



Workshop on Cell Biology and Genetics: Summary Statement



Introduction

A workshop on the subject “Cell Biology and Genetics” was held on 23-24 October 2017 at the Casina Pio IV, the headquarters of the Pontifical Academy of Sciences (PAS) in The Vatican. The main purpose of the meeting was to bring together members of the Pontifical Academy with scientists from the Academia de Ciencias de América Latina (ACAL) to report on recent advances in cell biology, genetics and biomedicine. The fact that ACAL was founded 35 years ago during a special session of the PAS added a particular significance to this workshop, especially because ACAL has recently entered in a new period of vigorous renovation.

Latin America has enormous human capital, with a highly educated and civilized population of great potential. There is a long history of contributions to research. This includes Nobel Prizes awarded to Bernardo Houssay and Luis Leloir for work done in Buenos Aires and to Mario Molina from Mexico for explaining the chemical mechanisms that affect the thickness of the ozone hole. New institutes have been created in recent years that have powerful scientific capabilities, although many challenges remain.

The workshop encompassed a total of twenty presentations in the fields of biophysics and cell membrane biology, cell signaling and developmental biology, neurobiology, biomedicine and genetics. There were also reports about intracontinental scientific collaborations, science and technology initiatives of the US Department of State and the current state and activities of ACAL.

In addition, there was a special session devoted to discuss scientific cooperation in Latin America and networking with countries in the Northern Hemisphere.

From the presentations and discussions during the workshop, we have garnered a set of major scientific conclusions that indicate the prominent refinement attained in some areas of the biological sciences in the region. In addition, since this meeting provided a unique occasion to analyze ways to enhance science development of Latin American countries, we provide a set of recommendations that are potentially useful for scientists and public policy makers.

New scientific advances as revealed during the workshop

A wide range of advances in Cell Biology by experts in the field was covered at the workshop. At the cell membrane level: how transient receptor channels for heat and pain work (Ramón Latorre); how gap junction hemichannels mediate inflammatory signals (Juan Carlos Saez); and how mechanically-gated ion channels mediate auditory perception (Ana Belén Elgoyhen) were discussed. In Biophysics and Biochemistry topics presented included: molecular motors that package single DNA molecules into bacterial virus heads (Carlos Bustamante); novel bacteriophage recombinases that allow the design of new genetic circuits in plants (Elibio Rech); how superoxide free radicals cause detrimental nitration of proteins (Rafael Radi); how diabetic glucose levels in endothelial cells cause low grade inflammation via free radicals (Salvador Moncada); how the folding of glycosylated proteins is controlled by the addition and removal of glucose (Armando Parodi); the biochemistry of early life forms (Rafael Vicuña); how protein degradation in lysosomes by microautophagy is regulated by the Wnt growth factor (Edward De Robertis); and how hypoxia is sensed by a molecular machinery involved in cancer (Pablo Wappner). In plant genetics, discussions included: how chloroplasts signal to the nucleus to regulate their own synthesis (Patricia León); how Rhizobium bacteria that fix nitrogen and solubilize phosphorous increase crop production (María Luisa Izaguirre) and how forced expression of three transcription factors generates desiccation-resistant plants (Luis Herrera-Estrella). In biomedicine, topics included: the replication of Zika virus in human radial glia stem cells (Stevens Rehen); how genomics and personalized medicine help decrease the incidence of cerebrovascular stroke (Conrado Estol); how dietary supplementation helps prevent neural tube defects (Rafael Apitz-Castro); how new applications of lasers through biophotonics effectively treats skin cancers, warts, ulcers and other dermatologic diseases at very low cost (Vanderlei Bagnato); how protein aggregates of an RNA splicing factor are formed in 97% of cases of Amyotrophic Lateral Sclerosis (Francisco Baralle) and how immunotherapy targeting immune-evasion molecules such as PD-1 and Galectin-1 with monoclonal antibodies is revolutionizing cancer treatment (Gabriel Rabinovich).

Conclusions and recommendations.

1. There is general consensus regarding the lack of recognition from governments of Latin American countries of the critical role science plays in both cultural and socio-economic development. As a result, policies for strengthening scientific research and training of young scientists are generally lacking in government programs. This situation has a severe impact on various grounds, *i.e.* there are deficiencies in science education at all levels, funds allocated for scientific research are insufficient, initiatives aiming at linking the scientific community with the productive sector are almost nonexistent, etc.
2. An additional consequence of the above condition is that the relative size of the scientific communities in Latin American countries - when measured in relation to their respective general populations - is very small when compared to those of developed countries. Moreover, there are several Latin American countries whose contribution to the world's scientific productivity is virtually negligible.
3. Due to this lack of support many young scientists depart from their home countries and settle in countries of the Northern hemisphere, where they find the proper conditions to express their vocations. Most often these scientists remain abroad, progressively losing contact with colleagues in their home countries. It is proposed that ACAL should play a leading role in assessing the magnitude of this scientific diaspora and thereafter generate networks leading to new initiatives that will benefit Latin American countries, such as research collaborations, training periods for graduate students, participation in thesis committees, promoting novel research programs in the region, etc.
4. State Policies to provide the resources and infrastructure required to repatriate young scientists are inadequate. It will be important to develop long-term national programs to provide the infrastructure and resources needed to facilitate and promote high quality, internationally competitive research programs by young scientists. Science and technology should be viewed as fundamental engines for cultural and socio-economic development in Latin America.
5. There is also ample agreement in that international organisms such as the Organization of American States (OAS), UNESCO and the U.S. Department of State could contribute to science as an engine for development in Latin America. It is also proposed that ACAL, with its continental vocation, should take the lead in contacting these international organisms and work with them on suitable strategies to pursue this objective.
6. ACAL is a civil society formed by scientists for scientists and is independent from any government. It is ideally situated to reactivate the participation of the OAS in promoting exchanges horizontally between Latin American countries. In particular, short-term fellowships for Ph.D. students are greatly needed. In the past OAS had programs to promote scientific exchanges, but sadly no more. ACAL should attempt to convince the Ministers of Science and Technology of OAS, who meet periodically, of the urgent need to re-engage in STEM (Science, Technology,

Engineering and Mathematics) programs. Science is non-political and essential for progress.

7. The Howard Hughes Medical Institute had during the past 20 years a Scholars program that transformed biomedical science in Latin America by elevating many researchers who presently occupy leadership positions in their own countries. It was noted with sadness that the program was terminated. The workshop participants, many of whom were or are supported by HHMI, felt that this was the most effective dollar-for-dollar program ever funded by HHMI. Hope was expressed that the Latin Scholars program might be reactivated in future. A program that is ongoing and is having a huge impact in biomedicine is the PEW Latin American Fellows Program. It provides a two-year postdoctoral stipend to study in the U.S. and start-up funds to return to home country institutions. The 180 PEW scholars that have already returned are changing Latin American biomedical science. The PEW Charitable Trusts very generously prepared a report specifically for this Workshop. This report is provided in the Appendix below.

8. Regardless the outcome of the proposed initiatives, scientists should make a special effort in creating links with the various sectors of society. They must interact with the media to contribute to the education of the general public. They must also relate with the private sector, exploring prospects for innovation in the productive processes. Due to its high social relevance, a fluent relationship with authorities of the health sector is particularly relevant. Successful experiences in these fields will constitute the best arguments to convince governments that supporting science is indispensable today as we are living through an amazing convergence of biotechnology, molecular medicine and bioinformatics.

9. In the midst of these challenges, some interesting cases were also presented. For example, the Brazilian Academy of Sciences embarked on a plan aimed at expanding the interactions between scientists and politicians. As a result, the budget for science-related activities did not experience a decrease that would have been expected otherwise. A letter addressed to the President that was signed by several Nobel laureates may have contributed to this effect. On the other hand, in Uruguay the size of the scientific community has been increasing steadily and a national system for evaluation of scientists has been established. In addition, an Academy of Sciences has been recently created. Furthermore, the scientific community in Uruguay has had a decisive role in implementing the national plan aimed at replacing fossil fuels by renewable sources of energy. These paradigmatic examples of Brazil and Uruguay call for optimism and strongly suggest that soundly designed public policies in science promptly translate into social benefits.

The research presented at the workshop will be published as a volume of *Acta Vaticana Scripta Varia*, which will provide the world and the Church with a window into the remarkable recent advances in Cell Biology. The wonderful atmosphere at the Casina Pio IV contributed to discussions that hopefully will have long-lasting effects in the scientific development of the vast Latin American subcontinent. The participants were most grateful to the Pontifical Academy of

Sciences and Pope Francis for this unique experience.

Appendix:

Statement on the Pew Latin American Fellows Program for the Workshop at the Vatican on Cell Biology and Genetics

by Rebecca Rimel and Kara Coleman of the Pew Charitable Trusts

The Pew Charitable Trusts has a long-standing history of providing funding for the training of young scientific researchers. Founded in 1985, the Pew Biomedical Scholars Program provides unrestricted research funding for assistant professors in the United States (U.S.), giving them free reign to test out creative, potentially risky ideas that have the possibility to return large dividends. As part of this program, all current grantees attend an annual meeting—an aspect of the program that serves to promote community building, networking, and collaboration. These yearly meetings have historically been held in the Caribbean or Central America, and this led Pew Scholars, at a meeting in Mexico in 1989, to discuss their observations about the inequity of resources and support available to their Latin American contemporaries compared with researchers in the U.S.

At the 1989 Mexico meeting, the scholars approached Rebecca Rimel, the president and CEO of the Pew Charitable Trusts and founder of the Pew Biomedical Scholars Program, and Torsten Wiesel, M.D., then chair of the program, about their concerns. As Ms. Rimel and Dr. Wiesel discussed the best approach to supporting science in Latin America, they realized that it was not only important to provide funding to train talented scientists from Latin America, but that it was also crucial to incentivize them to continue their research in their home countries. At the time, Latin American science was suffering from an exodus of talented researchers seeking international training, who did not later return to invest in the local scientific infrastructure. Rimel and Wiesel determined that any program to further science in these regions should focus on the repatriation of scientists to Latin America as a top priority.

In 1991, The Pew Charitable Trusts launched the Pew Latin American Fellows Program. Today, the program provides 10 fellowships per year, each of which gives funding for two years of postdoctoral training in the U.S. An additional payment is awarded to each grantee who returns to Latin America to start his or her own lab. These funds are used to help purchase much-needed start-up equipment for the laboratory. In the program's 26-year history, 262 fellowships have been awarded to scientists from 10 countries in Latin America. Of those who have finished their training in the U.S., close to 70 percent have chosen to return to Latin America where they now run their own laboratories.

A program survey completed in 2013 revealed the remarkable impact the program has had on scientific communities in Latin America. In total, the 151 respondents reported training 1,469

individuals—technicians, graduate students, postdoctoral fellows, and visiting scientists—amounting to an average of nearly 10 scientists trained per alumnus. Alumni have published an impressive 2,237 journal articles, resulting in an average of 15 articles per respondent, following their Pew fellowship and many have earned numerous honors. There are multiple recipients of the Bernardo Houssay Prize, The World Academy of Sciences prizes, the John Simon Guggenheim Memorial Foundation fellowship, the Howard Hughes Medical Institute International Research Scholar award, and the L’Oreal-UNESCO fellowship for Women in Science. Notably, several have been inducted into the Latin American Academy of Sciences. Additionally, Pew program alumni continue to be active members in the Pew community, ushering in future generations of participants in the Pew program by promoting the call for applications to young scientists and participating in application review as part of regional committees.

The scientific community in Latin America continues to grow and strengthen—for instance, the number of scientific doctorates pursued increased about 10-fold in Argentina between 2000 and 2010, and numbers of scientific articles tripled for Peruvian scientists in the same time period. However, as with all research communities, there is still room for improvement, and several critical windows of opportunity exist. First, it is important that investments in basic biomedical research be viewed as a funding priority at both the government and university level. It can be very challenging to fund exploratory, rather than applied, research projects in the face of economic instability and social unrest. However, the importance of research to understand basic cellular processes cannot be understated. For instance, studies on the cellular system that degrades proteins ultimately led to the development of a cancer therapy. One thriving Latin American example of an effective investment is the São Paulo Research Foundation, a state agency which directs upwards of 37 percent of its funding to basic research. This region produces more than half of the scientific papers that come out of Brazil. While it takes time for basic research to yield dividends, providing scientists with the funding to perform exploratory research is the best way to spark groundbreaking discoveries that will revolutionize human health. Investments in lab facilities, equipment, and salaries are also important to sustaining a thriving research enterprise.

In addition to university and government support, it is important for local foundations and philanthropies to invest in the science in their region. In many Latin American countries, the percentage of gross domestic product spent on research and development is less than 1 percent, compared with 2-3 percent in more developed countries. Under these circumstances, there is a clear need for support from other funding entities to drive progress. In Argentina, Pew has established successful partnerships with two foundations in Buenos Aires: Fundación Bunge y Born and Fundación Williams. Together, these foundations provide additional repatriation funds to Pew fellows returning to Argentina. The partnership is mutually beneficial: the Pew fellows receive additional start-up funds, and Argentina is able to recruit highly talented scientists to their institutions by promoting the additional funding opportunity. Foundations in other countries could consider a similar model in order to recruit talented scientists to their region, and provide much-needed support.

Finally, scientific training in countries where the infrastructure is less developed continues to be an opportunity for investment. Over the many years that the Pew program has been in place, the number of applications from Argentina, Brazil, Chile, and Mexico has steadily increased—along with a parallel improvement in applicant quality. However, countries such as Colombia, Peru, and those in Central America continue to lag behind in applications. Many who are interested in pursuing higher education go abroad to obtain a Ph.D. because of limited options at home. As scientists continue to leave their home countries, it will exacerbate the already fragile scientific state. We encourage regional collaborations, equipment sharing, hosting students and postdocs, or inviting scientists to present seminars. Such small steps can help to strengthen the scientific communities and infrastructures across the region.

As Latin American science looks toward the future, investment in research and training is a way to support its talented and committed researchers and stimulate scientific advances and innovation.