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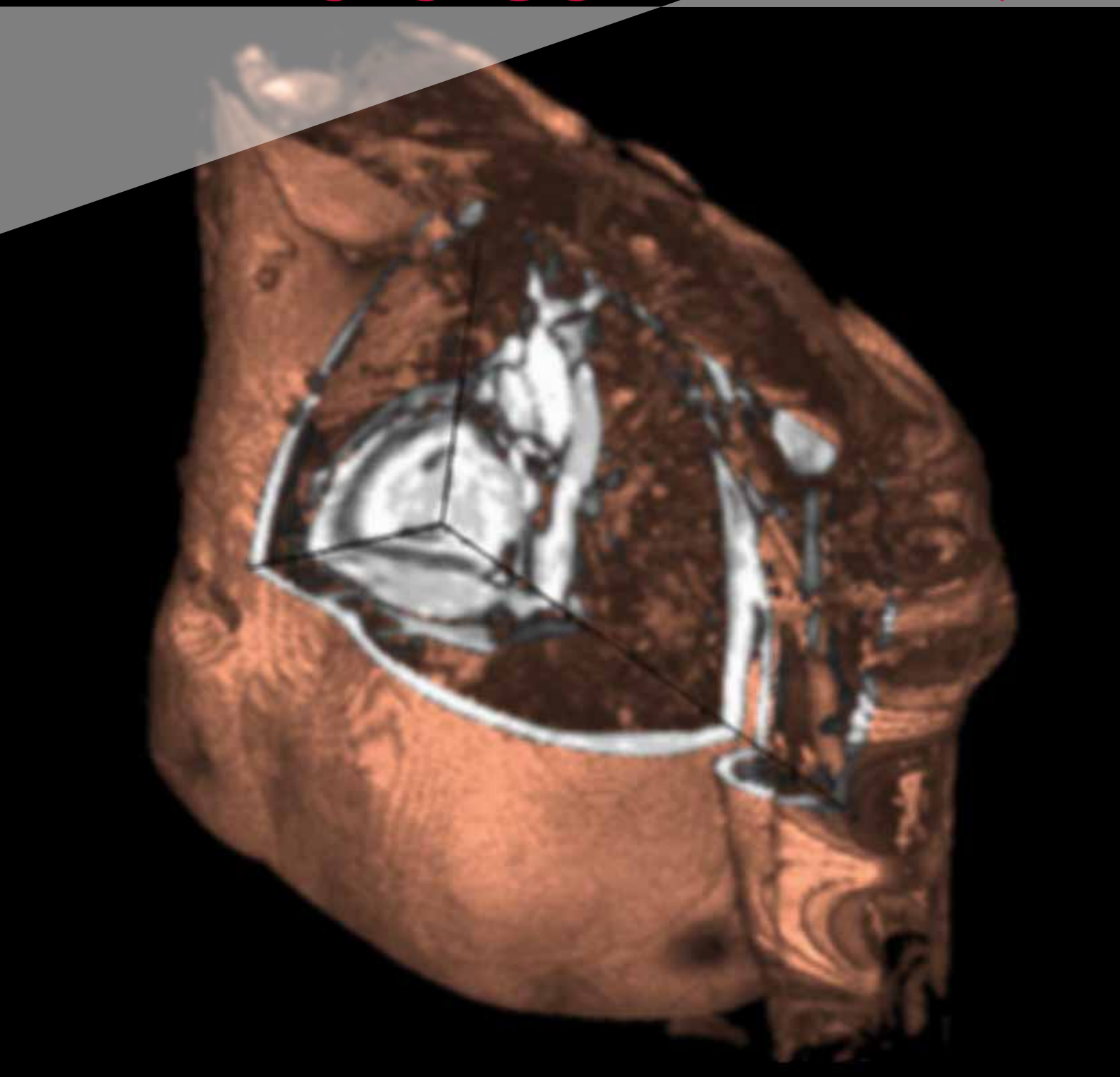
# cnïc PULSE

## autumn '17



# contents autumn'17

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CNIC Director **Dr. Valentín Fuster**

# WITHOUT TRANSFER, THERE IS NO INNOVATION

"As scientists we cannot live isolated from society". This was said by **Dr. Valerie M. Weaver**, the Director of the Center for Bioengineering and Tissue Regeneration at the Department of Surgery of the University of California in San Francisco, during the VI Edition of the CNIC Conference. And this is the truth: our duty as researchers, and members of a global society, is to make sure that our knowledge, our results are transferred in a way that benefit the whole of society.

Recently, the Secretary of State for Research, **Carmen Vela**, said that the transfer of knowledge between science and business should be a circular concept. Us researchers know that it is necessary to bring these two sectors closer together, science and businesses. We must break those barriers that still believe that companies need to be outside the university.

There is no doubt that the transfer of knowledge is the best way to give back the resources in research of the Public and Private Administration to the general population. The main source of knowledge is the academic world. The question is how to capitalize the investment in talent and resources that is made in the academic centers and to use those results for the benefit of society. The answer is the OTRI.

Since 10 years ago the CNIC has had a Technology Transfer Office (TTO), which in this short period of time has managed to transfer the knowledge and results of the laboratories and technical units of the center by providing an "added value" to the work, and in some cases, market products that have an impact on the health care of the general population. They also produce an economic return that allows us to continue investing in projects, hiring people, and in short, mobilizing the country's economy.

And, during this time the TTO of the CNIC has accomplished remarkable achievements, like the "Fuster Polypill", the first polypill approved in Europe for secondary cardiovascular prevention which was developed by CNIC researchers in collaboration with the pharmaceutical company Ferrer and that is approved for marketing in 55 markets in Europe and America; the collaboration agreement between the CNIC and its technological partner Philips, which allows the CNIC to count with the most advanced cardiovascular imaging technology in the entire spectrum, from ultrasound to hybrid equipment, through to CAT scans and Magnetic Resonance Imaging (MRI), and that has allowed for the development of the joint patent Philips-CNIC VF-3DESSOS, ultra-fast MRI, or the biomarker of the Pilar Martín Group, already patented for the diagnosis of acute myocarditis, and which is currently under negotiation for the joint development and licensing of the CNIC patent to a venture capital company to develop a biosensor capable of detecting the biomarker in patient blood samples in 30 minutes.

The conclusion is that without transfer, there is no innovation and without innovation, we are risking the future of research in our country. ■

# INPhINIT, THE TRAINING PROGRAM THAT CONTRIBUTES TO A GOOD DEVELOPMENT OF THE PROFESSIONAL CAREER OF THE RESEARCHER DURING THE PHD

The CNIC, as a "Severo Ochoa" center of excellence, participates in the International Predoctoral Program "INPhINIT" as a reception center for predoctoral researchers who wish to carry out their doctoral thesis in any of the center's laboratories. Promoted by the Social Project "Obra Social 'la Caixa'" and co-funded by the European Commission through the Horizon 2020-Marie-Sklodowska-Curie ActionsCOFUND program (Grant Agreement nº713673), the INPhINIT is a PhD scholarship program designed to integrate young international researchers in the best Spanish research centers, in the fields of technology, engineering, physics, mathematics, health sciences and life sciences.

Promoted by the Social Project "Obra Social 'la Caixa'", INPHINIT aims to support the best scientific talent and encourage high-quality and innovative research in Spain by hiring outstanding international students, who are in turn offered an attractive and competitive environment where to carry out a research of excellence. In every call, INPhINIT selects 57 young researchers of all nationalities who are offered a 3-year work contract to carry out their PhD in the accredited centers with the Severo Ochoa or Maria de Maeztu distinguishment and in the Carlos III Health Research Institutes. In addition, the researchers establish a professional career development plan which includes transnational, intersectoral, and interdisciplinary mobility opportunities. They will also be given a complementary training program.

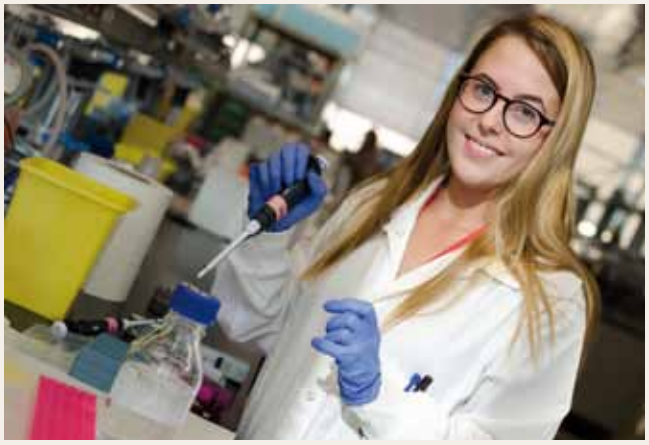
On this occasion, the CNIC welcomes **Rocío Muñiz**, who has already joined the group "Experimental Pathology of Atherosclerosis", directed by **Professor Jacob Fog Bentzon**. **Rocío** chose the CNIC over other centers that participate in this program because, in her opinion, it is one of the most important centers in cardiovascular research in Spain. "Both the facilities and the technology and ease are very good. I studied the Master's degree in Cardiovascular Research in the Netherlands and I knew for sure I wanted to do a PhD in a leading center in this field" "And why **Jacob**'s group?" "For two reasons: first, for the topic of the group, atherosclerosis, a chronic disease that causes most heart attacks and ischemic strokes. Atherosclerosis has always caught my attention because it affects thousands of people around the world every year and, nevertheless, the pathological mechanisms that trigger the disease are still not fully understood. Also, because my experience in the internship that I did in the past in this group was

**REQUIREMENTS TO ACCESS TO INPHINIT:**
At the time of hiring, the candidates must meet one of the following options:

- Have completed an official University Degree in Spain (or another country of the European Higher Education Area) which grants 300 ECTS credits, of which at least 60 ECTS credits correspond to the Master's Degree.
- Have a degree in a non-Spanish university not part of the European Higher Education Area which allows access to PhD studies. The verification of an equivalent level of studies previously mentioned will be carried out by the university when the admission process begins.

**TO BE ELIGIBLE, THE CANDIDATES MUST:**

- Be in the first four years (experience of research equivalent to full time) of their research careers without having obtained the PhD yet.
- Not have lived nor carried out their main activity (work, studies, etc.) in Spain for more than 12 months in the 3 years prior to the date of hiring. Short stays such as holidays will not be taken into account.
- Have a demonstrable level of English (B2 or higher).



**THE PROGRAM OFFERS:**

- 3-year contract.
- Very competitive salary.
- An award of 7,500€ for the PhD, in the case of the completion of the thesis in a period of 3.5 years.
- Additional training in transferable skills.

For more information: **www.inphinitlacaixa.org**

very satisfactory and I learned a lot. Finally, **Jacob** is an excellent group leader."

INPhINIT collaborates with the best research centers in Spain, which welcome the INPhINIT interns in one of their PhD programs. INPhINIT aims to revolutionize European doctoral training in terms of quality, excellence of the researchers, scope of the benefits offered and the expected impact. **Rocío** learned about the INPhINIT program during her internship at the CNIC. "My experience at the CNIC was very positive, which led me to look for scholarship possibilities with the intention of returning to the center to do the PhD once I finished my studies and stay abroad. With this intention, the scientific management department of the CNIC recommended the INPhINIT program as a very good option to do the doctorate."

Among the reasons which most motivated her to apply is the fact that it is a new program of the La Caixa Foundation, which in itself has a great prestige, aimed at international students and offered a three-year contract as a PhD student in research centers of excellence such as the CNIC. In addition, she adds, "because it offers a complementary training program to contribute to good development of the professional career of the researcher during the doctorate." **Rocío** believes that initiatives of this kind, that promote research, are absolutely "necessary" to promote research in Spanish centers. "It is important to instill the recognition of the value of research from a social point of view, especially in regards to the personal effort and ethical values of the people involved, and as a way to achieve long-term sustainable socio-economic development." In her opinion, initiatives, such as INPhINIT, will undoubtedly "contribute to this by holding on to national and international talent for the completion of projects organized in Spanish centers."

However, the researcher believes that, in Spain, unfortunately, the PhD scholarship program options are limited. "Spain has good research centers and excellent scientists, but many students, both Spanish and international, decide to continue their scientific training outside the country due to the scarcity of quality programs, which do exist in some northern European countries, such as The Netherlands, Sweden, Denmark, etc." From her stay at the CNIC, **Rocío** hopes to "do a good PhD and develop my professional profile as a researcher, learning from mistakes and achieving results." ■

# CNIC COORDINATES A NEW EU PROJECT TO TRAIN A NEW GENERATION OF SCIENTISTS FOR THE FUTURE

Last January 1st 2017, the project "4D Analysis of Heart Development and Regeneration through Advanced Optical Microscopy" was launched. This Industrial Doctorate (EID) project, financed by the European Commission and coordinated by **Professor Miguel Torres** from the Carlos III National Cardiovascular Research Center (CNIC), with the collaboration of **Dr. Nadia Mercader** from the University of Bern (Switzerland), has a budget of 1, 5 million euros and a duration of four years. The main objective of this project, contemplated within the framework of the European Union's H2020 Program is to promote collaboration between academic research and industry. "It's a training project that involves 12 European institutions for the training of young scientists", says **Professor Torres**. The European Union has placed their trust in the CNIC for this "tremendously competitive" project to coordinate these 12 institutions and carry through this project that seeks to train "a new generation of scientists for the future", adds the project coordinator.

The benefits of free and open exchange between universities and industry might seem obvious, and likely to have a positive impact on society; however, the industrial and academic sectors often work in separate worlds. For **Prof. Torres**, turning this situation around is one of the key challenges of this new project.

The project will include 6 predoctoral researchers from universities across Europe who have joined the program after a rigorous selection process that took into account the excellence in their academic record. Each of these predoctoral researchers will be jointly supervised by an academic researcher and an industrial sector supervisor and will spend half of their training at the industrial partner's facility. At the end of this period, they will defend their doctorate in one of the prestigious universities that are part of this network.

## 4D HEART

"Heart disease is a big health problem, especially in Europe. The effects of heart failure in terms of individual and social suffering, as well as the loss of work hours, are in fact very relevant. The cost of dealing with these issues is tremendous, and it is estimated that countries will not be able to cover the costs of treatment for all the people that are expected to have a cardiovascular problem in the next 20 to 30 years. And, the problem is that it cannot be cured, in the best-case scenario, it can be stabilized. There is no real solution, therefore any research that could lead to a new therapeutic approach for a regenerative cure would be a great step forward", says **Dr. Torres**.

According to **Dr. Miguel Torres** the real-time image of the growth and regeneration of the embryonic heart could discover the cause of the adult heart disease and lead to potential treatment. "The project is based on the study of the heart through the image, applying different light analysis techniques to capture and model how hearts develop and function. We are studying two models: the first, the mouse, which is a very useful model since it is a mammal and it is the best model we have where we can do embryology (studying unborn children or no pregnancies). And, the second is the zebrafish, which is further away from humans, but is a useful model since it allows the possibility to look at the development of the heart of an embryo in real-time. And why is the study in real-time important? Some adult heart conditions originate at this stage of the embryo and genetic analysis link the genes of the development of the heart to adult heart disease."

## TRANS PROJECT

For the coordinator of the 4DHeart, the project brings together certain characteristics that make it special: it is transnational, "that is, students have to do their thesis in a different country"; it is transdisciplinary, "it's about analyzing in great detail, using the new imaging technologies, how cells behave during the development of the heart and during its regeneration, which implies joining together different subjects: biology, physics and bioinformatics." And, in addition, it is a translational project, "in which the academic institutions collaborate with the universities and the companies."

This project involves 12 institutions, four research centers, four universities and four companies that are part of the European international sphere. The companies that participate in 4DHeart are recognized world leaders in the field of innovation:

- Acquifer, that integrates experience for the development of experiments, instruments and tools required for screening applications of organisms and cells.
- Leica Microsystems' Life Science Division, a Company that supports the image needs of the scientific community through advanced innovation and technical experience for the visualization, measurement and analysis of microstructures.
- Philips Iberia, one of the Product Divisions of Royal Philips Electronics.
- Bitplane, one of the leading companies in Interactive Microscopic Image.

The training will take place in collaboration with the following academic centers:

- The University of Bern (UBERN), a leading institution in areas of research with great social and scientific importance. Its representative will be **Professor Nadia Mercader**.
- The Optics and Biosciences Laboratory of the National Scientific Research Center (CNRS) in Palaiseau (France), which counts on an interdisciplinary group of researchers and scientific projects coordinated by **Professor Willy Supatto**.
- The **Professor Julien Vermot** Laboratory at the Institute of Genetics and Molecular and Cellular Biology (IGBMC), one of the main centers of basic multidisciplinary research in Europe.
- Idiap Research Institute (IDIAP), with the participation of the group of Computational Bioimage, led by **Professor Michael Liebling**.
- The Autónoma University of Madrid (UAM), Carlos III University of Madrid (UC3M), University of Starsbourg, and Instituto de Empresa are also participants. Additionally, they will count on the training given by **Juan Sarasua**, expert on Science Communication Strategies.

Beyond the training of the participants for their future postdoctoral research, 4DHeart will expand their professional possibilities at the end of their training period. The training provided through this Industrial PhD project is very thorough and extensive, so that, upon completing the program, students will be able to choose from the different academic research careers, the private sector, patent protection ■

# 'ACÉRCATE': A+ SCIENCE STUDENTS TRAIN AT THE CNIC

Once again, eight of the best senior high school students in Spain, with a 10 out of 10 average in the last 2 years of high school, have been the lucky recipients of a scholarship for the 'Acércate' program, organized by the Carlos III National Cardiovascular Research Center (CNIC) within its CNIC-Young Training Plan. The objective of this plan, a personal goal of the General Director of the center, **Dr. Valentín Fuster**, is "to attract and train the brightest young people from the earliest ages to create a pool of excellent researchers in the field of cardiovascular research."

The call, open to senior high school students throughout the country, finished off this year selecting three students from Andalusia, three from the Valencian Community, one from Castilla-La Mancha and another student from Madrid. Including those of this year, in total 96 students have already participated in the program, 37 are men and 59 women. On this occasion, the eight young students, **Aster Adel Gamil Eskandarous**, **Irene Cánovas Cervera**, **Ana María Frías Serrano**, **Carmen García Fernández**, **Pilar González Marchante** and **Marta Hernández Solís**, together with **Raúl Albaladejo Carrera** and **Gabriel Portero Campillo**, besides participating in the 'day to day' of a center of excellence in research such as the CNIC, they were able to share their experiences and doubts with the center's researchers, and also with **Dr. Fuster**, Director of the CNIC. **Dr. Fuster** believes that starting the training program in such early educational stages is key in attracting future researchers because young people are the "future of research in our country."

During the 15 days that they are at the CNIC, students perform various activities that help them get in touch with research, such as transgenesis activities, comparative medicine, proteomics, genomics or bioinformatics, among other activities. Also, on the last day of the program, they must make a presentation to their research supervisors.

In addition to being in touch with the latest technology and the most advanced experiments, the 'Acércate' program has a playful side too. Therefore, the youngsters stay in a Residence Hall for 15 days, anticipating what is sure to be their university life. In addition, they complete a leisure program that includes cultural and recreational visits.

From all the training programs available at the CNIC this is the one that is aimed at attracting the youngest talent.

The sustained support of the Pro CNIC Foundation is essential so that, year after year, it can continue to be celebrated and to capture talent from the earliest stage. "We are very satisfied with this concept that we started 12 years ago", adds **Dr. Fuster**.

## REAL RESEARCH

The students rated the program as "incredible". **Carmen** recognizes that as soon as she got to know the program, she did not think twice about it: "The Program was introduced to me as a unique opportunity, both to expand my knowledge and to gain experience." The Cádiz-born student **Ana Frías** was clear that the Program could help her to have "a vision of what research really is and, therefore, to decide if in the future I would like to dedicate myself to it."

*Julia Redondo, Rebeca Acín, Guadalupe Sabio, Leticia Herrera and María del Valle Montalvo*

## 'ACÉRCATE (GET CLOSE) TO CNIC RESEARCH CONFERENCE'

With the objective of "bringing science closer" to the young, the 'Acércate (Get Close) to CNIC Research Conference' was held at the CNIC, in which around 200 junior and senior high school students from the Bilingual School Zola Villafranca, Nueva Castilla School, Zurbarán School, Santa María del Camino School, and the Vallmont School, were able to learn how to become a researcher or what the research career really involves.

One of the objectives of the CNIC is to attract young talent to the most advanced cardiovascular research. The 'Acércate' Program invites eight brilliant final year high school students from around the country to spend two weeks at the center. However, interest in research may start earlier and this is the opportunity offered by Science Week. Thanks to the collaboration of the staff of the center, the CNIC shows its work to junior and senior high school students and hopes that this activity will encourage many scientific vocations.

*'Acércate' students in 2017*

For **Marta**, the experience has been "tremendously enriching", as it has allowed her to get inside a very well prepared center for translational research, while **Gabriel** appreciates that cultural and recreational activities are included to make this an incredible experience. And **Raúl** believes that "the Acércate Program is a unique wonder in Spain. The CNIC seems like an incredible center to me, not only because of its size, resources and number of staff working there, but also because of the coordination among the different departments that make the existence of such a leading and high quality – at the level of American and Northern Europe- research center possible." ■

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO (USA)

# Valerie M. Weaver

## "MOST OF THE FINDINGS WE HAVE ACHIEVED HAVE BEEN THROUGH SERENDIPITY"

Dr. Valerie M. Weaver is the Director of the Center of Bioengineering and Tissue Regeneration at the Surgical Department of the University of California in San Francisco. Dr. Weaver has been leading the interdisciplinary research in Oncology for more than 20 years. Her current research focuses on the contribution of cell-intrinsic matrix as well as extracellular forces in oncogenesis and in the development of cancer. Her accomplishments have been recognized with different awards: Breast Cancer Scholar Award and A Scholar Expansion Award from the Defense Department; the AACR Pancreatic Action Network Award, and the Women in Cell Biology MidCareer Award, in acknowledgement of excellence in her scientific career. The researcher participated in the Sixth Edition of the CNIC Conference, entitled "Mechanical forces in physiology and disease", a scientific event that gathered together international experts in the field of mechanobiology, from different areas of experience: technology, cellular biology, animal models, human disease, development, etc.

For you, what does it mean to be a scientist?
At this moment developing a scientific career is a privilege. We have endless tools at our reach; we ask ourselves the most interesting questions that lead to very original ideas, and there are more and more young people that get involved in this passionate career that is research.

Since when have you been interested in science?
In my case, it was very natural. It was as though the natural thing to do was to develop a scientific career. For some reason, research was in my nature. And, I knew it since I was very young. The problem was that my family was very traditional and my mother was very surprised, almost in shock, because that wasn't what a young woman should do with her life at that time. Fortunately, things have changed a lot and nowadays most women can freely choose what they want to study and be what they want to be. I have tried to give the most of myself and have dedicated a large part of my work to sponsoring other young people so that they have what they need in order to be able to develop their scientific careers.

In your opinion, what personal qualities should a researcher have?
There is no doubt, that having a mentor helps in developing a scientific career, but a researcher should have many other qualities. In my opinion, the most important quality a researcher should have is curiosity: the more interest they have in answering questions, the more possibilities they have in making a good scientific career. In addition, they must be creative. Most scientists, and I see a lot of this in my classes daily, are intelligent, and in order to be a researcher you have to be, but it is not enough. No matter how much training you have and how intelligent you are, there is another requirement to be a good researcher: humbleness. Because, in reality, we are not discovering things, but rather, learning from what is already there. Being modest enables us to see things, listen to other people, learn from others' ideas that help us see our work in a different way and be humble enough to admit the truth when we find it. The key is knowing what the truth is. And, supposedly, we should be the "seekers of the truth". And, that is what I try to do when I make up a team of researchers from different subjects and ethnic, social, economic and cultural groups. The idea is that they are able to reflect about how they want the world to be.

What "truth" are you looking for at this moment?
I would like to look into the relations that the mother cells have with their microenvironment. Concretely, I'm working on determining how the interaction of stromal-epithelial cells regulate the tissue development and homeostasis. Specifically, my group is exploring the molecular mechanisms by which these extracellular matrix receptors modulate the cellular destination. We are investigating how the mechanical and topological properties of the matrix, that are related with its composition and organization, regulate the function of the matrix's receptors, in order to alter the cellular behavior. Our investigation program is divided into two fields of investigation. The first one is centered on the

understanding of how the composition and organization of the matrix influence the development of the breast tissue and the tumor development, and the second, focuses on figuring out the role that the strength of the extracellular matrix has on the destination of the embryonic and adult mother cells.

Why did you choose this field in particular? What do you think you can contribute to it?
I'm aware that there are many intelligent people researching in this field, but what I believe that I can contribute to this line of research is the capacity to integrate and combine different approaches, from the nano, going through the research of tissues, and reaching the clinic. This way, travelling from the most basic to the clinic, we can define with the clinical researchers what the most important things are to going back to the nano, and in that way, work in that direction. My idea of research covers from the smallest – the nano, until the patient. That's why I work from the most basic till the clinical.

"The most important quality a researcher should have is curiosity: the more interest they have in answering questions, the more possibilities they have in making a good scientific career."

Working in just in one area is not enough for me. I believe that at one point of this line, we can find the truth. And, there's something that I'd like to highlight: I wouldn't be able to do this type of research if I didn't have such great collaborators or such a great team. In some ways, I see myself as an "integrator or conciliator" of different ideas, areas, perspectives, etc.

### How should the scientific advances be transmitted to society?

As scientists, we cannot live isolated from society. In my case I try to have lots of relationships, for example, with patients that could really benefit from my research, and also with other groups of people. All the groups need to collaborate with one another. Most of the findings we have achieved have been through serendipity. And that is why I think modesty is important, we cannot believe that we know it all. The reality is that a lot of times you make a discovery in something that you were not really working on. For example, recently we discovered something that we had never worked on before and now we are doing a pilot clinical trial on chemoprevention with the clinical researchers. Not in a million years would I have been able to predict that I'd have these results. Every time that I think I know what I'm doing, something happens that makes me go back, to the most basic. And, that's marvelous. However, we cannot forget that we are in debt with society. Our obligation is to transmit what we are doing. If we are arrogant and we distance ourselves from society, the image that we give is very negative. Us researchers are a privileged group and we have to be conscious of this. For example, for me it's a privilege that I was invited to CNIC to talk about science. ■

**CNIC Conference: 'Mechanical forces in physiology and disease', 4th and 5th of November 2016.**

**Invited by Jorge Alegre-Cebollada, Nadia Mercader, María Montoya and Miguel Á. del Pozo (CNIC) and by Martin Schwartz, from Yale University (USA).**

UNIVERSITY OF CHICAGO (USA)

# Marcelo Nobrega

# "BIOINFORMATICS WILL BE KEY IN THE FUTURE"

**Dr. Marcelo Nobrega works at his Laboratory of Human Genetics at the University of Chicago (USA) on the architecture and function of genes in their regulatory networks. For Nobrega, understanding these processes is crucial, because it is believed that the malfunction of the regulatory programs of the genes might be the cause of many human diseases, like obesity or diabetes. Dr. Nobrega's team identified what appears to be the real obesity gene, Irx3, which regulates the body mass and body composition. His study was published in *Nature.* His work also focuses on the regulation of genes that control cardiac development and congenital heart disease. Dr. Nobrega gave a seminar at the CNIC entitled "Regulatory genetic variation and human diseases", invited by Miguel Manzanares.**

What exactly is your field of research?

I have always been fascinated by the mechanisms and processes that underlie and trigger diseases. After finishing my degree in medicine, I started to train as a researcher and I realized how powerful genetics is in obtaining information about different mechanisms involved in pathologies. That's why I decided to focus my career on the field of genetics. The idea is that if we can compare different groups of patients with different variations and genetic profiles, this will allow us to investigate the specific mutations of each one. In addition, time plays in our favour because technology is getting better each day; for example, thanks to the Human Genome Project we can analyse the genome of many individuals and obtain information on the genes and the mutations involved in several diseases, like the cardiovascular pathology. And now we know that the mutations are not in the genes but outside of them. 99% of the genome is stable, it doesn't suffer alterations; but in reality, we know very little about what occurs in this "grey area" of the genome. And it is precisely these mutations that make us more susceptible to a heart attack, cancer, diabetes, etc. This is where I develop my work. I work on the design of technologies to relate these mutations, already identified outside the genes, with the specific mechanisms of certain diseases.

What type of mutations are they?

They are called non-coding mutations. The part of the genome that codifies the proteins involves merely 1% of the genome. The genome has three million letters, but only 30,000 of these letters produce proteins. So what does the rest of the genome do? It is possible that part of the answer to that question lies in its importance to regulate the expression of the genes. For example, each cell of our organism has the genetic information to produce insulin, but only some of the cells of the pancreas do it. Why do only the ones in the pancreas know how to activate this gene if all of our cells have the same genetic code and the same instructions? And the same occurs with the heart. It is fascinating. Somehow, these cells know how to use the different parts of the genome to develop their identity. And it is precisely in the part of the non-coding genome where this information is transmitted to the cells in order for them to activate a certain gene, and others not. We think that when there are mutations in these switches that activate or deactivate genes this balance is lost, and that is how diseases are provoked.

Do you know when, how or why these mutations are activated?

These switches are basically clusters of what is called transcription factor binding sites; they are DNA binding proteins that have the capacity to recruit other proteins to activate or deactivate genes. And what we believe is that these mutations have the capacity to alter or modify these transcription factor binding sites. We believe that when there is a mutation, the transcription factors do not bind to the DNA correctly, and therefore the target gene is neither activated nor repressed. And this has pathological consequences.

And is this the cause of the origin of diseases, like in the example that was published on the obesity gene?

What we found at that time is a switch inside a gene that activated a gene which everyone thought was the obesity gene. No, in reality it is not the gene that causes obesity, but the switch. It's difficult to understand that it is the mutations of certain mechanisms the ones that activate and convert a good gene into a "bad" one. And, what we know is that the same that happened with the obesity gene is what occurs in many other diseases.

Could these switches then be converted into pharmacological targets?

Not really, no. However, when we study the genetic causes that favour a greater predisposition to cardiovascular disease, we will definitely find the genes that are involved in such predisposition. And by studying the functions of these genes we will get information on the mechanisms that could become targets for future therapies. But under no circumstances could these be switches.

What made you orient your professional life to research?

I studied my medical degree in Brazil. In fact, I was a very precocious student, as I began studying it when I was just 15 years old. It was my mother's fault, because she started taking me to school when I was just two years old, and that's why I was so advanced. But, in reality I did not want to study medicine, it was not my dream. I liked biology, physiology... That's why during the first two years of my degree I was very pleased, because everything is very basic. The problem started when we got to the clinic: it was boring. What I liked was knowing how things were produced, the mechanisms involved and why it could go wrong. Fortunately, I got the opportunity to work in a research laboratory, first at my university in Brazil, and later on, in temporary stays in the USA. I loved what I saw in these laboratories and when I finished my medical degree, I applied for a research program in the USA. And that was 22 years ago. Since 11 years ago I have my own laboratory in Chicago, with a total of 9 researchers working there.

What is, in your opinion, the one quality that a young researcher should have?

The truth is that the current situation in research has changed a lot. In some cases, for the worse, if we talk about financing, consequently, now you have to be very patient if you want to work in this field because things advance very slowly. For that reason, my principal advice is "don't give up". Then there are many other aspects that must be taken into account: we are talking about a very competitive field, so you have to work really hard. You have to give 100% of all your capacity and be very ambitious in your day to day. Ask and ask yourself questions every day and try to give answers. And if you fail, start over again. And another thing that I always insist on is that in the scientific careers there are many corners; not all scientists are going to run a laboratory, there are other options in science: assistant, scientific reporter, work in the industry. Something that I recommend is that in the last years of the doctorate you should decide exactly what you want to do.

You say that it is a complicated time for research, but also fascinating, right?

That's right. If we put aside the economic financing, it's a privilege to research at this moment that we find ourselves in. Right now we have tools and knowledge that just a few years ago was a chimera, especially in the field of genetics and genomics. In fact, we are in a time of transition, or almost revolution. Bioinformatics will be key in the future, and it is already almost now. You cannot be a competitive scientist in the future if you do not master this field. In fact, I do not master it myself, which is why I need to get enough money to attract those experts who do to my laboratory. The programs that do not approach "coding" as a fundamental science work will surely fail.

Does that mean that in 10 years science as we know it today will be completely different?

We are going to continue using the same technologies that have been developed in the last 10 years but in a more sophisticated way. And precisely thanks to them, we are going to be able to polish the questions that we ask ourselves, which will be more and more complex. And so our research is going to focus on these complex mechanisms in order to redefine our ideas and hypothesis. There are more and more professional experts in bioinfor-

**"The romantic idea of the "Eureka" moment, does not exist" • "The intellectual satisfaction comes from the possibility of solving problems of nature that nobody has succeeded in doing so until now"**

matics analysis, while researchers, like myself, are very experienced, we do not have the training required to analyse those data bases in the right way. As I said before, I try to fill in that "gap" in my laboratory by hiring those professionals in data analysis and make them part of our laboratories. However, in the future, the good researchers will be those that combine these two areas: they will be the ones who will find the most interesting jobs, the ones who will develop innovative areas of knowledge... At least in the next 10 years. Further than that, it is hard to say.

What is a normal day like in your laboratory?

I must admit that I hate administrative work. I am not very disciplined when it comes to organization, so I try to delegate these tasks. I know it's a necessary part of my job in order for my laboratory to run well, but I have oriented my career in a way that the most part of my time is "protected", so I can dedicate a lot of time to my lab. But as part of a community, I still have to devote some hours to administrative work. In my case, it is not more than 5 to 10 hours a week. But, that doesn't mean that I spend the rest of the time researching, I actually spend most of it writing scientific articles, reading and acting as a mentor for my students

Do you remember any particularly important or disappointing moment in your career?

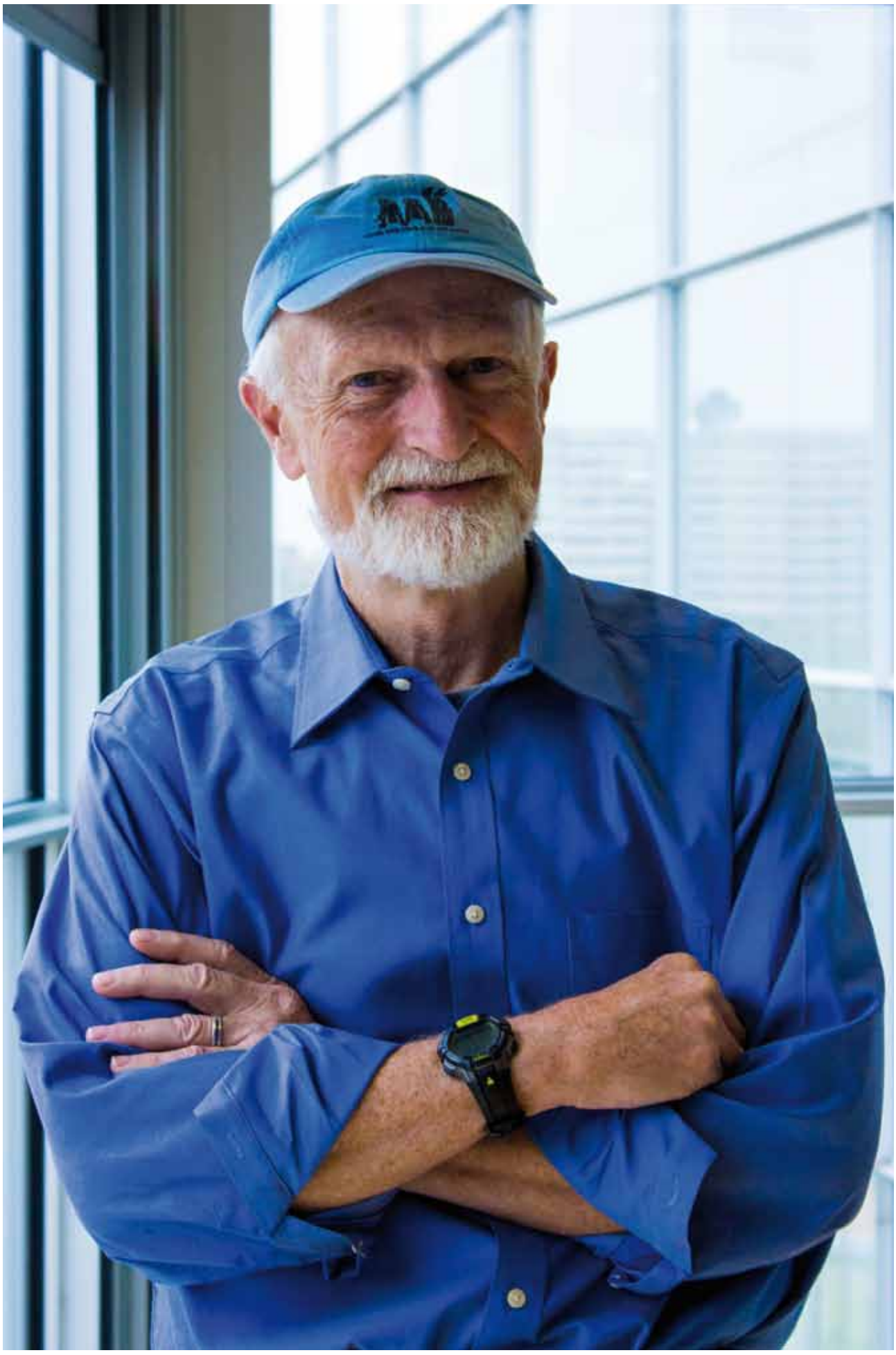
The scientific field is full of failures. The day to day is monotonous, boring and sometimes frustrating. You have to be obsessed with what you're doing, but it has to be that way. It's the only way to go forward and solve problems, and little by little, continue progressing. The romantic idea of the "Eureka" moment, does not exist, at least I've never experienced it before. But there are little moments of intellectual satisfaction that make it possible, step by step, for all the pieces of research to come together. And I think people should be pleased with such a special job. The intellectual satisfaction comes from the possibility of solving problems of nature that nobody has succeeded in doing so until now. And, if you do not have that capacity, it will be difficult to make researching your career. Passion must be constant.

What is your opinion of CNIC?

I had never been at CNIC, but I have always wanted to come. I have informally collaborated with my host **Miguel Manzanares**, many times before and from no won we are going to establish a formal collaboration between our laboratories. Nobody has the experience or knowledge necessary to do everything alone, and most certainly, Miguel's group is one with whom we will collaborate. ■

**Seminar "Regulatory genetic variation and human diseases".**

**Invited by Miguel Manzanares.**

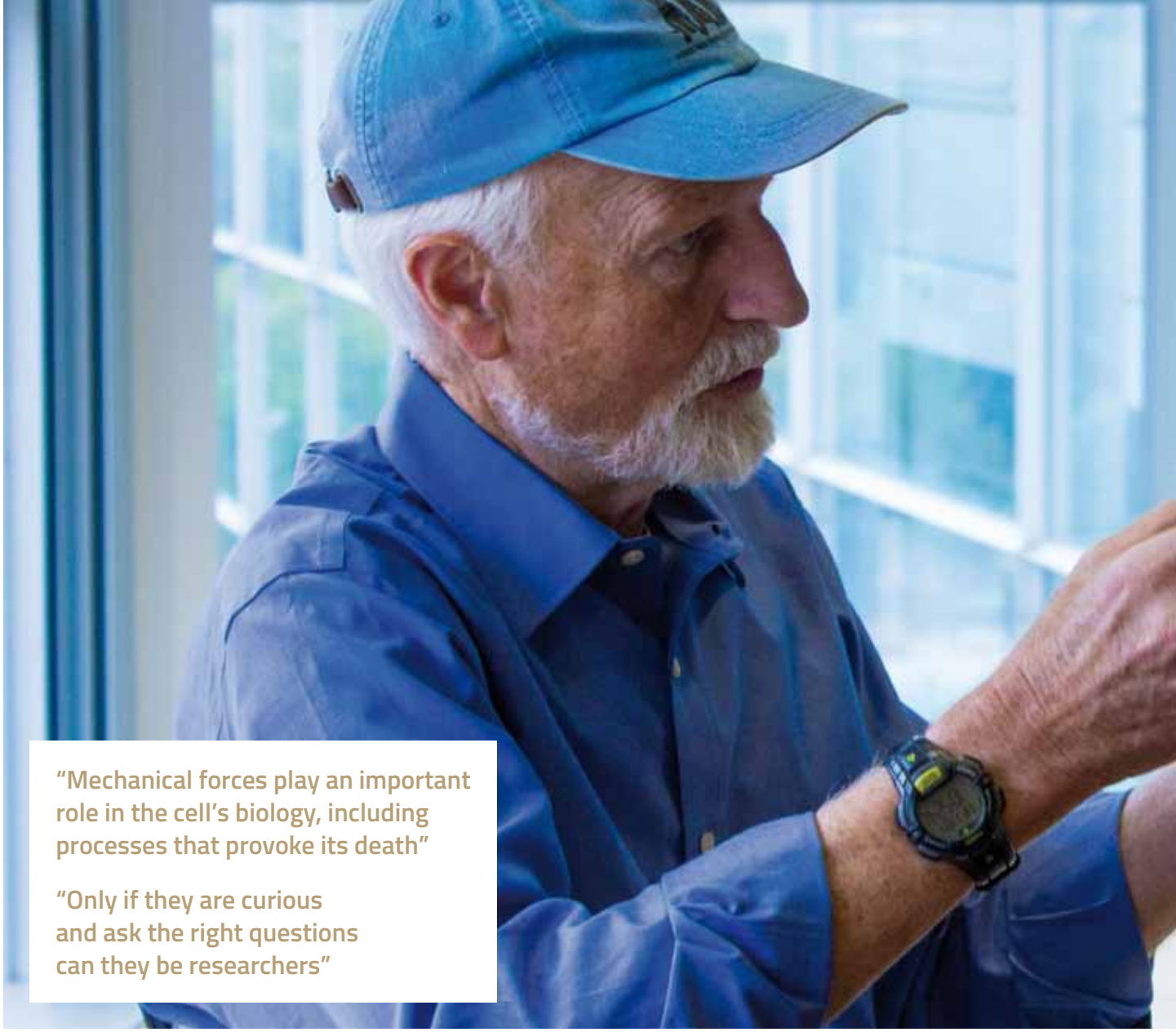


MECHANOBIOLOGY INSTITUTE (SINGAPORE)
COLUMBIA UNIVERSITY (USA)

# Michael Sheetz

## "BASIC RESEARCH HAS THE POSSIBILITY TO GO BACK AND UNDERSTAND THESE BIOCHEMICAL MECHANISMS AND FIND ANSWERS"

Professor Michael Sheetz, one of the pioneers in the field of Mechanobiology, is the director of the Mechanobiology Institute of Singapore and professor at Columbia University in the USA. Michael Sheetz has been working in the biomedical field for more than 40 years and has been one of the biggest promoters in the study of molecular motors. His achievements led to the discovery of the kinesin motor protein and revealed the steps by which molecular forces convert chemical energy into mechanical work. His discoveries, for which he was awarded the Lasker Award in 2012, permitted the discovery of drugs for both heart problems and cancer, among other illnesses. Professor Sheetz participated in the VI edition of the CNIC conference called "Mechanical forces in physiology and disease", a scientific event organized by the CNIC researchers Jorge Alegre-Cebollada, Nadia Mercader, María Montoya and Miguel Á. del Pozo and by Martin Schwartz, from the University of Yale (USA).



"Mechanical forces play an important role in the cell's biology, including processes that provoke its death"

"Only if they are curious and ask the right questions can they be researchers"

You were one of the first people to use this type of mechanical techniques in biological research. Why did you center your research in this field?

Thanks to the help of bioengineers, we can access extremely useful tools to investigate and get in depth knowledge on these forces that influence the cellular environment. The context is the following: our cells interact with other cells and with the extracellular matrix, and have the information inside them to associate in the right way and in the right quantity. For example, in twins, all these forces and all these biomechanical factors are working on the two twins essentially in the same way, but independently. And that makes the final result almost the same. Our big challenge is to determine why and how these events are produced. And for that we need to work in collaboration with bioengineers, biochemists and biological physicists. In the past, this whole process had been overlooked because the biologists were dominated by biochemistry. Now we are trying to go into detail about these biophysical and mechanical elements because until now we have been unable to understand how these physical forces are produced.

Are these factors involved in all the diseases?

Yes indeed. Cancer is the first in which we are certain, but little by little we have seen that these mechanical forces are involved in the development of cardiovascular disease, among others. Mechanical forces play an important role in the cell's biology, including the processes that provoke its death.

What can we expect in the future of this field of research?

It seems risky to talk about short-term results. That's why we have so many problems with politicians. They are only willing to finance research that offers short-term results, one year, for example. But one of the reasons why I continue in this field of research, in addition to the fact that I really enjoy it, is because I'm not entirely sure what I'll be doing in the next six months. Asking questions and finding answers in this field is very exciting. Actually, I only know what we already know now but it's not what I'm interested in at this moment. I want to ask myself more questions and find out more. I don't think that we can go forward until we have a more global knowledge of all the structures that are involved in the integration of the mechanical forces; and this is a long way. We have to gradually construct a structure of knowledge from the bits, of the blocks of information

that we find out, in order to be able to advance in this knowledge.

When did you decide to research in this field?
For many years, I have worked in the field of biochemistry and biochemical physics. I started to become interested in the physical controls and their influence on biological activity and when I started to investigate this field in more detail, it became clear to me that the physical promotors were critical elements in understanding the classical biochemical model, which biophysics had not incorporated until now. This makes it necessary to go back and ask the same questions and investigate the same issues already analyzed like, for example, how the cell relates with its surroundings and with the cell matrix, to determine what is going on in individuals.

Do you remember any important or especially discouraging moment in your career?
Rather than an important discovery, which our laboratory makes quite frequently, from a personal point of view it was very relevant to understand that we were not working or researching in the right way. This happens sometimes when you are conducting an experiment and the results are different from what you had thought at first. It's on that occasion when you have to find someone to confirm that what you are doing is not correct. And it's precisely in these circumstances that you truly understand why the results are not what you had predicted in the first place.

Is it about learning from your mistakes?
They are not exactly mistakes, but rather it is nature itself that is signaling the right way to obtain new information that is correct.

What is, in your opinion, the one quality that a young researcher should have?
Curiosity. Their decision to be a researcher and to follow this career must be marked by their desire to truly discover how certain events occur and develop in the most detailed and precise way possible. Only if they are curious and ask the right questions can they be good researchers.

How important is the figure of a mentor in research?
I'm going to tell you an anecdote about an old German teacher whom the students demanded his attention. One day he threw a fish at them and told them: "come back in two years with what you have learned and tell me about it". It's certainly not, the best way to act as a mentor. What we try to do at our center in Singapore is for physicists, chemists and biologists to work together, in the same space where there are no walls or separation of any type, therefore the laboratories are together, so they can speak amongst each other and share what they are doing, what they are seeing, in their different scientific languages. We all know how difficult it is for physicists to explain their findings to biologists, and the same is true with physicists, biochemists, etc. And this interrelationship is very valuable because it makes the researchers go back to some issues that were already assumed, and it is possible that they may have to reconsider them and look at them in another way. It's a challenge.

Is it similar to what occurs between clinical researchers and basic researchers?
Right. However, one aspect must be taken into account. Doctors and clinicians have one basic principle: not to cause any type of harm. That is why they work with methods that have been proved no to provoke any harm, despite the fact that in some cases they don't generate a real benefit for the patient either. If you analyze the research rationally with some drugs, these are very fragile. However, basic research has the possibility to go back and understand these biochemical mechanisms and find answers. It is the first step, to understand the most basic mechanisms, in order to advance in the design of treatments. ■

**CNIC Conference: 'Mechanical forces in physiology and disease'. 4th and 5th of November 2016.**

**Invited by Jorge Alegre-Cebollada, Nadia Mercader, María Montoya and Miguel Á. del Pozo (CNIC) and by Martin Schwartz, University of Yale (USA).**

UNIVERSITY OF ILLINOIS (USA)

# John A. Rogers

Dr. John A. Rogers, from the University of Illinois (USA) has spent years applying his knowledge of bioengineering on health. His group tries to understand and exploit interesting characteristics of "soft" materials, like polymers, liquid crystals and biological tissues, as well as hybrid combinations of these with other unusual types of micro/nano materials, in the form of tapes, wires, membranes, tubes or the like. Some of his contributions are related to the field of portable electronics and biosensors, a technical development that could be the next revolution of the digital era.

# "WE CAN CARRY A PERMANENT DIAGNOSTIC LABORATORY IN OUR ORGANISM"

Rogers' group has published a study in the magazine *Science Translational Medicine* on a skin patch, which is very small in size and thickness, and has the capacity to analyze in real time four biomarkers found in sweat that are essential to check our state of health. A very cheap, single-use device that can be put on the arm or on the back and that can send the results of the analysis to our mobile phone and warn us of the measures that we should take in case our health is at risk. Rogers trusts that these systems, which can also use other fluids like tears, will be used in the future to diagnose a number of diseases.

What is the current situation on the investigation of these bio-integrated electronic systems in the field of cardiology?

At the moment we are working with these platforms on the heart, the brain and the skin. But we think they will have many more applications. We are trying to develop, for example, batteries which are compatible so that in this way, we can integrate the devices inside the organism and not only use them externally. We don't want to stop at the heart, brain and skin. Our intention is to generate platforms for the pancreas, kidneys, etc. This is just the first step.

What would the applications of these platforms be?

The brain is a very sophisticated organ. Many times we do not know how it works, how some diseases develop, etc. That's why if we can get more in-depth knowledge on it through these devices we will start to get some answers to the fundamental questions in neuroscience. This is just one example of how these new tools will allow us to go more in depth in neuroscience research. But in addition to researching, these technological platforms have a diagnostic application. Actually, they have two very defined uses: research, to make new biological discoveries and clinical, as a diagnostic tool.

In your opinion, are these devices ready to use in the clinic on a routine basis?

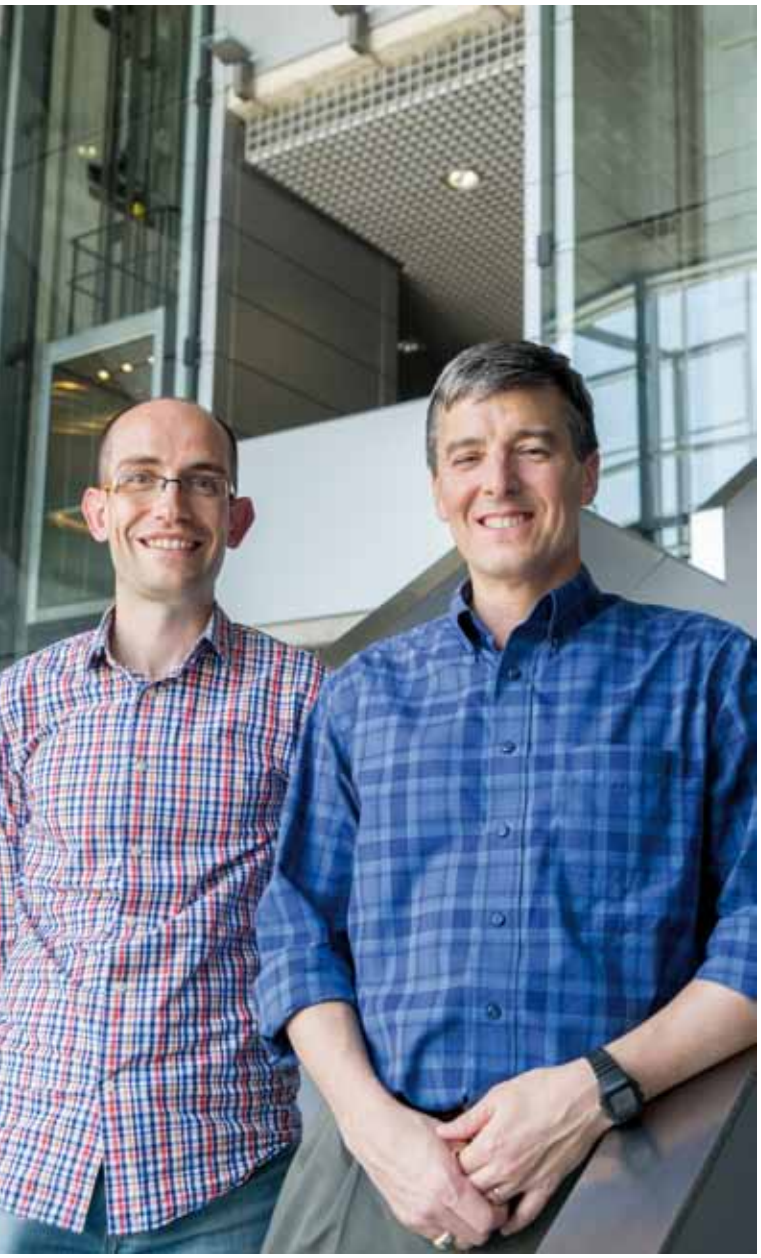
We are already working with and trying on our prototypes on people. I'm referring to the devices that are put on the skin, like the one I have on right now and that provide us with information about certain physiological parameters related to our health. This type of platforms are unique because they adapt to our skin and, depending on the specific area of our body where they are located, they can measure a series of physiological parameters that can usually only be done in hospitals. Thus, if for example they are placed on the chest, they will measure the heartbeats without the need for an electrocardiogram, with a greater clinical fidelity than an electro, since the measurement is done in a continuous way over time. Other devices can evaluate the level of oxygen in the blood, the pulse, the body temperature, etc. The number of applications of the "external" devices on the skin is very extensive. Furthermore, we continue to work on the internal devices, those that can be integrated inside the organism, especially in the brain or the heart, although at the moment we have only worked on animal models, and we hope to start testing on humans next year.

Do they also have therapeutic applications?

Although our work is focusing on diagnosis, these devices also have a therapeutic application. For example, the devices integrated in the brain or the heart could generate small stimuli that would control the heart rate, like a sophisticated type of pacemakers, but they can also be combined with optogenetic systems in order to perform optical stimulation, etc. And in the future we hope to work together with microfluidic research and integrate drugs that are released at the right time and place.

In the future, will we all have a doctor incorporated into our body?

**"These type of platforms are unique because they adapt to our skin and, depending on the specific area of our body where they are located, they can measure a series of physiological parameters that can usually only be done in hospitals"**



Something like that. With these devices we can carry a permanent laboratory of diagnosis on our bodies which controls the main physiological health parameters. But the idea is not to take on the work of medical professionals, if not to provide them with more precise and high-quality information in real time.

What is the biggest challenge that these devices pose?

In my opinion, the biggest challenge that all of these bioelectronic devices pose is the safety in clinical practice and its subsequent approval by the health regulatory authorities that will allow their production on a larger scale for use in health. Furthermore, another of the challenges that we will be faced with in the future, as bioelectronics becomes increasingly more sophisticated, is related to batteries. That is to say, their size must be reduced, but mainly to obtain batteries that, for example, can be charged inside our own body through movement. New and revolutionary ideas are greatly needed in this field.

Why did you decide to focus on the health applications of your research?

I have been in the field of materials engineering for years, and from the beginning I have been working on the design of flexible electronic devices. We discovered that all of our work could be of interest to the neuroscientists, although we had never actually thought it would be of any interest to health. But, thanks to clinicians and biologists we have found ourselves in this exciting career, and also thanks to the students, who are very enthusiastic in this field.

What advice can you give to people who begin their career in scientific research?

Throughout the years, I have worked with many young researchers in my laboratory. I try to instill in them some values, like being generous, and try to make them understand the importance of getting really good training. But in the last years I have realized that they have to begin contemplating their career from a multidisciplinary point of view. They should know how to collaborate with researchers from other areas that have a lot of experience in other fields. In summary, generous, good collaborators, and with an interdisciplinary mindset. For me, these are key.

How important is a mentor in a scientific career?

It is possible that at this moment this is the most important task that I currently perform. I do it with real pleasure and it gives me great satisfaction to see how some of my students have a very important scientific career. I believe it's not just researching, but rather that mentoring is a way to educate the future mentors to do the same thing that many of us are doing.

It is your first visit to CNIC. What possibilities for collaboration have you seen?

Of course, it would be very interesting to collaborate with a center like CNIC in the future. We have many areas of research in common in the cardiovascular field; and this center, apart from its facilities, also has incredible experience. I believe that after some of the meetings we have had during my stay in Madrid, we will most likely find ways to work together. ■

**Seminar "Soft, Bio-integrated Electronic Systems for Cardiovascular Research".**

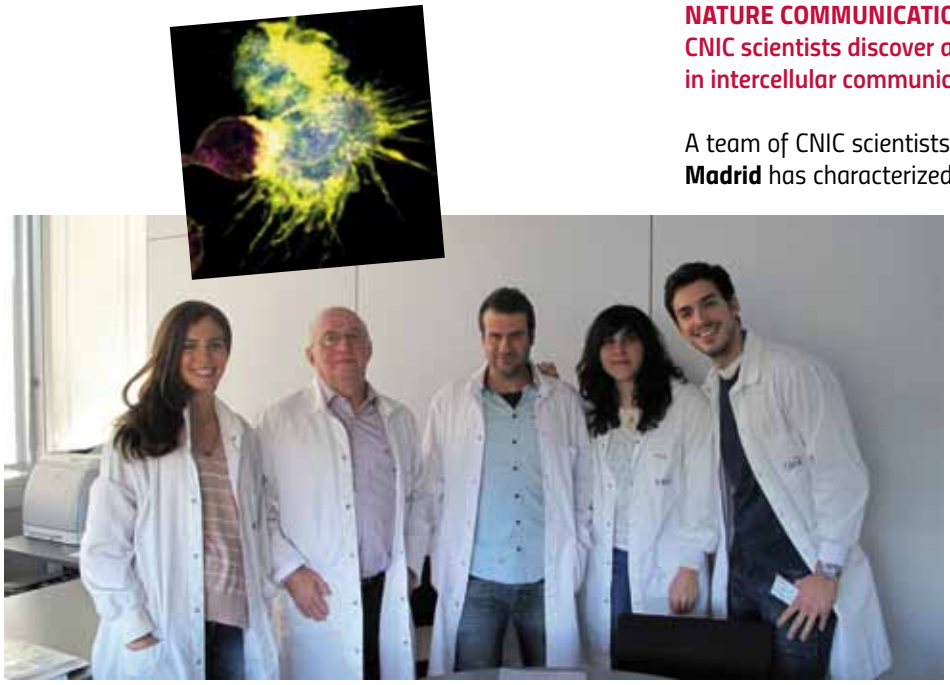
**Invited by Jorge Alegre.**

# EXCELLENCE IN COMMUNICATION SCIENCE

## **LEADING JOURNALS** PUBLISH CNIC SCIENCE

A 'scientific dogma' overturned, a new target for the treatment of aggressive lymphomas, the mechanism through which a decades-old drug stems the spread of injury after a heart attack, and the discovery that inhibition of an enzyme prevents and reverses the formation of aortic aneurysms in Marfan syndrome and related diseases.

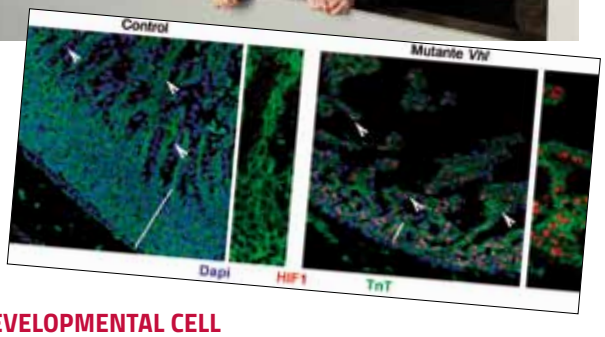
These are some of the scientific highlights published by CNIC research groups over the past months in leading science journals such as ***Circulation***, ***Nature Communications***, ***Blood***, ***Developmental Cell***, ***Nature Medicine***, ***Nature Communications***, ***Journal of Experimental Medicine***, and ***JACC***.



Villarroya-Beltri, C., Baixauli, F., Mittelbrunn, M., Fernández-Delgado, I., Torralba, D., Moreno-Gonzalo, O., ... Sánchez-Madrid, F. (2016). *ISGylation controls exosome secretion by promoting lysosomal degradation of MVB proteins.* ***Nature Communications***, 7, 13588. doi:10.1038/ncomms13588

### NATURE COMMUNICATIONS
### CNIC scientists discover a key signal in intercellular communication

A team of CNIC scientists led by **Prof. Francisco Sánchez-Madrid** has characterized a cell signal that impedes intercellular communication and could have a central role to play in biomedical strategies such as gene therapy, vaccine design, and immunotherapy. The study, published in ***Nature Communications***, characterizes a signal that impedes the secretion of nanovesicles called exosomes. Cells secrete exosomes as a means of intercellular communication; however, certain viruses can use exosomes as "Trojan horses" to facilitate their propagation and entry into neighboring cells. The signal, called ISGylation, was in the past viewed mainly as an antiviral signal, although some studies show that it can also be activated by other stimuli such as a lack of oxygen, aging, and cancer. The new research shows that "in these situations, ISGylation can affect the secretion of exosomes, and therefore communication between cells."




## DEVELOPMENTAL CELL

### Hypoxia signaling plays a physiological role in heart formation

Scientists at the CNIC led by **Dr. Silvia Martín-Puig** have demonstrated the fundamental role of the hypoxia response in the correct formation of the heart ventricles. Hypoxia, a drop in the levels of oxygen, triggers a complex adaptive response to reestablish the tissue supply of nutrients and oxygen. The key elements of this response are the hypoxia-inducible transcription factors, or HIFs, which mediate the activation of a multitude of genes that guarantee a transitory adaptation to the lack of oxygen.

The CNIC team identified discrete metabolic territories within the embryonic myocardium; the study uncovers the molecular mechanisms through which HIF1 establishes this metabolic boundary between different types of cardiomyocytes to regulate the maturation of the contractile muscle and the formation of the conduction system. The study, published in ***Developmental Cell***, describes the importance of the hypoxia pathway in an essential physiological process, the formation of the heart chambers, establishing the importance of hypoxia outside of disease settings.

The study findings advance knowledge on the molecular processes linking the metabolic status of the myocardium to its maturation and function and also open "new opportunities for therapeutic intervention" to modulate HIF signaling or directly adjust the metabolic state in order to improve heart function in cardiovascular disease.

Menéndez-Montes, I., Escobar, B., Palacios, B., Gómez, M. J., Izquierdo-García, J. L., Flores, L., ... Martín-Puig, S. (2016). *Myocardial VHL-HIF Signaling Controls an Embryonic Metabolic Switch Essential for Cardiac Maturation.* ***Developmental Cell***, 39(6), 724-739. doi:10.1016/j.devcel.2016.11.012

## NATURE MEDICINE

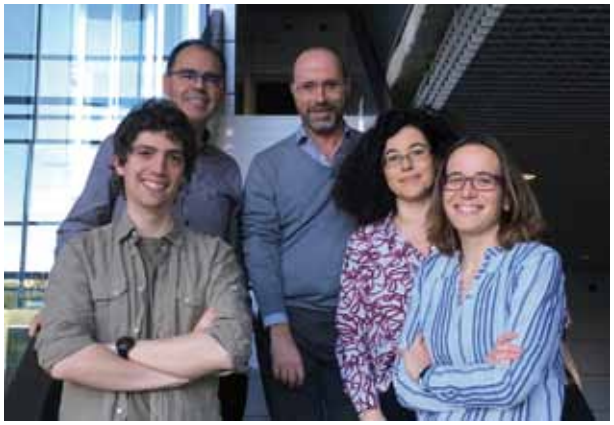
### Inhibition of a specific protein prevents and reverses aortic aneurysm in models of Marfan syndrome and similar diseases

The inhibition of a protein—inducible nitric oxide synthase or Nos2—in the arterial wall is able to reverse aortic disease in a mouse model of Marfan syndrome and other types of aneurysm. The findings, published in ***Nature Medicine***, suggest a major potential for NOS2 inhibitors in the treatment of thoracic aortic aneurysm. The study was codirected by **Dr. Miguel Campanero** of the CSIC Instituto de Investigaciones Biomédicas Alberto Sols and CNIC scientist **Dr. Juan Miguel Redondo**.

An aneurysm is a swelling or abnormal enlargement of a portion of an artery, resulting from a pathological weakness in the blood vessel wall. For long periods, an aneurysm is an indolent condition that provokes minimal or no symptoms; however, it is an extremely dangerous condition prone to sudden, catastrophic, and often fatal complications. Effective treatment therefore requires early and accurate diagnosis, close patient management, and surgical repair when conditions allow. The vessel dilatation increases the risk of arterial rupture, and current pharmacological treatments are therefore aimed at reducing pressure on the vessel wall. However, these treatments are of limited use because they do not arrest the deterioration of the aortic wall in aortic diseases, including Marfan syndrome, a disease caused by defects in the fibrilin-1 gene. The only truly effective therapy available is surgery, but this dangerous intervention is indicated only when the risk of rupture is deemed greater than that of surgery. Moreover, surgery does not cure or stem the underlying condition, which is progressive and not confined to a specific artery wall segment. There is therefore a need to identify the mechanisms underlying aortic wall degeneration and to discover new pharmacological targets for slowing the natural progression of these diseases.

The research team on this study identified 2 potential therapeutic targets for the treatment and prevention of aneurysm: the metalloproteinase ADAMTS1 and the nitric oxide synthase NOS2. The study demonstrates that mice lacking Adamts1 develop a disease similar to Marfan syndrome and that the genetic inactivation of Nos2 expression prevents aortic disease in these mice and in a mouse model of Marfan syndrome. But the study goes further, also demonstrating that pharmacological inhibition of nitric oxide production rapidly and effectively reverses aortic dilatation and aortic medial layer deterioration, both in mice lacking Adamts1 and in the mouse Marfan syndrome model.

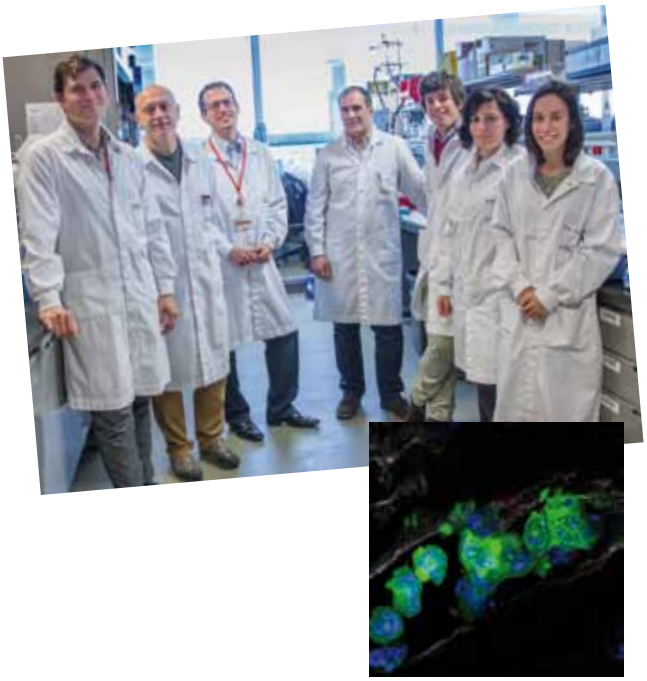
Oller, J., Méndez-Barbero, N., Ruiz, E. J., Villahoz, S., Renard, M., Canelas, L. I., ... Redondo, J. M. (2017). *Nitric oxide mediates aortic disease in mice deficient in the metalloprotease Adamts1 and in a mouse model of Marfan syndrome.* ***Nature Medicine***.
doi:10.1038/nm.4266



## BLOOD
### A new treatment target for aggressive lymphomas

An estimated 400 000 people worldwide are diagnosed with lymphoma every year, and B cell lymphomas kill more than 200 000 people every year. CNIC scientists have identified a possible therapeutic target for 2 types of very aggressive lymphoma. The CNIC team discovered that the microRNA miR-28 regulates the terminal differentiation of B lymphocytes, blocking the growth of B cell lymphomas. The study, published in Blood, establishes the therapeutic potential of synthetic miR-28 analogs for inhibiting the growth of Birkitt lymphoma and diffuse large cell lymphoma. These findings could lead to the development of the first miRNA analog therapy for the treatment of B cell lymphoma and provide the basis for human trials.

Bartolomé-Izquierdo, N., De Yébenes, V. G., Álvarez-Prado, Á. F., Mur, S. M., López del Olmo, J. A., Roa, S., ... Ramiro, A. R. (2017). *miR-28 regulates the germinal center reaction and blocks tumor growth in preclinical models of non-Hodgkin lymphoma.* ***Blood***.
doi:10.1182/blood-2016-08-731166

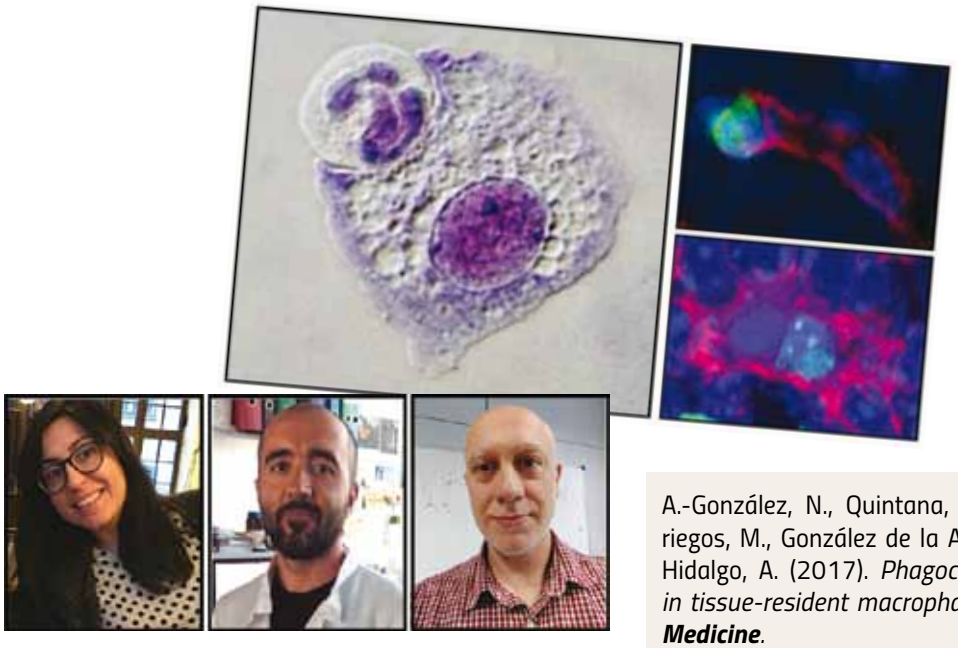


## NATURE COMMUNICATIONS
### A decades-old drug stops the spread of injury after a heart attack

Acute myocardial infarction is a serious disease that affects more than 50 000 people a year in Spain. Treatment has advanced a great deal in recent years, especially in the extensive use of coronary angioplasty, in which a catheter is used to re-establish blood flow through the blocked coronary artery. Nevertheless, many heart attack survivors have seriously impaired heart function that limits their long-term health and generates major health-system costs. The search for treatments to limit the irreversible damage caused by a heart attack is an extremely important research area in terms of both patient care and health policy. In an article published in ***Nature Communications***, CNIC scientists report a new mechanism of action of metoprolol, a drug that can limit the damage produced during a heart attack if administered early.

The team led by **Dr. Borja Ibáñez**, Clinical Research Director at the CNIC and a cardiologist at the Fundación Jiménez Díaz University Hospital Health Research Institute (IIS-FJD), has identified the mechanism that explains why this drug is so beneficial: rapid administration of metoprolol during a heart attack directly inhibits the inflammatory action of neutrophils, a type of blood cell. The reduced inflammation translates into a smaller amount of damaged tissue in the post-infarcted heart. The finding opens the route to new applications for this cheap, safe, and simple drug.

García-Prieto, J., Villena-Gutiérrez, R., Gómez-Tech, M., Bernardo, E., Pun-García, A., García-Lunar, I., ... Ibáñez, B. (2017). *Neutrophil stunning by metoprolol reduces infarct size.* ***Nature Communications***.
doi:10.1038/NCOMMS14780



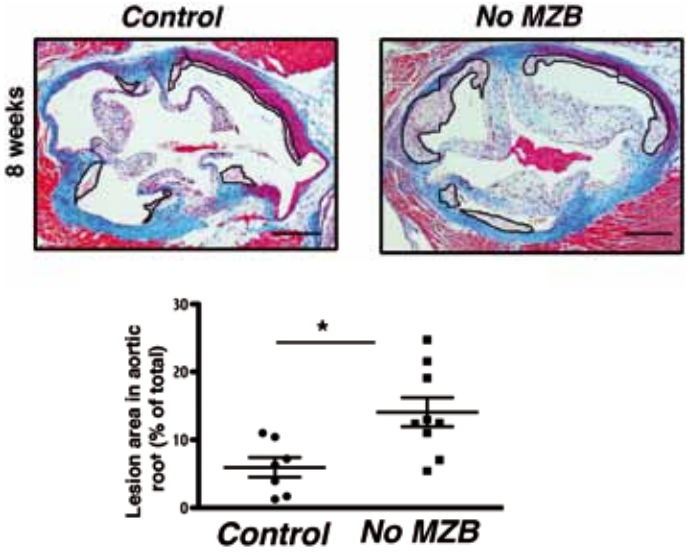
## JOURNAL OF EXPERIMENTAL MEDICINE
### Cell "cannibalism" trains our defenses

Phagocytosis is a biological mechanism whereby specialized cells ingest and degrade old, dead, or damaged cells to prevent their accumulation from causing tissue damage. A CNIC-led study has now reported that phagocytosis appears also to have an educational role. The ***Journal of Experimental Medicine*** report is the fruit of a joint effort by teams from the Spanish National Cancer Research Center (CNIO), the Spanish Superior Scientific Research Council (CSIC), and groups from the USA, and was coordinated by **Noelia Alonso-González** and **Andrés Hidalgo** of the CNIC. The study shows that phagocytosis not only eliminates useless cells, but also trains macrophages, the immune cells that carry it out.

It is a paradox of nature that death is a prerequisite for the continuation of life. This is no more evident than in our own bodies, in which billions of cells in the intestine, the blood, the skin, and other tissues die every day so that new ones can take their place. Scientists have long been interested in how organisms eliminate the debris from these expired cells. One of the commonest mechanisms turns out to be that specialized cells eat the old, dead, or damaged cells. This digestive process, called phagocytosis, is carried out by cells called macrophages, a name that means "big eaters".

An important conclusion of the study is that the act of ingesting expired cells trains the immune system in how to maintain tissues in a clean and healthy state, and that macrophages play a very important role in this process. The study identifies in detail the molecules that carry out important tasks in the phagocytic process in each tissue, from the gut to the liver and bone marrow. Surprisingly, the researchers found that each tissue has its own specific molecular toolkit for eliminating unwanted cells. According to **Alonso-González**, "This discovery suggests that it should in principle be possible to modulate phagocytosis in individual organs, without altering events in neighboring organs. One could, for example, promote the elimination of dangerous cells in the spleen without risking elimination of beneficial cells in the lung." Although any therapeutic application lies in the future, the study, in describing how the body maintains itself clean and healthy, suggests that in time it may be possible to coordinate the work of these cleansing macrophages to our benefit.

A.-González, N., Quintana, J. A., García-Silva, S., Mazariegos, M., González de la Aleja, A., Nicolás-Ávila, J. A., ... Hidalgo, A. (2017). *Phagocytosis imprints heterogeneity in tissue-resident macrophages.* ***Journal of Experimental Medicine***.
doi:10.1084/jem.20161375




## NATURE MEDICINE
### 'Unexpected' role of an immune cell subtype in the protection against atherosclerosis

Marginal B cells, a subtype of immune cell, appear to protect against atherosclerosis. The findings were published in ***Nature Medicine*** by a team including researchers from the CNIC and Cambridge University (United Kingdom). In this first study to examine the role of this specific B cell subtype, the research team not only shows that marginal B cells protect against atherosclerosis but also describes the mechanism through which they carry out this protective function.

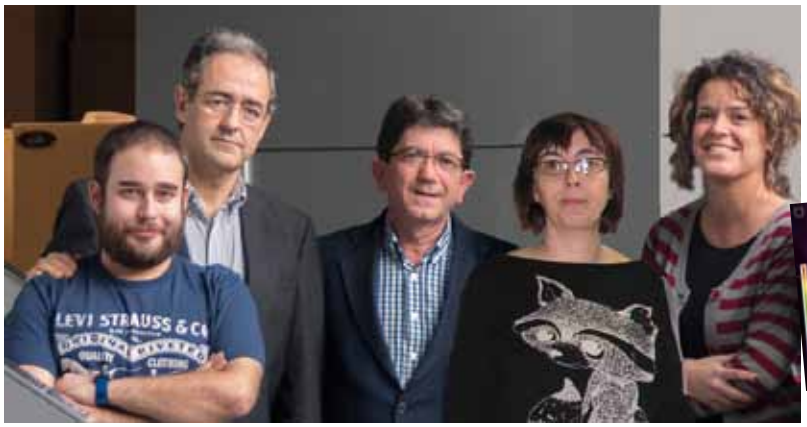
Nus, M., Sage, A. P., Lu, Y., Masters, L., Lam, B. Y. H., Newland, S., ... Mallat, Z. (2017). *Marginal zone B cells control the response of follicular helper T cells to a high-cholesterol diet.* ***Nature Medicine***.
doi:10.1038/nm.4315

## NATURE COMMUNICATIONS

### CNIC scientists discover an essential mechanism in the immune response

A study led by **Dr. Almudena Ramiro** and published in ***Nature Communications*** demonstrates an essential role for the transcriptional regulator CTCF in antibody production. The research shows that CTCF is required for the ability of B-lymphocytes to correctly protect the body against infection. In the absence of CTCF, the immune system does not function correctly, a finding with implications for vaccine research. The study reveals an essential function for CTCF in the orchestration of transcriptional changes during the terminal differentiation of B-lymphocytes and advances our understanding of the mechanisms that regulate the immune response.

Pérez-García, A., Marina-Zárate, E., Álvarez-Prado, Á. F., Ligos, J. M., Galjart, N., and Ramiro, A. R. (2017). *CTCF orchestrates the germinal centre transcriptional program and prevents premature plasma cell differentiation.* ***Nature Communications****,* 8, 16067. doi:10.1038/ncomms16067



## NATURE MEDICINE

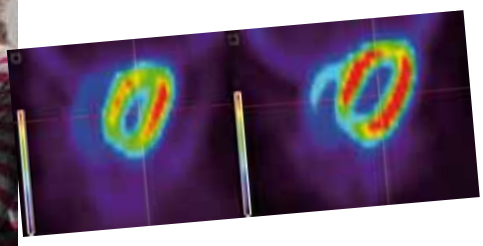
### A new anti-cancer drug linked to cardiovascular problems

Inhibitors of the enzyme Plk1 were recently authorized as an "innovative therapy for leukemia" by the US Food and Drug Administration (FDA). However, a study published in ***Nature Medicine*** by researchers from the Spanish National Cancer Research Center (CNIO) in collaboration with researchers at the CNIC suggests that prolonged use of these inhibitors can lead not only to hypertension but also to blood vessel rupture and severe cardiovascular problems.

Progress toward personalized medicine depends on knowing the function of each of our genes and proteins and selecting the appropriate drugs targeting these proteins according to the specific alterations in each patient. In recent years, regulators of the cell cycle, the process that controls the proliferation of tumor cells, have demonstrated their usefulness against various cancers, including breast cancer. Among the new drugs used in this strategy is the Plk1 inhibitor volasertib, which has shown very promising results in acute myeloid leukemia and was recently recognized as an "innovative therapy" by the FDA due to its effectiveness against this type of tumor in clinical trials.

In the new study, the CNIC research group led by **Juan Miguel Redondo** participated in the characterization of cardiovascular defects in mice with decreased Plk1 activity, resulting from genetic deficiency and treatment with volasertib. Together with scientists at the Centro de Investigación del Cáncer (CIC) in Salamanca, the Universidad de Salamanca, and the London Research Institute, the CNIO and CNIC team found that while volasertib treatment of a mouse strain with low Plk1 levels did not cause growth defects, it did cause artery rupture and secondary cardiovascular effects. These results indicated that the arteries are more sensitive to Plk1 inhibition than other adult tissues. The team went on to show that Plk1 is essential for the contraction of cells lining the artery wall, an essential process for maintaining an appropriate blood pressure.

Cardiovascular disease and cancer are the main causes of morbidity and mortality in modern societies. The involvement of Plk1 in the control of both processes will have a major impact on future biomedical developments.



De Cárcer, G., Wachowicz, P., Martínez-Martínez, S., Oller, J., Méndez-Barbero, N., Escobar, B., ... Redondo, J.M. and Malumbres, M. (2017). *Plk1 regulates contraction of postmitotic smooth muscle cells and is required for vascular homeostasis.* ***Nature Medicine****.* doi:10.1038/nm.4364

## NATURE COMUNICATIONS
### The key to improved cancer immunotherapy

CNIC researchers have investigated how different subtypes of essential immune-response cells called CD8+ T lymphocytes cooperate to mount a stronger anti-tumor response. The results show that generation of an optimal immune response to cancer requires cooperation between two types of memory T cell—one circulating in the blood and the other resident in tissues—that can be reactivated with current immunotherapy strategies. These results, published in ***Nature Communications***, have the potential to improve current cancer immunotherapy strategies, especially in relation to the prevention of metastasis (dissemination of the tumor to organs distant from the site of origin).

Immunotherapy—the use of the immune system to fight cancer—is revolutionizing treatment, and was selected by the prestigious journal ***Science*** as the major scientific advance of 2013. According to study leader **David Sancho**, "Cancer escapes the control of the immune system because the cytotoxic T lymphocytes that should recognize and eliminate tumor cells are inhibited. Current immunotherapy is based on reactivating these T lymphocytes; however, little is known about how cytotoxic T cells can be generated more effectively, and in particular how immune memory can be triggered to prevent the development of tumors and metastasis."

The study suggests that an optimal anti-tumor immune response requires the generation of both circulating and tissue-resident T cell memory. Both memory T cells subtypes can be reactivated with current immunotherapy treatments, and reactivation of both requires DC1 dendritic cells. Cancer immunotherapy is not simply a treatment that can effectively promote the rejection of primary tumors; above all, it is a fundamental tool for impeding metastasis after surgery to remove the primary tumor.

Enamorado, M., Iborra, S., Priego, E., Cueto, F. J., Quintana, J. A., Martínez-Cano, S., Mejías-Pérez, E., Esteban, M., Melero, I., Hidalgo, A. and Sancho, D. (2017). *Enhanced anti-tumor immunity requires the interplay between resident and circulating memory CD8+ T cells.* ***Nature Communications***, 8,16073
doi: 10.1038/ncomms16073

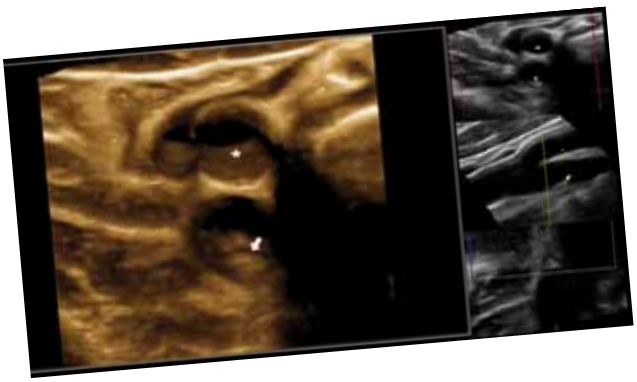
## JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
### 3D visualization of cholesterol plaques improves cardiovascular risk prediction

Three-dimensional ultrasound could become a central tool for identifying individuals at risk of developing cardiovascular disease. This is the conclusion of a report, published in the ***Journal of the American College of Cardiology***, from the CNIC-Santander PESA study (Progression of Early Subclinical Atherosclerosis), a collaborative project between the CNIC and Banco Santander that studies more than 4000 middle aged participants. The report demonstrates that total atherosclerosis burden is a very useful parameter in the stratification of individual cardiovascular risk, when considered together with classical risk factors (blood cholesterol, blood pressure, diabetes, smoking status, exercise, and obesity).

The results of the study, directed by CNIC Director General **Dr. Valentín Fuster**, show that among the study participants (mean age 45 years) the total atherosclerosis burden is twice as high in men as in women (63.4 versus 25.7 cubic millimeters), is higher in the femoral arteries than in other vascular territories, and increases with age.

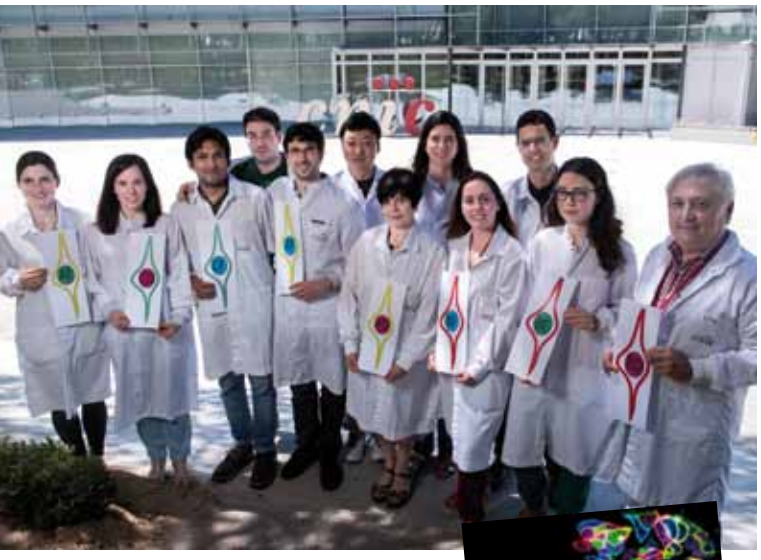
The CNIC scientists explored the most atherosclerosis-prone regions of the carotid and femoral arteries. In each territory, the researchers performed 3D ultrasound examinations of 6 cm arterial segments in both branches, centered on the carotid sinus and the femoral bifurcation. The study population included 3860 middle-aged participants with no disease symptoms and no history of myocardial infarction or stroke. All participants were Banco Santander employees based in Madrid. PESA is a prospective cohort study that monitors patients over several years. The patients were examined with a new ultrasound system made by CNIC technology partner Philips. The system uses a linear volumetric transducer that acquires 3D images of the arteries and atherosclerotic plaques.

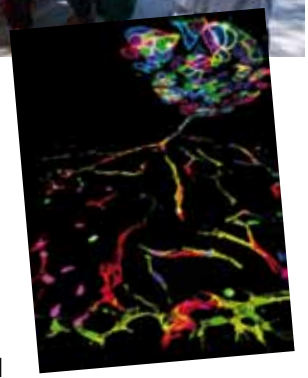
Although 3D ultrasound is still in the development phase, it has already shown clinical promise in several areas, including quantification of atherosclerotic plaque volume. Direct quantification of plaque volume by 3D ultrasound is more accurate than 2D techniques for estimating an individual's total plaque burden.



**Borja Ibáñez**, CNIC Research Director and a cardiologist at Fundación Jiménez Díaz university hospital commented that "conventional risk factors (blood cholesterol, hypertension, smoking, etc.) allow a broad prediction of the population risk of severe cardiovascular events (infarction or stroke); however, individualized predictions based on these risk factors are not very accurate. Now, with the ability to directly visualize atherosclerotic plaques and quantify their number and size in the body, we will be able to predict individual risk more accurately. The presence and extent of atherosclerosis gives direct information about how risk factors affect the arteries in each individual."

López-Melgar, B., Fernández-Friera, L., Oliva, B., García-Ruiz, J. M., Peñalvo, J. L., Gómez-Talavera, S., ... Fuster, V. (2017). *Subclinical Atherosclerosis Burden by 3D Ultrasound in Mid-Life: The PESA Study.* ***Journal of the American College of Cardiology****,* 70(3), 301-313. doi:10.1016/j.jacc.2017.05.033



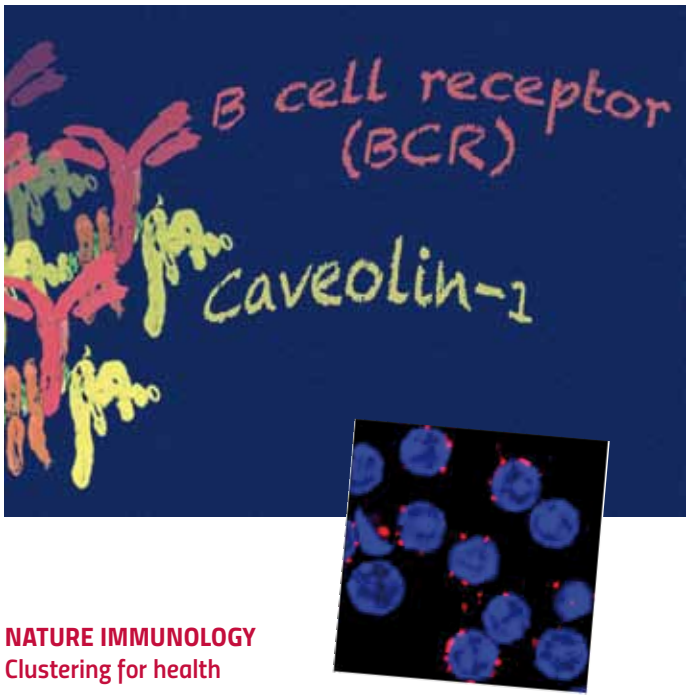


## CELL
### New methods for analyzing gene function

A study published by CNIC scientists in ***Cell*** will allow any researcher to induce and analyze multispectral genetic mosaics in vertebrate models such as mice and zebrafish. The new technology will allow a high spatio-temporal resolution definition of the function and interaction of genes during development and disease. Genes encode the information needed to synthesize proteins, the functional building blocks of our cells.

According to study leader **Rui Benedito**, the improved methods for studying gene function will allow researchers to "increase knowledge about how the genome operates in the multiple cell types that make up our bodies and understand gene interaction networks and their regulatory hierarchies." This knowledge, moreover, is crucial for the design of efficient therapeutic strategies to modify or correct genetic activity in disease.

Pontes-Quero, S., Heredia, L., Casquero-García, V., Fernández-Chacón, M., Luo, W., Hermoso, A., ... Benedito, R. (2017). *Dual ifgMosaic: A Versatile Method for Multispectral and Combinatorial Mosaic Gene-Function Analysis.* ***Cell****,* 170(4), 800-814 e818. doi:10.1016/j.cell.2017.07.031



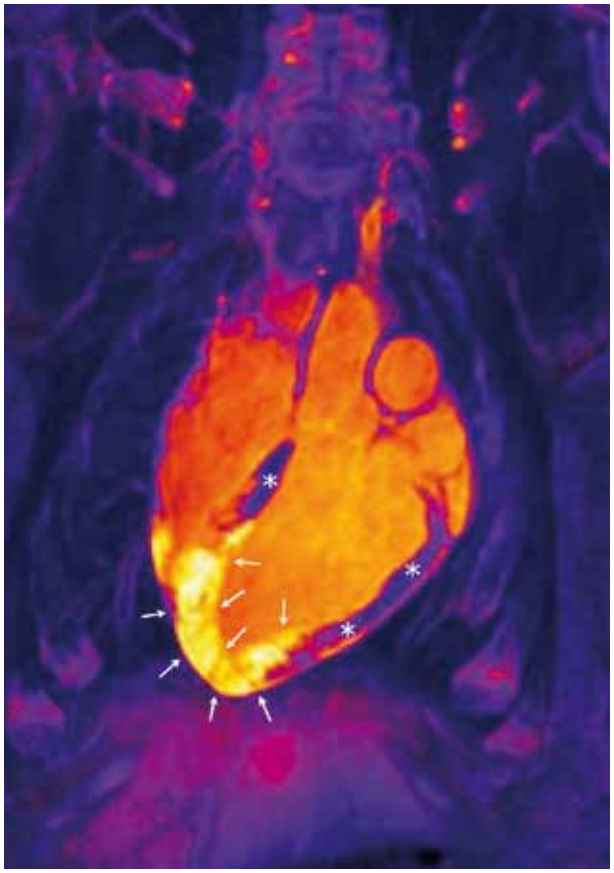

## NATURE IMMUNOLOGY
### Clustering for health

Our immune system protects us from multiple threats such as disease-causing microbes and cancer. However, when our immune system is activated inappropriately, it attacks the body and causes autoimmune diseases. Historically, autoimmunity has been considered the result of immune-system hyperactivity. Recently it has become clear that autoimmunity can also occur as result of weakened immune responses. In this situation, a strategy based on pharmacological inhibitors would be counterproductive, and an appropriate strategy would be activation or substitution. Working with this new concept, researchers at the University of Freiburg (Germany) and the CNIC have identified the protein caveolin-1 as a key regulator in a unique model of autoimmunity caused by insufficient immune function.

The team identified caveolin-1 as a crucial regulator of the clustering of receptors in the plasma membrane of B lymphocytes. Using experimental models, the authors showed that, in the absence of caveolin-1, B cell receptors are disorganized and, crucially, do not efficiently detect threats. As a result, B cells are not activated appropriately

and generate deficient immune responses. These results demonstrate for the first time that the organization of receptors in the B cell membrane ensures the correct activation of these cells.

Minguet, S., Klasener, K., Schaffer, A. M., Fiala, G. J., Osteso-Ibáñez, T., Raute, K., ... Del Pozo, M. Á. (2017). *Caveolin-1-dependent nanoscale organization of the BCR regulates B cell tolerance.* ***Nature Immunology***. doi:10.1038/ni.3813



## CIRCULATION / CIRCULATION RESEARCH

### Dogma overturned: new studies into inflammation in the infarcted heart could lead to changes in therapy

Scientists at the CNIC and the Fundación Jiménez Díaz (FJD) and Salamanca University Hospitals have demonstrated that the response of the human heart to an infarction differs significantly from what was previously thought. The study, published in 2 independent articles in the leading journals ***Circulation*** and ***Circulation Research***, overturns the established view that an infarction is followed by progressive repair of the myocardium.

The project arose from research begun more than 10 years ago at Mount Sinai Hospital in New York, directed by **Valentín Fuster**, who is an author on both of the new CNIC-led studies. Two years ago, the CNIC and the FJD University Hospital signed a collaboration agreement to coordinate their studies of cardiac muscle after an acute myocardial infarction. The study is the first in the world to study heart attack patients by MRI so soon after the re-establishment of blood flow. In addition to studies in patients, the team have also extended their investigation of infarction in pigs, the experimental model most similar to humans. The unique translational research infrastructure at the CNIC includes equipment for directly comparable imaging in human and animal studies, allowing the team to demonstrate that treatments during an infarction can change the composition of the cardiac muscle during the first hours after reperfusion and result in a much more rapid recovery of the heart. In the words of study author **Dr. Rodrigo Fernández-Jiménez**, "MRI provides an extraordinary ability to noninvasively visualize events occurring after an infarction in real time, including inflammation, tissue volume expansion, hemorrhage, and obstruction of the microcirculation."

The study was coordinated by Dr. Ibáñez, Director of Clinical Research at the CNIC and a cardiologist at FJD University Hospital. In his estimation, the discovery of the bimodal inflammatory response in the human heart "forces us to think about the best timing for MRI scans used in clinical trials to quantify irreversible injury and to monitor the effectiveness of interventions to reduce this injury. Until now, this question was not considered important, and cardiac imaging studies have been conducted on any day in the postinfarction period. The new findings show that the optimal time for these scans is between postinfarction days 4 and 7, when the second wave of inflammation/edema is prominent and affects the entire region that was shut off from the blood supply during the infarction."

This research project was possible thanks to the scientific collaboration between the CNIC and technology partner Philips Iberia. Physicist **Javier Sánchez-González**, a Philips researcher embedded at the CNIC, leads the technological development of these cardiac imaging projects, and his input is essential for transferring the initial findings from the CNIC to collaborating hospitals, so that the new algorithms can be tested in a clinical environment. ■

Fernández-Jiménez, R., Barreiro-Pérez, M., Martín-García, A., Sánchez-González, J., Agüero, J., Galán-Arriola, C., ... Ibáñez, B. (2017). *Dynamic Edematous Response of the Human Heart to Myocardial Infarction: Implications for Assessing Myocardial Area at Risk and Salvage.* ***Circulation***. doi:10.1161/CIRCULATIONAHA.116.025582

Fernández-Jiménez, R., Galán-Arriola, C., Sánchez-González, J., Agüero, J., López-Martín, G. J., Gómez-Talavera, S., ... Ibáñez, B. (2017). *Effect of Ischemia Duration and Protective Interventions on the Temporal Dynamics of Tissue Composition After Myocardial Infarction.* ***Circulation Research***, 121(4), 439-450. doi:10.1161/CIRCRESAHA.117.310901

# ALLIANCE FOR SCIENCE:

## TWO OF THE LARGEST RESEARCH COHORTS IN SPAIN JOIN TOGETHER TO WORK ON THE PREVENTION OF ATHEROSCLEROSIS AND ALZHEIMER'S

Alzheimer's disease and atherosclerosis are characterized by presenting a long and slow progression, which starts much before the appearance of the first symptoms. In the case of Alzheimer, alterations in the brain can start being produced up to 20 years before the characteristic memory problems appear. And the same occurs with atherosclerosis, since it is known that the formation of plaques in the arteries also begins 20 years before a heart attack or stroke can take place. Both Alzheimer and atherosclerosis share risk factors like obesity, hypertension, hypercholesterolemia, hyperglycemia and a sedentary lifestyle. In addition, it has been shown that cardiovascular risk factors cumulatively increase the risk of depositing the amyloid protein in the brain, which is also the main protein involved in Alzheimer's disease. Nonetheless, it remains unknown whether both diseases share an underlying process.

This association has led the CNIC and the research center of the Pasqual Maragall Foundation, the Barcelonabeta Brain Research Center (BBRC), to start a collaborative project in order to investigate the relationship between atherosclerosis disease and Alzheimer's disease. The agreement includes studies of vascular image, cognitive image and neuroimaging in their respective cohorts, which add up to more than 6,000 healthy individuals, the largest initiative worldwide in this sense.

According to the Director of the Pasqual Maragall Foundation, **Dr. Jordi Camí**, "the experience accumulated by the BBRC and the CNIC gives us a unique opportunity to investigate and understand the relationship between Alzheimer and atherosclerosis". For his part, the General Director of the CNIC and principal researcher of the PESA-CNIC-Santander study, **Dr. Valentín Fuster**, affirms, "we have spent years speculating with the idea that the risk of the development of cardiovascular disease is related to the risk of development of cognitive impairment and Alzheimer's disease. Up until now they were hypothesis based on aggregated data, but this collaboration will help us decipher if there really is a real nexus between both these entities or even if both are different spectra of the same process."

### MULTIPLE CLINICAL DATA

The main advantage of the project is the richness of the multiple clinical data obtained in the participating cohorts: the Alfa (Alzheimer and Families) Study cohort of BBRC has 2,743 participants between the ages of 45 and 75, and the PESA-CNIC-Santander (Progression of Early Subclinical Atherosclerosis) cohort of CNIC, with 4,184 participants between the ages of 40 and 55. The volunteers that participate in the Alfa cohort, take cognitive, genetic, neuroimaging and clinical tests, as well as others, every 3 years, since 2012. The objective of this infrastructure, financed by "La Caixa" Social Work project, is to understand the natural history of the disease and to identify the risk factors and biological indicators that could contribute to its development. From now on, the participants will also get ultrasounds and CAT scans, in order to detect if they are in the pre-phase of atherosclerosis and to evaluate their evolution along with the risk of developing Alzheimer's disease.

On the other hand, the participants of the PESA-CNIC-Santander Study, are evaluated every 3 years using the latest non-invasive cardiovascular imaging techniques to detect the presence of atherosclerotic disease in the carotid, aortic, coronary and iliofemoral territories. Thanks to this agreement, the participants' APOE gene will now be determined, which is the main genetic risk factor for Alzheimer's disease, and a subgroup will perform cognitive tests and new neuroimaging techniques in

order to investigate if cognitive deterioration is produced or brain changes in individuals with varying levels of atherosclerosis. The data obtained in both cohorts will be analyzed by a multidisciplinary team from BBRC and CNIC. This exchange of material, ideas, results, personnel, and experience between both institutions will allow the advance of knowledge of the relationship between the vascular and cerebral changes that are produced in atherosclerosis and Alzheimer's disease.

### COLLABORATION CNIC & SEC

The collaboration between the CNIC and the Spanish Cardiology Society (SEC) has led to the creation of a plan of postgraduate training for doctors specialized in cardiology, which according to **Dr. Andrés Íñiguez**, president of the SEC "responds to our society's commitment with excellence and the promotion of quality in the cardiology services in our country. There is no quality assistance without quality of research. We are very pleased to have been able to carry out such an ambitious plan together with one of the world's leading centers of cardiovascular research."

For **Dr. Valentín Fuster**, General Director of the CNIC, "the excellence in research, effective translational medicine, and training are basic pillars of the CNIC. Since its creation, the center has made an exceptional effort to identify and train the most talented and outstanding individuals in cardiovascular research. This effort is coordinated under the umbrella of the center's global training program, the CNIC-YOUTH Training Program, which covers all levels from secondary education to postdoctoral training and that of medical and scientific professionals."

**Borja Ibáñez**, Director of the CNIC's Department of Clinical Research and cardiologist at the Fundación Jimenez Díaz University Hospital in Madrid, who directly supervises the three training programs for young cardiologists, comments that, "these training programs have different objectives according to the training stage of the participants. In the past, similar programs have achieved important results and currently there are cardiologists in different national and international hospitals that have a permanent link to the CNIC through concrete projects that began to take shape during their time at our center." ■

## CNIC-SEC-YOUTH TRAINING PROGRAM FOR DOCTORS

This Training Program is divided into three distinct programs, all of which have already opened their application processes, and can be done through the CNIC website: www.cnic.es

**CARDIOYOUTH SEC-CNIC**

The objective of this program is to create a profile of cardiologist-researcher of excellence through a specific training in statistics and methodology, clinical and translational training in the latest techniques of basic research used in cardiovascular biomedicine, all of which are focused in the cardiology specialty. This will be a two-year training program with an additional third year. The first year will be in the United Kingdom studying a Masters in statistics and methodology at the prestigious London School of Hygiene and Tropical Medicine. Under the direct supervision of **Professor Stuart Pocock**, world leader in this field. The second year will be at the CNIC, integrated in a research group. The third year is optional and could include 25% of the time dedicated to the CARDIOYOUTH program. This program aims to train the future cardiologist researchers and integrate them in a network formed by national hospitals and the CNIC.

**INVEMIR SEC-CNIC**

The purpose of this program (which lasts between four to six months) is to complete the training of the cardiology residents in their last years of the MIR training, through a project of research at the CNIC laboratories, under the supervision of a scientist. The eight resident doctors chosen by the SEC and CNIC will also have the opportunity to establish links in order to continue to develop their research projects at their respective National Health Centers counting with the support of the SEC and CNIC, even after they finish their training.

**RES@CNIC SEC-CNIC**

The third program will train 20 professional doctors during their first resident stages in the MIR cardiology program, offering them the opportunity to be in touch with cardiovascular research at the CNIC laboratories. This way, the resident students can get to know first-hand the latest techniques in biomedical research that are being researched at the center's laboratories under the supervision of one of its scientists. Furthermore, they will also receive a theoretical training about cardiovascular research.

# TTO OR HOW TO CAPITALIZE THE INVESTMENT OF TALENT AND RESOURCES OF THE ACADEMIC CENTERS

The Technology Transfer Office (TTO) of the CNIC is responsible for ensuring the diffusion of scientific and technological advances generated by the center to a greater number of users who can evaluate their interest in developing these technological advances to generate new products, processes, applications and services. The TTOs are intermediaries in the science-technology-enterprise system, and their mission is to boost relations among the agents of the system, explains **Noelia López Martín**, in charge of the office at the CNIC. For this, "the TTO are in charge of identifying the technological needs of the socioeconomic sectors and to improve the transfer of knowledge between the public and private sectors, thus contributing to the application and commercialization of the results of the R & D generated in the universities and public research centers." The TTO concept is not something new. The TTO originated at the end of 1988 as structures to encourage and facilitate cooperation in R & D activities between researchers and companies, both in the national and European framework. The first offices designed to bring research results together emerged in Spain 30 years ago, although originally they were in charge of national and international calls to finance projects.

With the passage of time, the Public Administration "understands that the resources invested in research - public financing - can have an economic 'return' that allows for the continuation of investing in projects, hiring people and mobilizing the surrounding economy. In the end, it is about 'giving value' to the results obtained in the research and marketing them", says **Noelia López**. The main function of the public sector is knowledge in R & D, while the marketing of such knowledge is, to a large extent, the responsibility of the companies. The paradox is that the main source of knowledge is the academic world.

The question is how you can capitalize the investment in talent and resources that is done in the academic centers and use those results for the benefit of society. The answer is the TTO.

## DUTIES OF THE OTRI

- Detection and evaluation of innovative technologies that can be exploited commercially. "It's about identifying ideas in the CNIC that have the potential to be commercialized and be used to treat and diagnose any disease," clarifies **Noelia López**. In the case of the CNIC, she explains, it is important to know all the laboratories and technical units of the CNIC and their research areas to identify which lines of work could be susceptible to transfer. Also through internal training at the CNIC we make it so that it is the researchers themselves who come to the TTO with ideas that can be transferred.
- Assessment of the maturity of the technology and the potential industrial interest.
- Financing, management and protection of the intellectual property of the CNIC through patents and other intellectual property rights. The objective is to study the idea from a technical, economic viability point of view (if there is financing), if it can be protected by intellectual property right, to study the market.
- Searching for the status of the technique in scientific article databases and patents.
- Promotion and dissemination of the research activities and results of the CNIC, through platforms of offer/demand and attending the partnering/brokerage events.
- Identify commercial license opportunities for the CNIC's Technological Offers portfolio.
- Negotiate terms and conditions of licensing contracts.
- Transfer of technology through entrepreneurship: creation of spin-offs.


- Promotion of collaboration agreements between researchers and local, national and international industry, and, follow-up of private R & D projects.
- Negotiation, management and follow-up of material transfer agreements (MTA) and Confidentiality Agreements (CDA).

The TTO of the CNIC, directed by **Enrique Lara**, works closely with a prestigious patent agency for advice on intellectual property rights and counts on the legal advice of an international firm specialized in this field. **Noelia** explains that a patent application is "a very good negotiation tool. Having a patent gives value to the results." The patent is a title granted by the State to have territorial market exclusivity, depending on where the application is filed. But to be able to present a patent application the object that is protected has to be 'new' - nobody in the world must have done something like it - and taking into account the status of the technique, "it does not have to be obvious for an expert in the matter to have come up with this invention."

## WHAT BENEFITS DOES IT PROVIDE FOR THE CNIC?

The R & D results obtained by the researchers are property of the CNIC, since it is the center that provides the resources to achieve these ideas. The CNIC can then license your product to a company to market it. But we must not forget that many of the ideas are unable to be licensed, despite the fact that they many years have been invested in their research and development.

Another form of knowledge transfer is through scientific collaboration or contracting services. In this way, the CNIC can exploit its great potential in scientific and technical capacities. For example, the CNIC has state-of-the-art equipment and infrastructures and both laboratories and technical units generate new animal models and research materials in-house. All this allows us to address unique R & D projects and makes the CNIC a center of reference.

## PATENTS

- Fuster Polypill: The first polypill approved in Europe for secondary cardiovascular prevention was developed by CNIC researchers in collaboration with the pharmaceutical company Ferrer. It is approved for commercialization in 55 markets in Europe and America, thanks to having received the approval of the European Medicines Agency, as well as the national agencies. Since September 2017, in Spain a 40 milligram dose of atorvastatin is available, an option with a higher dosage than the previous one, of only 20 milligrams of atorvastatin which has been available since January 2015. It is indicated for patients who have overcome a cardiovascular incident and require treatment to reduce the risk of a second incident. The medication, fruit of public-private collaboration and marketed under the name of Trinomia, includes three active ingredients: an antiplatelet drug to prevent the formation of thrombi, acetylsalicylic acid, a statin to control cholesterol levels and to stabilize atherosclerotic plaque, atorvastatin and an ACE inhibitor, and Ramipril, an antihypertensive that prevents remodeling of the heart that occurs after a heart attack. The fact that Trinomia has been developed by the CNIC and Ferrer makes it an example of how Spanish innovation can be a leader even worldwide.
- Ultrafast Magnetic Resonance: The collaboration agreement between the CNIC and its technological partner, Philips, allows the CNIC to have the most advanced cardiovascular imaging technology in the entire spectrum, from ultrasound to hybrid equipment, through CAT scans to Magnetic Resonance (MRI). The aim is to advance in the prevention, diagnosis and

more effective treatment of cardiovascular disease thanks to the technology that Philips will update as advances in this field are made, and according to the signed research program. Thanks to this collaboration agreement, the Philips-CNIC VF-3DESSOS joint patent has been developed. MRI is the best technique to see the function and anatomy of the heart, but it is a technically complicated test with examination times of over 30 minutes. The new Philips-CNIC VF-3DESSOS joint patent has shortened scan times to less than 1 minute. This joint technological development represents a milestone in the field of cardiac imaging.

- New generation of vectors: In 2016 the CNIC formalized a license agreement with the Spanish company VIVEBiotech for the development of a new generation of non-integrative viral vectors that can be used for genetic transfer and in this way modify tissues and cells. It is expected that this technology will be available for marketing during 2018.
- Atrial Fibrillation: The CNIC also has a collaboration agreement with Correvio International Sàrl for the study, both in animal models and patients, of mechanisms involved in atrial fibrillation in order to transfer the results to clinical practice. It involves a drug that has already come out and does not work the same way in all patients. The company wants to determine the mechanism of action in order to achieve a better selection of patients.
- Biomarker in myocarditis: After more than 10 years of work, **Pilar Martín Fernández**'s group has discovered and validated a biomarker that has already been patented for the diagnosis of acute myocarditis. Currently, a negotiation is underway for the joint development and license of the CNIC patent to the venture capital company to develop a biosensor able to detect the biomarker in patient blood samples in 30 minutes, which would be an essential tool in clinical practice for the differential diagnosis of acute myocarditis and myocardial infarction, since acute myocarditis sometimes mimics a myocardial infarction and the differential diagnosis can be very complicated. At the moment the results are positive.
- Among others, other patents in development are: New radiopharmaceuticals for in vivo diagnosis; Treatment and Diagnosis of Thoracic Aortic Aneurysm; P38 inhibitors for the treatment and prophylaxis of liver cancer; New therapeutic agent for the treatment of lymphoid neoplasms; Use of selective agonists of Beta-3 adrenergic receptors for the treatment of pulmonary hypertension, and New therapy for the treatment of myeloproliferative diseases. ■

## The first polypill approved in Europe for secondary cardiovascular prevention was developed by CNIC researchers in collaboration with the pharmaceutical company Ferrer

## The collaboration agreement between CNIC and its technological partner, Philips, allows the CNIC to have the most advanced cardiovascular imaging technology in the entire spectrum

# THEIR ROYAL MAJESTIES
## THE KING AND QUEEN VISIT THE CNIC

KING FELIPE AND QUEEN LETIZIA MET WITH REPRESENTATIVES OF THE COMPANIES THAT MAKE UP THE **PRO CNIC FOUNDATION**

Accompanied by **Dolors Montserrat**, Minister of Health, Social Services and Equality; **Carmen Vela**, President of the Board of Trustees of the CNIC and Secretary of State of Research, Development and Innovation, and **Jesús F. Crespo**, Vice-president of the Board of Trustees of the CNIC and Director of Carlos III Health Center, **their Majesties the King and Queen** visited the CNIC in February of last year. Their Majesties got to know about the most relevant investigations that are taking place at this center of excellence, thanks to the explanations of **Dr. Valentín Fuster**, General Director of the CNIC and **Luis de Carlos**, President of the Board of Trustees of the Pro CNIC Foundation.

Their Majesties met with the representatives of the 14 companies and institutions that through the Pro CNIC Foundation have achieved that since 2006 CNIC has become a leading institution worldwide, as demonstrated by its renewal as one of the "Centers of Excellence of Severo Ochoa". At the meeting, **Dr. Valentín Fuster**, General Director of the CNIC, was also present. He explained the current situation of the center, whose financing is guaranteed until 2020, with a contribution of 100 million euros in this period.

The Pro CNIC Foundation is made up of a group of companies that in 2005 signed an agreement with the Ministry of Health, where they committed to financing the center. The agreement also included the incorporation of the prestigious cardiologist **Valentín Fuster** to lead this ambitious scientific project. As a result, CNIC became the first elite research center in Spain articulated through a Foundation that combines public and private, in both funding and management. During this decade, "the Foundation has contributed significantly to the development of the center. On one hand, economically, providing more than 20% of the total budget in these last years, and on the other hand, with its participation in the management of the Center through its Board of Trustees and Executive Commission", indicated **Luis de Carlos**, President of the Pro CNIC Foundation.

## SOCIAL COMMITMENT

Additionally, added **Luis de Carlos**, the contribution of the companies not only means a firm commitment to R&D, but also "a firm commitment to an issue of great social interest: the health and quality of life of the Spanish people". **De Carlos** underlined how the stable funding that the Foundation gives to CNIC allows research to be planned on a long-term basis and permits investing in training during all stages of the research career.

Furthermore, in these last years, the Pro CNIC Foundation has also contributed to the improvement of health in citizens by promoting healthy habits. "In all the companies that are sponsored by Pro CNIC, Comprehensive Health Plans that have favorably impacted employees and their families, have been put into operation, under the supervision of **Dr. Fuster**. Pro CNIC has also approached society with more general campaigns such as "Women for the Heart", that **her Majesty the Queen** knows very well, or launching mobile applications such as "The Circle of Health" with healthy tips and challenges."

On his part, **Dr. Valentín Fuster** highlighted that thanks to this funding formula, it has been possible to develop a global training plan, called CNIC-JOVEN, which brings biomedical research closer to young people and allows the creation of a quarry of researchers of excellence in the cardiovascular field. He also mentioned the use of "applied medicine" as one of the significant features of the CNIC and how important it is for the private sector to support the work of centers like the CNIC, a "paradigmatic model of private-public collaboration".

Their Majesties and the rest of the authorities visited the laboratories of the center and were able to speak to three research group leaders from the CNIC, **Dr. Ana Dopazo**, **Dr. Jacob Fog** and **Dr. Enrique Lara**, in order to know first-hand some of these projects that are being conducted at the CNIC. Finally, Their Majesties, attended a scientific debate called "Cardiovascular Research Excellence in Spain". Also present were the three winners of the Princess of Girona Foundation Award in Scientific Research of CNIC **Dr. Borja Ibáñez**, **Dr. Guadalupe Sabio** and **Dr. Rui Benedito**, as well as the CNIC researchers **Dr. Pilar Martín**, **Dr. Almudena Ramiro** and **Dr. David Sancho**. ■

# VALENTÍN FUSTER, NEW PRESIDENT OF THE HEALTH ADVISORY BOARD

**Dr. Valentín Fuster** has been appointed new President of the Health Advisory Board to replace the deceased **Dr. Joan Rodés**, who was the President of the Advisory Council until his death earlier this year. In the official presentation of **Dr. Fuster** as President of the Council, the Minister of Health, Social Services and Equality, **Dolors Montserrat**, paid special recognition to the efforts of the General Director of the CNIC to convey to the citizens that "we must be active protagonists of our own health." In addition, she highlighted "his generosity in accepting the presidency of the Advisory Council, putting all his experience and knowledge at the disposal of the Ministry of Health, Social services and Equality, the national health system and the whole country."

During the presentation, **Dolors Montserrat** recapped his extensive professional career, as he is, among other things, Director of the Cardiovascular Institute of Mount Sinai Medical Center in New York, Prince of Asturias Prize Winner in Research and General Director of the CNIC, which is a reference in the world for its research excellence. He is also President of the Nutrition and Obesity Study Observatory of the Ministry of Health; whose mission is to promote a healthy life.

The Minister also expressed his gratitude to **Dr. Rodés** for his legacy, as he was able to put "Spain as leader in hepatic science not only in Spain but also the rest of the world. Both the international medical community and our National Health System are in debt to him."

"The challenges we face in the National Health System of the future are numerous and the Health Advisory Council will have a key role in helping us overcome them", said the Minister. Among these challenges, the Minister pointed out the demographic as one of the main ones, which makes it necessary to continue promoting "prevention strategies that contribute to a more active and healthy ageing."

On his part, **Dr. Fuster** highlighted that he faces this challenge with great enthusiasm and that "his motivation has always been the research of what is health in order to contribute something to its improvement." To conclude his speech, he added: "I believe strongly in this country. We must try by all possible means to ensure that health is a priority and to strengthen all areas that make it possible - the promotion, the research and health care." ■

VALENTÍN FUSTER:
"We must try by all possible means to ensure that health is a priority and to strengthen all areas that make it possible - the promotion, the research and health care"

Dolors Montserrat highlighted Dr. Fuster's generosity "in accepting the presidency of the Advisory Council, putting all his experience and knowledge at the disposal of the Ministry of Health, Social Services and Equality, the national health system and the whole country"

# A BENEFACTOR NAMES THE CNIC HIS UNIVERSAL HEIR

An anonymous citizen committed to scientific research and health has decided to name the Carlos III National Center for Cardiovascular Research (CNIC) as his 'universal heir', thus donating in his will all his assets to the CNIC. The selfless action of this anonymous benefactor is not very common in Spain, although it is in the Anglo-Saxon countries where there is a greater tradition of what is called 'charity'. In our country it is not common for people to donate their money for research projects, although there are often individuals who want to help and do not know how to do it. Some scientific institutions try to promote sponsorship through campaigns, since the funds provided by citizens can be used to generate new research contracts, improve equipment or allow researchers to get in contact with the best centers of the world by doing exchanges or short-term stays there.

## RESPECT FOR RESEARCH

In this case, the benefactor is someone who apart from his generosity, also has a deep respect for the work of Spanish scientists, whom he considers to be at the forefront of the scientific community, as well as a very close personal experience to the world of health, having been able to observe in the day to day of the hospital activity the need to equip medicine with new advances through research and thus understand how both disciplines complement each other. Precisely, for this generous benefactor the CNIC represents a clear example of transfer of research to the improvement of health and for that reason has deserved special consideration.

The CNIC appreciates its benefactor's support for investigation. Philanthropy, a way to connect individuals with institutions dedicated to research that increase the quality of life and improve society, is an act of generosity not sufficiently recognized today. The good news is that in our country there are more and more people committed to science and in this way or another, they participate economically in the promotion of research. Society should consider health research as a highly valuable asset, as an investment of which we are all jointly responsible for and that will give us a better approach to the health problems that many of us or our relatives will have in the future. ■

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# SECOND ANNIVERSARY OF THE AWARENESS CAMPAIGN "WOMEN FOR THE HEART"

Cardiovascular disease is still the leading cause of death in Spain. It represents 30% of total deaths, a percentage that places it above cancer (27,86%) and respiratory system diseases (11,08%).

Since 2014 the Mapfre Foundation, the Pro CNIC Foundation, the Spanish Heart Foundation and the Community of Madrid, have been promoting the Awareness Campaign "Women for the Heart". The main objective of this Project is to inform the population about the importance of the early recognition of the symptoms and the need to maintain healthy lifestyle which contributes to reducing the impact of cardiovascular disease in women.

On its second anniversary, the Minister of Health, Social Services and Equality, **Dolors Montserrat**, highlighted the importance of prevention and the need to keep up with the good work of "boosting the promotion of health and power of women against cardiovascular diseases".

According to the Deputy Minister of Social Policies and Family of the Community of Madrid in little more than two years, the campaign has benefited 78,000 Spanish women, who have received free medical exams on the buses that have travelled around more than 50 municipalities.


The project, backed up by the General Director of the Carlos III National Cardiovascular Research Centre (CNIC), **Dr. Valentín Fuster**, will count on the unconditional support of the journalist **Ana Rosa Quintana**, the singer **Mónica Naranjo** and the athlete **Ruth Beitia**, deluxe ambassadors of this initiative, and whom throughout the year will contribute selflessly in broadcasting messages that are key to helping women identify the warning signals and prevent a heart attack. ■

# VISIT FROM THE HEALTH AND FOOD SAFETY COMMISSIONER OF THE EUROPEAN COMMISSION

The Health and Food Safety Commissioner of the European Commission, **Vytenis Andriukaitis**, visited the Carlos III National Centre of Cardiovascular Research (CNIC) accompanied by the Minister of Health, Social Services and Equality, **Dolors Montserrat**; the Secretary of State of Investigation, Development and Innovation, **Carmen Vela**; the Executive Director of the Spanish Agency of Consumption, Food Safety and Nutrition, **Teresa Robledo**; the General Director of the Carlos III Health Institute, **Jesús Fernandez Crespo**; the Manager of the CNIC, **Alberto Sanz**, and **Borja Ibáñez**, Director of Clinical Research and **Vicente Andrés**, Director of Basic Research at the CNIC. ■

# THE JAPANESE AGENCY FOR RESEARCH AND MEDICAL DEVELOPMENT AT THE CNIC

The Japanese Agency for Research and Medical Development (AMED) is an institution dedicated to improving medicine through research and development in Japan. Through its President, **Mr. Makoto Suematsu**, the Managing Director of the Foreign Affairs Department of AMED, **Mr. Masahiko Noda**, and the First Secretary - Commissioner of Science and Technology – of the Japanese Embassy in Spain, **Mr. Masahiro Aoki**, the AMED visited the facilities of the Carlos III National Center of Cardiovascular Research (CNIC), accompanied by **Alberto Sanz**, Managing Director of the CNIC, **Borja Ibáñez**, Director of Clinical Research, and **Vicente Andrés**, Director of Basic Research of the CNIC. ■

# INTERNATIONAL WOMEN AND GIRLS IN SCIENCE DAY AT THE CNIC

What barriers are there in becoming a researcher? What must be changed in the formal and informal educational system to get rid of the stereotypes that impede equality in Research and Development? Are the quota systems, removal of language barriers, gender biases in evaluation or the co-responsibility of institutions and families to conciliate personal, professional and family life, positive? These are some of the issues that were debated at the International Women and Girls in Science Day at the Carlos III National Cardiovascular Research Center (CNIC), who counted with the presence of **Carmen Vela**, Secretary of State for Research, Development and Innovation; **Ana Puy**, Director of the Women and Science Unit (UMYC); and **Jesús F. Crespo**, Director of the Carlos III Health Institute.

Science and gender equality are essential to meet the Sustainable Development Goals, included in the UN's 2030 Agenda. In the last 15 years, the international community has made a big effort to inspire and promote the participation of women and girls in science. Unfortunately, women are still faced with barriers preventing them from fully participating in this field. According to a study conducted in 14 countries, the probability of female students completing a bachelor's, master's and PhD in a science-related field is 18%, 8% and 2% respectively, while the probability for male students is 37%, 18% and 6%.

In order to be able to achieve full and equal access and participation in science for women and girls, and moreover to achieve gender equality and empowerment of women and girls, the UN General Assembly decided to proclaim February 11th as International Women and Girls in Science Day.

## RESEARCH CAREER

The CNIC has participated in this initiative with this conference, and showed a video with several testimonials from female researchers at the CNIC in different stages of their research career, with which they intend to motivate future female researchers not to give up their vocation despite the difficulties they may find along the way. Furthermore, participants were able to know first-hand the different stages of the scientific career and the importance 'mentoring' has on the education of the youngest. ■

# MARCH FOR SCIENCE: 'MOVE FOR THE CNIC'


Nothing better to take care of our cardiovascular health than to preach by example. Therefore, Promega Biotech Ibérica S.L. organized, in collaboration with the CNIC the March 'Move for the CNIC', a socially responsible initiative aimed at promoting the cardiovascular activity of the CNIC workers, and whose participation will be linked to helping with the program 'Approach', aimed at fostering the interest of research in young people.

This sports day to support scientific research and promote cardiovascular health was held at El Pardo and included a 10 km track, where the participants, sports 'enthusiasts' of the CNIC and of Promega Biotech Ibérica S.L. and their families opted for walking, jogging, cycling or any other healthy modality. For each person enrolled, Promega Biotech Ibérica S.L. gave an economic contribution to the CNIC's training programs.

"Promoting cardiovascular health through this type of initiative is a great idea because it introduces the concept of health within the community and the working environment," says **Dr. Valentín Fuster**, General Director of the CNIC. **Gijs Jochems**, General Director of Promega Biotech Ibérica S. L, said that his company works to promote the healthy habits of workers with initiatives such as the one that is now being done with the CNIC, "a collaborative partner necessary in this event that in the end pursues the workers' personal and professional well-being". ■

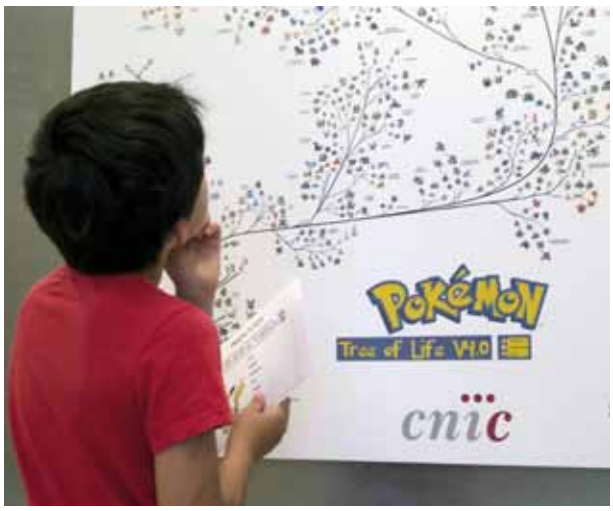
For each person enrolled in the March 'Move for the CNIC', Promega Biotech Ibérica S.L. gave an economic contribution to the CNIC's training programs


# THE CNIC PARTICIPATES IN "SCIENTIFIC WEEKEND"

The VIII edition of the "Scientific Weekend", the science fair for all audiences, was celebrated for the fourth consecutive year at the National Museum of Science and Technology (MUNCYT) in Alcobendas on the 27th and 28th of May, with the collaboration of the Social Work "la Caixa". More than 40 institutions from all over Spain participated in this weekend, including the CNIC. All of them prepared more than 200 activities, workshops and games so that the visitors of this fair in Alcobendas could learn all about science and technology. The boys and girls who approached the stand of the CNIC were able to discover first-hand everything they had ever wanted to know about the functioning of the heart. For example, they saw a heart through the microscope, something that can only be done in a laboratory with the most sophisticated technology. They also discovered the shape and the sound that the heart makes. Furthermore, they could also see how the sarcomere contracts, the anatomical and functional unit of the striated muscle.

Two of the other activities organized by CNIC consisted of explaining the genetic code with the help of Harry Potter using gummy amino acids, which was used to explain how proteins are made, and to reconstruct Pokémon's phylogenetic tree.

In addition, during the "Scientific Weekend", other activities were also held, like discovering eggs that bounce and change color, "scientific magic", virtual reality, science in the kitchen, seeing a "chair to weigh astronauts", learning robotics or immersing into the exciting world of science through experimentation. ■




# DR. VALENTÍN FUSTER TEACHES MASTER COURSE "MOLECULAR, CLINICAL & POPULATION BASES OF CARDIOVASCULAR DISEASE AND HEALTH"

The director of the CNIC and the Cardiovascular Institute of Mount Sinai Hospital, **Dr. Valentín Fuster**, taught the course "Molecular, Clinical & Population Bases of Cardiovascular Disease and Health", organized by the International University Menéndez Pelayo (UIMP), sponsored by Ferrer Laboratories, where he tried to "motivate and teach for the future" more than 300 attendees, most of them cardiologists, although other experts in internal medicine or other specialties also attended. This year, it also counted with the presence of professionals from over 15 countries, many of them from Latin America and Europe.

For the first time this course was held in Cardona (Barcelona), the city that launched the 'Cardona Integral' initiative, a project where health becomes a priority issue for the citizens of Cardona and a tool for social and economic promotion of the city. The event also served to inaugurate the Convention center, CCCardona.

During the course, **Dr. Fuster** analyzed the foundations for healthy ageing, a healthy middle age, and a healthy childhood and adolescence. "Taking care of our health is a matter of individual responsibility and a general change of attitude and lifestyles. And you must insist on an important message: it is never too late to take care of yourself", said the General Director of the CNIC. "Promoting healthy lifestyle habits, which include not smoking, avoiding obesity, regular physical activity and a healthy diet routine, should be the foundation of current strategies to improve cardiovascular health among the general population," he stated. ■

**VALENTÍN FUSTER:**
**"Taking care of our health is a matter of individual responsibility and a general change of attitude and lifestyles. And you must insist on an important message: it is never too late to take care of yourself"**

# cnic AWARDS AND SCHOLARSHIPS

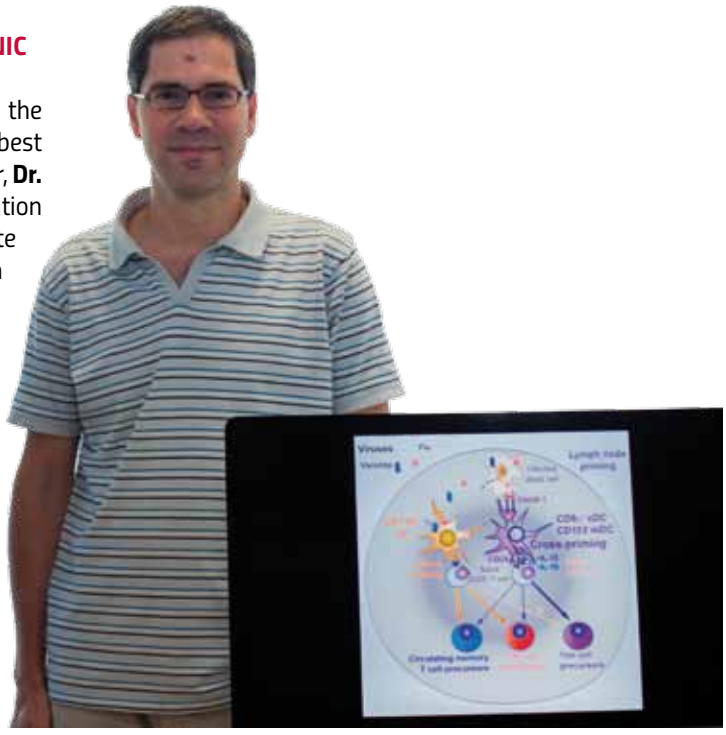

## DR. BORJA IBÁÑEZ AWARDED THE XII BANCO SABADELL FOUNDATION AWARD FOR BIOMEDICAL RESEARCH

The jury of the XII Banco Sabadell Foundation Award for Biomedical Research has acknowledged **Dr. Borja Ibáñez Cabeza**, Director of Clinical Research at the Carlos III National Centre of Cardiovascular Research (CNIC), as the winner of the 2017 award for his innovative contribution to the fight against cardiovascular diseases through the transfer of basic knowledge and technology to the prevention and treatment of this pathology. The prize is endowed with 50,000 euros and aims to acknowledge the trajectory of young researchers in the field of biomedicine. In the twelfth edition of the Biomedical Award, a total of 58 applications were submitted which included basic, clinical and epidemiological research profiles. The jury of this award has been presided over, once again, by **Dr. Carlos López Otín**, professor at the University of Oviedo.

## THE EUROPEAN UNION GRANTS 2 MILLION EUROS TO THE RESEARCH OF DR. DAVID SANCHO AT THE CNIC

The European Research Council (ERC) announced the winners of its Consolidator Grants to the 314 best researchers in Europe. Among them is a CNIC researcher, **Dr. David Sancho**, for his project "Functional characterization of mitochondrial metabolic adaptations to innate sensing in dendritic cell subsets", which will receive an amount of 1,995,000 euros over the next 5 years. The total amount of subsidies granted by the European Research Council of the European Union (EU) is 605 million euros and are part of the EU's Research and Innovation Program, Horizon 2020 "Science of excellence".

**Dr. Sancho**'s project focuses on immunometabolism, an emerging field of research that can generate new targets for the manipulation of functional responses in immune cells. As explained by the CNIC researcher, there are pioneer studies that show how the detection of microbes or danger signals modify the metabolism of immune cells. "We are interested



in the metabolic consequences of detecting danger signals from microbes or tissue damage by dendritic cells. Our previous work has shown that the recognition of microbes by macrophages changes the flow of electrons in the mitochondrial transport chain and that this modification alters the bactericidal capacity of the macrophage and its pattern of cytokine production."

The objectives of Dr. Sancho's project are: 1) characterize how the detection of danger signals from microbes or tissue damage modulates mitochondrial metabolism in dendritic cells in mouse and human; 2) dissect the molecular mechanisms that connect the detection of these signals and the mitochondrial metabolism; 3) address the impact of the manipulation of mitochondrial biology on the metabolism and function of mouse and human dendritic cells; 4) evaluate possible therapeutic approaches through the manipulation of mitochondrial metabolism in dendritic cells in animal models of disease, which are essential as a preclinical approach.

## GUADALUPE SABIO RECEIVES LEONARDO SCHOLARSHIP TO RESEARCHERS AND CULTURAL CREATORS OF THE BBVA FOUNDATION

Researcher **Guadalupe Sabio**, of the CNIC, received one of the 50 Leonardo Scholarships to Researchers and Cultural Creators of the BBVA Foundation in the area of basic research for her project "Inhibition of P38gamma as possible therapeutic target for liver cancer". The 2017 Leonardo Scholarships for Researchers and Cultural Creators have now been awarded in seven out of its nine categories — Basic Sciences; Biology, Environmental and Earth Sciences; Biomedicine; Information and Communication Technologies, Other Engineering areas and Architecture; Economics and Business Management, Legal and social Sciences; Humanities; and Literary Creation and Theatre. **Dr. Guadalupe Sabio**, is also, one of the 100 women chosen among the Top 100 Women Leaders in Spain in 2017, an initiative aimed at boosting the presence of women in all areas. With this recognition, **Dr. Sabio** becomes part of the very select group "Top of Honor", among which are also **Her Majesty Letizia Ortiz**, **Almudena Grandes**, **Amaya Arzuaga**, **Amaya Valdemoro**, **Carmen Alborch**, **Carmen Iglesias**, **Irene Milleiro**, **Julia Otero**, **Margarita Álvarez**, **María José Alonso** or **Marta Martínez Alonso**, among other important figures.

## EDUARDO OLIVER GRANTED YOUNG RESEARCH AWARD OF THE SPANISH SOCIETY OF PHARMACOLOGY

**Eduardo Oliver** has been granted the Young Researcher Award of the Spanish Society of Pharmacology, recognition that this society grants to its members under 35 years of age with the best scientific career. This award has a prize of 1200€, which is to be divided with the other award winner **Miguel Romero**, from the University of Granada. This award is added to the one received last year by the Federation of European Pharmacological Societies for the publication of the article "The zinc transporter ZIP12 regulates the pulmonary vascular response to chronic hypoxia" (***Nature***, 2015; 524:356-360), where he is the main author.


## THE BANK FOUNDATION "LA CAIXA" PAYS TRIBUTE TO BIOMEDICAL RESEARCHERS

The 'Imprescindibles' campaign of the Bank Foundation "La Caixa" wants to recognize the importance of research in the welfare of people and the contribution of scientists who dedicate their lives fighting against diseases and preserve one of the most highly valued assets: Health. **Isidro Fainé**, president of the Bank Foundation "La Caixa", and **Jaume Giró**, General Director of the Bank Foundation "La Caixa", accompanied by doctors **María Blasco**, **Valentín Fuster**, **Maite Mendioroz**, **Eduard Gratacós**, **Bonaventura Clotet** and **Pedro Alonso**, presented the new advertising campaign that this year wants to give voice to the leaders in the field of research of excellence that work to respond to the great challenges of humanity in health issues, with the aim of fighting the diseases that have the greatest impact on the rest of the world. The campaign gathers the testimonies of the scientific leaders and explains the most important points of their research. Among them are **Dr. Fuster**, General Director of the CNIC, who notes that "there are two keys to promoting cardiovascular health: Science and Education." ■

# cnïc PULSE

## otoño '17