ann.

DR. KIESSLING: I was the other reviewer and we put it into the maybe category based on the fact that she was going to try to do this all by herself and that half the project won't work if they don't get a third antibody. But the area is brand new and really exciting and these people are pivotal. I mean this is a whole new area of gene regulation and these people are the major players. So I would be happy to see this funded.

DR. LANDWIRTH: Okay. So we have a new recommendation that it be moved to the yes column. Is there any objection, any oppose here? And if not, we will do that. Thank you.

The next project is a Yale project, 011, the PI is Sasaki. The title is Cortical neuronal protection in spinal cord injury following

transplantation of dissociated neurospheres derived from human embryonic stem cells and it received a score of 2.1. The reviewers comment, please.

DR. HUANG: So this --

DR. LANDWIRTH: I mean who presented --

DR. HUANG: So this -- this proposal deals with spinal cord injury and the idea is to take neurospheres derived from embryonic stem cells in culture and then put them into the spinal cord and then to assess brain function upstream from that -- that innovation.

This was a very strong proposal. The strengths include the clinical relevance of the subject matter and also the PI is a qualified physician scientist. The only concerns with it were that the PI had not had that much experience with human embryonic stem cells. Aside from that, there were no -- no major weaknesses.

COURT REPORTER: One moment please.

(Off the record.)

DR. HUANG: So we put it in the maybe category, because of its score which was 2.1 and at that point we didn't realize how many of the grants would be in the yes category and whether it would fit. My recommendation would be that this is a strong grant,

strong PI and important subject matter. So I would put it in the yes category.

DR. LANDWIRTH: Were the other -- Bob, were you the other?

MR. MANDELKERN: I was the other reviewer --

DR. LANDWIRTH: Please.

MR. MANDELKERN: -- with Dr. Huang and originally I thought this should not be considered. However, having listened to Dr. Huang's remarks and in collaboration on the phone previously, I do support also now moving it into the yes column.

DR. LANDWIRTH: So we have a new recommendation that this project be moved from the maybe to the yes column.

DR. JENNINGS: Could I just ask a point of information?

DR. LANDWIRTH: Yes, please.

DR. JENNINGS: Could you explain to me what a neurosphere is?

DR. LANDWIRTH: The question is what is a neurosphere?

DR. HUANG: It's a collection of cells grown and cultivated -- like human embryonic stem cells,

they will aggregate into temporary bodies, but a neurosphere is a three dimensional collection of cells that are predominately human neurons. So they are not a uniform cell type, but they're actually a collection of cells. And in that collection, they will also begin to show a differentiation into different types and interactions between the cells.

DR. JENNINGS: Thank you.

DR. LANDWIRTH: So we now have a recommendation that this project be moved to the yes column. Is there any objection from anybody? If not, please. Thank you.

The next project is Yale project 031, the PI, Dr. Qiu, Potential Use of Embryonic Stem Cells in Treating Type I Diabetes in the NOD Mouse Model.

VOICE: What was the point listed?

DR. LANDWIRTH: 2.1 was the score that proprietary information in that proposal. The reviewer?

DR. WALLACK: Again, it's a young researcher. I think the researcher was actually trained at UCONN, if I'm not mistaken. And it's -- if the person is assumed they -- that he's very, I think, responsible job at Yale. He's supported strongly by the University and again I can't comment on the science, but I can

comment, as you all can, in the printed documents that this particular -- without reading all of it, I will just quote five or six words. And it is therefore very much likely to advance the field that the -- that the research is involved with. I know that the lab that the -- that the scientist is working with is already involved in this kind of research. So I would assume there would be a lot of support there. It had a fairly good rating of 2.1. I think it's the kind of the thing that we should be funding.

DR. LANDWIRTH: How's again -- how did it get in the maybe column, I'm sorry if you said it.

DR. WALLACK: I would fund it.

DR. LANDWIRTH: How did it get in the maybe column first time around?

DR. WALLACK: I don't recall to be honest with you. I think, again, I think it was similar to what Paul was talking about in that it was of that category of 2.1, we weren't sure exactly where we were going with the other project and we were putting it in the holding bay. But unlike the specific concern about the previous one I commented on about the amount of time and so forth, I don't think there was that kind of -- of concern here.

DR. LANDWIRTH: Okay. Dr. Canalis,

anything you want to add that?

DR. CANALIS: No problem, that's fine. Sounds good to me.

DR. LANDWIRTH: So the suggestion is to move it to the yes column, is that right?

DR. CANALIS: Yeah.

DR. LANDWIRTH: Milt?

DR. WALLACK: Yes, yes, yes, yes.

DR. LANDWIRTH: Okay. Any other discussion? Is there any objection to that? Then we will so move it, please. Thank you.

The next project is a UCONN project and the PI is the Choudhary. Differentiation of Embryonic Stem Cells -- no -- yeah. To Neural Crest Derived Trabecular Meshwork Like Cells Implications and Glaucoma, 2.1 was the score. Ann?

DR. KIESSLING: This is -- this is this really interesting application to look at glaucoma and I think this is exactly the kind of thing that we would like to be studying with human embryonic stem cells. I don't remember exactly why we put it in the maybe and it's possibly because it had a score of 2.1 and 7.17. Who was the other reviewer on this? It was you.

DR. LANDWIRTH: I was, yeah. To be honest

with you, I don't recall exactly why we did that. But here we have Dr. Fishbone is going to tell us.

DR. FISHBONE: No, I would wonder if the person who suggested putting it in the maybe column could re-express why they said that. Otherwise, we don't know the reason.

DR. LANDWIRTH: That's what we're trying to remember. My notes --

DR. FISHBONE: I know, but it's usually not the primary or secondary --

DR. LANDWIRTH: Oh, oh.

DR. FISHBONE: It's usually somebody who says I'd like to put it in the maybe.

DR. LANDWIRTH: Okay. Anybody recall the discussion that we had around that particular project?

DR. FISHBONE: Okay. I note --

DR. KIESSLING: I mean this is --

DR. FISHBONE: -- Ann was very in favor of it and all of sudden it ended in the maybe.

DR. KIESSLING: This is a very -- I mean this is actually really exciting. This is really going to be hard to do, but this is a very exciting project. Was there something about the budget? Was there something about who -- who was doing this?

DR. LANDWIRTH: I don't think we had a personnel question about this or a budget question, I don't recall that. But be that as it may --

DR. KIESSLING: No, I mean I was very excited about it. So it could be just because it was -- I just didn't want to put it in the no.

DR. LANDWIRTH: Okay. So we're now looking at a recommendation that it be -- that it be moved to the yes column. Is there any objection to that?

MR. MANDELKERN: The number on that again, Jul.

DR. LANDWIRTH: Pardon me?

MR. MANDELKERN: Could you repeat the --

DR. JENNINGS: Thirty-three, Bob.

MR. MANDELKERN: 033.

DR. JENNINGS: Yep.

MR. MANDELKERN: Thank you.

DR. KIESSLING: I mean the nice part about this application is they've actually recognized the fact that they're not going to get the cell type until they do co-culture with more than one type of cell. So they're sort of going out into an important new area.

DR. LANDWIRTH: Okay. So hearing no objection to that recommendation, we'll move that one to

the yes column too, please. Next will be --

VOICE: Juli, was that 037?

DR. LANDWIRTH: 033. 037 is coming up now.

VOICE: Oh, 003. That was yes.

DR. LANDWIRTH: Yes, 033 is a yes, 037, a UCONN project, the PI is Dr. Li, the title is Developing an Assay Using Embryonic Stem Cells to Screen and Evaluate Anti-Cancer Drugs. The score was 2.2 and the reviewers please. Who reviewed that one?

DR. KIESSLING: Yeah, we -- we did.

DR. LANDWIRTH: Okay. Go ahead.

DR. KIESSLING: You and I did. I'm not as enthusiastic about this grant as I am about Choudhary's grant. I think that this application is the one where there's a lot -- a lot to be learned about cancer stem cells and I'm not sure that -- that this -- that this application is going to yield nearly as much information as some of the others.

DR. LANDWIRTH: And --

DR. KIESSLING: So I would actually move to move this one to the no category.

DR. LANDWIRTH: Yeah. I think, as I recall, that was the concern of the reviewers as well

that it's underestimating how complicated this is. So our recommendation is that that be moved to the no column.

DR. KIESSLING: Well -- well, an interesting thing about this application is that cancer stem cells are like adult stem cells, they probably don't divide very often. But this investigator seemed to think that they were going to divide regularly, so that was the real naïve opinion about what -- you know, the -- what stem cells do.

DR. LANDWIRTH: Any other comments about that? Any objections to moving it to the no column? If not, please move it. Well, the next one is part of the database question. We have that one. How do you want -- yeah, the next one -- sorry, a mic.

Okay, the next one is the UCONN -- the UCONN project, what was the number again? Here it is, yeah. Oh, 043 and that's the one about the Connecticut Stem Cell Database, a bioinformatics resource for stem cell research and I think we discussed that in connection with the project also from UCONN and the number for that one is 41.

VOICE: I think the other one was 041.

DR. LANDWIRTH: 041, PI there being

Nelson, which is also a database related project and that was the reason that we put it on a maybe. Recognizing that it's a very important opportunity to have a database in Connecticut, but wondering why these were two of them, one from the Health Center campus and one from UCONN campus. So how can we help work on that?

DR. GENEL: Well, I mean there's no perfect solution here. There are a couple that I would offer. One is on theoretical grounds. I really wonder whether or not something like a database should be incorporated within one of the core grant.

VOICE: Not with --

DR. GENEL: Oh, one -- oh. On a philosophical basis, I have to wonder whether or not a more appropriate place for a database is within one of the core grants. But leaving that aside, what I would recommend probably is the simplest thing to do is to move this one to the funding category, but with the caveat that they be encouraged to collaborate in collaboration with Dr. Nelson.

Since this is the one that achieved the highest score, recognizing that the content of the two is somewhat different, but I think that, that might be one way of splitting the baby.

DR. LANDWIRTH: Ann, did you want --

DR. KIESSLING: I talked this over with Amy, I think we should listen to -- Amy has some thoughts about this.

DR. GENEL: I'm sorry. No problem.

DR. LANDWIRTH: Amy, please.

DR. WAGERS: I think I'll just reiterate a little bit what I said before and that is that both -- so I reviewed only one of these, but both of them, it's my understanding, will take already publicly accessible data and sort of rework it into another format for analysis and display.

And so I think the point about whether or not this is appropriate for a seed grant mechanism is something that we really should think about, because this is not necessarily something that will foster additional larger projects that will come out of it. It might, but, you know, since the input data is data that's already out there and accessible to the community, it's not entirely clear how what is going to be proposed here will do something transformative for the scientific community.

There's also some scientific issues as far as the particular -- with the Gryk proposal, the particular area of (indiscernible) they want to focus on,

which is receptor like and pairs, which historically the activity of those don't correlate well with RNA levels and so you would always want -- need to go from this analysis to do your own analysis to confirm what they had done.

Whatever analysis they do, there are issues of how to resolve conflicts in trying to compile together data from many, many, many different labs with different levels of stringency in their cutoffs, how they will deal with these conflicts, what the quality control for the data going in will be and then the long-term question of if it's a seed grant and it's published -- or and it's funded for two years and that supports the database, at the end of two years what happens to the database and how do -- how does it get maintained?

And I think that's one of the reasons this would be more appropriate for some sort of resource type core and -- and I don't know, in the grant that I looked at, there wasn't a real discussion about how what they were doing would fit in to national efforts which are headed in the same way.

So I would actually not be in favor of putting these as a high priority for funding, either one of them.

DR. LANDWIRTH: Okay. Bob.

MR. MANDELKERN: I would like to say that I'm not in favor of putting this into a yes category, because I think our mandate is to try to do science and that we are the only committee in Connecticut who has the opportunity to fund fundamental science.

Database can be funded by many other skills, many other areas, but we have the mandate to go to science and to fund as many projects in human embryonic stem cell research that we can.

So I think it is good to look that we have already said yes to three, six, eight, ten seeds in science and I would object to putting this in the yes category for the reasons I mentioned.

DR. LANDWIRTH: Steve?

DR. LATHAM: Another consideration that's similar to what was mentioned before is that the seed grant doesn't offer sustainability and if you want a database to be accessible over time, then after the first year on a seed grant or the second year, they're going to have to come back for more somewhere. Which is why I think it -- Mike's right, I think it belongs in a core grant that has a supporting part.

DR. LANDWIRTH: Ann, do we want to revise

our recommendation?

DR. KIESSLING: I think this is just a tough call, because these grants are very similar, we've got them here side by side. They both have the same specific gains. I think there's a real need for an easier way to get the information together, but I don't know that this is what we want to do with seed grant money. I sort of agree with that.

So I don't have as much issue with making the database or sustaining it as I think this is not one of things we want to do with our $10 million. So probably the University of Connecticut as a system needs to set aside the resources to do this, perhaps in their bioinformatics core or something like that.

I think this is important, I don't think it's our mechanism. I don't think we have the mechanism for it.

DR. LANDWIRTH: It sounds like we're hearing a recommendation to put this in the no column, both of them, on the grounds that it's not appropriate for a seed grant. Any objection to that? Mike, did you want to make one last comment?

DR. GENEL: No objection, but is there -- can we be assured that this be communicated back that we

feel that this does need support, but not within the mechanism. In other words, something ought to go back to both of these investigators and to the institution indicating that our feeling was that this was necessary, but that a different mechanism needed to be --

DR. LANDWIRTH: I'm sure that, that can be -- that can be done.

DR. GENEL: You can do that, okay.

DR. LANDWIRTH: So that both of them get moved to the no column, Nelson and Gryk. Now, we're going back to --

DR. WALLACK: Juli. On UCONN 041 --

DR. LANDWIRTH: I know you agreed that it should be done.

DR. WALLACK: UCONN 041. Wait, no, no, the recommendation back about why we're not funding it.

DR. LANDWIRTH: Right and that information is going to get --

DR. WALLACK: But that letter of -- of description of why we did this will definitely go back to them?

DR. LANDWIRTH: That's -- I'm told, yes. Am I correct?

MS. HORA: Yes, we can put that in. There

also will be minutes from this meeting and a full transcript available.

DR. WALLACK: But they're not going to read the minutes. They need a --

MS. HORA: Yes, we can put that in a letter the way we did on earlier suggestion.

DR. WALLACK: Great. Okay, great.

DR. LANDWIRTH: The next one.

DR. CANALIS: I have a comment.

DR. LANDWIRTH: Please.

DR. CANALIS: Now, we were supposed to fund -- to use about ten percent of the funds for new, you know, seed grants.

DR. JENNINGS: No, we're not less than 10 percent.

DR. CANALIS: This was ten percent or higher.

DR. JENNINGS: Right.

DR. CANALIS: Yeah, with that you're going down with the English. At least ten percent, we're already at 20 percent and I think as a good reminder just to keep it in mind.

DR. LANDWIRTH: Yeah.

DR. CANALIS: Because we have not looked

at the other grants and I think in principle in all fairness to the other grants, we need to keep some parameters be undefined in mind. So at this point, you know, it should be a good reason to move a maybe to the yes category. You know what I mean? We're already at 20 percent of the funds. It's a good -- something that we really should keep in the back of our minds.

DR. LANDWIRTH: Right. Okay, it's a point well taken. Thank you for that. But we still have -- we do have to run through the rest of them and we need to be cautious about our decisions and that's one of the reasons they were ranked according to their score.

Okay, we're now this is the Yale -- this is Yale project 035, PI is Massaro, Regulation of (indiscernible) Differentiation in a Human Embryonic Stem Cells. The score was 2.5 and the proprietary information involved and I -- who were the reviewers?

MR. WOLLSCHLAGER: The reviewers were?

VOICE: Skip.

MR. WOLLSCHLAGER: Dr. Kiessling and Dr. Huang.

DR. KIESSLING: Who is this? I'm sorry.

DR. JENNINGS: It's Massaro.

MR. MANDELKERN: Massaro, YSME-035 is next

in line.

MR. WOLLSCHLAGER: Dr. Canalis, were you a reviewer on that?

DR. CANALIS: I don't recall that.

MR. WOLLSCHLAGER: I have that as Dr. Kiessling and --

DR. LANDWIRTH: My mistake. Kiessling and Milt Wallack. Go ahead.

DR. KIESSLING: That -- that's the application from the very strong laboratory, but a pretty weak application. I would definitely move this to not be funded.

DR. LANDWIRTH: Okay. Milt, comment?

DR. WALLACK: The same.

DR. LANDWIRTH: So we have a recommendation that it be moved to the no column.

DR. KIESSLING: Yeah, this was the application that has a great literature review and -- and very, very, very sketchy description of the experiments to be done.

DR. WALLACK: 035.

DR. LANDWIRTH: We can move it to the no column, thank you. Okay, next -- yeah, next project is a UCONN project, 003 and the PI is Wang. The title is

Rapid Real -- yeah, Rapid Real-time and inside of MRNA detection in living human embryonic stem cells with nanoprobes. The score was 2.5. And reviewers are Dr. Arinzeh and --

VOICE: Comment please.

DR. LANDWIRTH: Give a summary of where it was, how it got to the be in the maybe column and what you think we should do now?

DR. ARINZEH: Yeah, well, I'm not exactly sure why it's in maybe, but the role -- this is a proposal to investigate nanoprobes. Nanoprobes were a detection of MNRAs and human embryonic stem cells and there are a lot of scientific issues in the proposal why -- why are you -- you know that they were able to synthesize the nanoprobes, but then it concerns about why were they targeting MRNAs and just there were a lot of -- so my recommendation is no. There was a lot of issues that --

DR. LANDWIRTH: Any comments? Any more comments on that?

DR. FISHBONE: Can I just --

DR. LANDWIRTH: I'm sorry. Dr. Fishbone.

DR. FISHBONE: Yeah, I think I had put a maybe on it, because it looked like a very technical

project. I withdraw my maybe.

DR. LANDWIRTH: Well, yeah. It can't be a maybe, it has to be yes or no.

DR. FISHBONE: No, I'm withdrawing my maybe to a no.

DR. JENNINGS: He said he withdraws it.

DR. LANDWIRTH: Okay. Alright, so we have a recommendation that it be moved to the no column. Any objection to that? If not, please move it to the no column.

Next one is UCONN project 014, the PI is Chamberlain. The title is the Role of Polycomb Impressive Complex 2 in the maintenance of pluripotency in human embryonic stem cell. It received a score of 2.5 and Dr. Huang and Dr. Genel, please.

DR. HUANG: So this is the proposal by a young investigator who has shown that PRC2 is important in mouse embryonic stem cell differentiation by working on the knockout paper and now proposes to do the same thing in humans, but to do it by RNA eye. It was -- so that -- so one of the key strengths is the investigator's previous experience in this -- in the same system.

The detailed critique talks about the fact that once a cell is not pluripotent, it doesn't matter if

it's multipotent, it just isn't pluripotent. But that might be sort of a semantic distinction. We had put it in the maybe category, because despite its score the investigator had a lot of experience before in the mouse system and this was a very strong proposal.

So, you know, with the score of 2.5, I don't know whether we can justify putting it in the yes category. On the other hand, I think if -- I wish there were a place to leave it, so that in case we do have additional funds available, this is a strong grant. I just can't raise it to the priority to put it ahead of other grants into the yes category.

DR. LANDWIRTH: Okay. Mike.

DR. GENEL: I would leave it till we finish.

COURT REPORTER: You need to stay on the microphone.

DR. LANDWIRTH: Well, leave it where?

DR. GENEL: Maybe. What I am envisioning is that once we have gone through the definite yeses through all the categories, we'll have a better idea of whether we have any fudge room or not.

So I would like to leave this -- leave a few of these as maybes until we go through the rest of

the categories, otherwise then let's -- then I would leave it out. But I think there's value in having a few left over until we go through all the categories.

DR. LANDWIRTH: I may ask for some protocol advice on that, because we didn't -- we didn't state that as an option for the ones we just determined to be either yes or no. So what do you think?

DR. GENEL: Why don't we have an option to stay in maybe?

DR. LANDWIRTH: Pardon me?

DR. GENEL: Why don't we have an option to stay in maybe?

MR. SALTON: I think that what I would recommend is that Dr. Huang and Dr. Genel, is we can move this to no and then before we render final decisions, anyone can request that a no be brought back up for one final look, if there's -- if -- and you do it that way.

DR. LANDWIRTH: Okay.

MR. SALTON: And if you want to put it up above the category of nos in some way, but that way it's just like anything you can reserve an option to bring it back.

DR. GENEL: I would recommend Juli, that we not do what Henry suggested, but if we don't want to

leave it for later, at least leave it for the last item in this discussion of the maybes. That would not be inappropriate.

DR. LANDWIRTH: Last, I think, was five last items.

DR. GENEL: Well, maybe the other four will go, you know, we'll eliminate.

DR. JENNINGS: Mr. Chairman, if I may, I think the whole object of leaving it in the maybe category is that we -- we need to look at the other grants, the investigative grants and the core and group grants and then know how much money we have left over at the end. So in my mind it does make sense to have some category for projects, small projects that we might fund, if there's a little money left over at the end.

DR. GENEL: Yeah.

DR. JENNINGS: I don't think it makes sense to do what Milt just suggested and decide at the end of this session, I think if we're going to do this at all it has to be decided after we've allocated the bulk of our $10 million.

DR. LANDWIRTH: Just in time, look who's back.

DR. GENEL: Well, I would suggest being

not. The interim chair has to handle the question on the floor. I would suggest that we go with 014 in maybe. Let's leave one in maybe and then we'll get back to it. No big deal. We can do that. It seems to be the sentiment.

DR. WAGERS: I want to put my two cents in, I really liked this grant. So I think Paul has got a really good point. This is -- this is a tough call. This is a human embryonic stem cell grant. It's a very interesting area of research.

I didn't read it in detail, but if there's any possibility that we can fund this type of grant as a seed grant, we should really give it a chance.

DR. HUANG: Well, my -- my inclination is to put in the yes category. However, I realize that we're at the point where we decided at the beginning that we would use as a starting out point for how many seed grants we would fund. And I don't want to make it equivalent to the other ones, that's why I said to leave it in maybe. But my inclination is I would like to see it funded, but I don't know whether we can go over the limit.

DR. GENEL: I'm going to make a recommendation, Juli, based upon what Ann and Paul said

that we table it until the completion of the other four maybes and we'll consider that one as the last maybe.

DR. LANDWIRTH: I think we do that. We may have easy judgments on the other four and have nothing -- nothing more to deal with. Is that alright? Okay, let's just hold that one off in the corner where it is now and go on to the other four and see where we are at that point.

Next project is UCONN 054, Srivastava is the PI. Identifying the Metabolic Profile of Self-renewing Stems Cells and it received a score of 2.5 and Dr. Genel and Amy Wagers were the reviewers.

DR. GENEL: Well, yeah I think we -- given the priorities and so forth, I would take it off, although I'm still tempted.

DR. LANDWIRTH: Give us a little summary again of what it was.

DR. GENEL: Well, this was a chemical engineer who wanted to spend some time during the summer to work out a systems approach -- a model -- a systems model for stem cell and I think by spending some time in Wisconsin. But and I -- you know, in a perfect world I would fund it, but we don't have the money.

DR. JENNINGS: How much money are they

asking for?

DR. GENEL: 170, 180,000.

DR. JENNINGS: So it's almost as big as the other.

DR. GENEL: It's almost as big.

DR. JENNINGS: And this is two weeks in Wisconsin is -- it's not important.

DR. LANDWIRTH: Amy, comment?

DR. WAGERS: So I actually had recommended putting it in the no category at the outset, so I'm -- I'm in agreement.

DR. LANDWIRTH: Okay. We're hearing that this go over to the no category, any objection to that? If not, please move it.

We are now up to UCONN project, 020, PI is Crocker. The title is Cytokine Regulation Human Embryonic Stem Cells Derived Neural Pre-cursor Differentiation and received a score of 2.7 and reviewers are Charles Jennings and Mike Genel.

DR. JENNINGS: Can I get just a second to?

DR. LANDWIRTH: This Crocker, 020.

DR. JENNINGS: Okay. I'm almost there and I think I remember it. Okay, so what they're doing, they will be converting human embryonic stem cells into neural

progenitor cells or neural stem cells and then they wanted to look at the effect of inflammatory cytokines.

So it is known that inflammation restricts the ability of the brain to regenerate to repair itself and so understanding that may be of interest and might also be relevant to the efficacy of the neural transplantation therapy. They're looking at one specific -- possibly the matrix associated in the pile of protases on their regulators which are called TIMPS. And so that was my summary.

I'm just trying to remember what we recommended. I remember being -- I was lukewarm about this and the referees, I think, were also lukewarm. I guess --

DR. GENEL: If I can Charles? As I recall, this is a fellow who had just come from Scripps and had just arrived at UCONN when he wrote the grant

DR. LANDWIRTH: Right.

DR. GENEL: Had a great deal of promise, was highly regarded, and my reaction, I wrote down on here, it's too bad we don't have enough money. I still feel that way, you know, it's too bad we don't have enough money.

DR. LANDWIRTH: Right.

DR. GENEL: So considering where we are, I think I would, for simplicity, I would move it over to the no category, but it's a pity.

DR. LANDWIRTH: Right. Charles, you okay with that?

DR. JENNINGS: Yeah, I'm okay with that.

DR. LANDWIRTH: So we have a recommendation now that that be moved to the no category. Is there any objection to that? If not, please move it. Thank you. Next project is a UCONN project, 052, with PI is Amano. That was the Germ Cell Therapy by Nuclear Transfer Derived Embryonic Stem Cells. It received a score of 2.75 and the reviewers were Amy Lee, oh, and Steve Latham.

DR. LATHAM: I think this got into maybe because I saved it from being put in no and now I put it back in no. I thought that the reviewers had given it a lower score than they justified in their discussion of it, but it is entirely a mouse study and I can't justify saving it given these priorities.

DR. LANDWIRTH: Amy.

DR. WAGERS: I agree.

DR. LANDWIRTH: You agree with that, so we have a recommendation that be moved over to the no

column? Any objection to that? If none, please move it.

We are now up to UCONN project 055. The PI is Yao. Method Development for Formulative Analysis of Proteins Phosphorlyation and embryonic stem cells. It received a score of 2.75 and Treena Arinzeh and --

VOICE: Dr. Fishbone.

DR. LANDWIRTH: --and Gerry Fishbone were the reviewers. A comment from one of you, please?

DR. ARINZEH: Okay. I'll start. Okay, it looks at -- this proposal looks at the protein phosphorlyation and will try to characterize protein phosphorlyation in human embryonic -- human embryonic stem cells. And so it's coming up with new analytical methods to do so. And so the issue here is that reviewers will even comment on this proposal.

They said that it's an overlap from the PI's other 2006 grant and so they gave them a score of 2.75 based on that. So it overlapped with the 2006 grant and this year's core facility grant from the PI. So based on the reviewer, you have to say that -- I said no, but they didn't comment on the scientific merit of the proposal, so.

DR. LANDWIRTH: So your view now is that --

DR. ARINZEH: I still say no. I mean it is developing analytical methods, so it really should belong like a core grant anyway.

DR. LANDWIRTH: Okay. Thank you. Gerry, do you have any comment?

DR. FISHBONE: Nothing to add. No, I would vote no.

DR. LANDWIRTH: Okay. So we have a recommendation to move it to no. Any objection to that? We move it. Okay. Now, that's the one we left?

VOICE: Chamberlain, already discussed, we were going to reconsider it.

DR. LANDWIRTH: Okay. And we're back now to the one that we left for reconsideration, it's 014, the PI is Chamberlain. Role of Polycomb Request Complex 2 in the maintenance of pluripotency in human embryonic stem cells. Dr. Huang.

DR. HUANG: If I could, I now propose that we put it in the yes category. The strengths of this are that the topic is very, very important, in terms of figuring out cromatin proteins are bind to cromatin and effect early differentiation of stem cells.

The -- specifically, this investigator has been participating in the mouse work and was one of the

people who knocked out the gene in mice, showing that it's important and now is going to do RNA on human cells. So I would now put it in the yes category.

DR. LANDWIRTH: Mike, comment?

DR. GENEL: Let me just read the first portion of the overall evaluation. This is a very intriguing seed grant application by a young investigator who is likely transitioning from a post-doc to a junior faculty position.

The grant has significant potential for generating novel information regarding early stages of human embryonic stem cell differentiation. That's just exactly what we created the seed grants to do.

DR. LANDWIRTH: So your recommendation is that it be moved to the yes column?

DR. GENEL: Yes.

DR. HUANG: Yes.

DR. LANDWIRTH: Any objection to that? Okay. Right, now we have the nos, which are nos forever, unless somebody has one that they'd like to revisit? They're going to come off the board. Okay. Thank you very much. I would like to turn the floor back over to our leader.

MR. WOLLSCHLAGER: Okay. If I understand

then procedurally, we're not going to consider any of those yeses for any funding right now. We're going to move to the next category. I don't know if you're going to have to sort of move those yeses somewhere.

DR. JENNINGS: We're going to need the board space. Why don't we just peel them off and pile them on the floor right over there?

MR. WOLLSCHLAGER: It's perfectly fine to do that, make it easy.

DR. JENNINGS: Yeah.

MR. WOLLSCHLAGER: We just put them down there.

DR. JENNINGS: We need -- I mean we need the board space and --

MR. WOLLSCHLAGER: We need the space again, right. I mean the nos are the -- you know.

DR. GENEL: Yeah, they're nos forever.

MR. WOLLSCHLAGER: Nos are nos forever at this point.

DR. JENNINGS: Just peel them all off and put them into two piles.

MR. WOLLSCHLAGER: And the yeses I would just --

And I don't have a -- I don't have a

camera phone with me, but we have a record of all the yeses and we just make sure we keep them together. Alright, the next categories are -- well, we have core and group and then the established investigator. I don't know that we articulated a particular order this time around or do we?

DR. GENEL: I would suggest we do the core and the group and then -- because I think that will help define how much money we have available to do the programs.

MR. WOLLSCHLAGER: And I think actually that was spelled out this morning, yeah.

DR. GENEL: Was it?

MR. WOLLSCHLAGER: Yeah.

DR. GENEL: Okay.

MR. WOLLSCHLAGER: So starting with core proposals or -- and core proposals and group are both going to receive 14-minute description and discussion regardless of their peer review score. So we'll start with the cores?

DR. JENNINGS: Where are we starting off?

MR. WOLLSCHLAGER: We're starting with reviews of the core applications.

DR. JENNINGS: So that's category SCP, is

that right?

MR. WOLLSCHLAGER: SCD, D, as in David.

DR. JENNINGS: But aren't we going from lowest to highest score?

MR. WOLLSCHLAGER: Perhaps, to be consistent, we should go from the worst score to the best scores, which is what we did with the seed grants.

DR. JENNINGS: Yes, that's right. Lowest rank --

MR. WOLLSCHLAGER: So we're going to start with the --

DR. GENEL: Why do we need to be consistent? I think it was -- I think it's a much better process if we start from the top and go down rather from the bottom and go up, because it would be much more efficient in terms of our time.

MR. WOLLSCHLAGER: Okay. Easy enough. Okay, so in that -- so as folks pull out their papers, we're going to start review of the core grants, that's SCD -- D.

We're going to do it by rank order with the best, that is the lowest number, and the first application to be reviewed then would be 08-SCD-YALE-004, Lin, with a score of 1.45. And I don't have the names of

the -- the reviewers are Dr. Canalis and Dr. Wallack.

DR. WALLACK: I would be very supportive of this project.

COURT REPORTER: Can you talk in the mic?

DR. WALLACK: Yeah, I will. I'd be very supportive of the project. They've got an excellent rating or review and I'll read from just the last three sentences here. The project is essential to the future of stem cell research at Yale and in the state generally.

My only concern is that the actual space allotted to the embryonic stem cell core may not be sufficient to support future expansion of these activities. But the presentation, the documentation, I read thoroughly. I was extremely impressed by the documentation and by the description of why this was required and I would enthusiastically support this application.

DR. LANDWIRTH: The other reviewer?

DR. CANALIS: Yeah, I --

DR. LANDWIRTH: Yes, Dr. Canalis.

DR. CANALIS: I do agree, you know, basically it's very similar to the application we reviewed initially. Which his -- the grants have been cut significantly. I believe it was a 50 percent cut and

basically he's reapplying requesting for additional funding for the next, you know, for an additional period of time.

It's the best score in the category. He has proven track record. You know he's -- he's made the appropriate progress, you know, I think I fully agree with Milt on this.

VOICE: Ernie, could you speak into the mic, I couldn't hear you.

DR. CANALIS: I try. Honest to God, it's -- we're very close. I mean --

DR. WALLACK: We agree.

VOICE: We agreed, okay. That's what I have to hear. That's fine. I just wanted to hear that much. Thank you, Dr. Canalis.

DR. CANALIS: You know, I thought I'd --

DR. LANDWIRTH: So the recommendation from the reviewers, from our reviewers, is that it be a yes on funding?

DR. FISHBONE: Could I -- should I ask a question?

DR. LANDWIRTH: Any other comments? Yes, question.

DR. FISHBONE: Is the 2.5 million that

they're requesting, is that the 2.5 that we didn't give them last year or is for new and different?

DR. WALLACK: As I read the grant application, it was clear to me that this was more advanced sort of factors they were bringing to the table. So that I think that the implication of the question is accurate and that is that some of it will fit in to some of the things that they didn't -- weren't able to fund before.

What I was impressed about is that it went one step further, while still being consistent with the idea that it will give their researchers the ability to exist in year three and four. So on all of those levels I was impressed by it, as well as the way that the documentation was put together.

DR. CANALIS: I agree.

DR. LANDWIRTH: Thank you. Charles?

DR. JENNINGS: I just want to point out that the amount of money that they're asking for is greater than the entire amount that we've spent in the morning session.

MR. WOLLSCHLAGER: Yep.

DR. JENNINGS: And I think it requires a little more -- a little more discussion before we write

them a check for two and a half million dollars. So my first point is that my recollection is that last year, they applied for four years funding with a budget of five million and then we cut back to two years funding with a budget of two and a half million.

So and if they're asking for another two -- only one year has passed since then, so this is not simply an extension of what they were doing before, right, I would like some better understanding as to why they need two and half million now as opposed to a smaller amount, which is going to -- that's quickly going to consume our budget.

DR. CANALIS: I missed the point.

DR. LANDWIRTH: Can we -- do we have any concise --

DR. JENNINGS: Can you give us some sort of breakdown as to how they're going to spend that money? I mean is it mostly salaries, is it new equipment? Is it?

DR. CANALIS: Oh, that's what you're looking for.

MR. WOLLSCHLAGER: If I could just add to that? The requirement under the RFP was that, I believe, for core facilities was they had to enunciate that there

wasn't going to be an overlap on prior funding for -- so that should be addressed in the proposal.

DR. JENNINGS: But what's the duration -- what's the duration of funding for this one?

DR. CANALIS: It's not reported on here.

DR. WALLACK: As I said to Gerry, my response to Gerry is that it goes further than those things -- at least from what I recall, but those things that they were talking about a year and a half ago.

DR. JENNINGS: Right.

DR. WALLACK: So it's going to, I believe, fill in some of those areas that they will need to go forward in the year three and four.

DR. JENNINGS: Right.

DR. WALLACK: But I also clearly walked away from reading the application with the idea that it was taking their whole process even further.

DR. JENNINGS: Right.

DR. WALLACK: So that that's why I said I was satisfied on all of those various levels.

COURT REPORTER: Alright, one minute please.

(Off the record.)

DR. CANALIS: This -- the overall funding

would carry him to May, 2011. He gives -- on page 11 of the grant, he gives a very good detail of his current funding and resources of the funding.

Frankly, I reviewed this two weeks ago, so the exact details are not as fresh in my mind as they were. But, you know, gave the impression when I read it that he -- it was obviously the continuation of the previous core, but yet made appropriate changes, you know, based on his previous experience, you know, requested different type of equipment. He justified this. The scientific review is virtually flawless.

DR. JENNINGS: Would the first year of funding overlap with the funding that we awarded them last year or is it --

DR. CANALIS: I would request a 30 minute break for me to go and re-read to answer specifically.

DR. JENNINGS: Yeah, we probably don't want to do that right now.

DR. CANALIS: Which I'd be happy to do, you know. When I read it I felt --

DR. KIESSLING: The cover letter says that -- the cover letter says they're out of money in February of 2009.

DR. WALLACK: Charles, my understanding is

that -- both that -- Ernie's on this. I read it more recently than two weeks ago and I read it with that kind of eye, so while it's a 136 page document.

DR. JENNINGS: Yeah, no, I know.

DR. WALLACK: So that I can't tell you the specifics of that answer.

DR. JENNINGS: Yes.

DR. WALLACK: But I was clearly satisfied as I believe Ernie is also stating that it fit the categories appropriately to warrant the funding.

DR. JENNINGS: Right.

DR. WALLACK: I have no reservations about it.

DR. LANDWIRTH: Can I just make a suggestion that we're going to be dealing with funding questions tomorrow and for today we just want to decide whether we want to put this in that category, so that we have a chance to deal with that tomorrow.

DR. JENNINGS: I mean if that's the question, I certainly have no objection to going --

DR. LANDWIRTH: Yeah, we may be funding it tomorrow and deciding tomorrow how -- funding it for how much.

DR. JENNINGS: We can reserve -- I think

this year we have the clear right to ask for less than -- to give them less than they asked for.

DR. LANDWIRTH: Okay. Bob.

MR. MANDELKERN: I would like to comment on this grant also. I took occasion also to read it through from beginning to about page 100 and I was struck very highly in support of it, because in terms of all our own criteria, the ability to perform the commitment, the potential for collaboration, the ultimate high stakes benefits for the State of Connecticut, they correlated the application with every one of our criteria in remarkable fashion. And I think their ability to do so was based upon the work that they've done and what they expect to do.

Some of it is, you know, projected future, hiring further investigators and so on, which they've already succeeded nobly in doing. So I think the report should be -- the proposal should be pushed to yes and it's an outstanding job I felt they did documenting their case in requesting the funds.

DR. LANDWIRTH: Gerry.

DR. FISHBONE: Could I? It seems to me we've been caught in a little bit of a time warp, because of the way that the original request for applications

went out. In other words, we asked them to apply it for four years with -- for the core grant and then we only gave them enough to cover them for two years and whereas most of the other grants were like for two years. And it seems to me that in order for them to continue, even if they were just continuing what they were doing in their original application, they would need another 2.5 million, because that's what they needed for four years. And it sounds like they're actually doing more and enhancing things.

So I'm almost sorry I opened this Pandora's box. You know I think the reason we're in this bind is they're not asking each year for a certain amount and then the next year coming back for a certain amount.

They needed $5 million to start with -- we only gave them two and a half. So it's not unreasonable, as Ann says, they'll run out of funding in February and it's not unreasonable to continue to fund them at the same level.

DR. LANDWIRTH: Okay. So I hear -- is there any more discussion?

DR. WALLACK: Recommendation to put it on the funding side.

DR. LANDWIRTH: Recommendation to put it

on the funding side, is there any more?

DR. JENNINGS: I agree.

DR. LANDWIRTH: So let's move it then, if there's no objection? Let's move it to the funding side please under yes.

The next project is a UCONN project, 003. PI is Aguila and the title is Flow Cytometry Core for the Study of Human Embryonic Stem Cells and it received a 1.5 score.

DR. JENNINGS: Okay. I want to put --

DR. LANDWIRTH: And the reviewers are Ann. Oh, Charles.

DR. JENNINGS: I'm one of the reviewers. I don't -- who is the other reviewer on this?

VOICE: Mike.

DR. JENNINGS: Mike.

DR. LANDWIRTH: Mike, is that it?

DR. JENNINGS: Do you want me to start? Okay.

DR. LANDWIRTH: Okay, Charles, go.

DR. JENNINGS: Okay. So this is an application for a Flow Cytometry Core. This is equipment for analyzing and sorting of human stem cells and other types of cells. They're asking for a million dollars

over four years and the PI, whose name I think is Hector Aguila, is a very established investigator who is already running a Flow Cytometry Core at UCONN and they already have six machines. So some of these machines are quite expensive, they can cost up to a half a million dollars each. I think there's no doubt that these machines are essential for many aspects of stem cell research.

But they're not asking for a budget to buy a new one, UCONN recently spent half a million dollars to buy state of the art cell sorter and they wanted one that would unencumbered by federal funding and can be used for embryonic stem cells and they have that now.

So what this -- what this is proposing is really to provide the support of operating this core facility. And so my -- I'm just looking, because I think the key issue here is whether this is a reasonable budgetary request. I think this -- there's no doubt in my mind that there ought to be some sort of cell sorting core and that many of the purposes that this proposes are reasonable.

I think they're asking for too much money and I'm just as I'm speaking I'm looking for the -- my detailed notes on this. Yes, so and I would point out, I think it would be good to get some comment from Amy

Wagers in the course of this discussion, since Amy is actually running a comparable core up at Harvard Stem Cell Institute that does at least some of the things that they are proposing here.

So my first concern is that they're asking for 20 percent support for the -- for the Director. So I'm not convinced that it requires 20 percent of a senior investigator's time in order to oversee a core facility. And they are also -- I'm going to flip to the budget page, so that I don't misstate it, but they were also asking for a -- sorry, this is not -- it's complicated. They're asking for a full-time post-doc and a full-time technical assistant. One of the referees pointed out that operating a core facility is not really an appropriate activity for a post-doctoral fellow who is supposed to be in training.

And they've asked for 43,000 for various service contracts for these things. So the machines are expensive to maintain. They break down every so often. The service contracts are extremely expensive to keep them operational and that seems like a reasonable thing to be wanting.

I'm concerned that this is just -- this is too much money. I am not convinced that it will be used

only for human embryonic stem cells or even for stem cells. I think there are a lot of other applications of that could use us, who are doing, you know, general immunology research that doesn't necessarily have any link to stem cell research and I don't think it's our job to be subsidizing general purpose immunology research at UCONN.

So I'm sympathetic in principle to the -- to supporting this, but I think that this is too much -- to much money to be asking. I think I am echoed to -- I think I'm echoing here some of the comments made by the referees, so finally I'm concerned about some of the -- you know this is about separation of funding, I'm sorry.

The referee is confused by the inclusion of a post-doc in the budget and agrees that this is not an appropriate position for a trainee and thinks that's not justified. And --

DR. LANDWIRTH: Charles, do they -- I just question the distribution of the usage of that equipment is not spelled out in any detail to satisfy you that it won't be --

DR. JENNINGS: They list the potential uses for it, because -- this is like 60, 70, almost an 80 page grant, so as far as -- I think that they did list

like users and -- yeah, they do. They identify on page 18, they list 18 already funded stem cell researchers. It's already funded through our program who are either using or planning to use Flow Cytometry, so that seems reasonable. Another 22 from UCONN and UCONN Health who are applying to us now that would like to use it.

Of course, we won't -- we've already decided not to fund some of those people. So -- so I think the bottom line is that there is -- you know, there is really a user community for this, but I'm not convinced that -- that that's the only user community and it -- I'm not sure that we should be subsidizing for the facility that quite clearly serves a broader community than just stem cells. And I do think the PI is credible.

The PI is already running a core facility on a smaller scale. I think it right to give them some funding, I just am not convinced that we should be giving a million funding. I'm also not convinced that we should be supporting or that we should commit now to four years worth of funding for -- for this. I mean what I think might be reasonable would be to commit to two years and then, you know, if they continue to provide the community service, we can extend the funding.

I would make this -- I think this is

different from a situation in which they're asking to build something from scratch and acquire a lot of capital equipment, in which I think you really do need a long-term commitment in order to make it worthwhile.

Here we're really talking about salaries and the continuation of services upon the core facility for which the capitol expenditure has already been made. So I don't think there's any sort of structural reason why we need to commit to four years as opposed to three years or two years or one year or whatever.

And so I would favor a shorter period and a lower funding rate per year. So I'm looking at cutting this by at least -- at least twofold in terms of the budget.

DR. LANDWIRTH: Mike, you're a second reviewer on that?

DR. GENEL: Well, I share some of the concerns. Let me point out that this Dr. Aguila is also the PI for a program project using Flow Cytometry which we will be reviewing in the program projects with an almost identical budget, although it's only -- it's a million dollars. So there's some -- there's a fair amount of overlap in what -- that I would see in that.

The other thing that I would point out is

that the Yale Center also has the same machine that they just purchased according to what I read and offered as part of core facilities for the rest of the state and I'm not familiar enough with the technique. It seems to me this a technique that you really want to have close by. You don't want to run up and down the turnpike to use.

DR. JENNINGS: I think it's essential to have it on site. You don't want to be carrying your bifurcate cells, you know, not even across the city let alone across the state. So --

DR. GENEL: Well, listen. This certainly is something that I think deserves funding and I think the question -- I don't know that it's for us to determine precise elements of the budget. I think that has to be negotiated.

DR. LANDWIRTH: Well, then it seems to be the issues of funding in terms of amount and time period are something we can consider tomorrow. So the question for today, it seems to me, is if we arrive at a satisfactory formula for that, will it be something we're going to fund as a yes?

DR. GENEL: Yes.

DR. JENNINGS: I would say yes. I think they've made a good case for the need for providing some

facilities.

DR. LANDWIRTH: Bob, comment?

MR. MANDELKERN: Yes, I wanted to support Charles in his position now of saying yes. I read the grant. A lot of the science, of course, escapes me as a layperson, but it seemed to me that they were seeking to fulfill a very important need with this science. That they felt there was a definite need to have this equipment and that it was being asked for and I think we have to say yes and then tomorrow we will determine just what the levels are, if there is some feeling that it's over asked.

But for now we have to say yes, because it's a worthwhile project, it is only one basis point off from the Yale grant, which we just voted yes to, at the 1.5 score and that is -- 1.45, pardon me, and this is a 1.5 score. I think in -- with all due diligence, we should vote this into the yes category.

DR. LANDWIRTH: Okay, so we have a recommendation that --

DR. WALLACK: Juli, a question through the chair to Mike Genel. Is this -- is this -- I'm having -- could you clarify something?

We funded the UCONN core last time, a year

and a half ago, for 2.5 million I think. Is it your interpretation that this is an extension of that funding?

DR. JENNINGS: No, it's a different --

DR. GENEL: Well, it's different -- it's a different core. Now, I mean one could -- you know, one could question whether or not this could be combined as a single core. I think reality is that I think the physical location of this is somewhat different than the rest of the core facilities at UCONN.

DR. JENNINGS: My -- my recollection is that --

DR. GENEL: This is a core facility, but not part of the UCONN core.

DR. JENNINGS: That's exactly right. My recollection is that the UCONN core that we funded last year did not include Flow Cytometry. So I would see this as -- I think a complimentary core facility that's likely to be valuable to a lot of people.

DR. LANDWIRTH: So we have a recommendation that this be placed in the yes column and remembering that we have some issues about funding levels to be discussed tomorrow. Is there any objection to that? If not, let's move it there please. And now with great pleasure, I defer the chair to our leader.

DR. JENNINGS: Can we take a break?

DR. LANDWIRTH: Dr. Galvin.

DR. GALVIN: Is now a good time to take a break?

DR. LANDWIRTH: Oh, no, oh, okay. Want to take a break?

DR. GALVIN: Good time to take a break.

DR. LANDWIRTH: Okay. Break time.

(Off the record.)

MR. WOLLSCHLAGER: Alright, if folks can take their seats back, please. Just a reminder, we're doing the core grants, 14 minute maximum discussion of them all. At this point, we've only got two of them done, so we need to keep moving along.

The next proposal under consideration is -- I'm sorry, I can't read by writing -- is 007. PI is Han. Amount requested is two and a half million and the title is Integrated Proteomics and the score was a 2.25 from peer review. Principal reviewers on this are Dr. Wagers and Dr. Landwirth.

DR. WAGERS: Okay, so this is a grant that brings together six investigators, three of them at the Farmington campus and three of them at Storrs and the focus of the grant is on establishing an integrated

analysis of human embryonic stem cells using proteomics, metabolomics and chemical biology.

The grant -- basically the idea is to identify proteins, metabolites, phosphor proteins that are -- and kinases that are expressed in human embryonic stem cells with the idea that cataloging all of these might be useful in understanding what these stem cells do. This is a $2.5 million proposal.

The score is obviously quite a different category from the last two that we have talked about and I think part of the issue is that -- and this was pointed out by the reviewers -- there's a lot of effort going on in this core, but it's not clear the sort of central hypothesis or central goal that's going to be achieved and how that's going to be useful.

So things that one could wonder also they will use only NIH approved lines not unapproved lines, so in theory this is a proposal that could be funded through an NIH mechanism. There are novel aspects to it, but the integration wasn't -- the components of the core wasn't all that clear.

And there's issues of the sort of scale of what they want to do and how they'll prioritize what -- what will come in. They say that in addition to directly

profiling these cells and making that information available -- which I would actually argue is not really a core facility, that's more of a project in and of itself, if they're going to be generating this data. And they say that in addition to generating this data, they will help others around them to apply these kinds of proteomic approaches to their studies as well.

But there's not a clear discussion about how these different activities will be prioritized, what kind of group that they can handle, what kinds of numbers of projects would, you know, probably be able to be supported. There's a lot. They include in the application many, many, many letters from many, many, many different investigators that say, you know, this is exciting and we would make use of it although these are fairly general types of support letters and it doesn't give a good or a clear impression of how -- how all this would be -- would be facilitated.

Also, they promise to give training to these individuals in these different labs should the technologies that they are using through this kind of a core bank mechanism becoming very important in their own research. But then you have to wonder since much of this relies on very specialized pieces of equipment, whether

there will be ample time on those pieces of equipment if you train all of these investigators to use them, whether the sort of capacity will be there.

And so I guess I was -- I was less enthusiastic about this grant. I thought a major component of it actually relies on generating enormous amounts of human embryonic stem cells and profiling them without a clear direction of where that information is going -- is going to take you. There are absolutely some interesting and novel aspects to this that I think might have been stronger even as, you know, a group proposal or a seed grant proposal individually to try to -- to look at these novel profiling types of approaches in human embryonic stem cells and it's sort of brought down by -- by the generics in their transcriptional profiling and sort of hybrid but not speculative that aren't particularly innovative in any way and the questions about how this enormous amount of work is going to be channeled. So that's -- that's my impression of it.

DR. GALVIN: What would be your recommendation?

DR. WAGERS: Oh, sorry. My recommendation. I think I would probably put it in the no category. I think in light of the other priorities

that we have and the strong support for the two cores that we've discussed previously, it would be hard for me to argue that this would be a stronger core, especially since I have some -- some question really about how much of it actually fits into a core mechanism.

DR. GALVIN: And Dr. Landwirth, did you have comments?

DR. LANDWIRTH: I'm afraid I can't comment very much on the technical aspects, but I'm a little concerned about how the organization aspects come through. The peer reviewers described this as a proposal of four interrelated projects and a dedicated stem cell sub-core. The table of contents talks about four cores and a sub-core. And I don't quite get that and then nor do I follow how it relates to the core that's already there. So I'm a little concerned about this proliferation of cores. So I follow that -- Amy's lead on that recommendation.

DR. GALVIN: We have recommendations from the two reviewers that it go into the do not fund. Is there agreement with that? Anybody disagree?

DR. JENNINGS: I would just like to ask a question, Mr. Chairman. Since there are like three or four separate components and they're not terribly well

integrated, are there any components here that are interesting enough that they might stand on their own, since we do have that option?

DR. WAGERS: I guess I hadn't looked at it from that standpoint. So they're sort of the two components that were the most innovative are one is a foster protein profiling where we're basically able to take specific domains of proteins, SH2 domains, that recognize particular phosphorlyation modifications on proteins and use those to catalog what proteins might be signaling in embryonic stem cells.

The other is a chemical biology approach that uses modifications that are active enzymes, but there are some concerns there about whether those chemical probes would modify, in fact, the signaling properties of the stem cells themselves.

I think in all of the cases, perhaps because of the space limitations, is the whole concept of what really they were going to study here wasn't elaborated so clearly. As I recall, the most -- you would kind of want to compare -- compare cells in different states in order to understand the biological processes that get them between those two states. And in many of the components they talked really just about

profiling embryonic stem cells in a sort of standard culture condition. In one they talked about plus minus FGF signaling.

I think these are really interesting applications that could be developed into an idea that would really test the hypothesis and, you know, provide new information, but as they are written, I don't really see them as core facilities so much, because they really require inputs of novel agents in sort of a biological rationale for setting that up.

DR. JENNINGS: In fact, one of the senior investigator grants from Bruce Mayer actually has what sounds like a very similar thing, which is to do phosphatizing profiling using SH2 domains and that scores well.

I'm one of the reviewers on that and I think that's worthy of very serious consideration. I don't know if Bruce Mayer is the PI or the co-PI for that section you mentioned. If so, that would be a strike against this one.

DR. WAGERS: Sorry, I can look here, I don't remember all the names, I didn't write them all down.

DR. GALVIN: You're checking on that Dr.

Wagers?

DR. WAGERS: Yes, I'm trying to find it here.

MR. MANDELKERN: As I recall from our discussion last year on a different core grant proposal, which had very high ranks for part of it and mediocre for the rest of it, which pulled down the overall score.

We were told that we cannot spin out any piece that the core grant has to stand as a whole. Since we did not in the RFP say we would spin out pieces. So I think it's all or nothing based upon the recommendation we had from counsel last year in relation to the SCNT core.

MS. HORA: We did make some modifications to the RFP this year that allows us to consider parts of grants. We are not bound the way we were last year.

DR. WAGERS: To answer your question --

MR. MANDELKERN: I stand corrected. I was on the drafting committee, I don't recall it. I'll have to look at the RFP. Thank you, Marianne.

DR. WAGERS: To answer your question, yes, Bruce Mayer is the PI of the Phospho-Tyrosone profiling component of this core grant.

DR. JENNINGS: So I then vote not to fund

this and evaluate Mayer's proposal later on its merits.

DR. WAGERS: That's fine with me.

DR. GALVIN: It sounds like we have a consensus no. That's it.

MR. WOLLSCHLAGER: Alright, the next core for consideration is 001, Lee, it's for 2,005,000. It received a peer review score of 2.5. It's name is Establishing the Connecticut Therapeutic Cloning Core Facility - From Startup Technology/Feasibility Tests to SCNT/ntESC Derivation Services or something of that sort. And the principal reviewers are Dr. Arinzeh and Professor Latham.

DR. LATHAM: This is -- first, there's a central ambiguity. This is a proposal from Evergen, which is a private company in Storrs closely allied with Gerry Yang and his group. What it appears to be is an effort -- because of the rules last year that Mr. Mandelkern was just mentioning, there was a hybrid grant last year that contained a core proposal and some group projects proposals. The group projects proposals did not meet with this committee's approval, because the thought was that you needed a core in place before you could go forward with those group project proposals.

This now is an effort to create a core

that you have to have in place before you can go forward with those group projects proposals. We couldn't fund just the core, because it was part of a hybrid proposal last year. But this time it's housed in Evergen, although there is comment in the proposal to the effect that they're thinking about making it a 501C(3) public benefit corporation.

So the application comes from a private for-profit firm, but they express willingness in the application if the core is funded to house it -- well, they don't say willingness, they say they're investigating it with tax lawyers and others, to house it in a 501C(3).

There's a big chunk of the grant proposal that's actually repeated twice that details the history of the proposal in last year's grant making and Gerry Yang's ties to the proposal. The promise is basically to set up a stem cell nuclear transfer center and an embryonic stem cell core in Storrs for use in close cooperation with UCONN Storrs group and I'll leave it at there and let you say more about science than I can, if you would?

DR. ARINZEH: Yeah, I mean that's -- that's pretty much what I had to say and then in addition

to that would just be that -- I mean, you know, I just looked at the science in terms in the group and their capabilities. I mean obviously this is a very good group -- a good -- a good team that could potentially pull this off.

But it does seem a little ambitious to do this in two years, what they plan to do, which is do training and have all these lines and -- I guess these are human cells, so everything has been based on animal cell or -- so.

DR. LATHAM: And I'll add that one of the peer reviewers' comments -- the peer review on this is very, very short and it basically says these people are absolutely terrific, they have all the capabilities they say they have. However, it says, the uncertainty over this proposal must be about the long-term value of this approach to the derivation of disease or patient's specific HES cell lines. Given the rapid progress that has been made in development of methods for direct reprogramming, direct reprogramming would seem to be a more fruitful area of research with far greater long-term potential. So that seems to be the motivation for the score being the way it is. So.

MR. WOLLSCHLAGER: Are either of you

making recommendations?

DR. LATHAM: I guess I would recommend no, somewhat reluctantly, because it does seem as though it's -- I think last year when we looked at this, we were excited about the core element of the hybrid grant. I just -- the reason I'm leaning no is that I'm a little worried about the housing of it now in Evergen with the gesture that it could potentially be housed in a non-profit corporation. Perhaps that could all be worked out in the contracting process, but I'm a little worried about who's really going to be doing this.

DR. GALVIN: Dr. Arinzeh, any recommendations?

DR. ARINZEH: I guess I want to say maybe, but I'm leaning towards no. But, you know, like I said I think just from the size and the group itself, I just think it's a very -- I mean I like the group, in terms of, you know, what they -- what they're capable of doing. So.

DR. LATHAM: Maybe someone else on the committee could speak to the question whether it would be useful to have a core facility like this in Storrs.

DR. JENNINGS: So you're looking -- I'm in recusal.

COURT REPORTER: Dr. Jennings, put the microphone on.

DR. JENNINGS: I'm sorry. I said I am in recusal on this, since I'm a former consultant to Gerry.

MR. MANDELKERN: The only -- the only addition I might make, Steve, is, is my understanding that Evergen is a quasi-private. That is a partnership between Evergen and UCONN. That it's a quasi-public, quasi-private. Am I right, Dr. Wallack?

DR. LATHAM: All I can judge by is that its called Inc.

MR. WOLLSCHLAGER: I can only speak that there is been presented to our office, but not approved, a draft proposal for UCONN to invest money into Evergen. That is a very questionable proposal from our office perspective as far as even the ability of the University to invest as if it was the treasurer's office.

So I don't know of any -- the only information I can contribute on that question is that our office has not approved and sent back even the whole concept of UCONN investing.

Now whether there's some other kind of operational partnership, I'm not aware of that.

DR. GALVIN: Now, are we going to consider

the potential science that could be created and if so, what weight does that have in comparison to our concerns or lack of clarity about exactly who the entity is or represents?

DR. KIESSLING: I unfortunately didn't read this application and I promise I will do so tonight in detail. But one of the -- one of Connecticut's strengths is this team that can do somatic cell nuclear transfer. There are very few teams in the world that can do this. And it's -- for instance, this is something that's really lagging in California, for their $300 million, they don't have a team like this.

So at some level, this would be to Connecticut's advantage to either improve this technology or even address the question as to whether this is a more effective way than induced pluripotency for reprogramming a cell.

I haven't read this grant in detail, I don't know what it's strengths and weaknesses are, but the -- but the technology is unique to this team.

DR. GALVIN: So are you saying that you really are not terribly concerned about sorting out which quasi it is and -- or which, you know, whether it's a 501 or something else, that doesn't make any difference to

you?

DR. KIESSLING: No, I -- at some level it's probably better if it's a small company. I mean that's what Connecticut wants to do is develop companies. So I mean this money is supposed to go to developing companies, not universities. So it's very possible --

DR. GALVIN: So what -- what do you think of the science?

DR. KIESSLING: The science I think right now is basically unproven. I mean we can do this in mice. We can obviously clone all kinds of large animals. Nobody understands the efficiency of reprogramming adult stem cells in any useful way and that's a big question all over the world. And now that we can reprogram cells in other methods besides passing them through eggs, it becomes a different question. But there are very few teams in the world who can really do this.

DR. GALVIN: Would you be more comfortable discussing this in the morning?

DR. KIESSLING: Yes.

DR. GALVIN: Put it in maybe.

DR. FISHBONE: If I could add something to what Ann just said? I think she made a very important remark that we're one of the few places in the world

where somatic nuclear transfer is being worked on from a research point of view. And since we don't know whether the induced pluripotential cells will do the same as embryonic stem cells, it may be worth, you know, some investment -- I don't know what the sum of money is -- in order to keep this work going on. Because without support, it's going to stop and we will never know whether that's, you know, a viable method of -- of being able to transplant embryonic stem cells in humans.

DR. GALVIN: I think that's a very worthwhile comment as was the preceding comments from Dr. Kiessling. I think when we look back at this, we -- we have to make some -- excuse me -- some value judgments about what portion of this particular endeavor, if not all of it, we wish to endorse. And what I hear from my two valued colleagues is -- is that there is a piece of technology we need to preserve and I think the group needs to look at this first thing in the morning after Ann has had a chance to peruse it for the quality of the science that it -- I hear two -- I hear several things. I hear one is there's some doubt about who is the entity, but I hear something else about it's very important to preserve the technical abilities and something else that has to say something with is the science that's going to

use these technical abilities sound or should we just look at some way -- are we doing good projects and preserving the technical abilities or are we doing something with perhaps less than great science and in the process preserving this technical capability? And we need to sort that out. I would appreciate if we could Dr. K's opinion tomorrow, if she should have a chance to --

DR. KIESSLING: I'm sorry.

DR. GALVIN: -- review it.

DR. KIESSLING: I looked for this and didn't find it.

DR. GALVIN: Oh, Dr. Canalis, yes.

DR. CANALIS: It's 3:00, I'm waking up again Commissioner.

DR. GALVIN: Good.

DR. CANALIS: If it's UCONN, I am in conflict. If it's not UCONN, I'm not. And if it's not UCONN and it's a company, I think tomorrow when this is re-discussed, I think we need to pay clear -- close attention to escrow related issues and that they're all in place. Because we know, you know, escrow's quality would be in place at University of Connecticut and Yale, but on private companies, that could be a question that

needs to be resolved.

DR. GALVIN: If it's UCONN, I can't vote on it either. So I think that's one of the -- another question we need to resolve is are we voting on a UCONN project, which you and I cannot vote on, or is this significantly distinct from the University of Connecticut and from the Health Center that the UCONN-connected members of the committee can vote on it.

DR. CANALIS: But the request regarding escrow still remains, you know, in place, particularly if it's not UCONN. I think companies should have, you know, a clear record.

DR. GALVIN: Yeah.

DR. LATHAM: If I may add one thing? This is also a low peer review score compared to what the core proposal from Gerry's group got last year. I don't remember who was assigned to review the hybrid last year, but it might be worthwhile to explore why it is that -- what this application is claiming to be is a re-visitation of the piece of Gerry's last year hybrid grant that -- that wanted to establish a core, which was last year very highly rated by the peer review committee. And if -- if it hasn't changed substantially and it's got a much lower rating, we should figure out why.

DR. CANALIS: Is lower better or lower worse?

DR. LATHAM: I'm sorry. It's got a much worse rating this year than the last.

DR. CANALIS: Okay. So last year it was better than this year?

DR. LATHAM: Correct.

DR. CANALIS: And it's the same proposal?

DR. LATHAM: On the face of the proposal, it claims to be basically carving out the core element of what had been a very highly rated hybrid proposal last year. Well, highly in the sense of good.

MR. MANDELKERN: Can I suggest that we go with the proposal to leave it at maybe with some further research on all our parts tonight and we can review it fresh in the morning?

DR. GALVIN: That's sounds like a winner to me.

MR. MANDELKERN: Excuse me?

DR. GALVIN: That sounds fine to me. I think that's a good proposition. So we shall place that in the maybe catalog and review it in the morning.

COURT REPORTER: One moment, please.

(Off the record.)

DR. GALVIN: That is number what, Mr. Wollschlager?

VOICE: One.

MR. WOLLSCHLAGER: That grant is number 001, that's SCD-001.

COURT REPORTER: Can you say that in the microphone?

MR. WOLLSCHLAGER: That is grant SCD, like David, 001. With a PI of Lee.

MR. MANDELKERN: That's what we were doing, 002.

DR. JENNINGS: 001.

MR. WOLLSCHLAGER: 001.

DR. JENNINGS: That is 001.

DR. FISHBONE: You know my -- my recollection of last year was that -- that the grant from UCONN was lower rated, like a 3.5. It's just a recollection. And it would be nice to have that information, if we can. But I think the reason was that some of the proposals in it, some of the sub-grants were not very good, which sort of brought down the overall.

DR. LATHAM: I think that's what the representation is on the face of this proposal was that the hybrid grant had in it a core proposal and then some

group proposals and that this -- that the peer reviewers thought that the group proposals depended on the pre-existence of the core. And then for technical reasons, the whole thing -- we couldn't partially fund one piece with the other.

DR. KIESSLING: I think the big difference this year is the introduction of induced pluripotent cells. I mean the reviewers are questioning putting $2 million into technology that may not be needed. If induced pluripotent stem cells had not been invented in the year 2007, I think that this would probably score very highly. If this were still the only way to do it.

MR. WOLLSCHLAGER: All right, so that's in the maybe category and we can talk a little bit about some other information we'll bring to the table tomorrow. So the next core grant then is SCD-002. It's the PI is Cecchi and the institution is the Zenith Biotech requesting 380,000 for a grant called Build-out of the Stem Cell Media Facility for Research and Production. And the -- I'm sorry -- and the peer review score was 3.75. Primary reviewers are Dr. Huang and Mr. Mandelkern.

MR. MANDELKERN: This is one of the grants where we succeeded in provoking an application from a

private company. Unfortunately, the quality of the science leaves a bit to be desired. This is basically a request to develop mortars and bricks to build a center for stem cell culture media products. They want to have an offices of a conference center built and their aim is worthwhile, but the science is very lacking in this application.

They propose to develop reagents that support growth, differentiation, development of tissue microorganisms. However, the proposal is largely a list of facilities to be developed and not of science. There is minimal presentation of the properties of the reagents to be developed and approaches to quality control and so on, criteria control, are very lacking.

I would encourage this private entity to reconsider its point of view and focus more on science rather than bricks and mortar. And with a score of 3.75, I -- I, with my colleague, who was Dr. Huang, my esteemed colleague, Dr. Huang, pardon me. We must suggest a no category for this application.

DR. GALVIN: Any other members wish to comment? Move that to the no column.

MR. WOLLSCHLAGER: And the final core grant application under consideration is SCD-005. Excuse

me. And the PI is Hiskes, 230,900. It received a peer review score of 4 and the title is Human Embryonic Stem Cell Research Ethics, Oversight and Education. Reviewers for this grant are Dr. Kiessling and Professor Latham.

DR. LATHAM: I'd like to say a couple things about it to begin. First, I think we should all ignore the peer review score, because the peer review -- this is a non-scientific proposal and the peer review score was on the basis of what appears to have been a policy decision by the peer review committee that I think is really for this body rather than them.

A few minutes ago, we were talking about the database proposals and we said that where they really belonged were in the core category to support core research. This proposal, I think, falls into that area. This is basically a bid by UCONN to have its escrow and educational support systems for their stem cell research be funded instead of, as they describe it in the application, being an unfunded mandate.

So the idea here is to pay for escrow staff, educational services, training by the escrow to researchers on ethics issues, and I think it's a logical part of supporting the core to have it get funding.

One of the reviewers -- or there's a

statement in the peer reviewers' document that I think backs up why they gave it such a low score and they said well doesn't UCONN get overhead in its grants anyway? What's it spending its overhead on, if it's not spending it on escrow and other things.

But I think it's really for this Committee rather than for the peer review committee to decide whether it's a good idea for our funding monies to go toward ethics support of the projects.

DR. KIESSLING: I have a slightly different view of this. I am actually very sympathetic with this need. However, I believe that the reviewers were right. Most of the escrow committee functions come out of indirect costs. So we're already at some level funding some of the escrow functions. In that, I would love to see from this particular investigator a proposal for specific ethics focused activity. If they want to develop a course, if they want to -- ask a question, if they want to do something. But to support UCONN's escrow committee as a core facility, I don't think is -- I think that's already mostly done out of the 25 percent indirect costs.

DR. GALVIN: Any further comment? Yes, Mike.

DR. GENEL: I agree with Ann. I think we're opening up a Pandora's Box when we start to fund activities that really ought to be institutional responsibility.

DR. KIESSLING: This group wants to do more than that. I think they really do want to develop a sound ethics educational program for the State of Connecticut and I think that this team is uniquely qualified to do that. That's not what this application is. So I would really like to see an application from this group that's either asking an ethics question or developing a set of guidelines or something.

DR. JENNINGS: Mr. Chairman, if I may?

DR. GALVIN: Yes, Charles.

DR. JENNINGS: I think that raises at least legal questioning, what is -- what is our mandate under the law? And certainly supporting research is our mandate and certainly the ethical review is part of supporting research and make where -- where -- how that should be paid for, but it must be paid for.

I think a separate question is whether -- whether we should be supporting bioethics research, scholarly activities that go beyond the managery oversight and I think -- independent of whether we think

that that's a worthwhile scholarly activity, I raise the question whether we're even allowed to allocate funds to that purpose under the statute.

DR. GALVIN: I certainly share some of your apprehensions about that and -- and share some of the other comments about whatever, that it is, in fact, most likely a part of reasonable overhead by the fact -- by the University.

I don't see -- and I think echoing Ann's remarks -- I don't see a specificity of this dealing with a particular problem that has to do with stem cell research, although it could. But I think since it would -- the activity benefits the whole University, you almost have to look at it as a part of overhead. Any other comments? If not, what is the sense of the Committee? Yay, nay or maybe?

MR. MANDELKERN: Nay.

VOICE: Nay.

DR. GALVIN: All right, that's negative. That goes in the --

DR. LATHAM: Well, I disagree. I would say yay.

DR. GALVIN: Okay. So do we want to take a vote?

MR. WOLLSCHLAGER: Well, we haven't -- we haven't -- we haven't taken any votes today, we've been trying to do it by consensus. But I guess it would be necessary to go on the record if we can't reach a consensus.

DR. LANDWIRTH: We can go maybe. Did somebody say maybe? Or Steve say --

DR. LATHAM: Also, it's for $230,000.

DR. KIESSLING: I was going to say this is a pretty small amount of money. I'd actually like to leave this is the maybe category. I think this should be revisited. I think it also needs to be -- the budget needs to be looked at with the respect to the fact that some of their activities are already -- should be funded by UCONN.

DR. GALVIN: I have to disagree with you. What would change overnight to take it from a maybe to a yes or from a no to a yes?

DR. KIESSLING: How much money we have.

DR. GALVIN: Is that a reasonable determinate? Are we fitting the money to the science or the science to the money or do we want $250,000 to go into this rather than into a piece of science or attract a new -- a new individual or a new researcher? So I'm

not sure what will change overnight, but if you want to reconsider it tomorrow, we'll reconsider it tomorrow.

DR. KIESSLING: I'd feel more comfortable doing that, because I think this is a unique problem.

DR. GALVIN: I'm just not sure it's a problem we're going to be able to solve very -- very easily without figuring out fractional overheads and a lot of kind of difficult stuff. But we'll put that into maybe.

MR. WOLLSCHLAGER: That completes the first cut at reviewing the cores. I know the Commissioner would -- would remind us and encourage everyone to review the nos up there, because once they're no, they're going to stay nos. And we'd like to do that and if I understand it, the Commissioner would wait until tomorrow for reconsideration on the two maybes.

DR. GALVIN: That's -- that's correct. And then once again I would urge you all to make sure that you understand which two are the yes and which two are the nos. It's hard for me. I can make it out pretty well, but it's hard to tell sometimes which grant you're talking, that they're all -- they're all relatively small print, at least for me, and they're all on green paper.

So if there's something -- if there's

something in the no that you thought should be reconsidered, now is the time to say so.

MR. WOLLSCHLAGER: Alright, then, next order of business and we're going to need -- Pamela, I guess we're going to need to rearrange things a little bit, because we're going to keep going.

MS. HARTLEY: Okay.

MR. WOLLSCHLAGER: And so I guess you want to get the two -- you want to be able to have these taken off the board, but appropriately categorized so we can revisit them tomorrow.

DR. JENNINGS: If we're doing the blue ones next there's room to keep them on the board.

MR. WOLLSCHLAGER: Well, that's true, with the blues we could just keep going. You're right. Thank you.

Alright then in that case we're going to continue with the same time frame which is 14 minutes. We're looking at the C category grants now, that is for -- C is -- C is what? C is hybrid or group grants. Group grants. We're going to go in order of best rated by peer review to worst rated. Which means the first grant would be SCC-005, submitted by Redmond, requesting basically $2 million, peer review score of 1.25 and the title of that

proposal being Translational Studies in Monkeys. And the two primary reviewers we have Dr. Kiessling -- oops, I'm sorry, that may be wrong. Dr. Jennings and Dr. Fishbone, I believe that's correct.

DR. JENNINGS: Gerry, do you want me to take the first crack at it?

DR. FISHBONE: My pleasure.

DR. JENNINGS: Okay. So this is a project from Gene Redmond, a professor of psychiatry at Yale and it's the highest score in this category. I believe it's the highest scoring in any category. They're asking for $2 million over a period of four years.

I felt that my bottom line is they make a very strong case and I'm going to come down in favor of this one. So what they're doing is studying human embryonic -- the human embryonic stem cells --

COURT REPORTER: Microphone?

DR. JENNINGS: I'm sorry. Oh, I'm sorry. Let me move over because the cord is just not moving. So they're working on human embryonic stem cells as a potential therapy for Parkinson's Disease. So this is an idea that's been extensively explored in mouse studies and to a lesser of mouse and rat studies and to a lesser extent in monkeys and there have been a few human trials.

They're not with embryonic stem cells.

And so the idea is to -- is to do a large scale study, so I believe it's 16 monkeys in year one and then 24 monkeys in year three and so all the monkeys will be followed for a period of two years. And the work is going to be done in St. Kitts, which I have to look up, but it's apparently St. Kitts and Nevis and it's the smallest -- one of the smallest countries in the Americas. It's a little island in the Caribbean, which somehow got populated by African Green Monkeys. I guess they were brought there by pirates and they ran wild and there's now 25,000 of them in terms of wild commonly on the island.

So this research facility takes advantage of that and the point here is that this is a very valuable opportunity to do primate research, monkey and primate research that is increasingly expensive in the United States. And this facility has been around for I think 20 years. It's operated by a non-profit organization called The Axion Foundation, which is based in Connecticut. So although physically the location is out of state, it is overseen by an entity that's incorporated in Connecticut. And so I'm very much hoping that there won't be any procedurals issues with that, but

I raise it because it is an issue to the discussion.

And what they're planning to do is differentiate the human embryonic stem cells to different -- to different stages in the dopamine neuron lineage and then they will put them into monkeys that have been treated with the toxin known as MPTP, so this is a very standard model of acute Parkinson's Disease and they will characterize the monkeys' behavior in great detail. So that one of the features of this colon in St. Kitts is they have intensive on-site staff, they can get this relatively cheaply to provide both veterinary care, which is particularly important if you're talking about monkeys who have treated with a toxin, they need -- they're very expensive to maintain and look after them to make sure that they're properly -- they're properly treated. And also they'll be monitoring their behavior very continuously to see how the symptoms, the change of time following these neuro-drops.

So the idea is you turn the embryonic stem cells into dopamine neuron precursors and you put them into I think three different locations in the substantia, nigra and the striata, the areas that are affected in Parkinson's Disease. They will monitor the outcome over -- over a substantial period of time. Will then

sacrifice the animals and look in great detail to see what has happened, the survival of the graft and how the cellular events in the brain correlate with the behavioral improvements that they expect to see in the transplantation -- as a result of the transplantation.

So I was impressed at the thoroughness of this. It's a substantial budget and a lot of it is salaries. But there's the facility to produce human embryonic stem cells. I'm not -- I don't -- it wasn't absolutely clear to me -- well, I haven't read every page of this grant, I wasn't absolutely clear what stem cell lines they'll use, although they will be using non-federal ones. So this clearly is not a federally fundable project at the moment. And there's substantial effort devoted to culturing and differentiating and characterizing the embryonic stem cells and then there's the -- all of the surgery and the behavioral monitoring and the post-mortem examination.

So to me it's -- it had a -- it had a flavor of rigor and thoroughness. I think these kinds of studies need to be done on a fairly large scale in order to get significant results and they are -- they appear to be doing that. And -- and to me, most importantly, this is something in which there is a clear therapeutic

concept. I think it's very well established. Moving into primates and studying systematically -- not human -- primates what primates correlate with successful therapy seems like an essential step towards a human cellular -- cellular therapy for Parkinson's.

So I liked this very much and the referees comment, the proposal is excellent, very well written and has the potential and the investigators have the experience to move to clinical trials in Parkinson's Disease. Certainly Redmond has a very long and impressive track record in this field. So -- so I would concur with that.

The only negative comment is they say the study is -- it's not novel as compared to several other studies using the NOD embryonic stem cells. So, you know, I think that I would say in response to that -- and I haven't gone back and done a thorough examination of the literature, but, you know, conceptually certainly the idea is out there. This I think is a very thorough -- thorough study. I think more of this kind of thing is needed. One needs a very substantial body of animal data, before you can start with human embryonic stem cell therapeutic trials -- I'm sorry, human clinical trials and I think this is an important step on that path. So

I'm in favor of support -- of funding this one.

DR. GALVIN: Okay. But this -- but it's outside the state and outside the country. And the money is being -- the money is going to be spent in St. Kitts.

DR. JENNINGS: No, not so. Let me clarify the budget. So most of the -- most of the budget goes to salaries of people at Yale. So it's a Yale project with a subcontract to the Axion, which is based in Connecticut but operates the facility in St. Kitts. So the -- let me give you the amount. Out of the two million budget 583,000 is the subcontract to Axion and the office actually provide there -- it's a well presented grant. They provide tabulated posts of the -- of doing this with Axion -- doing this in St. Kitts versus what it would cost at either the Yale Primate Center or the New England Primate Center and it's a very large price difference. I mean they're not exactly comparable, I think because they're -- it's a different species of monkey, but it's --

DR. GALVIN: Well, they're not -- they're not comfortable with this species of monkey, did I hear you say?

DR. JENNINGS: I said the cost may not be exactly comparable, but there is an impressive cost

savings in doing this through the St. Kitts' facility. So it's a grant to Yale with a subcontract to a foundation in Connecticut that operates a facility in St. Kitts. The PI is a professor of psychiatry at Yale, who is also a co-director of the facility in St. Kitts and will fly back and forth and will supervise and in some ways perform hands-on work himself at the St. Kitts facility. So this is basically a grant to Yale in my -- in my eyes.

DR. GALVIN: Yeah, but some of the money is going to be spent outside the country.

DR. JENNINGS: Some of the money, yes.

DR. GALVIN: And there's going to be coming -- comings and goings back -- I'm sure that the St. Kitts trips won't all be totally disregarded by folks that would like to get out of the rain. But I am concerned about our charter to spend -- to spend the money in Connecticut and I'm not -- I'm not sure about this. This looks like a way to sort of -- just a moment -- you know, I have some business feelings about this. Yes, Mr. Mandelkern.

MR. MANDELKERN: If I may reference this report that Charles just reported on? Page 54, may I read, Chairman, for a moment? We are aware of the

position that the Connecticut Stem Cell Initiative money should be spent entirely within the state. However, we believe that this project should be an exception for the use of primate resources which are not available in sufficient quantity anywhere in the United States. Even the largest pharmaceutical companies are lacking primate facilities and the federal regional primate centers and most university animal care facilities have been heavily subsidized by federal dollars. The bulk of the project resources will be spent within the state, but the project is dependent on primate resources which are essentially unavailable in the United States.

There was a conference on this question, the result of which the process was substantially funded for the expansion of the St. Kitts facility by Harvard, John Hopkins, Rush University, University of North Carolina and the Burnham Institute, which have chosen to collaborate with the Axion Research Foundation on stem cell and gene therapy studies. This is within the report that Charles just referenced and it also has great reference -- I don’t want to take the time of the Committee to read any further, but page 54 gives detailed explanation of the supervision of the work in St. Kitts by people from Connecticut, which has over 22 years

experience in working on this project in St. Kitts. So there's a long record of supervision and careful expenditure of dollars --

DR. GALVIN: St. Kitts isn't Connecticut.

MR. MANDELKERN: No, I hardly think so. It's got a different climate Dr. Galvin.

DR. GALVIN: Yep, I understand -- I understand that. I'm not sure that we -- whatever you want to call it, Corporation A subcontracts to Corporation B to do something outside of Connecticut. Are we going to approve this one and make -- I heard the word in one of the other of your dialogues about an exception to policy. Now, are we going to make an exception to policy for a firm that has -- or a university that has -- that has a Connecticut base but wants to do their work in Wisconsin or Oregon or California?

So I'm concerned about this and I'm concerned about granting an exception to policy bearing in mind that we're not dealing with business funds or our funds, we're dealing with taxpayers funds who have a right to expect that -- that the money will be spent in Connecticut as they were told several years ago and that it would have -- I think it would have to be something

that would be overwhelmingly in favor of doing something outside the states before the average person who files a Connecticut 1040 Form would be comfortable with.

And that is my opinion and perhaps Gerald Fishbone has some more opinions?

DR. FISHBONE: Nope. I was the second reviewer and I think there is no question that the quality of research is tremendous, the importance of the work is great, everything about it is -- is really terrific except for the structure of how it's financed. And I think we're going to need some direction maybe from Henry as to whether this is even possible to do, even if we wanted to do it.

I mean my feeling is everything about it is terrific, but I'm not sure that it's -- it's within our province to be the funders.

DR. GALVIN: I get the same feelings, but I'm the guy who has to go back and tell the General Assembly if we're trying to continue -- or enhance our project that I'm the one who will have to answer the question, why did you send a half a millions dollars out of the -- not out of the state, out of the country. And I'm not sure that those I hear people are going to move back and forth and, you know, I can understand some

reasons for doing that, but I'm not -- once again, I'm not sure that the average guy who makes 50 grand a year and pays $8,000 in tax and something to the state is going to buy into that and I'm the guy that has to sell it. So you're going to have to sell me.

DR. KIESSLING: What percentage of the budget is for the primates?

DR. JENNINGS: It's just over 25 percent. So it's 580,000 roughly or 583,000 out of a budget of $2 million.

DR. GALVIN: Travel and consultants and subcontract, I have 609,000.

DR. FISHBONE: Yeah.

DR. KIESSLING: So that's the --

DR. GALVIN: You wanted to know --

DR. JENNINGS: But some of that is not --

DR. GALVIN: Yeah, we're starting to run over time on this grant, but I can tell you what I'm going to hear is this is a boondoggle so people can go down to the --

DR. FISHBONE: No, no --

DR. GALVIN: I'm not telling you -- I'm not saying that the truth of the matter is anything other than what Charles has presented. I'm telling you what I

am going to hear, this is a boondoggle. People are going to go back and forth to St. Kitts, you could have done it here in the states and you didn't.

DR. FISHBONE: Mr. Chairman.

DR. GALVIN: Yeah.

DR. FISHBONE: I'm sorry to interrupt.

DR. KIESSLING: Does Connecticut --

DR. FISHBONE: They make a compelling argument as to why you could not do it here in the states.

DR. KIESSLING: Does Connecticut have a primate facility?

DR. GALVIN: It's got to be better than that if I'm going to take it to the taxpayers.

DR. KIESSLING: Does Connecticut have a regional primate facility?

DR. GALVIN: No, they don't. But they -- they really don't -- people really, Ann, don't really care about that.

DR. KIESSLING: No, I understand.

DR. GALVIN: They think why can't you do it here?

DR. KIESSLING: Where's the most -- where's the closest regional primate facility to

Connecticut?

DR. JENNINGS: New England.

DR. KIESSLING: Oh.

MR. MANDELKERN: May I make one comment, Dr. Galvin?

DR. GALVIN: Yes.

MR. MANDELKERN: We have had 87 grant request proposals. The score on this proposal is number one of all categories and it is clearly documented in the hundred-odd pages why it is necessary to pursue this research in St. Kitts, where the only available supply is. I also might make one last point and I will shut-up. This is a project which talks of going -- excuse me -- to clinical trials, if they succeed in their research, which could lead to amazing therapeutic effects in a disease which affects a million to a million and a half people in the United States.

The potential benefit to the State of Connecticut is remarkable. It is mind boggling and would put us in the forefront of the international community of stem cell research, if we fund this and it is successful. Thank you.

DR. GALVIN: Well there’s a lot of ifs there, but I think -- it is my opinion, having been, you

know, tossed around on the -- on the sea of the General Assembly, that there will be a lot of push back if this comes -- if this becomes an issue, which it could, and I'm not even sure we can legally do this and I'll have to ask Attorney Salton to give us an opinion about can we spent the money out of the continental United States?

MR. SALTON: Well, I think we had a discussion about this last year and my opinion then has not changed from that, which is that the statute requires that we provide funding for the advancement of embryonic and human adult stem cell research in this state.

Now, at that time, we did discuss the possibilities of an exception and that exception would be an example where the Committee came to the conclusion that the unique circumstances are such that it would be infeasible and unreasonable to expect a research program which is fundamentally located in Connecticut, for example, to build a proton accelerator when there's one that's existing in Arizona or something, because you wanted to use that resource as a component of your research here in Connecticut or that it was a supporting element of the research in Connecticut.

So I'm not going to be the person who says -- you know, but this certainly is some -- that this is

the situation in this case, but I think that's the -- that's really the parameters. If you have a research project which is largely based in Connecticut with a Connecticut -- not just a façade or a front door, but an established and eligible institution in Connecticut and they say listen, it makes no sense for us to build something here for this particular project. It makes it economically -- it's unreasonable and it's a waste of taxpayers' money, rather than to outsource this component of a research project which is otherwise then returns come to the state and is integrated into research being done in the state, I think the Committee can reasonably do that.

But on the other hand, for someone to say there is a in Dubai are research labs run by UCONN and really the money is going to go in the UCONN front door and then the research activities and the funds will all be spent in Dubai and UCONN is just merely using it's principal office here as the façade, then that doesn't meet the interests or the intent of the legislature in creating the fund.

The -- it's clear in the legislative debates that created the fund in this program, that part and parcel of what was expected of this whole activity

was the development of research in the state. So I can't -- having not read the proposal, I can't parse out where you are in that continuum between something that's merely -- Yale is really sort of the front door and the money is passing through Yale out to St. Kitts or whether or not really the research is fundamentally being done at Yale, but they're using resources or services located outside the state, because it's really economically not -- perhaps in this case -- legally possible to set up a primate center in Connecticut without federal funding being involved and federal funding would then put -- would make the human embryonic stem cell research desirable in this case, not impossible.

DR. GALVIN: Yeah.

MR. SALTON: So that's something that the Committee will have to parse out based on the review of the application, but that's the basic parameter. It's legally possible if you fall within the appropriate end of that continuum.

DR. GALVIN: Okay. Let's put this over into the maybe, so we can discuss it tomorrow. But I will tell you right now, I may not be able to support this when subsequently interrogated while trying to move some things ahead and I -- for stem cells. And as I've

said several times, it's not what the science is and the high quality of the grant and that's a very good way to do things, it is the perception that the average voter and his or her elected Senator or representative will have reviewing this and not -- not understanding some of the nuances and we will -- we will consider it again tomorrow.

DR. CANALIS: Commissioner.

DR. GALVIN: Yes, Dr. Canalis.

DR. CANALIS: A brief comment. Frankly, I really have difficulties with this. You know in view of the limited amount of funds that are available and with the sentiment that part of the purpose was to create a research environment in the State of Connecticut, to allow funds to go outside the state, outside the country, frankly, I couldn't be supportive of that.

You know with the limited resources that we have available, you know, I think it's -- I really want to offer my position straight out. It can go in the maybe, but my position is not going to change.

DR. GALVIN: Oh, I agree with you and I think that economic times are tough, that's all you have to do is have somebody say wait a minute you spent $500,000 in St. Kitts? It's not going to fly. We'll

talk about it again tomorrow.

I think we have an opportunity to do one more.

MR. WOLLSCHLAGER: Alright, we have time then for 08-SCC --

MR. MANDELKERN: Excuse me. What has been the disposition of that?

MR. WOLLSCHLAGER: Maybe.

DR. KIESSLING: It's maybe.

MR. MANDELKERN: Oh, maybe. Thank you.

MR. WOLLSCHLAGER: You're welcome. It's -- okay we're looking at then 08-SCC-UCHC-006, Hla, received a peer review score of 2.75.

COURT REPORTER: Wait one moment.

MR. WOLLSCHLAGER: Oh, what's that?

(Off the record.)

MR. WOLLSCHLAGER: You're right, it's 2.7, Aguila. Okay. So it's -- I take that back, it's SCC-003, Aguila, 2.7. And it's entitled -- it's entitled Development of Assays for Clonal Dissection and the reviewers here are listed as Dr. Huang and Dr. Genel.

DR. HUANG: Mike is not here. I don't know if I should proceed.

MR. WOLLSCHLAGER: Please.

DR. HUANG: So this proposal is from University of Connecticut and the PI is Aguila and the proposal is to develop a totally synthetic animal-free biomemitic culture plate system to grow clones of human ES cells.

So the proposal deals with the issue that ES cells are heterogeneous and that in order to purify them that we have to separate them into single cells and then grow each of the cells clonely. But as we do that, the cells may not stay pluripotent and it may change their characteristics.

So the two parts are first to look at the heterogeneity inherent in human ES cultures and to use flow cytometry to clone and select them. The second is to develop biomemitic matrixes that allow the growth of the ES cell clones in such a way that maintains their pluripotency.

The proposal received a score of 2.7. The part one looking at the heterogeneity was felt to be important, but the approaches were not felt to be innovative by the peer review committee.

Part two, developing the new matrixes was thought to be very innovative and novel. It was also felt that the cost of the proposal was high, particularly

in project one which did not use innovative techniques.

Just parenthetically the PI of this proposal, Dr. Aguila, is also the PI of the core proposal up on the board, one of the two that we put in the yes category. And as you recall, the -- the purpose of that core was to develop the flow cytometry facilities for UCONN.

So I would say in light of the score and the weaknesses, I would propose to put this in the no category.

MR. WOLLSCHLAGER: Dr. Genel is not here.

DR. KIESSLING: Is this a -- is this more than one investigator?

COURT REPORTER: Speak in the microphone.

DR. KIESSLING: Is this more than one project? Is this a couple of --

DR. HUANG: This is two projects. One is to look at heterogeneity by flow cytometry and the second is to develop the main biomemitic matrixes to grow the cells.

DR. KIESSLING: Different investigators?

DR. HUANG: The one PI, different investigators, correct. Right.

MR. WOLLSCHLAGER: We'll look for Dr.

Genel, but in the meantime any other comments or discussion from any of the members of the Committee?

DR. GALVIN: Okay. Where is -- we're beginning to lose members. Is Dr. Canalis gone for the day or is he -- just step out for a moment? Okay.

DR. KIESSLING: He's calling St. Kitts.

DR. JENNINGS: Making a reservation.

DR. KIESSLING: He's making a reservation.

VOICE: He's coming.

DR. GALVIN: Okay. Well, while we're waiting for these two learned gentlemen to return, please direct your attention to the two grants listed under no. If for some reason you don't think they should be there, now is the time to speak up because they will not be here in the morning.

DR. HUANG: Dr. Genel, while you were out, I presented my thoughts on 003, Aguila, which was to look at heterogeneity and ES cells as part one and part two to develop biomemitic matrix material to grow ES cells. And I recommended that it be put in the no category because of the weaknesses of lack of innovation in part one and the high cost.

I also pointed out that the PI was -- is one of the PIs on the -- the core, one of the cores.

DR. GENEL: I'm in complete agreement.

COURT REPORTER: Microphone please.

DR. GENEL: No, I'm in full agreement. I thought there was duplication of effort here in terms of some of the other applications and I -- in particular, I thought -- in some respects I thought it was a little bit contrived to fit into -- to fit into the category. So I would agree with putting this into a no category.

DR. GALVIN: Anyone else have a comment to make?

DR. FISHBONE: Could I -- could I ask a question? From the review, I have the impression that there are two parts to this and the first is not novel and the cost is very high. The second by contrast is novel and that's the development of the matrix, the matrixes that may contribute to stable clonal growth. Are we allowed now to split that into parts or not? And is there any feeling by the reviewers that part two would be worthy of funding and not part one?

DR. GENEL: Well, I'll tell you my own idea of this in a rather tight funding climate is that, no, you -- they made a choice to put this into a -- into a program project and that we -- it's an up or down phenomenon. That's basically how I'm looking at it.

DR. FISHBONE: But the question I was asking.

DR. GENEL: Huh?

DR. FISHBONE: That was the question I was asking.

DR. GENEL: Well, we did that last year, we really were up and down on our program projects --

DR. FISHBONE: But -- yeah, but they've changed the ground rules.

MR. SALTON: That's correct. Last year we were on an up and down because of the way the request for proposal was drafted. We amended the request for proposal this year to allow partial funding at the -- at the request of the Committee.

DR. GALVIN: Is there any --

DR. GENEL: Well --

DR. GALVIN: Go ahead.

DR. GENEL: Well, in that case it moves up to a -- to a principal investigator category and it goes in with the rest of the violet -- the violet grants, if we want to do that, but I would not fund it separately as a program project because it's no longer a program project.

DR. GALVIN: Any further comments? Okay. Is there any sentiment? I hear negative

votes. Is there any sentiment to further consider or to give a yes vote to this proposition?

MR. MANDELKERN: In view of -- in view of the many drawbacks, I think this should be put in the no category because of the caveats mentioned by Dr. Huang and I don't think we should start parsing proposals at the moment. I think it can go into the no with a score of 2.75.

DR. GALVIN: Okay. We can put that -- anybody opposed to putting that into the no category? Please do. And I will just tell -- rather -- not trying to be the voice of doom and gloom, I will advise the group that we are looking at difficult financial years where we may have to justify not only the -- not only to try to justify additional funds, should we -- should that be the feeling of the group, but we also may have some trouble hanging on to the 10 million. We hear that low revenues, high expenditures and some fairly difficult economic predictions. Our sister states are all in economic budget negativity. We are not, but we could be and we -- as you consider one of our other proposals, you need to think -- we need to think about what is going to be our posture and how we're going to present this to the people who control our money.

And we will adjourn today and resume tomorrow at --

DR. WALLACK: Well.

DR. GALVIN: Yes.

DR. WALLACK: Do we want to stop in the middle? Can we finish this series at least?

DR. GALVIN: No.

MR. WOLLSCHLAGER: Folks who are waiting to get their tickets back do have your parking coupons, so you can get out?

(Off the record.)

MS. HORA: Yes, we did speak to the hotel staff. The room will be locked, but they advise you not to leave laptops here. So if you want to leave notes and that kind of thing, it will -- it will be locked.

DR. WALLACK: So the notes we can leave here.

MS. HORA: Yes.

(Whereupon, the meeting was concluded at 4:00 p.m.)