

ESTADO FINAL RESOLUCION DEL CONSEJO Observaciones: _____ _____	FECHA <div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 30px; height: 30px;"></div> <div style="border: 1px solid black; width: 30px; height: 30px;"></div> <div style="border: 1px solid black; width: 30px; height: 30px;"></div> </div>	<div style="border: 1px solid black; padding: 5px;"> <div style="border: 1px solid black; width: 40px; height: 20px; margin-bottom: 5px;"></div> <div style="font-size: 0.8em;"> 1. APROBADO 2. PENDIENTE 3. RECHAZADO 4. A FISCALIA </div> </div>
--	--	---

This is only for internal use of FONDAP

EVALUATION REPORT CENTERS FOR ADVANCED RESEARCH

I. PROJECT INFORMATION

CENTER'S NAME CEMC

DIRECTOR Andrés Stutzin

II. EVALUATION PANEL

NAME	ORGANIZATION/ INSTITUTION	E-MAIL	SIGNATURE
REVIEW 1			

III. PROGRAMS EVALUATION (please fill up as many forms as programs exist within the Center)

PROGRAM'S NAME

PRINCIPAL INVESTIGATOR: Cecilia Hidalgo

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	x			
Accomplishment of objectives and goals of the reported program	x			
Quantity of the results reached regarding the objectives and goals	x			
Quality of reached outcomes related to proposal objectives and goals	x			
Degree of integration with other ongoing programs of the Center	x			
Diffusion of the results	x			

PROGRAM'S NAME

PRINCIPAL INVESTIGATOR : E Jaimovitch

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	x			
Accomplishment of objectives and goals of the reported program	x			
Quantity of reached outcomes related to proposal objectives and goals	x			
Quality of reached outcomes related to proposal objectives and goals	x			
Degree of integration with other ongoing programs of the Center	x			
Diffusion of the results	x			

If there had been none, please disregard this question

PROGRAM'S NAME				
PRINCIPAL INVESTIGATOR : Andrew Quest				
ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	x			
Accomplishment of objectives and goals of the reported program	x			
Quantity of reached outcomes related to proposal objectives and goals	x			
Quality of reached outcomes related to proposal objectives and goals	x			
Degree of integration with other ongoing programs of the Center	x			
Diffusion of the results	x			

PROGRAM'S NAME				
PRINCIPAL INVESTIGATOR: Andr�� Stutzin				

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	x			
Accomplishment of objectives and goals of the reported program	x			
Quantity of the results reached regarding the objectives and goals	x			
Quality of reached outcomes related to proposal objectives and goals	x			
Degree of integration with other ongoing programs of the Center	x			
Diffusion of the results	x			

--	--	--	--	--

PROGRAM'S NAME

PRINCIPAL INVESTIGATOR: Sergio Lavandero

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	x			
Accomplishment of objectives and goals of the reported program	x			
Quantity of the results reached regarding the objectives and goals	x			
Quality of reached outcomes related to proposal objectives and goals	x			
Degree of integration with other ongoing programs of the Center	x			
Diffusion of the results	x			

PROGRAM'S NAME

PRINCIPAL INVESTIGATOR: Luigi Devoto

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	x			
Accomplishment of objectives and goals of the reported program	x			
Quantity of the results reached regarding the objectives and goals	x			
Quality of reached outcomes related to proposal objectives and goals				
Degree of integration with other ongoing programs of the Center		x		
Diffusion of the results	x			

PROGRAM'S NAME
PRINCIPAL INVESTIGATOR: Claudio Hetz

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	x			
Accomplishment of objectives and goals of the reported program	x			
Quantity of the results reached regarding the objectives and goals	x			
Quality of reached outcomes related to proposal objectives and goals	x			
Degree of integration with other ongoing programs of the Center	x			
Diffusion of the results	x			

PROGRAM'S NAME
PRINCIPAL INVESTIGATOR: Luis Michea

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	x			
Accomplishment of objectives and goals of the reported program	x			
Quantity of the results reached regarding the objectives and goals	x			
Quality of reached outcomes related to proposal objectives and goals	x			
Degree of integration with other ongoing programs of the Center	x			
Diffusion of the results	x			

IV. CENTER EVALUATION

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Uso Interno
Degree of adoption of suggestions from the last report *	x			
Accomplishment of objectives and goals of the Center	x			
Quantity of reached outcomes related to proposal objectives and goals	x			
Quality of reached outcomes related to proposal objectives and goals	x			
Degree of integration between the programs of the Center	x			
Creation and reinforcement of international networks	x			
Outreach	x			
Diffusion of results	x			
Establishment and tasks of the Advisory Committee		x		

RECOMMENDATIONS (see following concepts)					
<div style="border: 1px solid black; width: 40px; height: 40px; margin: 0 auto; display: flex; align-items: center; justify-content: center;"> XXXXXXXX </div>	<div style="border: 1px solid black; width: 40px; height: 40px; margin: 0 auto;"></div>	<div style="border: 1px solid black; width: 40px; height: 40px; margin: 0 auto;"></div>	<div style="border: 1px solid black; width: 40px; height: 40px; margin: 0 auto;"></div>	<div style="border: 1px solid black; width: 40px; height: 40px; margin: 0 auto;"></div>	<div style="border: 1px solid black; width: 40px; height: 40px; margin: 0 auto; background-color: #e0ffff;"></div>
APPROVE	APPROVAL WITH SUGGESTIONS	ADDITIONAL INFO.	PENDING	REJECT	FONDECYT USE
<div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 30px; height: 30px;"></div> <div style="border: 1px solid black; width: 30px; height: 30px;"></div> <div style="border: 1px solid black; width: 30px; height: 30px;"></div> </div>			<div style="border-bottom: 1px solid black; width: 150px; margin: 0 auto;"></div>		
Evaluation Date			Signature reviewer		

ANNUAL REPORT

EVALUATION COMMENTS:

The CEMC center for 2009-2010 is composed of 8 research groups (about 200 persons) and led by 7 PIs and 1 co-PI. They are assisted by about 25 associate researchers, 23 post docs , about 55 PhD students, 20 undergraduates and 30 technicians. CEMC activities include research and training programs and also aims to promote diffusion of science in Chile in other universities and for a large public and the organisation of scientific meetings. The CEMC center was approved for further five years of funding in 2007 and this review concern 2009/2010. The research activities of the center still remain focused on signal transduction mechanisms operating in normal and pathological situations in various tissues, underlying neuronal plasticity and neurodegenerative diseases, proliferation , apoptosis and cancer, hormone generation and effects, cardiac and skeletal muscles physiology including cardiovascular diseases. These pathologies involve in general calcium signalling cell, proliferation or cell death mechanisms and ion channels, these areas of research generating collaborations between PIs and their collaborators.

Research activities

In the period analysed, the number of ISI publications that has been produced has increased from 19 (2008/2009) to 27 and importantly also the mean impact factor which also increased from 4 to 5,78. Among the 27 publications, 10 are ranked within the top 10% of the field concerned which is also in progress compared to the past period (37% versus 25%). The number of Joint publications in CEMC and collaborative publications with national or international research institutions is rather progressing may be in relation with the increased visibility and communication of the center which has been developed.

Two important modifications can be noted since the last evaluation.

First , Andres stutzin has replaced recently Cecilia Hidalgo as center director in march. This was a previous recommendation to anticipate possible retirements for the future. The reviewer wants to underline the very important work done by Cecilia Hidalgo in the center during the past years and to put at her credit and evidently to all PIs the progress realized by the center in terms of number and impact of the publications and also for the quality of training of students and various initiatives for promotion and visibility of the research (meetings, courses, external communication, international collaborations...). No doubt for the reviewer that Andreas Stutzin will continue to promote this strategy and will bring complementary and also new impulse for the future period.

Second, a new PI is hosted by the center, Claudio Hetz following his successful period as an associate investigator. This also was a recommendation at the renewal of the center to prepare the future to take advantage during a period of time of the experience and high quality of the PIs who might be retiring in the following years. It is interesting to note that these younger researchers have specific topics of research but also develop joined research projects with senior PIs , so promoting research highlite and novel concepts issued from the laboratory including the redox regulation of ryanodine receptors and ROS (reactive oxygen species) modulation in pathological situations in a variety of cell types. It is expected that the associate investigator Luis Michea working on hypertension will also join the center as

a full PI next year. This will reinforce the cardiovascular research area of the center. It is pointed out that this year another talented young associate researcher, David Mears, left the center. One can hope that another one can be recruited in a one year future why not in the field of ion channel to support the new director who will probably increase his administrative tasks.

The individual projects concern various organs and tissues and various approaches. In particular, studies on calcium signalling, redox modifications, intracellular calcium releasing proteins such as RYR and IP3 receptors initiated by the senior PIs on skeletal muscle induce collaborations between various PIs in neuronal, endocrine, ovarian, cardiovascular cells.

The group of C Hidalgo focuses on the key role of redox regulation of RYR in the Calcium-Induced Calcium -Release in cells. They showed that ROS stimulate RYR-mediated calcium release in neuronal and pancreatic cells (two papers in press). Interestingly, these studies concern neuronal process such as spine formation but also integrate functions such as special memory are investigated and potential implications in neurodegenerative diseases are proposed. This also provided publications in very good international journals such *Antiox.Redox.signal* and two in revision (*J Biol Chem*, *Endocrinology*). Several publication with S Lavandero are noted in this period.

The work of the group of E Jaimovich on calcium signalling in skeletal muscle and neurons is original since it concerns gene expression. A study which concerns human muscle from DMD (Duschenne dystrophy) is accepted in the excellent "Faseb Journal". The interest of the study is attested by a grant from AFM (French Muscular Dystrophy Association). Another work on fiber plasticity is in press in another journal of reference: *J Gen Physiol*. Interestingly these studies constitute the thesis project of students of the group. This follows recent studies in the past year on RYR receptors in cell physiology also in high standard journals: *J Biol Chem*, *Cell Calcium* *Am J Physiol*. Several specific points under study may have high physiological relevance in muscle physiology and pathophysiology. Because E Jaimovich is an expert in calcium imaging initially in skeletal muscle cells, collaborations are also carried out in other cell types and in collaboration with several PIs. These include new studies examining the role of RYR isoforms in hippocampal spine formation under the action of BDNF and in memory. International connections are established with international collaborators also focused on the redox regulation of RYR receptors in skeletal muscle and heart (France, USA, recently Belgium)

The group of A Quest is focused on cancer, aiming to identify the parameters involved in caveolin-1 function as a tumor repressor. The group demonstrated recently the inhibition of target genes such as survivin and COX2. Caveolin-1 expression level appear to be a major player of angiogenesis, a work which is expected to lead to a paper shortly. A new hypothesis studied in collaboration with the new co-PI (C Hetz) is the role of caveolin-1 in the UPR (Unfolded Protein Response). This group also provided interesting data published in high impact factor journals. Numerous collaborations are reported with associate researchers such as L Leyton (2 papers in 2010) and other PIs on Thy-1 induced adhesion in astrocytes via P2X7, TRPM4 and proliferation (A Stutzin with a paper in press in *J Cell Physiol*) open new translational research by combining several expertises. Clinical issues are reported.

The group of Sergio Lavandero is focused on cardiac cells and in particular survival signalling following lesions of reperfusion related to ischemia and the search for mechanisms of cells death. He collaborates with all the PIs of the center, and has a large number of national and international collaborations for instance in USA, Canada, Spain, France, Germany. In addition to good publications (*BBA*, *Apoptosis*, *FEBS letters*, *BBRC*..) and some through the international collaborations reach high ranked journals (*Cell Death Diff* with G Kroemer in the past year and *EMBO J* in 2010). Osmotic stress such as ischemia/reperfusion-induced cell death involves various signalling pathways to produce necrosis, apoptosis, and autophagy. They reported for instance mitochondrial dysfunction associated with hyperosmotic stress. They combine studies of ischemia/reperfusion with protocols involving ROS, RyR receptor and proteasome which allows collaborations with other PIs. National collaborations may lead to clinical applications (angio II peptide) with other PIs. Many PhD students are trained in joined programs leading to interesting work (endocrinology in press). I would encourage however to try to publish cardiac studies in cardiology journals.

The group of Luigi Devoto is strongly associated to clinical practice and clinical research. This group works on ovarian steroids in the regulation of human corpus luteum demise and the influence of steroidogenesis on endometrial cells from normal and polycystic ovary women. Their research is highly related to clinical and pathological situations and to human health application. The contact between clinicians and basic researchers is fundamental for reaching this aim and for promoting innovative studies. For instance this research may lead to understand clinical problems such as frequent early pregnancy loss in PCOS women. As mentioned in the past although the group is largely oriented towards clinical applications their association to the center promotes exchanges interactions between fundamental and clinical research and allows in a reverse way to set up protocols at the cellular level in order to understand clinical situations and possibly find clinical applications. Access to human sample can be a bonus in the field. The collaborations with other PIs is also important for training PhD and postdoctoral students. It is quite important that medical students have also a scientific culture for the development of translational research not only in the field of endocrinology. The group publishes regularly in international dedicated to this field such as in *Gynecol Endocrinol* in 2010 (2 papers) or *Fertil Steril* in which they can combine basic research and pathological human endometrium samples.

Claudio Hetz is now a new PI of the center and based on the innovative research and high standard publications of the two past year this decision seems quite appropriate. His work concerns misfolding of proteins occurring during stress injuries. ER (Endoplasmic reticulum)-stress triggers a complex adaptative response named UPR (Unfolded Protein Response) which aim to restore homeostasis in the organelle. Of major importance, specific misfolded proteins are a feature of neurodegenerative pathologies including Prion, Parkinson, Alzheimer, and ALS. His work is then related to the elimination of these misfolded proteins through the ER-stress pathway. His strategy is to use approaches to modify ER stress levels together with animal models of neurodegenerative disease. In addition to a paper in *PNAS* (2008) and a remarkable work in the top ranked journal *Mol Cell* in 2009 with editorial comments, he also is the first author of another top paper in *Genes&development* in 2009 obtaining the cover illustration and editorial as other international comments. Another collaborative work is published in another high impact journal (*PloS Biol*) in 2010. The work of C Hetz is innovative, it evidences the new role of ER stress pathway in the accumulation of toxin proteins in major neurological diseases, a world problem of Human Health. These studies should help to identify new therapeutic drug strategies in neurodegenerative disorders which is a major issue. His group appears highly competitive in this field. It is not clear to me how many students he has in his group. It might be recommended that CEMC helps to hire a post doctoral fellow. It is also not clear to if he is quite independent of L Glimcher since she published the high impact factor papers as a senior author.

Luis Michea is another associate investigator focused on cardiovascular damage induced by mineralocorticoids in hypertension and calcification. The aim is to understand how aldosterone exerts its deleterious effect in the cardiovascular system with as a goal to develop pharmacological strategies (MR antagonists) to prevent in particular chronic renal failure. The therapeutic interest of MR antagonists is explored within his group using Chronic Renal Failure (CRF) patients and relevant animal models of CRF. His studies aim to have clinical implications for patients with end stage renal disease. Consistent with this, using Luis Michea demonstrated the beneficial role of spironolactone in a paper published in 2009 in "Hypertension" with an editorial comment highlighting the impact of the research. They also look for biomarkers of acute kidney transplant rejection. They also provided another work published in "Hypertension" in 2009 concerning ENaC channel and NO production in small arteries. The effect of aldosterone in a model of autoimmune disease and in vascular calcification, in anti-fibrotic properties and in inflammation was mentioned in the last evaluation. It has recently been published in *J. Immunol* (2010), a very good journal. Collaborations with a world specialist (F Jaisser in Paris) on resistance arteries and within the center with C Hetz have been developed this year and are promising for the future. This will help naturally to be a new PI in CEMC in a near future.

Andreas Stutzin is now the new director of CEMC. His group is focused since a few years on the interesting family of TRP channels and in particular on studies in epithelium cell lines and primary

cultures of the function of TRPM4 in cell death, proliferation and migration. This new research program is quite well integrated in a main research axis of the laboratory and initiates obvious collaborations with other PIs. In addition They will focus on the modulation of TRPM4 by oxidative stress following their previous studies which evidenced H₂O₂-induced TRPM4 activation associated with cell death. This group has high expertise in structure-function studies and their technical expertise is complementary to that of the others PIs. The project of obtaining a transgenic mouse based on a dominant negative TRPM4 construct (under the control of specific promoters of the prostate and CNS) which was in development is now under investigation and validation. This line will be mated soon to TRAMP mice to study the development of prostate cancer. They study the H₂O₂-induced TRPM4 activation with a publication in revision in J Biol Chem. Another study mentioned in the past evaluation was the swelling-induced ATP release which activates P2X₄ receptors. It has been recently published also in J. Biol. Chem (Varela et al 2010) which I considerer as a high impact factor but also a highly cited international journal. Collaborations with other PIs have also been completed (AQ) using a modern strategy (shRNA), a work in press in J .Cell.Physiol (2010)and with the new PIs (C Hetz) on the IP₃-mediated Calcium release in MEF cells, a work to be submitted soon. These collaborations are strongly related to studies of calcium signalling in cells, a process which governs most physiological functions and when altered is the trigger of many pathologies.

Training Activities and Networking

The training activity continues to be excellent since the renewal of the center with the listed participation of all PIs and associates to the training of graduate students, post docs and other young investigators. Since the beginning of the center, the PIs participate to several PhD programs in the University of Chile. As recommended in the two past years, they put efforts to prepare the students to the practice of English which is essential for future postdoctoral applications, for writing papers and to participate to international meetings. Interestingly, the PIs also participate to undergraduate programs and can meet a large number of potential PhD students from different universities which appears as an important means to select the best and motivated students for research with perhaps complementary scientific backgrounds.

Finally, the post doctoral training which also involves all PI is linked to the organization of several courses and meetings on the main research topics of the center such as calcium signaling, cell death, translational research...

An impressive list of collaborations is mentioned in the document and attested by collaborative publications most of the time of very high impact factor. All PIs give invited lectures which attest for their international visibility in their field.

General comments

In my opinion, the PIs have achieved the scientific goals stipulated upon CEMC in the last annual report. The publications record includes average, very good and also excellent papers. One must notice that the highest impact publications are often in collaboration with other prestigious international institutions. But this is not a critique because it is a long process for all recent centers over the world to increase the impact factor over a certain level. The impact factor of the papers produced by CEMC including those involving national collaborations has increased regularly each year to reach a very good international standard. In addition, The impact factor must not be considered as the only evaluation parameter. For instance, Journals such as J. Biol. Chem , J Physiol London and many others in special fields which have a medium impact factor, are considered as references and are highly cited. It is a similar situation for applied medical journals. The average of the publications of the center has significantly increased the two past years and the reviewer can only encourage the PIs to maintain this level and this progress. This will be stimulated by the presence of young PIs or young researcher having an international experience. I will still emphasize that the quality of the journal looks to me more important that the total number of papers. The strategy to integrate the two co-PIs as full PIs looks seems very positive and promising for

the center in the future. It might be worth considering to add a new co-PI in the scientific area of the new director considering that he will spend more time to administrative tasks. I also renew my support to A Stutzin who is a talented scientist who will continue to promote CEMC activities in the following years.

One major point was the construction of a new building to house most of the PIs in the same place. As mentioned in the document the strong earthquake of magnitude 8,8 had major impact on this project which was more than delayed and probably suppressed. The reviewers mentioned in the past that this project was very important for the future of CEMC. However, one can be happy that a new plan was rapidly proposed (dec 2010) by the administration of the medical school at the Universidad de Chile. Now, a space around 3000 m² will be dedicated shortly to welcome 6 of the 7 PIs and an associate. The reviewer is quite happy of this decision. I and other reviewers were thinking that having at least a nucleus of PIs at the same place around common facilities was a major point for the development of the center, to promote exchanges and initiate collaborations between PIs and also between students. The renovation of the building really looks as an excellent initiative in spite of the critical situation induced by the earthquake. The fact that another PI with strong clinical activities is located in another place does not appear to me as a problem because it opens opportunities for human samples and to clinical developments, the most important was to gather all the basic methodologies and the fundamental research in a very proximal area.

Highlight of several strong points:

It seems to me that the strong points of CEMC are the same as previously reported

- Collaboration between PIs. They have made considerable effort to develop innovative programs and collaborations between them. The most significant issues are the identification of new signaling mechanisms, new targets or new concepts issued from PIs of the center (redox regulation of RYR receptors and subsequent dysfunction in calcium signaling : RYR and IP3 receptors, studies related to Caveolin-1, TRPM4, GLUT 4 and cell death, misfolded proteins, UPR and neuronal pathologies.....) which also have led to a large number of collaborative publications.

- Training of students involving co-tutoring with 55 PhD theses (including 12 completed) during the period 2009/2010. Also development of joint projects for post-doc between two PIs. Many efforts have been produced to improve the formation of young researchers (courses, seminars, lab meetings, retreat). The center appears as a major place to train students to scientific and medical research in Chile .

- National and International collaborations: Each PI has established collaborations with other Chilean institutions and universities. Networking is excellent concerning the research activities of the center including clinical research and the reviewer feels that the CEMC plays a pivotal role in the development of the research at different levels: at the local level in the university through exchanges between medical school and ICBM, at the national level with a significant number of joint programs and associated publications with other Chilean institutions and at the international level with long lasting research programs with scientists from famous institutions in USA , South America and Europe, usually leading to publications in very high ranked journals . The list of collaborations and of contacts abroad is impressive.

- Networking in teaching looks excellent: All PIs are involved in several PhD programs and in organizing post-graduate courses or symposia in the different universities of Chile. Training concerns both fundamental and clinical research. This offers to young researchers opportunities for international contacts and certainly opens possibilities for training in foreigner international institutions. This is an excellent way to bring new ideas and new expertises into the center. The performance of the new added PIs is a good illustration.

- It seems clear that CEMC common facilities are under the responsibility of the appropriate PIs and are organized as open platforms. They are reported as used by all PIs and collaborators . The development

of a virus facility, of flow cytometry and of confocal imaging was needed both for students training and for collaborative projects. They seem heavily used. The use of transgenic or KO mice models is under development at least for some PIs projects. This strategy, although it must be controlled and evaluated by a committee inside the center because of the cost, will be helpful to promote functional genomics studies.

-National and international visibility of the center have been increasing during the past years. It is difficult to consider such activities on a one year period. The participation of the PIs at international conferences as “invited speakers” or the increasing number of invited lectures all over the world, their participation in editorial boards of international journals, in review processes for journals or grants are also increasing. The organization of the 16th meeting on calcium binding proteins is an example of the international visibility of the organizing PIs . Some have been awarded or invited to write chapters in books or are members of advisory committees and have responsibilities in national or international scientific societies.

-Press reports to promote CEMC research has been enhanced during the present year and a relationship has been established with a private society.

- Success in granting in other Chilean programs seems good. The reviewer does not know in details the “limitations in external granting” for FONDAP institutions but this comment is raised each year by the PIs and should be considered by the institutions. An excellence center should benefit of all the funding possibilities to raise their level of activity and in particular to develop common facilities which might be open to researchers outside the center.

-The impact factor of the published papers is increasing. All PIs makes effort to publish in high ranked journals . The average performance is quite good and the score of the new co-PIs must be underlined. This also evidence the importance of networking and of postdoctoral training in other prestigious laboratories for the development of new research programs and new technical approaches when back to Chile.

Some Weaknesses

-Already mentioned before, it is important to associate *in vivo* studies and to promote the use of some transgenic mice

- To achieve both a better balance between post docs/students and to encourage post docs to focus on their own individual research projects/objectives in order also to get some independence and to stimulate publication of their scientific work. I am uncertain whether there are possibilities for extending the duration of a post doctoral fellows in order to finish projects which may improve the scientific productivity of individual labs and the institution. The development of post doctoral fellows to become eventually ‘independent’ principal investigators or at least competent research fellows represents one of the great challenges as more demands (ie. publications) are required to secure long term research positions. Also, post docs are expected to train PhD students and their contribution to the quality of the research is essential for any laboratory in the world. Because of the rather high number of PhD students, it is unlikely that they can all be trained by the PIs.

- The Web site is described as much more attractive and informative. It is not so easy to find it! (It would be interesting to add a link on any document given outside). The publications do not look well updated

- One of the main difficulties mentioned during the past years was the delayed construction of the new building (expected in 2009 at the renewal). As mentioned earlier in the review, the renovation of the medical school building to welcome most PI’s is an excellent initiative which will take out what was targeted as a weak point for the future.

ADDITIONAL INFORMATION REQUIRED FOR THE FULL EVALUATION OF THE ANNUAL REPORT:

If you require additional information or leave the evaluation pending, please indicate the documentation or explanations required to complete the evaluation. In case there are additional demands that the Center's director has to accomplish, these have to be explained so the director may take the necessary measures.

If you entirely reject the contents of the report (or significant portions of it) please indicate here the demands that should be posted to the Center' director.

RECOMMENDATIONS TO THE CENTER DIRECTOR:

(only if report is approved))

I encourage the director to continue to promote the quality of the research by maintaining and developing common facilities in the new building which will host most PIs after renovation.

I encourage a careful selection of the postdoctoral fellows, to promote conditions for them to get some independence and specific projects and to try to maintain their position for at least two years.

ESTADO FINAL RESOLUCION DEL CONSEJO Observaciones: _____ _____	FECHA <div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; width: 30px; height: 30px;"></div> <div style="border: 1px solid black; width: 30px; height: 30px;"></div> <div style="border: 1px solid black; width: 30px; height: 30px;"></div> </div>	<div style="border: 1px solid black; padding: 5px;"> <div style="border: 1px solid black; width: 40px; height: 20px; margin-bottom: 5px;"></div> <div style="font-size: 0.8em;"> 1. APROBADO 2. PENDIENTE 3. RECHAZADO 4. A FISCALIA </div> </div>
---	--	---

This is only for internal use of FONDAP

EVALUATION REPORT CENTERS FOR ADVANCED RESEARCH

I. PROJECT INFORMATION

CENTER'S NAME CENTER FOR MOLECULAR STUDIES OF THE CELL

DIRECTOR ANDRÉS STUTZIN

II. EVALUATION PANEL

NAME	ORGANIZATION/ INSTITUTION	E-MAIL	SIGNATURE
Reviewer 2			

III. PROGRAMS EVALUATION (please fill up as many forms as programs exist within the Center)

PROGRAM'S NAME Oxidative Stimulation of Calcium Release from Intracellular Stores: Possible Role in Excitable and Endocrine Cell Function
PRINCIPAL INVESTIGATOR: Cecilia Hidalgo

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	X			
Accomplishment of objectives and goals of the reported program		X		
Quantity of the results reached regarding the objectives and goals	X			
Quality of reached outcomes related to proposal objectives and goals		X		
Degree of integration with other ongoing programs of the Center	X			
Diffusion of the results		X		

PROGRAM'S NAME The cellular machinery for calcium-dependent regulation of gene expression in muscle cells
PRINCIPAL INVESTIGATOR Enrique Jaimovich

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	X			
Accomplishment of objectives and goals of the reported program	X			
Quantity of reached outcomes related to proposal objectives and goals		X		
Quality of reached outcomes related to proposal objectives and goals	X			
Degree of integration with other ongoing programs of the Center	X			
Diffusion of the results		X		

If there had been none, please disregard this question

●

PROGRAM'S NAME Caveolin-1 as a conditional tumor suppressor in cancer: identification of the mechanisms that control caveolin-1 expression and cellular parameters that define caveolin-1 function as a tumor suppressor.

PRINCIPAL INVESTIGATOR: Andrew Quest

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	X			
Accomplishment of objectives and goals of the reported program	X			
Quantity of the results reached regarding the objectives and goals		X		
Quality of reached outcomes related to proposal objectives and goals	X			
Degree of integration with other ongoing programs of the Center	X			
Diffusion of the results	X			

PROGRAM'S NAME Sergio Lavandero

PRINCIPAL INVESTIGATOR: Cell death & survival signaling in cardiac myocytes

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	X			
Accomplishment of objectives and goals of the reported program	X			
Quantity of the results reached regarding the objectives and goals	X			
Quality of reached outcomes related to proposal objectives and goals		X		
Degree of integration with other ongoing programs of the Center	X			
Diffusion of the results		X		

PROGRAM'S NAME Endocrine and molecular cross talk between the human corpus luteum and endometrium. Significance for infertility treatment and fertility regulation.

PRINCIPAL INVESTIGATOR: Luigi Devoto

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	X			
Accomplishment of objectives and goals of the reported program	X			
Quantity of the results reached regarding the objectives and goals	X			
Quality of reached outcomes related to proposal objectives and goals		X		
Degree of integration with other ongoing programs of the Center		X		
Diffusion of the results		X		

PROGRAM'S NAME: Regulation of the unfolded protein response and its role in neurological conditions.

PRINCIPAL INVESTIGATOR: Claudio Hetz

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	X			
Accomplishment of objectives and goals of the reported program	X			
Quantity of the results reached regarding the objectives and goals	X			
Quality of reached outcomes related to proposal objectives and goals	X			
Degree of integration with other ongoing programs of the Center	X			
Diffusion of the results		X		

PROGRAM'S NAME New cell targets and transduction mechanisms of mineralocorticoid dependent cardiovascular damage: focus in hypertension and vascular calcification.

PRINCIPAL INVESTIGATOR: Luis Michea

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	X			
Accomplishment of objectives and goals of the reported program		X		
Quantity of the results reached regarding the objectives and goals	X			
Quality of reached outcomes related to proposal objectives and goals		X		
Degree of integration with other ongoing programs of the Center		X		
Diffusion of the results		X		

PROGRAM'S NAME: The role of TRPM4 channels in cell cycle and non-apoptotic cell death.







PRINCIPAL INVESTIGATOR: Andrès Stuzin

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Internal use
Degree of adoption of suggestions from the last report *	X			
Accomplishment of objectives and goals of the reported program	X			
Quantity of the results reached regarding the objectives and goals	X			
Quality of reached outcomes related to proposal objectives and goals	X			
Degree of integration with other ongoing programs of the Center	X			
Diffusion of the results	X			

IV. CENTER EVALUATION

ITEM	Total/ Good	Partial/ Regular	Insufficient/ Deficient	Uso Interno
Degree of adoption of suggestions from the last report *	X			
Accomplishment of objectives and goals of the Center	X			
Quantity of reached outcomes related to proposal objectives and goals	X			
Quality of reached outcomes related to proposal objectives and goals	X			
Degree of integration between the programs of the Center		X		
Creation and reinforcement of international networks	X			
Outreach		X		
Diffusion of results	X			
Establishment and tasks of the Advisory Committee		X		

RECOMMENDATIONS (see following concepts)

					
APPROVE	APPROVAL WITH SUGGESTIONS	ADDITIONAL INFO.	PENDING	REJECT	FONDECYT USE

EVALUATION CONCEPTS ANNUAL REPORT

1. **Approve:** The reviewer recommends to accept the report in its present form since he/she considers objectives and goals fully accomplished and all relevant issues covered by the report.
2. **Approval with suggestions or minor observations**
 - 2.1 **Minor observations:** The reviewer recommends the approval of the report despite the justified incompleteness of some aspects that does not constitute an obstacle for the continuity of the Center activities.
 - 2.2 **Suggestions:** The reviewer recommends minor changes in order to improve the future performance of the Center.
3. **Additional information:** The reviewer requires additional documentation or specific explanations to fully evaluate the report.
4. **Pending:** The reviewer makes significant observations to the report and conditions its approval to the accomplishment of specific demands.
5. **Reject:** The reviewer has strong objections to the contents of the report.

EVALUATION COMMENTS:

It is clear that despite its rather short history (8 years) this center has already produced a remarkable output both in terms of publications and in number of PhD theses. The relocation of teams in closer geographical proximity should further reinforce interactions and visibility. The reported period covers September 1st 2009 to September 30th, 2010. Although the net increase in productivity is difficult to appreciate objectively on a one year term, the quantity and quality of the research executed at CEMC is very satisfactory and for each of the programs significant progresses have been done in line with the fixed objectives.

Concerning quantity, the number of publications increased from 19 (2008-2009) to 27. Most importantly, the majority has been published in competitive good and for some very high quality journals as the average IC of the published papers is nearly 6, thus taking into account the recommendation made in the previous review. Also there are 4 joint publications between groups as the proof of an increase of productive interactions within the center (2 in 2008-2009) and a good amount (9) of publications resulting from external collaborations. Of note, the new PI (Claudio Hertz) made remarkable contributions in the field of protein misfolding disorders, highlighting perturbations in the homeostasis of the endoplasmic reticulum and significantly contributed to this increase in productivity.

Although I do agree that changes and improvements would take some time to get measurable, last year recommendation can be reiterated as there are however too few papers co-signed by graduate students (i.e. zero for LD team and most of them by one in SL team).

All the teams have established national and international collaborations, this is very positive concerning the visibility of the center.

The most impressive performance of the center is however, the dedicated involvement of its senior members in training activities. As a concrete output of this effort is for example the ongoing tutoring of 55 PhD theses and the insertion into academia of 3 CEMC trained post-doc.

The center website is a good tool to improve visibility/communication. For some of the teams it should be up-dated to include for example their most recent achievements/ publications.

ADDITIONAL INFORMATION REQUIRED FOR THE FULL EVALUATION OF THE ANNUAL REPORT:

If you require additional information or leave the evaluation pending, please indicate the documentation or explanations required to complete the evaluation. In case there are additional demands that the Center's director has to accomplish, these have to be explained so the director may take the necessary measures.

If you entirely reject the contents of the report (or significant portions of it) please indicate here the demands that should be posted to the Center' director.

RECOMMENDATIONS TO THE CENTER DIRECTOR:

(only if report is approved)

- (a) **Core facilities** are of crucial importance for maintaining competitive research and to enable synergies of know-how between the groups. Therefore, I strongly recommend that hiring competent personnel to run them, and buying state of the art equipment be a priority. Along this line, I approve the director 's choice to buy a confocal spinning disk microscope instead of inviting the advisory board in 2010. Furthermore, in the CEMC area of research it becomes important that culture data are validated by in vivo experiments, therefore it is urgent to have access to a facility offering enough space and sanitary conditions to house mouse models.
- (b) **Cotutoring** of PhD and assign of post-docs on common projects between two groups is an excellent initiative which is to be encouraged/extended.

© Despite my comment above, an on **site visit of the advisory committee** should not be postponed for too long.

(d) **Infrastructure:** Adjustment to the situation created by the unexpected earthquake is certainly understandable and the alternative choice to refurbish /reallocate existing space is wise. It will be of the director responsibility to urge the agencies (Faculty/University of Chile) to deliver the space in a reasonable delay as proximity of the teams between themselves and of the teams with the core facilities is vital to their interactions, efficiency and productivity.