

NATIONAL PROGRAM FOR RESEARCH CENTERS OF EXCELLENCE
(FONDAP)

FINAL EVALUATION REPORT

This form is intended to facilitate your work as a referee and standardize the evaluation reports. Each topic is expected to be evaluated with concepts ranging from outstanding to poor and detailed technical comments supporting your points on the report.

If the Center report does not contain information on the given topic, please indicate so in your evaluation.

Your final overall comments and recommendations are an important part of the review process.

I. PROJECT INFORMATION
CENTER'S NAME: Center for Cell Regulation and Pathology
DIRECTOR: Dr. Nibaldo Inestrosa

II. EVALUATION PANEL			
REFeree NAME	ORGANIZATION/ INSTITUTION	E - MAIL	SIGNATURE
REFeree N° 1			

III. CENTER ACHIEVEMENTS

1.- Scientific achievements and their impacts to local, national and international community.

i.- Comments

The information provided tabulated the various accomplishments of the Center since its inception in 2000. The papers were listed non-redundantly but in order of investigator. This complicated dissecting the contributions of each laboratory head difficult. Of note, this review report did not benefit from a site visit and so there may be some inaccuracies and assumptions included that are due to misunderstanding of the report documentation provided.

1. Publications: The publications by the members of the center comprise 191 papers (primary and reviews) in ISI journals as well as 30 book contributions. I have broken down the primary contributions of the Center members. Note H indices may be slightly underestimated.

Dr. Nibaldo Inestrosa (director and a founding investigator) – 68 papers of which approximately 10% are reviews. Journals include J Biol Chem, Developmental Dynamics, Molecular Neurobiology, FASEB J, J. Neurochemistry. Productivity has been excellent and Dr Inestrosa has a life-time H-index of 41. Citations per year have been steadily increasing and his most highly cited papers in the past 10 years have been Opazo et al (2002) at 204 cites and Opazo et al (2000) at 172. Dr. Inestrosa's program focuses on the roles of the Wnt pathway on survival and functions of neurons and protection from Abeta toxicity. His research program is extremely productive and he has a notable international profile.

Dr. Enrique Brandan (founding investigator) – 34 papers (these all appear to be primary papers). Journals include EMBO J, J Biol Chem, J Cell Sci, Developmental Biology, J Cell Physiology. Dr. Brandan has an H-index of 24 and his most highly cited manuscripts from the past decade are Riquelme et al (2001) at 48 cites and Osses & Brandan (2002) at 45 cites. His research investigates the interactions of proteoglycans with signaling proteins such as the TGFbeta pathway and he has moved towards effects of syndecans on muscle regeneration.

Dr. Miguel Bronfman (founding investigator) – published 14 papers in journals such as J Biol Chem (3), FASEB J and J Neurochem. Dr. Bronfman has an H-index of 21 and his most cited papers over the past decade include De Ferrari et al (2004) at 95 and Alvarez et al (2004) at 56. Dr Bronfman's research is focused on PPARalpha/beta functions and over the course of the CRCP tenure has identified roles for these proteins in neuronal cells – largely as a consequence of the groups nucleation.

Dr. Francisca Bronfman – 15 papers (three have since been published in 2010) in journals such as EMBO Reports, FASEB J, J Neurochem, J Biol Chem. Dr. Bronfman's H index is 14 and her most cited papers over the last decade include Bronfman et al., (2003) at 85 and Bonfman et al (2000) at 49. Dr. Bronfman's research expertise is in neurotrophin signaling and intracellular consequences.

Dr. Alphonso Gonzalez (founding investigator) – 22 papers with a couple of reviews. The journals include Proc Natl Acad Sci (3), J Biol Chem, J Exp Med. I was not able to easily calculate an H-index but note that several of Dr. Gonzalez's papers had high impact, such as Bravo-Zehnder (2000) with 65 citations and Guerrero et al (2004) at 38. Dr. Gonzalez works on intracellular trafficking mechanisms and modifiers of these processes associated with disease.

Dr. J Pablo Huidobro-Toro (founding investigator) – 46 papers with one review. Published journals include the Eur J Pharmacol, J Biol Chem, J Neuroscience. Dr. Huidobro-Toro has an H index of 14. His highest impact paper in terms of citations was in J Cell Physiology in 2000, which has gleaned 135, followed by Acuna-Castillo et al in 2000 (47 cites) and Buvinic et al (2002) with 46. Dr. Huidobro-Toro is interested in purinergic receptor signaling and has developed and applied modern techniques in molecular pharmacology to this system.

Dr. Juan Larrain – 17 papers (including 3 reviews) since 2000 in journals such as, Nature Cell Biology, EMBO J, EMBO Reports, Development and J Biol Chem. Dr. Larrain has an H-index of 14 and his most cited papers are Larrain et al (2000) at 134 and Larrain et al. (2001) at 73. His Nature Cell Biology paper has been cited 42 times since 2006. Dr. Larrain is a developmental biologist evaluating the roles of proteoglycans on normal development in Xenopus and mouse. He notes a manuscript was submitted to and rejected by Developmental Cell. He is aiming high and should persist!

Dr. Maria Paz Marzolo – 18 papers (inc 3 reviews) in journals such as Traffic, J Biol Chem and J Neuroscience. Dr. Marzolo has an H index of 14 and examples of her highest cited papers in the past decade are Li et al., (2000) at 151 and Li et al. (2001) at 69. Dr. Marzolo is interested in the LRP-like protein functions and has also investigated the role of ApoER2 in Alzheimer's disease associated neurodegeneration.

As can be realized from these data, the 8 investigators have maintained publications in very good journals with occasional papers in the highest ranked journals. I included citations (and the H index) as the report had the former metric included in several places, but of course citations do not tell the whole story. That said, there is a trend towards the group publishing in higher impact factor journals and this is both a good sign and to be commended. Numbers of papers are not as meaningful as their quality. This team has had and continues to have international impact.

There is excellent evidence of synergy even though the core interests are diverse. These investigators have many common interests and are working well together.

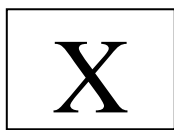
Overall, I would rate scientific productivity in terms of publications as at the high end of very good when judged internationally. To achieve a rating of Outstanding I would expect to see a greater number of papers in the top tier journals (impact factor > 10). Of note, Dr. Larrain has published in Nature Cell Biology and EMBO J/Reports and Dr. Brandan in EMBO J. Members of the group have published in PNAS and other very good journals. I would also note that my judgement of top tier journals is quite strict. There are 3000 biomedical journals and the top 30 (1%) of those that are not primarily review journals have impact factors greater than 17. I would not classify J Biol Chem for example as top tier. It is a very good journal but has an impact factor of 5.5.

The group has also made very good and frequent contributions to conferences and meetings with 14 conferences being organized under the auspices of the faculty. There is clear evidence of public outreach.

ii.- Evaluation



Outstanding



Very Good



Good



Poor

2.- Educational achievements and impact. Pay attention to integration of research and educational activities, and also in training advanced human resources, participation in PhD Programs.

i.- Comments

The best form of research education is in the form of successful training of students and fellows. The section on human resources (page 21-22) describes a vibrant PhD program that included development of a modern curriculum. Over 180 students (undergraduate, 1 Masters and PhDs) are listed and for those who have completed their studies towards a PhD, the average time to completion is 5 years which is within the norm. In addition, over 50 postdoctoral fellows have been trained over the past decade with a tenure of 2-3 years on average.

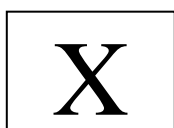
The report noted that there is not so much interdisciplinary interaction via co-tutorial theses due to the field of study, which is, in my opinion, a fair point.

It would be useful to know where the PhD graduates and fellows moved to once they completed their studies. How many stayed in academia, how many decided to do postdoctoral training abroad, etc. Without this information, it is difficult to compare the training success (aside from numbers). There is no evidence that this is a concern but these sorts of data help for relating the program to others. This is the sole reason for not scoring as Outstanding.

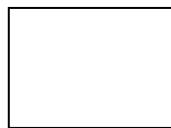
ii.- Evaluation



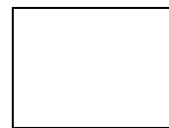
Outstanding



Very Good



Good



Poor

3.- National and international collaboration achievements. Pay attention to activities that contributed to national and international networking.

i.- Comments

It is clear that the investigators within the Center are highly collaborative as judged by co-authorship and interactions of their programs. The report focuses on the collaborations of the 5 senior investigators upon which the Centre was built. These examples are useful and indicate that these members work with other scientists both within Chile and internationally. This is not surprising as this is a mature and respected research group. There is also evidence presented showing the laboratory scientists participate in both national and international conferences and seminar programs.

Some information would have been useful for the more recent recruits – recognizing that they have had a shorter time to establish themselves. Even so, I have no concerns and judge the degree of research interaction as very good

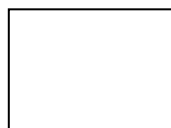
ii.- Evaluation



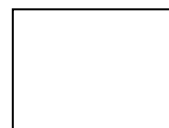
Outstanding



Very Good



Good



Poor

4.- Outreach Achievements. Pay special attention to those activities that tied the Center with the external community such as elementary or high schools, institutions, companies, among others.

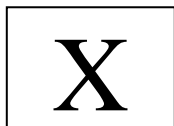
i.- Comments

While only half a page was used to describe the outreach activities, the content is impressive. The programs include two books aimed at the general public on topics of expertise within the Center (Alzheimers and Obesity). It also runs a seminar series for other researchers in Santiago as well as regular radio broadcasts of interviews with researchers. The Center staff take this responsibility for outreach very seriously.

ii.- Evaluation



Outstanding



Very Good



Good



Poor

IV. OTHER RELEVANT ASPECTS

If the Center report does not contain information on other relevant aspects, please indicate so in your evaluation.

i.- Comments

It would be useful to know of the history of the Center in terms of when people were recruited, their relationships with members (ex-trainees, etc) as this helps build a better picture of the organization of the group and rationale for the composition.

There should also be a confidential section for the Director to indicate his/her concerns regarding the progress over the past decade.

To reiterate, this review at 10 years typically involves a site visit where questions can be answered, facilities experienced, etc. Due to the earthquake, this was not possible. Indeed Dr. Inestrosa's own laboratory was damaged. Hence, the report generation occurred at a very difficult time for many of the scientists involved. The staff are to be commended for managing to assemble the information that they provided.

V. CENTER PROJECTIONS

Please comment about the center projections after the 10 -year FONDAP grant. If the Center report does not contain information on the Center projections, please indicate so in your evaluation.

i.- Comments

There was only a short section on the perspectives of the Center. It is unclear to this reviewer what the next steps and opportunities are, whether funding can be continued, etc. There is mention in this section of possible business developments but the Center has not accrued patents and there is no mention of other intellectual property so it is not obvious what the role of the Center would be with the pharmaceutical sector except perhaps in collaborating with expertise.

The impact of the FONDAP CRCP funding on the group is not easy to assess. The Center received the maximum allowed (600 million pesos per year). The Center has a current budget of over \$1,500 M\$ not counting the CRCP funds which ended in 2009. A significant grant to support regenerative biology was secured in 2009 which replaces 80% of the FONDAP funds and runs to 2012. With these funds in place, the integrity of the research group should be maintained although it may impact their research focus.

VI. INSTITUTIONAL COMMITMENTS

Please comment about the facilities available to the Center, the commitment of the administration of the leading and partner institutions to the Center, and the commitment of the partner institutions to achieve the Center goals.

i.- Comments

This is not possible to evaluate due to the absence of a site visit and lack of documentation. The report mentions that assistance from the faculty was initially lacking at the beginning of the Center but that relationships with the University administration were cordial.

ii.- Evaluation

☐

Outstanding

☐

Very Good

☐

Good

☐

Poor

VI. ADVISORY COMMITTEE

Please comment about the commitment of the advisory committee, and its contribution to the Center development.

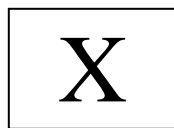
i.- Comments

This committee made three visits and the report notes the advice from the committee advisors was taken seriously and positively impacted the direction of the research of the Center. There is evidence for this in previous reports on the CONICYT web site. The frequency of 3 over ten years is low and a bi-annual visit might have allowed greater opportunity for impact.

ii.- Evaluation



Outstanding



Very Good



Good



Poor

VI. FINAL OVERALL COMMENTS AND RECOMMENDATIONS

Please provide a final overall and recommendations for the Center. Include here aspects that were not covered in the previous sections, which you consider significant for the Center.

i.- Comments

This is a superb example of a team of researchers working together to develop and nurture their mutual interests. The research areas they are pursuing have impact on human health (Alzheimers disease, lupus, tissue regeneration, fibrosis, nerve transmission, obesity and neurdegeneration). The group is using several model systems to elaborate and probe their research providing a rich environment for teaching and training and this has driven a highly productive stream of accomplished students and fellows.

The resources provided have been employed effectively and the emphasis on quality is apparent. Overall, the accomplishments of the group are compelling and admirable. In reading the initial justification for establishing the Center, it is easy to see that the ambitions and expectations of the founding investigators have largely been met. My evaluation is that this has been an effective and strong collection of scientists. If there had been the benefit of a face to face interaction, my evaluation may have been higher but I consider this to be an

excellent program that meets international standards and that is what I am comparing this program to.

ii.- Evaluation

☐

Outstanding

☒

Very Good

☐

Good

☐

Poor

NATIONAL PROGRAM FOR RESEARCH CENTERS OF EXCELLENCE
(FONDAP)

FINAL EVALUATION REPORT

This form is intended to facilitate your work as a referee and standardize the evaluation reports. Each topic is expected to be evaluated with concepts ranging from outstanding to poor and detailed technical comments supporting your points on the report.

If the Center report does not contain information on the given topic, please indicate so in your evaluation.

Your final overall comments and recommendations are an important part of the review process.

I. PROJECT INFORMATION
CENTER'S NAME: Center for Cell Regulation and Pathology "Joaquín V.Luco"
DIRECTOR: Dr. Nibaldo Inestrosa Cantín

II. EVALUATION PANEL			
REFeree NAME	ORGANIZATION/ INSTITUTION	E - MAIL	SIGNATURE
REFeree N° 2			

III. CENTER ACHIEVEMENTS

1.- Scientific achievements and their impacts to local, national and international community.

i.- Comments

The FONDAP Center for Cell Regulation and Pathology (CRCP) “Joaquin V. Luco” has fulfilled its mission as high standards research activity and scientific training were conducted in specific areas of cellular and molecular biomedicine. It has contributed to the advance of these disciplines and developed interactions resulting in a gain of productivity and visibility within and outside Chile.

Over the full period (2000-present), the CRCP center participants have contributed to eight Research programmes. These programmes were internationally competitive and dealing with important and actual questions in the fields of cell biology, developmental biology, physiology and neuroscience.

The data were concretized by an impressive number of original ISI publications (more than 200) with an excellent average IC (>to 5), together with participation to book chapters. Moreover, over the years an increasing number of postdoctoral fellows were recruited on the programmes.

At the national level, members of the center actively participated in university teaching programmes and welcomed 182 students, half of them for PhD training, the remaining ones as undergraduates. Scientific exchanges such as organization and participation to seminars and meetings have been actively fostered with other Chilean universities. Overall, the center has increased the quantity and quality of human resources qualified in Biological Sciences and contributed contributed in several important ways to developing the research infrastructure of Chile. Specific interest had been given to translational applications of the research via the creation of a Business Unit.

Finally, scientific information and training was given to the Chilean public through various channels.

ii.- Evaluation

☐

Outstanding

☒

Very Good

☐

Good

☐

Poor

2.- Educational achievements and impact. Pay attention to integration of research and educational activities, and also in training advanced human resources, participation in PhD Programs.

i.- Comments

PhD programmes:

The staff members:

- (1) coordinated core courses of two of the PhD programs of the Faculty.
- (2) contributed to the Medical Sciences PhD program of the Faculty of Medicine of the university
- (3) Students from these programmes made their PhD thesis research work at the CRCP

Scientific training:

The students had the opportunity:

- (1) to attend bimonthly scheduled FONDAP seminars.
- (2) to attend national and international meetings and courses.
- (3) to visit national and foreign laboratories, some of them choosing to perform a post doctoral stay abroad.

The Center during this ten years project trained :

- 51 postdoctoral fellows, most of them, but not exclusively, financed by the FONDAP-CRCP 1390001 project. Other supports came from CONY CIT and other financing sources.

(21) worked under Dr Inestrosa's supervision ; E. Brandan (7), A. Gonzalez (9), JP Huidrobro (5), M Bronfman (4), J. Larrain (3), MP Marzolo (1), F. Bronfman (1).

- 1) As a proof of attractivity, it should be mentioned that the number of post doc fellows dramatically increased during the second phase of the center.
- 2) Repartition among the teams is in strong favor of Dr Inestrosa whereas younger teams have few.

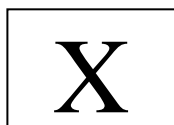
- 186 students graduates or undergraduates: Several defended or are in the process to prepare a thesis:

Here again, a majority of these fellows (47) worked or are working under Dr Inestrosa's supervision (41) or co-supervision (6); E. Brandan (22, 1 co-direction), A. Gonzalez (21, 2 co-direction), JP Huidrobro (25, 3 co-direction), M Bronfman (18, 1 co-direction), J. Larrain (14), MP Marzolo (14, 2 codirection), F. Bronfman (10).

- (1) Some of these students are co-directed by the group leaders as a proof of collaboration between the teams.
- (2) The younger groups are strongly involved in training students.
- (3) as for post docs, the number of students present increased by the second term of the

center.

ii.- Evaluation



Outstanding



Very Good



Good



Poor

3.- National and international collaboration achievements. Pay attention to activities that contributed to national and international networking.

i.- Comments

National achievements:

Thirteen courses, congresses and symposia have been organized inside Chile, mostly in Santiago, by staff members (Inestrosa (5), Brandan (1), Gonzalez (1), Larrain (1), Brofman (1), P. Huidobro (3). The attendance ranged from 200 to 30.

International interactions:

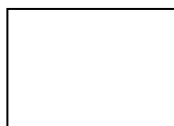
Over the decade, approximately 200 visits/interactions with foreign scientists and/or institution took place with a strong but not exclusive emphasis for USA and Europe. A good equilibrium exists between visitors coming to the center and visits abroad.

- (1) students have been involved in these contacts
- (2) more than 60 foreign scientists gave seminars
- (3) some were invited to participate to the congresses or courses (see above) organized in Chile.
- (4) Importantly some long lasting collaborations have been established with foreign laboratories.
- (5)

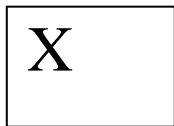
Participation to Editorial Board:

Dr Inestrosa is part of the editorial board of an international journal, the Journal of Biochemical Chemistry.

ii.- Evaluation



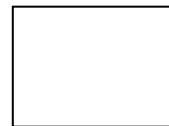
Outstanding



Very Good



Good



Poor

4.- Outreach Achievements. Pay special attention to those activities that tied the Center with the external community such as elementary or high schools, institutions, companies, among others.

i.- Comments

The Center staff carried out several types of activities:

- (1) Some were directed towards spreading and/or improving the content of biology courses. They were targeted to teachers such as a “Special courses for High School Teachers of Biology”. or to students and colleagues from other universities such as the weekly seminars and the monthly CRCP-MIFAB seminars.
- (2) Other targeted Chilean society such as radio programmes, mass media interviews, articles in newspapers, magazines and electronic publications accessible via the Internet,
- (3) Publication of vulgarization books on Alzheimer (Inestrosa) and Obesity (Marzolo)

ii.- Evaluation

☐

Outstanding

☒

Very Good

☐

Good

☐

Poor

IV. OTHER RELEVANT ASPECTS

If the Center report does not contain information on other relevant aspects, please indicate so in your evaluation.

i.- Comments

Research valorisation:

- Creation of a Business Unit Expertise aimed to foster the relationship with national and pharmaceutical companies. This unit had been instrumental in obtaining additional financial sources for the CRCP such as participation in a Center of Excellence in Science and Technology”

Honors received by staff members :

Dr Inetrosa received a National chilean prize in Natural Sciences 2008 , Dr Brandan became a

member of the academy and Dr larrain received a medal from the pontifical academy of sciences.

V. CENTER PROJECTIONS

Please comment about the center projections after the 10 -year FONDAP grant. If the Center report does not contain information on the Center projections, please indicate so in your evaluation.

i.- Comments

After termination of the CRCP center some or all (?) of its members plan to engage in a new initiative termed Center for aging and regeneration (CARE) they apply to with the help of the Business unit expertise (see above).

VI. INSTITUTIONAL COMMITMENTS

Please comment about the facilities available to the Center, the commitment of the administration of the leading and partner institutions to the Center, and the commitment of the partner institutions to achieve the Center goals.

i.- Comments

Although administration did its best to administrate the center difficulties were encountered to obtain decent and refurbished laboratories. This eventually happened but took too much time considering that research is submitted to international competition.

ii.- Evaluation

☐

Outstanding

☐

Very Good

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Good

☐

Poor

VI. ADVISORY COMMITTEE

Please comment about the commitment of the advisory committee, and its contribution to the Center development.

i.- Comments

(1) The Scientific Advisory Board visited the Center three times over the ten years.

(2) The FONDAP Reviewer Board also performed several visits.

Both boards gave recommendations. Among them was to avoid dispersion, to involve students in preparing publications as part of their formation, to initiate collaborations between the groups. Most of them were followed by the members although senior investigators, anxious to maintain their individuality, were reluctant to stronger changes in their research lines.

ii.- Evaluation

☐

Outstanding

☒

Very Good

☐

Good

☐

Poor

VI. FINAL OVERALL COMMENTS AND RECOMMENDATIONS

Please provide a final overall and recommendations for the Center. Include here aspects that were not covered in the previous sections, which you consider significant for the Center.

i.- Comments

Irrelevant as the center will be terminated

ii.- Evaluation

☐

Outstanding

☒

Very Good

☐

Good

☐

Poor