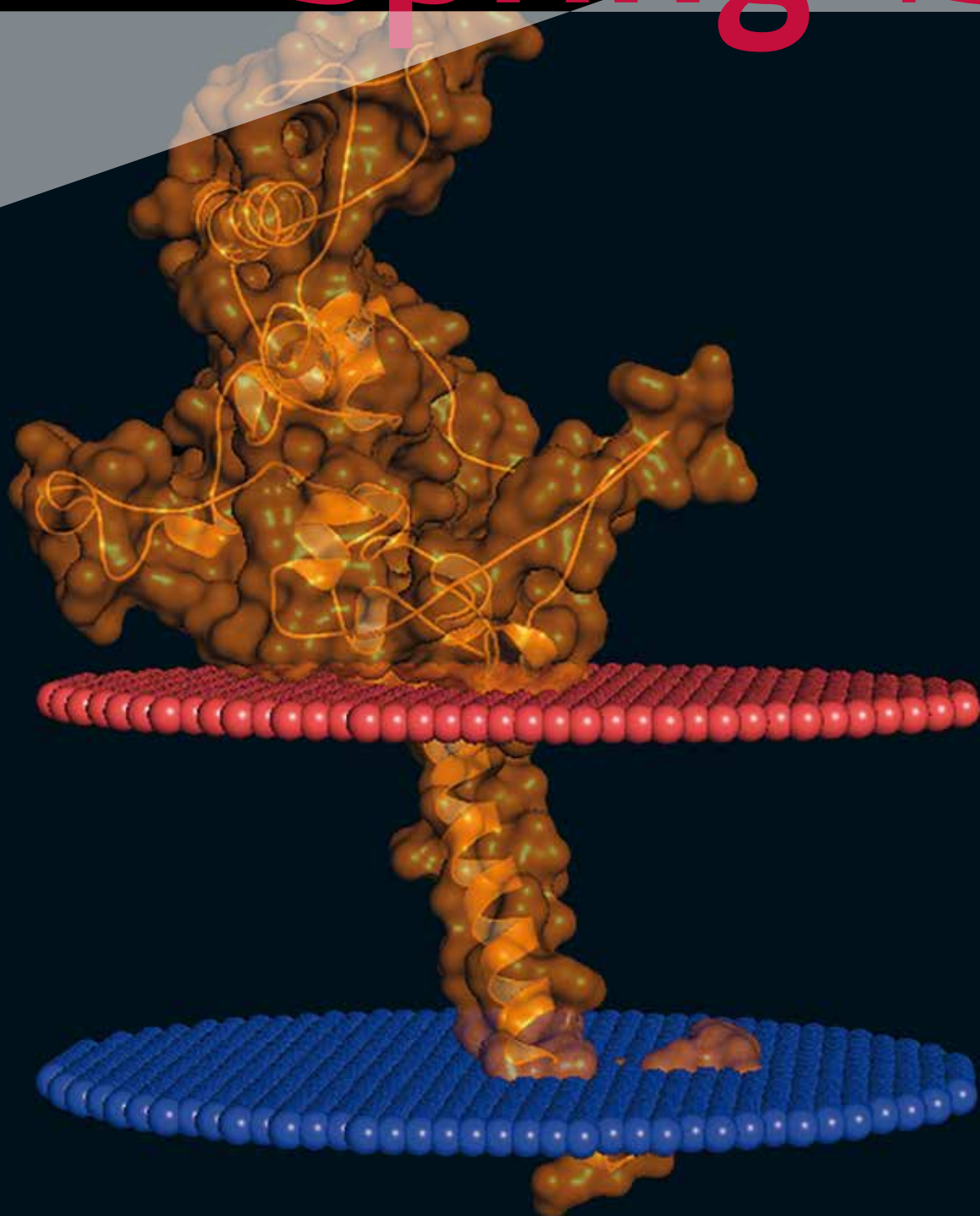


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WHAT'S ON
INSIDE SCIENCE
CNIC & SOCIETY

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spring'19



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Fundación **pro**cnic



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Thirteen of the most important companies in Spain have decided to renew their commitment with research of excellence by extending, until 2028, its agreement with the CNIC through the **Pro CNIC Foundation**. Since I joined the CNIC's management in 2005, the ProCNIC Foundation has been one of the strongholds of the center to ensure that the research carried out at the CNIC established a paradigm shift in Spanish cardiovascular research so that the re-

CNIC, GREAT TALENT MENTOR

sults reach the patient. This fruitful symbiosis has already produced great advances in the world of translational research, with obvious impact on the patient and society, such as the PESA-CNIC-Santander study, the first polypill approved in Europe for secondary cardiovascular prevention, the VF 3D-ESSOS patent for magnetic resonance software that has reduced the heart scan times to less than one minute, or the diagnostic kit that differentiates myocarditis from a heart attack in less than 30 minutes. In addition, many of our findings have been decisive for introducing changes to the recommendations of the European Society of Cardiology (ESC). However, there is something else that I cannot forget that, although less visible, permits this agreement with the Pro CNIC Foundation. It is



Dr. Valentín Fuster, General Director of Carlos III National Centre for Cardiovascular Research (CNIC)

the 'added value' that this agreement supposes and that has a positive impact on the operation of the CNIC. Thanks to Pro CNIC we have training programs that are recognized all over the world that not only serve to create the generation of future researchers, but also to attract talent from other countries, many of whom decide to stay at the CNIC and develop their research career here. CNIC and Pro CNIC act as a 'great mentor' of talent, regardless of where it comes from. I myself am a product of my mentors and had the luck, or the intuition, to let them guide me. And that is what we can do here.

In addition, the economic security provided by Pro CNIC establishes the CNIC brand and method, already internationally recognized by all researchers. The 'CNIC method' is fundamental to guarantee the rigor and excellence of our research and includes, as everyone knows, the application of our work for the benefit of society.

As **D. Luis de Carlos**, President of the Pro CNIC Foundation, affirms, "it is not enough to bet on traditional research, which may take years to reach the patient, but it is necessary to promote the so-called translational research, which is applied to humans as fast as scientific rigor allows it to be." ■

CNIC AND PRO CNIC: AT THE SERVICE OF RESEARCH AND IMPROVEMENT IN HEALTH

Since its refoundation in 2005, the National Center for Cardiovascular Research (CNIC), led by **Doctor Valentín Fuster**, has managed to position itself as one of the internationally renowned centers of cardiovascular research. This new phase was coordinated through an innovative joint-venture public and private sector model, in which the most influential Spanish companies actively participate in the CNIC through the Pro CNIC Foundation. The renewal of this agreement between the Pro CNIC Foundation, which groups together 13 of the most important companies in Spain -Acciona, Banco Santander, BBVA, Endesa, Mapfre Foundation, Mutua Madrileña Foundation, Ramón Areces Foundation, Repsol Foundation, Naturgy, Inditex, "la Caixa", Prisa and Telefónica-, and the CNIC until 2028, allows that the research carried out at the CNIC has a direct impact on the care and improvement of the health of the general population. In addition, part of its innovations are transformed into patents that generate an economic return and favor the development of Innovative Research and Development (R + D + I) in Spain.

In just 14 years, the CNIC has managed to reap achievements that have made it worthy of several awards and prizes of excellence. And, what is more important, its

research has generated substantial progress on how to approach cardiovascular disease, the first cause of death in the most developed countries.

Among the acknowledgments received, the one that stands out the most is the Severo Ochoa Prize, granted to the CNIC on two occasions, for accrediting before a panel of international experts, among which there were three Nobel Prize Laureates, programs of cutting-edge research and highly competitive at the international level.

There are two quantifiable parameters that define the success of a research center: the level of its scientific publications and the ability to attract revenue from external competitive funding sources. And the CNIC has triumphed in both indicators. In addition to publishing its results in the scientific magazines with the most impact in its area -**Cell, Nature, Science, JACC, EMBO**-, it is also the leader in obtaining national and international funds.

But undoubtedly, what is most remarkable about the CNIC is its capacity to change the way cardiovascular disease is treated and influence and improve the health of our citizens.



RESEARCH WITH REAL IMPACT ON THE PATIENT

Excellence and quality in research are achieved, mainly by ensuring human resources. A careful selection process of scientific personnel, its periodic evaluation by an external committee of excellence and cutting-edge technological supply have allowed the CNIC to establish a paradigm shift in Spanish cardiovascular research, transferring the results to the patient. Many of these findings have been determinants to introduce modifications in the recommendations of the European Society of Cardiology (ESC). Among those that the CNIC has achieved in these 14 years we highlight the following:

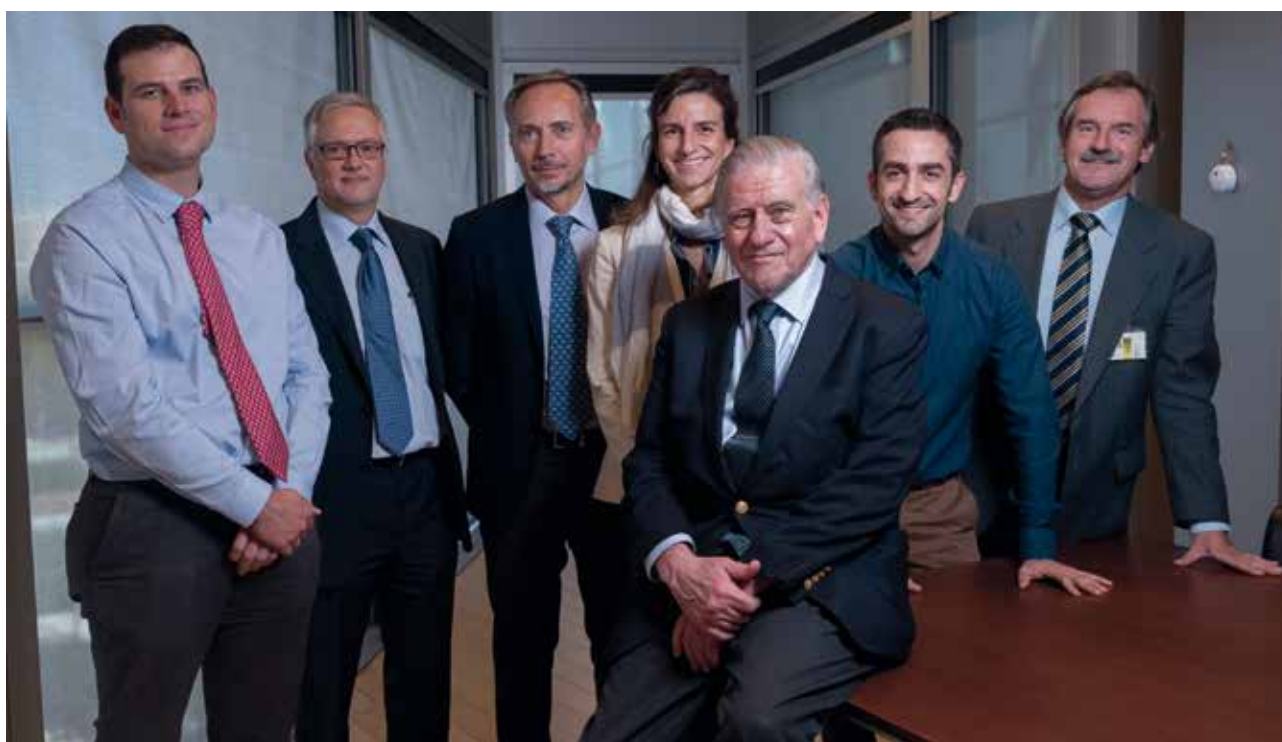


PESA-CNIC-Santander Study

The PESA-CNIC-Santander study, with more than 4,000 employees from Santander Bank, evaluates the presence and development of subclinical atherosclerosis (without symptoms) thanks to the use of innovative imaging techniques. It is providing essential information for the prevention of cardiovascular disease in apparently healthy people. In these past years, the study has shown, for example, that it is possible that a more effective reduction of 'bad' or LDL cholesterol is needed, even in those people classified as optimal risk; that a low 'energetic' breakfast (<5% of daily calories) duplicates the risk of atherosclerotic lesions; that little or poor sleep increases our cardiovascular risk, or that the 3D ultrasound is a key tool for identifying that risk. Its different findings have been published in several scientific articles and magazines like ***Journal of the American College of Cardiology (JACC)*** or ***Circulation***.

CNIC Polypill

The public-private collaboration between CNIC and the pharmaceutical company Ferrer produced the first polypill approved in Europe for secondary cardiovascular prevention. The drug, available in Spain since 2015, is indicated for those patients who have overcome a cardiovascular episode and require a treatment to reduce the risk of a second incident. The medication includes three active ingredients: an antiplatelet drug to prevent formation of thrombi, a statin to control cholesterol levels and to stabilize the atheroma plaque and an antihypertensive. Since its commercialization, the 'Fuster Polypill' has generated more than 1 million euros in royalties. This drug, approved in 50 countries and marketed as Trinomia®, offers an important advantage: its low price and simplicity, as patients only need to take one capsule, with the subsequent improvement in adherence.



Resonance in one minute: VF 3D-ESSOS

The agreement signed with Philips allows the CNIC to provide the most advanced cardiovascular imaging technology. Thanks to this agreement, a magnetic resonance (MR) patent has been developed, which is the best technique to study the function

and anatomy of the heart. The patent VF 3D-ESSOS software for magnetic resonance has reduced the examination time to less than 1 minute, compared to the more than 30 minutes that are currently needed. With this software, this technique can be used in more patients, improve diagnoses and reduce waiting lists.



Diagnostic kit for myocarditis

Myocarditis is a disease that is sometimes confused with a myocardial infarction, which makes it difficult to diagnose and can therefore lead to inadequate treatments. The CNIC has developed, validated and patented a biomarker for its diagnosis, and

is currently working on the joint development and license of the CNIC patent with a company to design a biochip capable of detecting the biomarker in patients' blood samples in 30 minutes, something that would be a fundamental tool in clinical practice for the differential diagnosis of acute myocarditis and myocardial infarction.





Creating a talent pool in cardiovascular research

Another one of the pillars of the CNIC is the attraction of young talent. **Dr. Valentín Fuster** returned to Spain to lead this project because he was convinced of the big talent pool that existed in our country, where there is a research base of excellence and that is very competitive. The private funding of the Pro CNIC Foundation has allowed the creation, and will continue to do so for the next 10 years, of a training and talent recruitment program which will identify and train the brightest youngsters that from the early stages of their education have shown interest in science and research.

This program, called **Young CNIC**, covers all the steps of the scientific career, from secondary education until the post-doctoral stage. Thanks to it, the CNIC has a talent pool of excellent professionals that will lay the foundation for research in the future. Since 2006, more than 6,000 participants in the different programs of training, have benefited from it. Many of these students who started in the initial programs when they were very young, now work in reputed research centers putting their talent at the service of science and the improvement of health. Some of them have gone through almost all of the CNIC programs and have remained in the center developing their research work.



Healthy Businesses

The advances of the CNIC have a positive effect on the fight against cardiovascular diseases, whose economic, social and human impact are reaching dramatic and unsustainable rates for the system. The technological and scientific advances in the treatments of cardiovascular diseases have managed to prolong, in many cases, the life of the patients, but the analysts coincide in that its application is an unsustainable expense for any health system.

Dr. Valentín Fuster is convinced that the approach to these diseases should radically change and many of his projects are focused on how to get to know and promote health, thus preventing illness.

The Pro CNIC Foundation has also joined this health promotion and, in recent years, has devoted an important part of its effort to the dissemination of healthy habits to all of society and, in particular, to the employees of its members.

The Pro CNIC companies have become promoters of healthy habits among its workers and their families with the support of the CNIC. These health plans in are very well-accepted by the companies' employees and have even received external awards recognizing this work. They are responsible companies that:

- Seek to end the number one cause of death in the world – cardiovascular pathology.
- Take care of the health of their employees and their families.
- Reduce the country's health expenses.

Promoting heart-healthy habits in society

With the advice of **Dr. Fuster**, the Pro CNIC Foundation has launched several campaigns to disseminate healthy habits to the Spanish society. The results have been very positive. It is worth mentioning the mobile app "The Circle of health" and the campaign "The tribe of the heart". The latter was launched through the Social Project of Mediaset Spain, together with the Pro CNIC Foundation and **Dr. Valentín Fuster**. "Having a healthy heart is in your hands" is the motto with which 'The tribe of the heart' took off. Taking proper care of this organ, that moves the world and gives us life, is the goal of this campaign, that seeks to create awareness through music, art and humor about the need to have healthy lifestyle habits in order to prevent cardiovascular diseases in children and adults.

Also worth mentioning is the initiative that is being developed together with the MAPFRE Foundation, also a member of the Pro CNIC, called 'Women for

the Heart'. This campaign started in 2014 to raise awareness and facilitate early recognition of the symptoms of cardiovascular diseases among women and promote healthy lifestyle habits. The campaign is allowing society to learn that cardiovascular disease is the first cause of death in women and that they too are prone to having heart attacks. ■



PRESIDENT OF THE PRO CNIC FOUNDATION

Luis de Carlos



THE CNIC AND THE PRO CNIC FOUNDATION: A MODEL OF PUBLIC-PRIVATE COLLABORATION

The Pro CNIC Foundation has just renewed the commitment, acquired by the 13 private companies that constitute it, to continue participating in the National Center for Cardiovascular Research (CNIC), directed by Dr. Valentín Fuster, until the year 2028. Thanks to this innovative example of public-private collaboration, the CNIC has established itself as a worldwide reference in the field of biomedical research. Consequently, the CNIC has been awarded the Severo Ochoa accreditation in recognition of its international excellence in the field of research. The Pro CNIC Foundation, directed by Mr. Luis de Carlos, is an entity through which these 13 pioneering companies channel their contributions for the funding of the CNIC, which has made it a benchmark for success in scientific patronage. In it, you can find the solidarity interests of some of the most important companies in Spain: Acciona, Santander Bank, BBVA, Endesa, Mapfre Foundation, Mutua Madrileña Foundation, Ramón Areces Foundation, Repsol Foundation, Naturgy, Inditex, "la Caixa", Prisa and Telefónica.

The Pro CNIC Foundation has extended the collaboration agreement with the CNIC until 2028. What is the Pro CNIC's participation in this agreement?

In 2006, the Pro CNIC Foundation was created to channel private funding to the CNIC. Through its Board of Trustees, companies not only give funding, but also participate in the decision-making and planning process of the center, contributing their business expertise in the daily management of the CNIC. We must not forget that cardiovascular diseases are the first cause of death in developed countries and, therefore, also in Spain. Every year, more than 120,000 people die in our country because of these pathologies that also cause more than 5 million hospital admissions. Due to this, it is essential to act in two areas: **prevention and research**. But faced with an epidemic of such magnitude, it is not enough to bet on traditional research, which may take years to reach the patient, but rather, it is necessary to promote the so-called translational research, which is applied to humans as quickly as scientific rigor allows. In this sense, one of the most important bets for Innovation and Research Development (i+R+D) was the creation of the National Center for Cardiovascular Research (CNIC). An ambitious project, leader in its field, that requires a double

way of financing to guarantee a high level of excellence in its activity. While a part of it is funded through public investment, the private funding comes from the Pro CNIC Foundation. This involves an intense work of scientific patronage and a referential public-private collaboration.

What does their participation in Pro CNIC mean for the companies?

The companies that make up the Foundation demonstrate with this contribution not only a resolute commitment to Innovation and Research Development (i+R+D) but also a solid commitment to an issue of great social interest: the health and quality of life of society as a whole. The advances of the CNIC have a positive impact on the fight against cardiovascular diseases, whose economic, social and human impact is reaching dramatic and unsustainable rates for the system. In short, the Foundation represents the high level of social responsibility of the member companies. Through this entity, they join together their efforts and channel their commitment to research and scientific patronage. A commitment that also means the great privilege to participate in the progress of our country with research as the main engine of development.

“In order to include, in clinical practice the projects that started in a laboratory, it is necessary to have an ongoing and especially sustainable investment”

What are the characteristics of this innovative model?

A fundamental strength of this commitment model is that it offers a more solid foundation than traditional forms of charitable financing, providing the CNIC with a more stable economic support than if it were based on sporadic donations from benefactors. This stability gives the CNIC greater freedom to commit to long-term and high profitability research strategies in collaboration with public and private institutions and allows a more efficient use of its own resources generated by competitive projects and the exploitation of its intellectual property rights. With this additional funding, the CNIC may invest in fundamental areas where public funding does not reach, for example, special programs for discovery and training of young researchers, external scholarships aimed at integrating basic and clinical research to respond to specific issues, acquisition of special research equipment and programs to encourage and keep valuable researchers. As a result of this collaboration, the CNIC not only has an important portfolio of programs of incalculable social impact already, but these results have also been improving exponentially throughout these years of collaboration. That is, the public-private collaboration itself has contributed to the excellence that has been recognized in turn with more external collaboration, through scholarships and international projects.

What would you highlight from the collaboration of these past years?

In these past years, perfectly quantifiable advances have been registered. For example, the number of publications with an impact index of greater than 10 (that is, those that are more cited in the work of other scientists and, therefore, have a special influence on knowledge) have multiplied by seven. Front-line magazines like **Cell**, **Nature**, **EMBO** and **Science** have collected studies directed by CNIC researchers on their pages. The translation from basic research to clinical research is one of the CNIC's distinguishing features. In order to include, in clinical practice the projects that started in a laboratory, it is necessary to have an ongoing and especially sustainable investment. Once again, the commitment of the members of the Pro CNIC Foundation, guaranteed until 2028, is essential for this research to have a direct impact on the quality of life, which already happens with some of the projects launched at the CNIC.

Any project in particular?

Among many others, initiatives such as the Metocard trial, which studies the beneficial effects of administering a beta-blocker, Metoprolol, to stop the damage of the heart,

to people who have suffered a heart attack. Current clinical practice recommends administering this drug once the patient has already arrived at the hospital, but the hypothesis of the CNIC's study, though very daring, proposes the administration of the drug while the patient is in the ambulance, on the way to the hospital, with a clear objective: to reduce the size of tissue that is destroyed after this common cardiovascular episode.

I would also like to emphasize that some of the findings that have been achieved at the CNIC, and that are the result of continuous years of research, have been decisive to include changes in the performance recommendations that the European Society of Cardiology (ESC) makes every year. The CNIC is mentioned nine times in the new ESC guides.

Another project which is closely linked to public-private collaboration is the polypill that, developed together with the Ferrer laboratories, agglutinates in one single tablet the necessary treatment after a first myocardial infarction (aspirin, statin and an ACEI), which means reducing health care costs and improvement in the quality of life of the patients (who will have to take one drug instead of three, which will also make it easier for them to follow the treatment). This drug is also a perfect example of how the research resulting from the collaboration between different entities can be profitable.

Lastly, we must also highlight the PESA CNIC-Santander Group and Botín Foundation program, where labor health and occupational risk prevention services of the Santander Bank collaborate with the CNIC to measure cardiovascular risk factors in volunteer employees. Thanks to this program, in a few years, not only will employees have healthier habits, but also clinical signs that currently go unnoticed and that could be indicators of cardiovascular pathology will have been identified and will allow early intervention in apparently healthy patients. More than 4,500 workers between the ages of 40 and 54 participated in the PESA program, and the analysis of the data will also provide valuable information about the heart attacks not detected in the general population.

One of the labels of excellence of the CNIC are the training programs and the recruitment of talent. How are these coordinated?

The CNIC-Young Training Plan deserves a chapter of its own. With the aim of attracting and training the brightest young people from the earliest ages (17-18 years old) and since 2006 the CNIC seeks to create a reserve of researchers of excellence in the field of cardiovascular research. The Plan is structured in several training programs, with an international and open approach that promotes periods of training in foreign centers and manages to attract talented young people from other places in the world. While collaboration with companies and private entities that make up the Pro CNIC Foundation is fundamental in all aspects of the center, it is even more essential in the area where youth training is concerned, since it is a long-term investment that counts on very little political return.

At this point, it is vital to emphasize the fundamental role of the researcher. It is well known that excellence and quality in research are achieved, mainly by ensuring human resources. A careful selection process of the scientific personnel, its periodic evaluation by an external committee of excellence and state-of-the-art technological supply (mainly in terms of cardiovascular imaging) guarantee productivity of the CNIC and promote a paradigm shift in Spanish cardiovascular research. This change of mentality is also observed when analyzing alliances of the CNIC, a strong supporter of teamwork that considers that it must be integrated with other entities that are directly related to health. The CNIC has established an extensive network of collaborations and contacts with the National Health Service System (SNS) to carry out projects of research, establish training programs and promote exchange and mobility of researchers between the CNIC and the SNS. It is important to highlight, for example, the INVESMIR program, which gives future doctors the opportunity to do a research project at the center's laboratories, supervised by CNIC scientists. Finally, the CNIC contributes very importantly to the Cooperative Research Thematic Networks and the activities of the Spanish Society of Cardiology.

What does the Severo Ochoa accreditation mean?

Thanks to these achievements, the CNIC has received the Severo Ochoa accreditation, as an international reference center in cardiovascular research. This accreditation, which has only been granted to 10 leading and cutting-edge centers, is valid for four years and will provide 1 million euros per year during this period. This recognition, awarded by a panel of international experts formed by renowned scientists, among whom include three Nobel Prize winners, will allow the CNIC to strengthen its research capabilities. This stability gives the CNIC greater freedom to commit to long-term high profitability research strategies in collabo-

ration with public and private institutions, as well as facilitate the way to other competitive calls, have preferential access to the large research facilities, enjoy flexibility in the hiring of personnel (scientists and technologists) and hold a scientific recognition that offers preferential visibility in obtaining patronage support, among other benefits.

How do you see the future of the CNIC and the Pro CNIC?

The recent renewal agreement signed by the secretary of Scientific Coordination, **Mr. Rafael Rodrigo**, and by me as president of the Pro CNIC Foundation, consolidates the CNIC as a world leader in the field of biomedical research. We are convinced that this innovative formula of public-private financing will allow the CNIC to remain as a world leader in cardiovascular research whose benefits are transferred directly to the patient. We have proven that it is an effective and sustainable formula that, ultimately, guarantees excellence in cardiovascular research, the only way to advance in the fight against what is known to be the first cause of death in developed countries and that is soon to become so in the poorest regions too.

And finally, I would like to give a special thanks to all the members for their constant involvement in the project and for their contribution to cardiovascular research. By the end of 2028 the companies of the Pro CNIC Foundation will have contributed more than 90 million euros to the project. It's definitely wonderful news for our country that this group of companies extends their commitment by demonstrating once more, through scientific patronage, its involvement both with innovative research development, essential for the competitiveness of our country, as well as for the substantial improvement of the quality of life of all the Spaniards. I think the CNIC is an example of a successful public-private collaboration and a model of the potential researcher of our country in the fight against cardiovascular diseases. ■



"The CNIC is an example of a successful public-private collaboration and a model of the potential researcher of our country in the fight against cardiovascular diseases"

MATRIX:

NEW AND INNOVATIVE TREATMENTS FOR CARDIAC TOXICITY, ASSOCIATED TO SOME CANCER TREATMENTS

**A PROJECT BY THE CNIC AND THE JIMÉNEZ DÍAZ FOUNDATION
UNIVERSITY HOSPITAL FUNDED BY THE EUROPEAN UNION
WITH AN 'ERC CONSOLIDATOR'**

The great advances in the treatment of cancer, a disease in which 4 million new cases are diagnosed every year in Europe, sometimes have a 'toll' to pay in the form of important adverse effects, such as cardiotoxicity. Up to 25% of patients receiving treatment with some of the most common drugs -anthracyclines and trastuzumab- develop some degree of myocardial toxicity, which can end up being very serious and condemn the cancer survivor to chronic heart failure or even to death from this complication.

The MATRIX Project led by **Dr. Borja Ibáñez**, Director of Clinical Research at the National Center for Cardiovascular Research (CNIC), has received an 'ERC Consolidator' grant from the European Commission, endowed with 2 million euros for the next five years, to develop new and innovative treatments for cardiac toxicity which is associated to some cancer treatments. MATRIX (Novel mitochondria-targeted therapies for cancer treatment-induced cardiotoxicity) will be jointly developed at the CNIC and at the Jiménez Díaz Foundation University Hospital (FJD) within a collaborative framework which started in 2015 to address the study of myocardial diseases.

Dr. Ibáñez explains that there are currently three major challenges in cardio-oncology: to know better the fundamental mechanisms responsible for the cardiac damage associated with these highly effective treatments; perform an early diagnosis of myocardial damage –nowadays this is only done when the damage is irreversible in many cases-, and develop specific therapies based on mechanistic knowledge -the treatments used today for cardiotoxicity are nonspecific and generally ineffective-. Based on the group's previous research in the field of mitochondrial biology and heart failure, MATRIX will address these three major challenges.

Mitochondria are the 'power stations' of cardiac cells and permanent damage to them produces severe and irreversible dysfunction of the heart muscle. MATRIX, explains **Dr. Ibáñez**, works on the hypothesis that the different effects induced by these drugs in the heart converge in a final mechanism of global deterioration in energy production by the mitochondria. "Thanks to the discoveries we have recently made in our experimental studies with advanced imaging, we are able to observe this damage in the mitochondria in a non-invasive way and very early on. Now- he adds -these findings will be transferred to the clinic for the first time." MATRIX will study, through these innovative cardiac magnetic resonance techniques, patients who start treatment with these drugs.

The main objective of the European Research Council (ERC) program is to finance 'ground-breaking' ideas that can revolutionize the health and society of the future. Its main criteria is to support research of excellence. The funded project is part of the ERC Consolidator Grant program which is aimed at young researchers, who have already shown great leadership directing their group, but are still in a consolidation phase. The ERC is the first European organization that collaborates in the funding of fundamental research projects based only on the criteria of a researcher's scientific excellence and the innovative strength of his/her ideal, regardless of his/her nationality or field of research.

The "Translational Laboratory for Cardiovascular Imaging and Therapy" directed by **Dr. Ibáñez** at the CNIC is eminently translational and, although it addresses issues related to biology and the mechanisms of disease and health, its ultimate goal is always to reach the patient. In fact, Ibáñez is also a cardiologist at the FJD Hospital and a group leader at the CIBER of cardiovascular dis-

eases (CIBERCV). His research-clinical duality places him in an ideal position to solve clinically relevant questions through basic and experimental research.

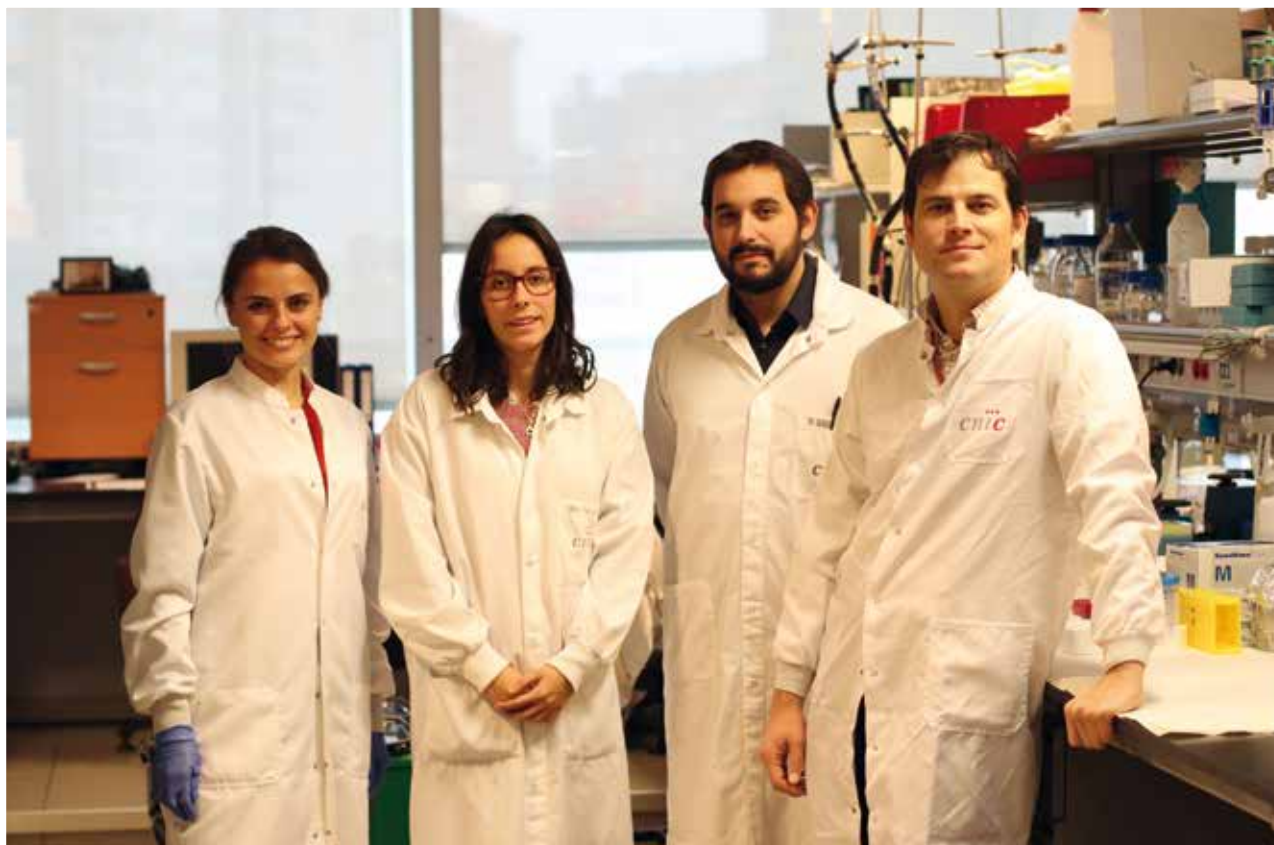
CARDIO-ONCOLOGY

In collaboration with the Jiménez Díaz Foundation University Hospital, the team has already started a clinical trial on humans within the Matrix study. "100 patients with lymphoma will be recruited and will receive chemotherapy treatment that includes high doses of anthracyclines.

All of them will have an advanced MRI- including new sequences developed by the group- before each cycle of chemotherapy, and they will also be monitored very closely".

One of the most 'innovative' and 'radical' treatments proposed by MATRIX is the auto transplantation of healthy mitochondria to replace those damaged by cancer treatment, something never done before and for which the group has very solid preliminary data which will help convince the European Commission of its viability. "It is about - explains the researcher - a radically new approach and that we intend to take to the clinic if MATRIX is successful. This would be a paradigm shift in the treatment of heart disease". ■

MATRIX works on the hypothesis that the different effects induced by these drugs in the heart converge in a final mechanism of global deterioration in energy production by the mitochondria



A CAREER AT THE CNIC



Alba García Escolano, Julio César García Rubio, Carlos Martí Gómez-Aldaravi and Eliú David Pérez Nogales are four examples of the talent pool of young researchers and doctors who have been trained, or are currently doing so, at the CNIC. **Julio César** and **Eliú David** met at the CNIC in 2007 and in 2015 were reunited once again at the same place. They have gone from being high school students with a grade point average of 10, to Cardiology residents, Julio at the Cabueñes Hospital, in Gijón, and **Eliú** at the Insular Hospital of Gran Canaria. **Alba** and **Carlos** are younger. Both benefited from Acércate and Cicerone Program and the CNIC Master Scholarship, and now they are doing their PhD at the CNIC.

How do you rate the training programs that the CNIC has to offer?

Carlos: Very positively. Each program is a good opportunity to enter in different levels of the world of research. In my case, both in high school and at the beginning of my degree, I found myself quite disconnected, especially on a practical level.

Alba: In my opinion they are very rich: they allow students from different branches and levels to get to know the world of research very up-close. Until my senior year

of high school, I only knew science as I read it on the Internet or saw it on television, but after going through the Acércate program and the rest of the programs, I realized what it means to actually do science: a hard road, but at the same time rewarding, that one never finishes traveling through completely.

Julio: The CNIC is a research center of excellence that has always considered training as an important pillar. I have had the enormous privilege of knowing it almost from its origins, when the building was not even functioning at full capacity, and right since then one could feel the teaching spirit of the center. The training plan CNIC-Joven has been evolving with time, significantly increasing the offer of programs, as well as the profile of people to whom they are directed at. Nowadays, it accommodates many different types of people, from those who have just finished high school to doctors who have already finished their specialty, and even graduates or graduates from other areas and post-graduate students too. It also offers scholarships that give the possibility to train future researchers of excellence abroad and programs that attract talent from other countries to the CNIC laboratories. In short, it is difficult to find a research center that has such a complete and diversified training program.

Eliú: At the moment, Spain is not really known for its support to research, to researchers and even less to the programs that combine clinical and basic research. At first, the CNIC brings the young person closer to research and, then, to the clinic. It does this in a simple way, and by providing everything that is necessary. This training offer is necessary and up until now, it is one of the few centers that promote it in such an energetic way.

How did you get involved in the Acércate program and what memories do you have from it?

Julio: I got to know the CNIC when I was 17 years old and was studying the Bachelor of Health Sciences. During my pre-university phase, I was very fortunate to have the support of José Ramón, my tutor and Physics and Chemistry teacher. Through him, I discovered research: we studied the relationship between the location of mobile phone antennas and cancer and we won fourth prize in the San Viator Research Awards. I have very good memories of all those afternoons we spent collecting and analyzing data. A few weeks before taking my university entrance exams, José Ramón recommended that I sign up to join an innovative research program offered by the CNIC. And that's how I got involved in the Acércate program. After going through a difficult selection process and demonstrating a good level of English through a telephone interview, I was fortunate to be one of the eight participants of that edition. I have very fond memories of those weeks and was very lucky to have such wonderful colleagues, all of them are great people, and some even close friends, like Eliú. We were the only two who chose Cardiology and we have continued to stay in touch both inside and outside the CNIC.

Carlos: My biology teacher at the time, was the one who first spoke to me about the Acércate program, already in one of our last few classes of my senior year of high school, while preparing for the university entrance exam. The truth is that I never thought they were going to give me a spot, but just for the sake of trying, I applied, and in the end was lucky. I remember most of all how intense the days were, they explained new things to us almost non-stop and it was very stimulating at the time. I learned a lot in the short time that the program lasted, and little by little I started realizing that they were very advanced things, things that I wouldn't have seen until the end of my degree, and sometimes not even. For example, I remember quite well what we learned about flow cytometry and how the basic markers of death worked, cell division, how to define cell populations; how qPCR works; mass proteomics, the confocal microscope, etc. These are concepts



and technologies that I have assimilated quite well now, but at the time I knew nothing about, and it would have remained like that for a long time, if it hadn't been for the program.

Alba: I had always liked Biology and at the end of my last year of high school and already a step away from the university entrance exams, I wanted to find out if there were any summer programs to know more about the science of this subject. Searching on the internet, I found the Acércate program and was one of the lucky ones who got to enjoy it. I personally have very good memories about this program. That year we rotated through different areas under a common context, which was to research leptin in mice, and I remember mostly how much I was impressed by microscopy and proteomics and the technology that surrounded it. During the program we applied different techniques and methodologies, and began to feel like young scientists. Lastly, I would also highlight the social aspect of this program, because thanks to its leisure and scientific activities very close ties were created among the participants.

Eliú: So much has happened since then! It was 2007 when I had my first contact with the CNIC and I remember that time with a lot of nostalgia. In high school I had just started an optional subject called "experimental sciences" where very few students had enrolled. I attended it for two years, **Carmen** and **Manolo** were the teachers. Their enthusiasm was contagious. Almost at the end of the school year, Manolo told me that he had sent my application to a research program that he came across, and thought that I could grow a lot by going there, that there were only seven people admitted in Spain but that we had to try. Soon I received the famous phone call in English and, without even realizing it, I was embarking on my first research adventure. The program could not have been more productive, nor of better quality. I had never seen a big laboratory until then, and I was fascinated. It seemed like I was in another world. We were given a manual that had to be studied beforehand, which I greatly enjoyed and still keep. We learned and conducted a vast majority of experiments that I had only seen in books, from electrophoresis (doing the whole procedure from the beginning, creating our own gels) to mass spectrometry (I admit that this was a little bit more difficult for me to understand how it worked). The dedication of all the

staff was incredible. That's where the seven of us, from different parts of Spain met, and today some are even work colleagues and, most importantly, friends. I cannot go without mentioning two of them, **Julio** and **Noelia**, my work colleagues. I defended our small project at the end of the pro-

gram with Noelia, and at the time she was three heads taller than me and was a very strong-minded woman, I was just a small and shy little boy who had not yet gone through the growth spurt ... we were a very strange pair. Afterwards, Noelia was also my university colleague during my Seneca university exchange program in Valencia. With **Julio** I have gone through a lot too, we both did the Cardiology residency, we met up again in the Res@CNIC program and he's a good friend, who I've had the pleasure of being a guide to in my little island.

Which people helped you the most throughout your career, teacher, tutor, etc.?

Carlos: It's difficult to pick just one specific person actually. In the end, I think we take a little bit from all of those that cross our path, and help us in one way or another: from my thesis directors **Fatima** and **Enrique**, to other CNIC people with whom I was lucky enough to work with during the summers or university professors with whom I did not even have a relationship with apart from the classes, up to of course my family, who has always been there for support.

Maybe during the time that it all happened, I could highlight **José Blanca**, who along with my genomics and bioinformatics teacher, **Ximo Cañizares**, were my directors of my final end of degree project in Valencia. Both of them, along with the rest of the group in which I worked taught me a lot and, possibly, made me decide to dedicate myself to bioinformatics, since then.

Eliú: Without a doubt, the main support has always been, and will be, my par-

ents. None of my ideas were ever crazy enough for their question to be no other than: "And what do you need? How can we help you?". Without them I wouldn't be half the person I am. Secondly, teachers, those people who are the real "influencers" of society. I deeply admire all those that took their time to teach me, but unfortunately I cannot name them all. **Eulaia Guerra**, my teacher throughout my whole childhood, an extraordinary woman in a small town in the Canary Islands who always taught us that first we had to learn how to be people and, later, learn knowl-

edge. We used to put Mathematics class on hold while the whole class called one of the classmates that had just had surgery, or at times stop just to solve problems between classmates. All while teaching us math, literature, grammar ... I do not know how she did it. Afterwards, in high school there were also three teachers that stand out, two of whom I have already mentioned, **Carmen** and **Manolo**, and also **Estrella** (my tutor and Biology teacher). Her human nature, enthusiasm for her work, unwavering moral to continue teaching, despite being a group of somewhat problematic students, makes you to never forget them, and to always feel grateful. And then at the CNIC, **Dr. Fuster** and all the staff I met there, they did something different too, they didn't just push, they twisted this career, they changed its direction. Without the CNIC, I would never have developed the interest that I currently have in clinical and basic research. Not only did I learn techniques, but also the symbiosis that exists between medicine and basic research, that one cannot advance without the other. Without basic research there are no new therapies and, without clinical research, you cannot get data from the population about these. Without these programs I probably wouldn't have decided to do an undergraduate in statistics and research methodology during my residency.

Julio: As **Dr. Valentín Fuster** indicates, the figure of the mentor is essential to help us focus on our objectives and motivate us to work to achieve them. In addition to **José Ramón** in the pre-university stage, during the degree I also had great support from several professors, among whom I'd like to mention **Professor Alfonso López Muñiz**, current dean of the Faculty of Medicine and Health Sciences of the University of Oviedo, **Professor Serafín Málaga**, professor of Pediatrics with whom I could collaborate in some studies, and **Professor Serafín Costilla**, head professor of Radiology. Currently, during my time as a resident doctor, I have felt especially supported by my tutor, **Dr. José Miguel Vegas** and **Professor Íñigo Lozano**, responsible for the Hemodynamics Unit and Interventional Cardiology of the University Hospital of Cabueñes, who is also my doctoral thesis tutor. I also have great admiration for **Dr. Jaime Baladrón**, director of the MIR Asturias Course, for his human nature and his enormous work capacity. He has also given me the opportunity to help be a teacher to others doctors, which is a truly rewarding job.

Alba: Ever since I was little I had always wanted to research, but the first person who showed me the love for my particular field was my tutor of the final end of degree project, **José María Ferrero**. He is an exceptional teacher and turned that project on computational models of fibers of Purkinje into an adventure that you just wanted to know more and more about: it propelled me to science. In that search, I met my current thesis director, **David Filgueiras**, who has helped me a lot and has taught me what research is like on a multidisciplinary team and beyond computing. A lot more people, in a direct or indirect way have fostered my vocation and have helped me, but I'd like to highlight the support that I have always received from my family and friends.





The four of you are back at the CNIC with different programs: Cicerone, Res@CNIC, etc. Was it your first choice or did you consider other options?

Eliú: Since I started residency and found out about this program I tried by all means to attend. It was complicated and I was a pain for the tutors, since I had to modify the entire first year training plan to include the program. In regards to the research group, I was in one of **Dr. Miguel Torres'** fields, directed by **Dr. Silvia Martín:** her group investigated the role of hypoxia in the development of the heart. There were some groups with a perhaps more clinical approach, which were a little more similar to my daily practice in the hospital; but nevertheless, I was interested that it be basic research, going back to it, in order not to forget it. It was a great experience, and I spent practically the whole day between the walls of the CNIC. It's true that it gave me a certain feeling of "maybe I'm missing something from the clinic, studying and hospital work ", so I stayed in the library till nighttime in order to be able to study "things for the residence". But nothing could be further from the truth, what it gives you and the change of perception of what is around you cannot compare to that time you invest in it. It's worth it, and I think a similar period should be included in the MIR training programs. I greatly appreciate everything the team taught me.

Julio: In the Acércate program, I doubted between studying Medicine or Biotechnology. Thanks to the advice of the CNIC researchers, I finally opted for Medicine as it is a more open career in terms of work perspectives. The day you hang a stethoscope for the first time around your neck is when you realize that you made the right decision. However, in my fifth year of Med school I felt the need to have contact with the basic research that I had discovered years ago in the Acércate program. That's why I joined to the Cicerone program with **Dr. Ignacio Flores.** They were two very interesting months of work. At the end of my degree, I

was certain that I wanted to do my specialization in Cardiology and I already knew the Res@CNIC program. When I visited the hospitals to choose the one to do my MIR at, an important factor for me was that they let me participate in the Res@CNIC program during R1. I finally chose the University Hospital of Cabueñes (Gijón), and I started working with the authorization already signed by the hospital to go to the CNIC in January.

Carlos: Honestly, it was my only option. I did not know other types of paid summer internship programs at that time, and given my positive experience at the CNIC I thought it was worth trying again. And I was lucky to get a vacancy for several summers during my studies, as well as to know many different research groups and quite varied research topics. The Cicerone program already provides a good opportunity to let you do things yourself and even think that you are helping the person who is teaching you, move forward with their work. It also allows you to learn about a certain topic in much greater depth and how to set up experiments to answer open questions.

Alba: I came back with the Master Scholarships and it was always my first choice., because I wanted to continue studying cardiac arrhythmias. In my case, I highly value this program because it allowed me to develop my final end of Master Project at the CNIC and learn and study more in depth about arrhythmias, assimilating everything for what I would later continue during my doctoral thesis.

Why the CNIC?

Eliú: It might be lack of knowledge, but I don't know any programs in other centers where young people, and later, health professionals, are encouraged, given financial, human and organizational resources to access this field. Actually, they make everything really easy, and once you've done one program, you'll be back. To me, the CNIC as has always had its doors open to receive the clinician: the "from

genes to the clinic" days are a clear example. The CNIC is not just a basic research center, it's also a link between basic and clinical research. And that's precisely what makes the CNIC so special.

Alba: the CNIC is the national center of reference dedicated to cardiovascular research, which is the field that I'm passionate about, and has cutting-edge technologies that allows high-level research to be developed. In addition, the presence of different groups and units facilitates collaborations, where multidisciplinary groups are created in which engineers, biologists, doctors, etc. participate, and which allow for the studies to be enriched with different perspectives.

Julio: In general, us doctors do not have much contact with basic research. During med school, the majority of the contents are clinical and our day to day is in the hospital and not in a laboratory. The CNIC, with its great commitment to translational research, is leading doctors to the lab and is bringing basic researchers closer to the patient. In this way, the center offers an exceptional opportunity for us clinicians to see first-hand what we are doing - for example, at the molecular level so that our field can advance. For residents who have just started specialized training, the Res@CNIC program means an initial contact with research. Thanks to the agreement with the Spanish Society of Cardiology, I trust that better conditions will be offered more and more to reach as many residents as possible. Then, if the residents are interested, they can stay longer in their last months of training (InvesMIR program), although sometimes it is difficult to organize the different shifts in order to be able to participate in this program. Knowing the center also helps to establish different collaboration agreements in the future with the different hospitals in the country.

Carlos: The CNIC is one of the best and best financed research centers in Spain and has all the latest technologies. Also, since it is a powerful research center, very different subjects are studied, so you can learn a lot even about things that do not directly affect your own work, but are very interesting scientific questions. At the same time, there are a lot of young people with whom to share the sorrows and joys of the thesis.

Carlos and Alba, you are currently at the CNIC in Enrique Lara and David Filgueira's groups, respectively. What aspects can you highlight about your work and your current training process?

Alba: In my case, I would highlight the opportunity to work with various types of high quality data: from magnetic resonance images to study the structure of the heart to optical cartography records to identify the electrical dynamics of arrhythmias. This allows connections between cardiac features to be established, that without the existing technologies at the CNIC, this would be practically impossible to study thoroughly. As an engineer, I process this data computationally, but my role is not limited to just this activity. Being able to develop my thesis at a center like this

has given me the opportunity to intrude in the experimental part to be able to obtain such data and be aware of its advantages and limitations. This is very helpful during the analytical process later. Finally, I would highlight the possibility of working with a multidisciplinary group in which biologists, biotechnologists, engineers and cardiologists join forces to research the arrhythmias. You realize how valuable this is when we discuss a topic and there are a wide range of opinions that allow high quality projects to be built, in every way.

Carlos: What I like the most about my work is the idea of being able to answer biological questions that cannot be done with more traditional methods, trying to decipher the underlying patterns that direct a coordinated response to certain stimuli; from a heart attack to an increase in pressure in the heart. In addition, bioinformatics gives you the opportunity to explore many ideas without the need to invest a big amount of time to generate experimental data derived from public data that has already been used for other objectives. It is also a very broad field that allows you to learn about very diverse topics -biology, computer science, statistics, algorithmics, mathematics-, and try to apply all that knowledge to solve a specific problem.

Do you think that these type of programs, especially Acércate, are useful to reach out to the young people and get them more interested in science?

Julio: Yes, programs like these are the ideal way to connect young people with science and attract talent to research. They allow you to discover first-hand the reality of science in our country. In my case, thanks to Acércate, I was able to orient myself and choose what degree to study - Medicine won over Biotechnology -.

Alba: I think that many young people who want to participate in these types of programs are already attracted by science, but need a little push to start their research careers in early stages. That's where the training offered by the CNIC comes in.

Carlos: It's hard to know what would have happened if I hadn't participated in these programs, for me, they were very stimulating and interesting, and it's possible that they helped me to choose which path to take.

Eliú: I have no doubt whatsoever. It is a completely unknown area to someone who's just finished high school. A little anecdote that illustrates this, although remembering it, makes me a bit embarrassed: when they accepted me into the Acércate program, I did a little interview for my town newspaper where they asked me my opinion about **Dr. Fuster** and his work. My response was that I didn't have the pleasure of knowing him. If a teenager is asked to name a famous athlete, musician, designer, they can probably name two or three. In the field of research, this is not the case. These programs do just that, they bring the reality and the world of the researcher to the young generations, exposing them to an area that they have never experienced, and that could generate interest and dedication.



ALBA GARCÍA ESCOLANO:

"I would highlight the possibility of working with a multidisciplinary group in which biologists, biotechnologists, engineers and cardiologists join forces to investigate the arrhythmias"

With your experience in the CNIC's different training programs, what would you highlight, and what aspects could be improved?

Julio: If I'm not mistaken, I think I'm the person who has participated the most in the programs: CNIC- Acércate, Cicerone, Res@CNIC and an Open Day experience some years ago. These are very powerful programs from a scientific point of view and are very well prepared for the candidates who participate in them. I have always felt very valuable for the CNIC as they seriously consider the feedback that we give them. Actually certain details are corrected from one year to the other in order to improve the programs. For example, with the Res@CNIC program, when I attended, there was no help for doctors who came from other communities. This issue was brought up at the final meeting of the program and the following year funding was obtained for this.

Alba: The CNIC programs stand out for their wide range of training at all levels, which allows you to enter into research sooner, during and after university. They definitely help you train and make important decisions related to the professional future in different stages of life. In addition, they allow you to get to know the activity of the various groups through seminars and have financial independence to research. In regards to areas of improvement, although this situation is evolving, in my case in particular, and after the Acércate program, I ended up thinking that there was no engineering activity (we had no contact with engineers) at the CNIC and that it was very unlikely that I would end up researching in this center. In that sense, it is necessary to emphasize the role of the engineer as part of biomedical research groups, although this occurs more and more with the presence of multidisciplinary teams and a greater number of seminars related to this area.

Eliú: I would highlight one point in particular: the sacrifice and dedication of everyone who works in research. It is amazing how, without complaint or tedium, every researcher took all the time necessary to clarify the issue at hand. They came on weekends to feed culture samples, take samples that needed to be processed on Saturday night or get certain devices that were very demanded during the week in untimely hours. We do not know how to appreciate this work, we do not value it and we do not give it the proper recognition. When you spend a few months with them, you learn this. Areas of improvement, not many really, maybe extend it to more people, but, like everything, this implies money, and the resources are not unlimited. On the other hand, I believe that the MIR programs and those offered by the CNIC during residency must be organized a bit better. I could not attend some of them because they do not contemplate such long periods of full-time dedication during residency. Maybe longer programs but on a part-time basis could encourage more residents to get involved and commit.

Carlos: I would highlight the wide offer there is at different levels. In the Cicerone program in particular, I think it's very positive that there are so many vacancies, so there are opportunities for more people. I also consider the financial endowment to be very important, which for example gave me the opportunity to have financial independence from my parents during the master. On the other hand, maybe the selection process could be improved. To give an example, in some European doctorate programs the candidates rotate through several laboratories a few months before deciding. While the Cicerone program can be useful for this purpose, which was my case, this is not usual. ■

DR. FUSTER RECOMMENDS 'TEAM WORK AND GOOD TUTORS' TO THE STUDENTS OF THE ACÉRCATE PROGRAM

EIGHT OF THE BEST SENIOR HIGH SCHOOL STUDENTS IN SPAIN, WITH A GRADE POINT AVERAGE OF 10, PARTICIPATED IN THE ACÉRCATE PROGRAM, ORGANIZED BY THE CNIC IN ITS CNIC-JOVEN (CNIC-YOUTH) TRAINING PLAN



Dr. Valentín Fuster, General Director of the CNIC, met up with eight of the best senior high school students in Spain, that participated in the 2018 Acércate Program and gave them essential advice to develop their future career in science and medicine: "Team work and good tutors or mentors".

"You are at a very important phase in your lives, and you need to start thinking about what you want to do and where you want to go", said **Dr. Fuster**, to whom these programs are key in the careers of the younger students.

"I myself, am the product of my tutors", he stated. **Dr. Fuster** advised them that "no matter how much you know; you always need a guide. I myself, right now, have some. The more complex life is, or a career is, the more important it is to have a mentor. It is he or she who will help you find your "talent", which in most cases goes

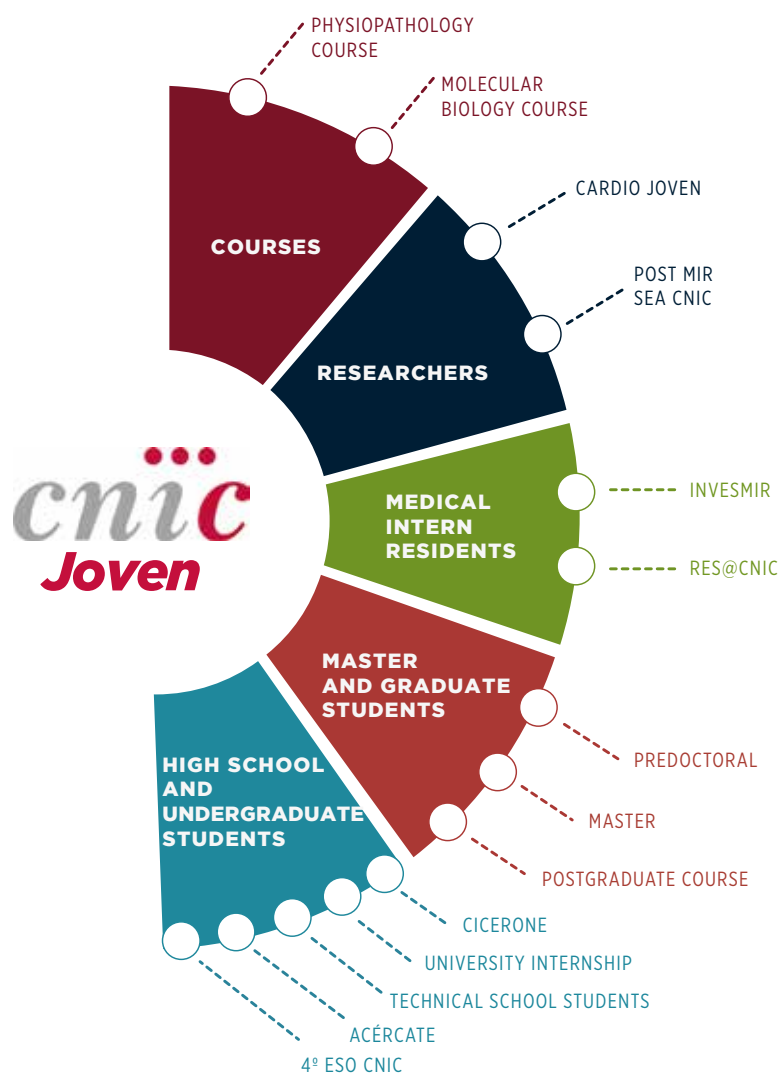
against "ambition". It will help you discover who you are", he advised. As for team work, "when I started out, it wasn't as important, but nowadays it is indispensable. In the future, your work won't make any sense if it isn't done on a team."

2018 PROGRAM

In the 2018 program, two students from the Community of Valencia participated, two others from Galicia, one from Extremadura, one from Canarias, one from Asturias and another one from Móstoles (Madrid). In total 104 students have already participated in the program, 38 males and 66 females. In the 2018 program, the eight young students were: **Raquel García Martín, Ana Hernanz Grimalt, Alba Arias Pascual, María Fernanda Hernández Martín, Belén Moldes Pais, Francisco Macía Guardado, Lidia González Teijido and Ana Montañana Pons.** ■

A COMPREHENSIVE TRAINING PLAN: FROM HIGH SCHOOL TO RESEARCHER

Training is a prime objective at the CNIC, therefore the center has developed a global training Plan called CNIC-Joven (CNIC-Youth) that covers all levels, from secondary education up to postdoctoral training and young professionals. A plan designed to bring biomedical research to young people and create a talent pool of future researchers of excellence in the cardiovascular field.



1. Coming out of class

The CNIC collaborates with the secondary schools of the Community of Madrid in different training programs:

- **Grade 10-CNIC.** Science students from eight different centers are at the CNIC laboratories between four to five days to explore possible scientific careers.

- **Practical Experience for students from Professional Training Schools.** This program brings together students from professional training schools to obtain practical curricular experience in the laboratories of the CNIC for three months. The CNIC has also signed collaboration agreements for internships throughout the whole school year (10 months) with the two existing Dual Centers in Madrid in the field of Biomedicine.

The CNIC also collaborates in this way with secondary schools from all over Spain:

- **Acércate.** The Acércate program offers top-performing senior high school students in the Social and Medical Sciences area, the opportunity to feel like biomedical researchers. The goal is to raise and increase interest in a biomedical research career. The participants spend two weeks at the CNIC, learning modern techniques used in biomedical research, conducting supervised experiments, operating sophisticated scientific equipment and presenting the results of their work, all under the supervision of the CNIC researchers.

2. Programs for university students

- **Cicerone.** Aimed at third and fourth year university and Master students that do their laboratory practice at the CNIC during the summer months. The duration

is 240 hours between July and September. Apart from completing a supervised research project, the students also attend CNIC seminars and workshops. The objective of the program is to give students first-hand knowledge of biomedical research so that they can make informed decisions about the possibility of studying a scientific career.

- **Curricular and Extracurricular Practical University Program.** The CNIC offers practical training for undergraduate and post-graduate students, including those who participate in the Erasmus program, completing their final end of year project, final end of master project, or Master of Arts.

3. Graduate and Master Students

- **Master Scholarships Program (CNIC-Acciona) and Carolina Foundation BBVA CNIC Master Scholarship Program.** These scholarships provide funds for students that study a master in a Spanish university to conduct their experimental Project in a laboratory at the CNIC.

- **Pre-doctoral Program (PhD).** Provides a unified framework for all researchers of the CNIC that are working on their thesis project to obtain a PhD. All pre-doctoral researchers are enrolled in this program, regardless of their source of funding. Their objectives are: to guarantee the uniform quality of pre-doctoral training at the CNIC and endorse fair and equal access of the pre-doctoral researchers to training opportunities.

- **Module of Introduction to research in cardiovascular diseases of the Molecular Biomedicine Master of the Autonomous University of Madrid (UAM).** This module provides a broad overview of cardiovascular biology, including the basic, clinical and translational research perspectives. Those who attend this course are students enrolled in the Master Program at the UAM, pre-doctoral researchers and participants of the CNIC and Res@CNIC SEC program.

- **Introduction to Research in Cardiovascular Diseases.** Post-graduate course run by the CNIC as part of the Master in Biosciences program.

4. Doctors of the present and the future

- **Res@CNIC Program.** In collaboration with the Spanish Society of Cardiology (SEC), this program offers resident doctors the opportunity, during the first years of their specialization, to learn about the latest cardiovascular research techniques that are used in the CNIC laboratories, under the leadership of a CNIC scientist. The residents that participate in Res@CNIC also receive training in theoretical aspects of cardiovascular

research through a didactic module led by experts. The program also seeks to create links and collaborations so that, when finishing their MIR specialization period, these professionals have the opportunity to undertake research projects in their respective hospitals in collaboration with the CNIC scientists.

- **InvesMIR SEC Program.** Offers senior resident doctors the opportunity, during their specialization period, to continue their training through a research project in one of the laboratories of the CNIC. An important goal is that the participants establish contacts and collaborations with the CNIC researchers that will support them, after completing their MIR specialization, in the search of their own research projects in their health centers of the National Health System.

5. The Researchers of the future

- **Cardio Joven (Cardio Youth).** Organized in collaboration with the Spanish Society of Cardiology (SEC), this program seeks to promote high-quality translational research in the cardiovascular area in the centers of the National Health System of Spain. It is directed at cardiologists who aspire to perform clinical work and advanced research in any of the Spanish National Health System centers and offers a training period to obtain a Master degree in epidemiology at the London School of Hygiene and Tropical Medicine.

- **Post MIR SEA CNIC.** Offers a one or two-year contract to medical professionals after their resident intern specialization (MIR) in cardiology or to cardiologists who are members of the Electrophysiology and Arrhythmias Section (Spanish Society of Cardiology - SEC), to work in a research project on electrophysiology and/or arrhythmias.

- **Post-doctoral Program.** Up to five-year stays to carry out supervised projects in the areas of basic, clinical or translational research.

6. Ongoing Education

- **Cardiovascular Physiopathology Course.** Organized by the CNIC, in collaboration with the Spanish Society of Cardiology (SEC), the course offers cardiologists a translational view of cardiology by introducing them to the study of physiopathology and basic research.

- **Vascular Biology Course.** Taught by the Director of the CNIC, **Dr. Valentín Fuster**, this course is part of the Menéndez Pelayo International University's summer program. Through the course, **Dr. Valentín Fuster** tries to "motivate and teach for the future". The majority of the participants are cardiologists, but experts in internal medicine or other specialties, also participate. ■

THE CNIC CONFERENCE ADDRESSES THE EMERGING CONCEPTS OF CARDIOVASCULAR BIOLOGY



A new edition of the “CNIC Conferences” called “Emerging Concepts in Cardiovascular Biology” was held at the National Center for Cardiovascular Research on November 16th and 17th. It brought together more than 100 scientists from 15 European countries, China, USA, Japan and Russia at the CNIC.

Coordinated by **Dr. Rui Benedito** and **José Luis de la Pompa**, of the CNIC, **Dr. José María Pérez Pomares**, of the University of Málaga, and **Dr. Didier Stainier**, of the Max Planck Institute for Heart and Lung Research, Bad Nauheim (Germany), the conference brought together researchers who are experts in fields such as studies of the mechanisms involved in the biology of blood vessels; in the role played by the cardiac endothelium in the development pattern of the heart and its impact on congenital heart diseases, and in the interaction between coronary angiogenesis and cardiomyocytes during tissue development and regeneration.

Data was presented and several aspects related to the mechanisms of blood vessel formation (angiogenesis) and the remodeling of vascular and cardiac tissues was discussed, especially in the context of cardiovascular disease.

The program included sessions which focused on the latest discoveries about the cellular biology of the vascular system, with special emphasis on the most important molecular signaling pathways and the transcriptional regulators that operate during development, physiological balance and heart disease and which are also fundamental to understanding the diversity and plasticity of cardiovascular tissues.

The lectures covered the fields of cell biology and embryonic development, vascular physiopathology, computational

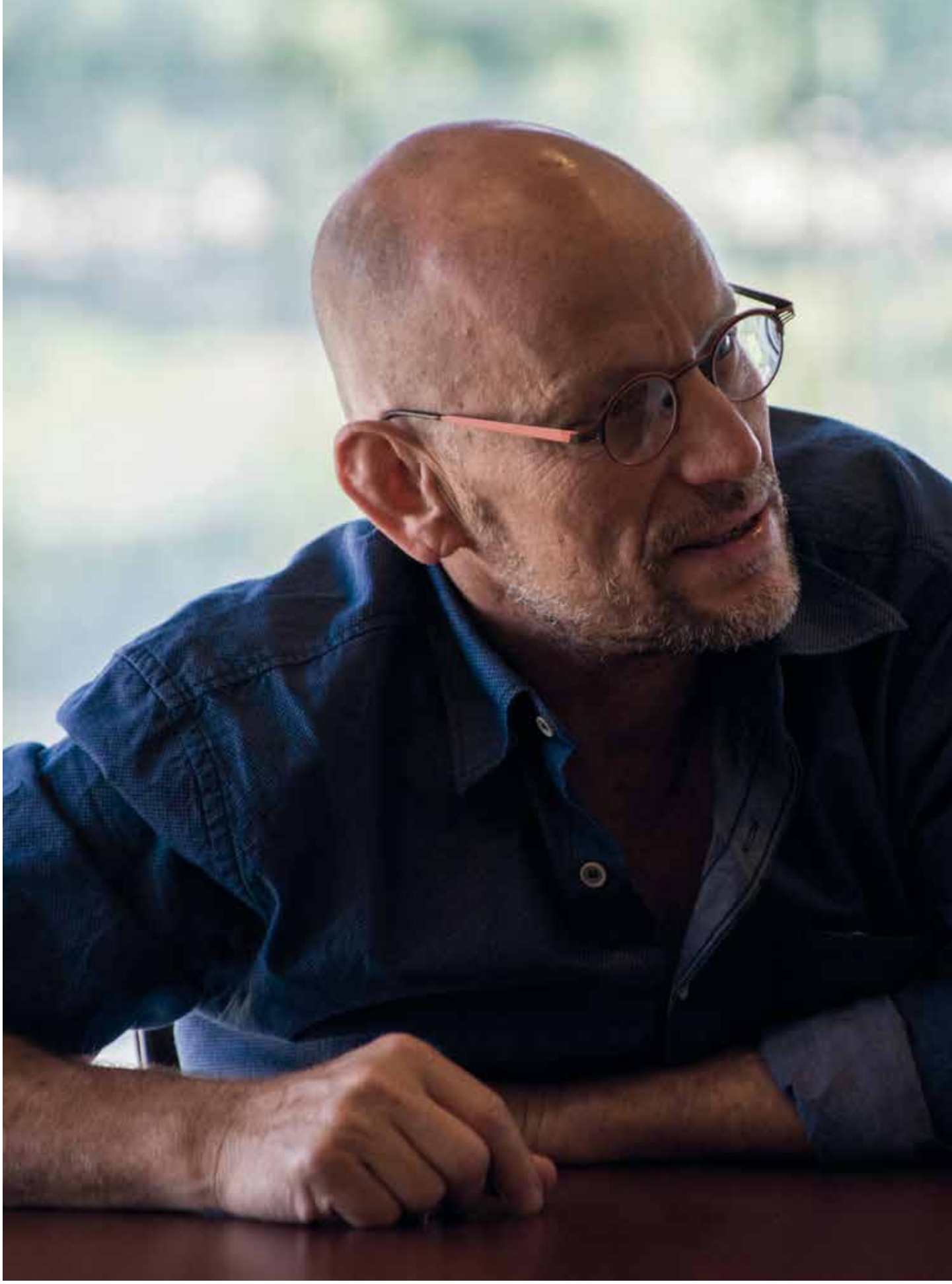
modeling, biophysical engineering, imaging techniques and regenerative medicine. There was also a special emphasis on the importance of the translation of these innovative concepts from cardiovascular biology to the clinic. Details of the program and guest speakers can be found at <https://cnic-conference.com/>

One of the other main objectives of the conference, and thus the sessions being organized in this way, was to stimulate communication between the most well-established researchers and those that are still in training.

In summary, the coordinators conclude, the meeting offered a forum for a general and up-to-date overview of the broad spectrum that cardiovascular biology research represents today.

UPCOMING CNIC CONFERENCE

The next CNIC Conference, entitled “New concepts of cardiovascular disease related to age”, will take place from October 24th to 26th 2019. Organized by the CNIC researchers **Vicente Andrés**, **Andrés Hidalgo** and **José Javier Fuster**, and Allan Tall, from Columbia University (USA), the meeting will cover four different topics of great relevance in this field: the Vascular-Neural-Immune axis in diseases related to age; Somatic mutations and clonal hematopoiesis in cardiovascular diseases; the aging of the immune system in cardiovascular diseases, and cellular senescence and cardiovascular disease. The Conference will address the new trends in this area, as well as the possible strategies to exploit this information therapeutically. ■





PROFESSOR ELDAD TZAHOR, DIRECTOR OF THE CELLULAR
AND MOLECULAR BIOLOGY LABORATORY AT THE
WEIZMANN INSTITUTE OF SCIENCE, IN REHOVO (ISRAEL)

Eldad Tzahor

"WE HAVE DISCOVERED
THE RECIPE TO
CREATE A
NEW HEART"

Eldad Tzahor's team centers its research on studying innovative mechanisms of cardiac regeneration and repair after an injury, a major challenge in current biomedical research. His laboratory of Cellular and Molecular Biology at the Weizmann Institute of Science, in Rehovo (Israel), combines innovative approaches to study cardiac regeneration in mammals, such as the role of the signaling pathway NRG1-ErbB2. In addition, they research the cardiac microenvironment as a means to improve the regenerative capacity of the heart and are manipulating the biophysical properties of the cardiac microenvironment (for example, the rigidity of the matrix) and its biochemical entities in search of conditions that facilitate cardiac repair mechanisms. Furthermore, they have also discovered that the Agrin protein can induce the regeneration of the heart of mammals, so it could have a great therapeutic potential for the treatment of ischemic heart disease. Their current studies examine the therapeutic effects of Agrin, whose administration in the injured heart of pigs causes a significant regenerative response. These findings will have implications for the improvement of current strategies to treat heart disease in humans. Professor Eldad Tzahor gave the Seminar "Novel strategies for cardiac regeneration in mammals" at the CNIC invited by Dr. Miguel Torres.

What is the current status of research in cardiac regeneration?

An important change is taking place. Years ago we could hardly think that it was possible to regenerate the heart after an injury; regenerating the cardiomyocytes was something unimaginable, especially after a myocardial infarction. But the work of my laboratory and that of others has shown that it really is not like that; yes, it is possible to reverse this fatal situation.

How? We know that cardiac cells can be renewed and these, in turn, regenerate the heart. Currently we are working on two possible ways to regenerate the heart: Agrin and ErbB2 approaches. The heart does not have the capacity to regenerate itself, but it is possible to cultivate stem cells in the laboratory, promote their differentiation from cardiac stem cells and transfuse them to the heart so that they integrate with the existing cardiomyocytes and "fill in" the cardiac injury and thus regenerate the tissue and reverse the damage.

But stem cell therapy for cardiac regeneration is still quite controversial. Many researchers affirm that it is a real alternative, but, in my opinion, I think it is necessary to look for other solutions. The reason that this therapy does not work as expected is that the cells, the transplanted ones and those of the patient, do not 'speak' the same language. In addition, the microenvironment in which they are transplanted, that is, the damaged heart, is a very toxic environment for the cells, which hinders their integration, and many of them end up dying. Only a few survive, so the cardiac function hardly improves.

So, what would be a more effective approach?

My idea is directed more towards the field of embryogenesis and the biology of development, areas in which **Miguel Torres** and **Nadia Mercader** of the CNIC also work, who investigate the formation of the heart during the embryonic phase. And we also rely on the evolution itself. If we

take the example of the zebrafish, we have seen that they are able to renew their heart after cardiac damage after two months. Some amphibians, like the salamander, also maintain this capacity, but the human being, we do not know why, has lost it. Or not? In the embryonic stages, and in neonates, the ability to regenerate the heart is maintained. The line of research that we are developing in my laboratory is aimed at identifying these signaling pathways in the heart of young mammals and how we can activate them in the adult phases so that they reactivate the regeneration of cardiomyocytes and repair mechanisms. That is, teach the adult heart to repair itself. In some way, by having the same capacity as it did when it was young.

How are you researching this?

My laboratory has identified two new models of cardiac regeneration, one of which has already allowed the design of a treatment that is expected to be in clinical trials in humans in two years. In fact, we are finalizing the tests on animals and the results are very encouraging. Essentially, we have understood that it is possible to reactivate the signs of heart repair, something that was unthinkable 10 years ago.

What are those two lines of research that you are referring to?

One of them is related to extracellular matrix proteins, a component that acts as cellular glue. We have analyzed these particles in newborn mice and compared them with those in the 1-week-old animals, which are unable to regenerate their heart. And that's how we have identified the Agrin protein, which was known to be related to neuromuscular connections - but not in the heart - that is present in newborn mice, but whose expression decreases in 1-week-old mice. And when we injected Agrin into the one-week-old mice that we had induced a cardiac injury, we saw that they were able to regenerate their heart. Now we are doing studies in pigs. A simple injection of Agrin manages to regenerate heart functions, reduce scars, etc. We are looking forward to the clinical phase in humans.

And the second line?

The second model is even more interesting, although I have more doubts about its transfer to clinical practice. The idea is, in some way, to analyze what has happened so that the cardiomyocytes lose the ability to regenerate. And we are seeing that the cardiomyocytes of mice that are just one-week old have lost the ERBB2 receptor, which is involved in heart growth. These molecules transmit a signal to cells, but have the drawback that they are associated with tumor development. We have proved that we can activate ERBB2 genetically only in cardiomyocytes. The problem is that due to this activation, the heart produces too many cells and can 'break' causing the death of the mice. But when we activated ERBB2 for only two weeks in mice with heart injuries, we have seen that the heart regenerates. It's magical! A complete regeneration of the heart occurs. Now we are working on a model of chronic insufficiency and we have verified that the activation of this receptor in the cardiomyocytes, only during two weeks, produced a new heart. A year ago we would never have believed it! We are very hopeful with this model because we believe that we have discovered the recipe to create a new heart. We hope to activate these molecules in humans.

And how do you resolve the risk of developing cancer?

We have to be very careful with this. We are talking about genetically manipulating all cardiomyocytes. You have to define the period during which the ERBB2 receptors should be activated. However, I am going to say something that may sound politically incorrect. In the same way that in some cases of cancer without therapeutic options high risk therapies are considered, the same can happen with the use of this therapy in patients with heart disease in which there is no other solution. Maybe it's a risk that would be worth taking. Activate the receiver for a week, 10 days or whatever is necessary, to regenerate the heart. And yes, only in very distinct patients whose problem would only be resolved with a transplant because, otherwise, they would die.

Could your research lead to a new scenario in cardiac regeneration?

We are already in a new scenario, but especially in heart failure. A year ago nobody could imagine it, but here we are. In mice we have been able to completely reverse heart failure and we are starting trials in pigs. It is certainly a new era in cardiac regeneration.

Are you collaborating with the CNIC in this field?

We are creating a network with **Miguel [Torres]** and **Nadia [Mercader]** and researchers in Italy and the United Kingdom to expand on mechanisms of endogenous regeneration. That is, teach the heart to regenerate itself through the reactivation of these mechanisms. I'm really optimistic with this line of network collaboration work. Sharing experience and knowledge is the best way to move forward.

How important is mentoring in the career of a researcher?

It is very relevant, of course. Young people are the future of research, so we have to help them in many aspects. When you are a young researcher you have many setbacks and, sometimes, it is very frustrating and you feel very lonely. Competition is very high and can discourage you. My job is to help them and guide them in their work. It is very important that you feel supported. Of course it's on my priority list! ■

Professor Eldad Tzahor gave the seminar "Novel strategies for cardiac regeneration in mammals", at the CNIC invited by Dr. Miguel Torres.

"Going abroad, at least for a while, is highly recommended for everyone, and especially for scientist"





ETH ZÜRICH (SWITZERLAND)

David Martínez Martín

HAS CREATED
A TECHNIQUE
THAT ALLOWS US TO MEASURE
IN REAL TIME THE MASS CHANGES
THAT CELLS EXPERIENCE
THROUGHOUT THEIR LIFETIME

Dr. David Martínez Martín holds a degree in Physics from the University of Valladolid with an Extraordinary End-of-Degree Award, and a PhD in Physics from the Autonomous University of Madrid, obtaining the Prize from the Royal Academy of Doctors of Spain. He has also done some training in the USA, Germany and Switzerland - where he ended up moving to in 2012 to work at the Federal Polytechnic University of Zurich (ETH Zürich), where he continues to develop his research career. With the aim of discovering how cells regulate their mass and size, Dr. Martínez Martín has created a technique that allows us to measure in real time the mass changes that cells experience throughout their lifetime (Nature). This technology makes it possible to measure the mass of individual cells or cell aggregates under culture conditions for days, with a resolution of milliseconds and a mass sensitivity of several picograms (0.1% of the mass of mammalian cells). Using his method, he has observed that the mammalian cells experience subtle mass fluctuations in a matter of seconds, or that the evolution of their mass is different when they are infected by a virus. He is currently preparing his transfer to Australia, where he has recently accepted an offer from the University of Sydney to start up his laboratory there.



"We observed a fascinating result: the mass of mammalian cells fluctuates slightly over time"

What is your line of research?

I work in biophysics and biomedical engineering. I am very interested in discovering the mechanisms that regulate cell growth. Although, they are considered the most elementary living units, the cells are actually complex autonomous systems. From a thermodynamic point of view, cells are open systems, that is, they are able to exchange energy and mass with their environment. Therefore, any model that tries to explain cellular functioning must include the exchange of mass and energy.

The mass and size of the cells is not random, but rather, it is intimately related to their biological function and physiology. For example, adipocytes in the human body are much larger than fibroblasts, and these in turn are larger than the beta cells of the pancreas. These facts suggest that the cells have mechanisms to regulate their mass and size. These mechanisms are essential in the formation of highly complex organisms such as humans, with a sophisticated architecture of tissues and organs. To this day, it is known that the origin of many diseases (cancer, hypertrophies, diabetes ...) is related to problems in the regulation of cell mass, so discovering the functioning of these mechanisms is a priority. Nonetheless, although characterizing mass changes of systems much larger or smaller than cells is done routinely, we did not have technologies that would allow this type of measurements at the cellular level with the necessary resolution. That's why I decided to work on the development of new instrumentation that will allow us to change this situation. This technology will open new ways to research cellular physiology in greater depth and will allow new diagnostic techniques to be established.

How does this instrument work?

It is based on a fundamental property of matter, which is inertia. A microscopic arm captures the cell or cells to be studied, and keeps them in culture conditions. With the help of a modulated intensity laser, a very slight oscillatory movement of the arm is induced in the atomic scale,

which allows a characteristic frequency to be located that depends on the mass of the cells. A second laser picks up the movement of the microscopic arm and sends it to an electronic system that analyzes it, extracting the information of the cell mass with very high precision.

The instrument is non-invasive and allows us to follow in real time (10 milliseconds of resolution) the evolution of the mass of the cells with a sensitivity of several picograms (approximately 0.1% of the mass of a human average cell). In addition, an inverted optical microscope is incorporated in the device and is fully compatible with transmission optical microscopy, fluorescence, confocal microscopy, etc. This allows simultaneous contrast of cell mass information with morphology and cell state.

What about the cellular environment?

To guarantee the cellular environment, we have also designed and built an environmental control system that guarantees the pH, osmolarity, temperature, and prevents contamination. This way the measurements can be made in a cultivated environment for days.

What information have you obtained so far?

A fascinating observation that we have made is that the mass of mammalian cells fluctuates slightly over time. We have detected fluctuations in mass at different time scales, but the fastest ones occur in just a few seconds. It is possible that these fluctuations are a fingerprint of the regulation system of cell mass regulation, although we still do not know its specific origin. The experiments we have conducted so far indicate that they are related to the metabolism and water exchange of cells with their environment.

We have also done research to see if the regulation of cell mass changes when they are infected by a virus. Specifically, we have worked with the Vaccinia virus, and we have discovered that the cells infected with this virus keep their mass close to a constant value, which allows us to easily distinguish between infected and uninfected cells. Taking into account these results, I am convinced that this tech-

nology will open up new ways to investigate the cellular physiology more in depth and will allow new diagnostic techniques to be established. For example, it could be used to develop new antibiotic sensitivity tests. Currently these type of tests take between 24 and 48 hours, but with our technology you could probably get the results in less than 30 minutes. An advance that could save many lives.

Would it be possible to understand how a healthy cell becomes cancerous?

One of the indications of the formation of a tumor, for example, in the mammary epithelium, is pleomorphism. That is, the manifestation of cells in that tissue with very different sizes. Therefore, I think that we could extract information of great clinical relevance by observing what happens to the mass of the cells during this type of processes.

Currently you are in Switzerland, but you will be moving to Australia. Is it the case of the Spanish scientist in search of an opportunity?

Science is a global activity; there are no borders. When I finished my PhD, I was lucky enough to be able to choose where I wanted to continue my career. I got a scholarship from the international excellence program EMBO (European Molecular Biology Organization) and I moved to Switzerland with the challenge of designing an instrument that would allow us to track the evolution of the mass of cells with great precision.

The project was very risky, a lot of funding was needed and the instrument had to be built from scratch. A project of this kind cannot be executed anywhere, but Switzerland had a very attractive environment. So I decided to go there and work with great scientists like **Professor Daniel Müller** and **Professor Christoph Gerber** (Kavli Prize in 2016).

I have been in Switzerland for more than 6 years and I am convinced that going abroad, at least for a while, is highly

recommended for everyone, and especially for scientists. It allows you to open up to other cultures, to get to know other ways of working, to master another language. It helps eliminate many prejudices and significantly promotes personal development. Currently these type of tests take between 24 and 48 hours, but with our technology you could probably get the results in less than 30 minutes. An advance that could save many lives.

Do you have any plans for collaborating with centers in Spain?

Collaboration with other specialists and other centers is essential. Spain has very good scientists and research centers, and I am currently in contact with several groups to study possible collaborations. In particular, I think that very interesting collaborations could be established with the CNIC.

How did you become interested in science?

Since I was a child I wanted to be an inventor. I loved the games in which I could build engines, electric circuits, water pumps, etc. In High School, I discovered that I loved mathematics and physics, and that they gave me the power to explain and predict many phenomena. That's why I decided to study Physics at the University.

This is your first visit to the CNIC. What's your impression?

I knew that the CNIC is a center of reference, and having the opportunity to know first-hand the excellent research carried out here has been very rewarding. The CNIC is a great example of how to connect basic research with clinical practice. ■

Dr. David Martínez Martín (ETH Zürich, Switzerland) held the seminar "Tracking a cell's mass in real time: a new indicator of cell physiology" at the CNIC, invited by Dr. Jorge Alegre.



WHAT'S ON **cnic** PULSE 34

A CARDIAC ARREST 'SURVIVOR' DONATES THE BENEFITS OF HER PROJECT TO THE CNIC

PAULA ELENA SUFFERED A THIRD-DEGREE ATRIOVENTRICULAR (AV) BLOCK, WHICH IMPLIES AN ABSENCE OF CARDIAC VENTRICULAR BEATS THAT LEAD TO A HEART IN CARDIAC ARREST, AND THUS HAD A **'NEAR DEATH EXPERIENCE'.**





PAULA ELENA RAMOS:
 “In the book I narrate everything I remember since I began to lose consciousness until I was discharged from the hospital, as well as the subsequent assimilation process”

On July 4th, 2014, **Paula Elena Ramos** left to be born again. Suddenly, without warning, without family history of such illness or previous symptoms, Paula Elena suffered a third-degree atrioventricular (AV) block. “This type of blockage consists of a complete failure of the transmission of the cardiac electrical impulse, from its origin in the atria to the ventricles, which are responsible for pumping blood from the heart. Therefore, this problem implies an absence of cardiac ventricular beats that lead to a static heart- in cardiac arrest- without pumping blood”, explains **David Filgueiras**, cardiologist and researcher at the National Centre for Cardiovascular Research (CNIC).

Paula Elena remembers very well how she began to lose consciousness and the stages that came after that - from the day she was admitted into the hospital until the day she was discharged. Later she went through a process of assimilation, not of the blockade itself, but of the week in the Intensive Care Unit and the operation she had to undergo; a very intense experience. All this is narrated in the book ‘BOX1. Story of the heart that sowed a galaxy in an electric body’, a text which originates from the need to disseminate data, experience and methods of dealing with a disease that there is so little information about; the lack of knowledge about heart blocks in young people and the misunderstood (and badly attended) pathological anxiety.

Also, another vital objective of **Paula Elena** who, after ‘being born again’ and undergoing a near-death experience, proposed to help in the research of this “rare disease” or “strange” event, as even medical professionals call it. “Being part of an extremely small percentage of survivors must be useful for something; Therefore, let’s start with research and dissemination”, she says. “In the book I narrate everything I remember since I began to

lose consciousness until I was discharged from the hospital, as well as the subsequent assimilation process”, comments Paula Elena.

RESEARCH IN ARRHYTHMIAS

The final objective of the sale of this book is to gather funds that will be fully used for research in arrhythmias that is carried out at the CNIC, specifically the group of Advanced Development on Mechanisms and Therapies of Arrhythmias directed by **Dr. Filgueiras**.

Paula Elena is especially grateful for the care and attention received from the cardiologist who implanted the pacemaker at the Can Misses Hospital in Ibiza, **Dr. Joaquín Seguí Bonnin**, now retired, and her current cardiologist, **Dr. Ricardo Ruiz Granell**, from the Clinical Hospital of Valencia. And of course to her second heart, a Medtronic pacemaker that she is totally dependent on.

The selfless attitude of this woman from Valencia is not very frequent in Spain, as it is in Anglo-Saxon countries where there is a greater tradition of what is called ‘charity’. In our country, it is not usual for people to donate their money for research projects, there are however, individuals who often want to help and do not know how. Some scientific institutions try to promote patronage through campaigns, since the funds donated by citizens can be used to generate new research contracts, improve equipment or allow researchers to get in touch, through stays and exchanges, with the best centers of the world.

“What **Paula Elena** did is an example for all of us”, says the General Director of the CNIC, **Dr. Valentín Fuster**. Starting from a very painful and traumatic experience, she has extracted a positive and altruistic project that should help us all continue researching.” ■

EXCELLENCE IN THE SCIENCE COMMUNICATION

MAJOR SCIENTIFIC JOURNALS PUBLISH CNIC RESEARCH FINDINGS

JOURNAL OF EXPERIMENTAL MEDICINE The dual and unknown function of the immune system

The cells of the immune system sustain life by infiltrating infected and damaged tissue and eliminating pathogens and cell debris. However, immune action produces a collateral damage of its own that can lead to autoimmune disease or contribute to the injury associated with myocardial infarction or stroke. Now, a new study led by CNIC researcher **Andrés Hidalgo** and published in the *Journal of Experimental Medicine* shows that in addition to its defense function and the associated damage to affected tissues, the immune system also plays an important role in the day-to-day function of healthy organs. The research results show that the immune cells called neutrophils help to maintain the normal function of healthy tissues.

The study, which is the result of more than five years of research and collaboration with laboratories in Europe, Asia, and the US, is important because it reveals that the immune system not only has a defense function that can damage tissues, but also is important for the day-to-day function of a healthy organism.

According to lead author **Hidalgo**, life is a continuous struggle between organisms. Large organisms, such as humans, provide a nutrient-rich environment for microbes and have developed an immune system to protect themselves against infection. To be effective, the immune system needs to be toxic, but this brings with it the risk of damaging the body's own cells and tissues. Commenting on the implications of this situation, study author **María Casanova-Acebes** explained that "the immune system is a two-edged sword, and the associated collateral damage can result in autoimmune disease or the injury accompanying a myocardial infarction or stroke. Therefore, one would expect immune cells to be excluded from healthy tissues in order to avoid unnecessary damage."

But the new study shows that neutrophils, one of the major immune cell types, not only enter healthy tissues but also carry out a range of functions unrelated to immunity.

The research results show that tissues that are especially sensitive to damage, such as the brain, are usually



'clean', or free of these immune cells; in contrast, other tissues, such as the lungs, liver, spleen, and bone marrow, are full of neutrophils, even in good health.

Moreover, the study shows that neutrophils perform a range of roles in several of these tissues, such as the intestine and lungs. According to study author **José Ángel Nicolás**, "an important finding of our study is that whereas the action of neutrophils is potentially dangerous in some tissues, in others it is beneficial; for example, maintaining the function of blood stem cells and preventing tumor metastasis in the lungs."

Casanova-Acebes, M., Nicolás-Ávila, J.A., Li, J.L., García-Silva, S., Balachander, A., Rubio-Ponce, A., ... Hidalgo, A. (2018). *Neutrophils instruct homeostatic and pathological states in naive tissues*. **Journal of Experimental Medicine**.
doi:10.1084/jem.20181468

SCIENCE

A new mechanism in the control of inflammation

In response to infection or tissue injury, our bodies react by activating the inflammatory immune response, which attacks the infection and repairs the damaged tissue. However, excess inflammation can sometimes have the opposite effect, increasing injury in a process known as immunopathology. Now, CNIC scientists have discovered a new inflammation control mechanism that allows the damage caused by the immune response to be controlled. The study is published in the journal **Science**.

The immune system reacts to infection and other causes of tissue injury by generating an inflammatory response. Inflammation is a defense mechanism that facilitates the recruitment of immune cells to the injury site; for example, the pancreas during pancreatitis, the kidney after a *Candida albicans* fungal infection, or the heart during a myocardial infarction. The function of these immune cells is to eliminate the source of injury that provoked the inflammation and to contribute to tissue repair.

According to lead author **David Sancho**, "The first immune cells to arrive at the infection or inflammation site are the neutrophils, and these cells are tasked with eliminating the source of the problem. However, neutrophils are very destructive and not only act on the infecting pathogen, but also damage the infected tissue. This tissue damage caused by our own defense system is known as immunopathology. It is therefore important to understand how our immune system can control the neutrophil inflammatory response to prevent it damaging our own tissues. The current study

shows that tissue infiltration by neutrophils is controlled by dendritic cells. These cells are better known for the essential role they play in directing the specific responses of T lymphocytes. The new study shows that dendritic-cell regulation of neutrophil infiltration helps to prevent excessive tissue injury."

Co-first authors **Carlos del Fresno** and **Paula Saz** emphasized the importance of understanding immune system regulation, both as a positive response, favoring the fight against infection or cancer and promoting tissue repair, and in its negative manifestations that can cause excessive inflammatory injury during infection, allergic reactions, and autoimmune disease. "This balance always exists in the immune system, and learning how to control it is the key to the fight against many diseases with an immune component."

The research was conducted in mouse models, the only experimental system that reproduces the complexity of the infections and inflammatory processes studied. These models can provide important insight into how to regulate the damaging immunopathological responses generated by our own defense systems. According to the CNIC researchers, knowledge in this area would be especially applicable to diseases characterized by massive neutrophil infiltration, whether this occurs as a response to infection or to tissue injury, as in a heart attack.



Del Fresno, C., Saz-Leal, P., Enamorado, M., Wculek, S.K., Martínez-Cano, S., Blanco-Menéndez, N., ... Sancho, D. (2018). *DNGR-1 in dendritic cells limits tissue damage by dampening neutrophil recruitment*. **Science**, 362(6412), 351-356.
doi:10.1126/science.aan8423

NATURE COMMUNICATIONS

Blocking hypertension with antihypertensive drugs prevents the development of a lethal disease

Researchers at the CNIC and the Consejo Superior de Investigaciones Científicas (CSIC) have discovered that effective control of high blood pressure with antihypertensive drugs prevents the development of aortic intramural hematoma (IMH), a serious and potentially lethal disease. The research has also identified specific proteins implicated in the disease, and the authors have generated a preclinical model for the study of IMH that will be useful for evaluating possible drug treatments. The study, published in *Nature Communications*, was co-directed by **Miguel Campanero**, of the Instituto de Investigaciones Biomédicas Alberto Sols (CSIC), and CNIC group leader **Juan Miguel Redondo**.

An IMH is an accumulation of blood within the wall of the aorta in the absence of dissection of the intimal layer (the innermost layer, in contact with the circulating blood). At early stages, an IMH can be reabsorbed spontaneously. However, in the long-term, IMH more frequently progresses to aneurysm, which is a dilatation or anomalous swelling of a portion of the aorta that can result in vessel rupture and death.

According to **Dr. Redondo**, both IMH and aneurysm are indolent diseases that cause very mild or no symptoms early on. However, as **Dr. Campanero** explained, the associated risk of sudden rupture "requires early and precise diagnosis, rigorous monitoring after detection, and appropriate treatment." Because there are no validated pharmacological therapies able to prevent harmful disease progression, surgery is the only effective treatment, especially for larger hematomas and those located in the initial portion of the aorta. However, surgery is risky, and the study authors emphasize, "it is essential to identify the mechanisms underlying IMH formation in order to develop pharmacological treatments able to efficiently block catastrophic progression."

The researchers have generated an animal model that accurately reproduces many of the characteristics of the human disease, allowing the research team to conduct an in-depth investigation of the molecular mechanisms underlying the origin and progression of IMH. The study revealed that one of the triggers of this disease is high blood pressure and that various drugs widely used to reduce blood pressure in patients and mice completely block the formation of IMH in the preclinical model.

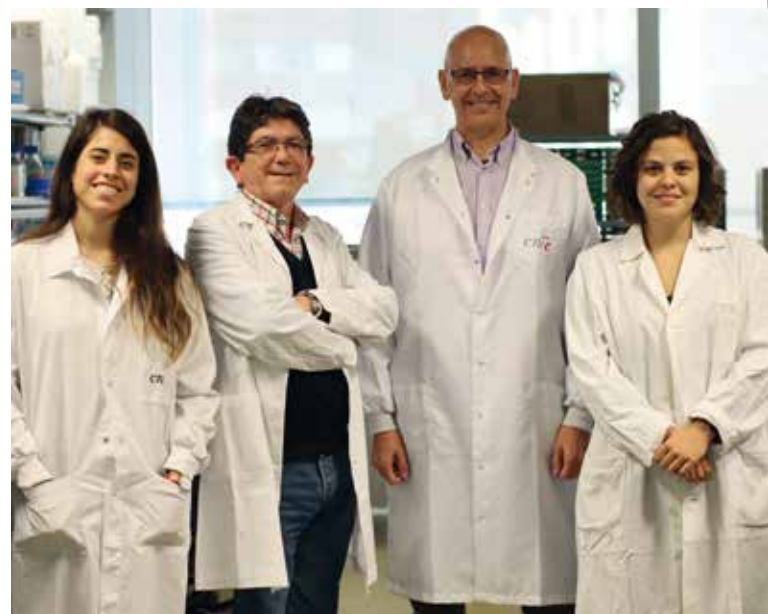
Analysis of the molecular mechanisms underlying IMH revealed that induced deficiency of a protein called Rcan1 in the cells of the blood vessel wall activates a protein called myosin light chain, which is involved in vessel formation. According to the authors, the study shows that "pharmacological inhibition of

myosin light chain activation effectively prevents IMH formation."

Working with the CNIC Proteomics Unit, the research team conducted a screen to identify proteins able to interact with Rcan1. This analysis identified 11 proteins that specifically interact with Rcan1, and according to **Dr. Redondo**, "one of them, the protein Gsk3- β , is a strong candidate as a mediator of IMH formation."

Gsk3- β inhibitors have been used for many years to treat a number of psychiatric disorders, and the researchers are therefore interested in comparing the incidence of IMH, aortic dissection, and aneurysm in patients treated with these compounds with that in the general population. "Now we have a good preclinical model of IMH, we can analyze the mechanism underlying its catastrophic progression in detail and begin to evaluate drugs able to slow or stop it."

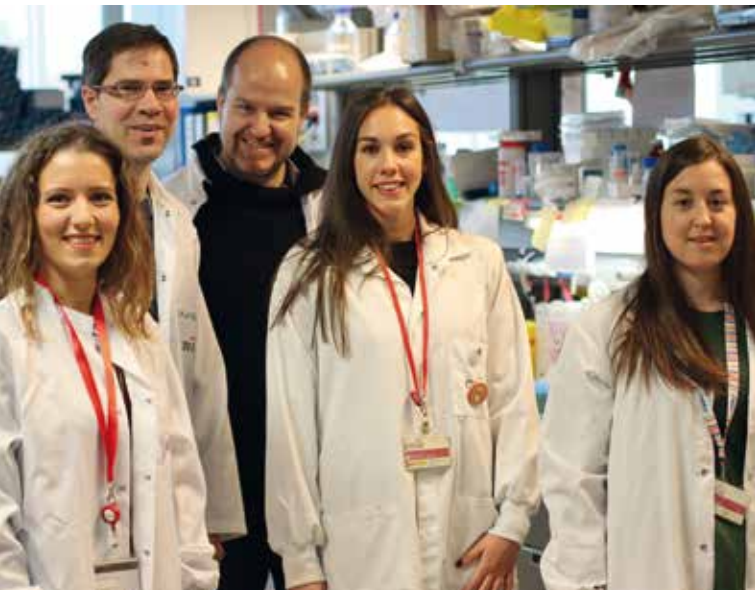
The study received funding from the Spanish Ministry for Science, Research, and Universities, the Madrid regional government, the CSIC, the ProCNIC Foundation, the Marfan Foundation (USA), the Marató Foundation, and the CIBER cardiovascular research network (CIBER-CV) linked to the Instituto de Salud Carlos III.



Villahoz, S., Yunes-Leites, P.S., Méndez-Barbero, N., Urso, K., Bonzon-Kulichenko, E., Ortega, S., ... Campanero, M.R. (2018). *Conditional deletion of Rcan1 predisposes to hypertension-mediated intramural hematoma and subsequent aneurysm and aortic rupture. Nature Communications*, 9(1), 4795. doi:10.1038/s41467-018-07071-7

IMMUNITY**CNIC scientists identify a new “watchdog” that controls intestinal bacteria**

The immune response to our intestinal microbiota—the community of microorganisms that live in the human gut—ensures that these microorganisms remain in their proper place. When the intestinal immune barrier is damaged, the gut bacteria can spread and cause inflammation throughout the body. Now, a study by scientists from the CNIC and the Department of Immunology at the Universidad Complutense in Madrid reveals a new mechanism in the regulation of this immune barrier.



The study, published in the journal *Immunity*, identifies a mechanism through which intestinal bacteria such as *Lactobacillus* strengthen the intestinal barrier to support a mutually beneficial relationship and prevent inflammation. The results have potential implications for the treatment of diseases featuring the spread of commensal bacteria outside the gut, as occurs in some metabolic disorders.

The study was directed by **David Sancho**, who heads the Immunobiology lab at the CNIC. He explained that “these intestinal bacteria contain or secrete molecules that bind specifically to the receptor Mincle (Clec4e). Mincle is expressed on the surface of antigen presenting cells of the innate immune system known as dendritic cells, and its function is to strengthen the intestinal barrier.”

The intestinal barrier restricts the localization of commensal microorganisms so that they stay in the intestine. This barrier can be weakened by some diseases and specific factors such as diet, leading to the systemic inflammation associated with autoimmune and metabolic diseases.

The research team propose that a new treatment strategy for these conditions could be the use of

probiotics (‘beneficial’ intestinal microorganisms) or prebiotics (nutrients that promote the growth of beneficial microorganisms); however, the mechanisms underlying this strategy are so far unknown.

The researchers were interested in understanding how commensal gut bacteria contribute the maintenance of the intestinal barrier that keeps them in the environment where they are beneficial. In animals lacking Mincle, there was an increase in the number of bacteria able to escape from the intestine and reach the liver, where they caused inflammation and metabolic changes. These findings highlight the potential of Mincle as a target for future therapies aimed at strengthening the intestinal barrier in situations when it is damaged or weakened.

The research team also observed that the intestinal barrier in mice was strengthened by treating them with commensal microorganisms such as *Lactobacillus* during early postnatal development. This effect was achieved through the interaction of these bacteria with Mincle expressed on dendritic cells in the intestine.

Martínez-López, M., Iborra, S., Conde-Garrosa, R., Mastrangelo, A., Danne, C., Mann, E.R., ... Sancho, D. *Microbiota Sensing by Mincle-Syk Axis in Dendritic Cells Regulates Interleukin-17 and -22 Production and Promotes Intestinal Barrier Integrity*. *Immunity*. doi:10.1016/j.immuni.2018.12.020

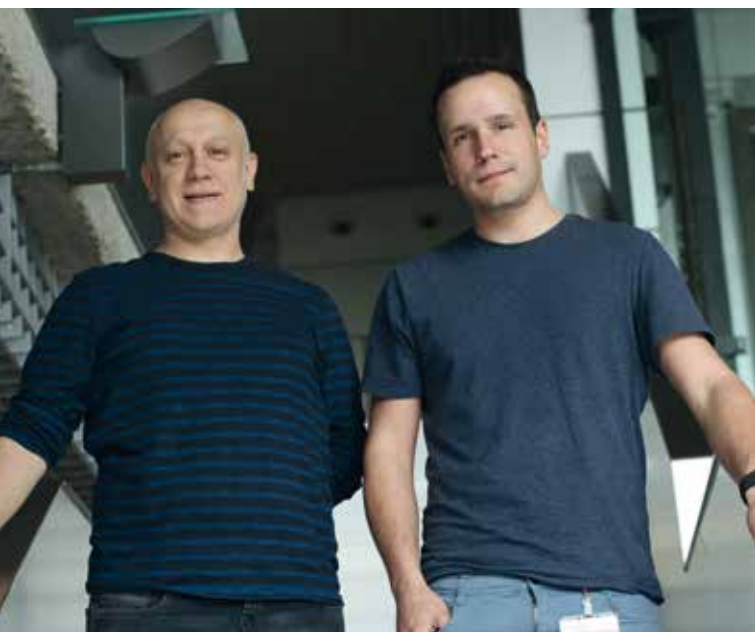
IMMUNITY**CNIC scientists discover an immune “clock” that controls infections and cardiovascular disease**

CNIC scientists have demonstrated the existence of an immune “clock” that coordinates the day/night cycles through the activity of a class of leucocytes called neutrophils. Neutrophils constitute the body's main line of defense, but their action can also damage healthy cells of the cardiovascular system. This newly discovered clock determines when neutrophils are activated and when it is time to eliminate them from the circulation. Describing the findings, first author **José María Adrover** explained that the researchers have identified “a series of molecules in the neutrophil nucleus and cell membrane that respond to diurnal (circadian) patterns in lightness and darkness and regulate the migration and localization of neutrophils in the body.” The study was carried out by the CNIC research group led by **Andrés Hidalgo** and is published in the leading journal *Immunity*.

The immune system, especially through the action of neutrophils, ensures peaceful coexistence with microorganisms by efficiently eliminating those that cause infection. Nevertheless, this comes at a price, because

the often disproportionate action of the immune response damages healthy tissue. According to **Andrés Hidalgo**, "This is what happens, for example, during myocardial infarction, stroke, and acute lung injury. The biological challenge is to control the immune system so that it protects against infection but does not cause collateral damage to the body." The new presents a response to this challenge that could have important repercussions for health care.

Due to the worldwide high prevalence of infectious and cardiovascular diseases, the study could have wide-ranging clinical implications. The team is currently working on ways to manipulate this immune clock with drugs to induce diurnal or nocturnal immunity, depending on the needs of each patient. This therapeutic approach could be valuable for people at risk of cardiovascular events and also for immune-compromised patients susceptible to infection.



Adrover, J.M., del Fresno, C., Crainiciuc, G., Cuartero, M.I., Casanova-Acebes, M., Weiss, L.A., ... Hidalgo, A. *A Neutrophil Timer Coordinates Immune Defense and Vascular Protection*. **Immunity**. doi:10.1016/j.immuni.2019.01.002

JACC

Sleeping less than 6 hours a night increases cardiovascular risk

People who sleep less than 6 hours a night may be at increased risk of cardiovascular disease compared with those who sleep between 7 and 8 hours, suggest the results of the PESA CNIC-Santander Study published in the **Journal of the American College of Cardiology (JACC)**. The study indicates that poor-quality

sleep increases the risk of atherosclerosis—the build-up of plaque in the arteries throughout the body.

"Medicine is entering a fascinating phase. Until now we have tried to understand cardiovascular disease. Now, thanks to studies like PESA CNIC-Santander, we are beginning to understand health," said **Valentin Fuster**, CNIC General Director and JACC editor-in-chief.

Study author **Dr. Ordovás** explained that "cardiovascular disease is a major worldwide health problem, and the several approaches used to prevent and treat it include drugs, physical activity, and diet. This new study emphasizes that we need to include sleep as one of our weapons in the fight against heart disease—a factor that is neglected in our society every day. This is the first study to show that objectively measured sleep is independently associated with atherosclerosis throughout the body, not just in the heart."

Previous studies showed that lack of sleep increases cardiovascular disease risk by increasing risk factors such as blood glucose, blood pressure, inflammation, and obesity. Describing the study, Dr. Ordovás explained that "the goal of our study, which included almost 4000 PESA CNIC-Santander participants, was to evaluate the impact of sleep duration and interrupted sleep on atherosclerosis. We found that participants who slept for less than 6 hours per day or who had a very fragmented sleep pattern had more cholesterol plaques than those who slept for longer or had uninterrupted sleep". First author **Fernando Domínguez** concluded, "Sleep duration and quality are of vital importance for cardiovascular health."

The new study differs in several ways from previous studies on sleep and heart health. Crucially, it is larger than many earlier studies and was conducted in a healthy population; in contrast, many previous studies included people with sleep apnea or other health problems. Another important difference is that whereas other studies relied on questionnaires to determine how much sleep participants had, the new study used actimetry to obtain objective measures of sleep. As **Dr. Ordovás** pointed out, "What people say and what they do are often different."



Domínguez, F., Fuster, V., Fernández-Alvira, J.M., Fernández-Friera, L., López-Melgar, B., Blanco-Rojo, R., ... Ordovás, J.M. (2019). *Association of Sleep Duration and Quality With Subclinical Atherosclerosis*. **Journal of the American College of Cardiology**, 73(2), 134-144. doi:10.1016/j.jacc.2018.10.060

CIRCULATION

Expression of a molecule in blood cells predicts atherosclerosis risk

Earlier detection of cardiovascular disease is a step closer thanks to the findings of team of CNIC scientists led by **Francisco Sánchez-Madrid** and **Pilar Martín**. The researchers found that the expression level of the molecule CD69 in blood cells inversely predicts the appearance of subclinical atherosclerosis (developing before symptoms appear) independently of classical cardiovascular risk factors.

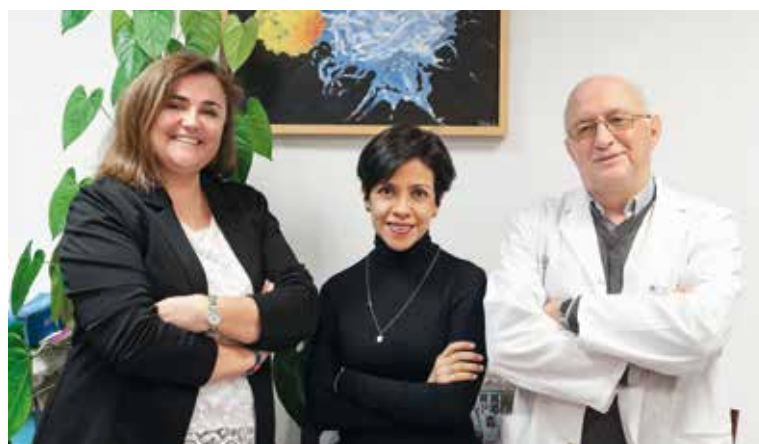
Atherosclerosis is characterized by the accumulation of lipid deposits in the artery wall, but the disease is usually not detected until after it has caused a clinical event such as a myocardial infarction or stroke. Because of the diminished quality of life experienced by affected individuals, treatment after symptoms appear is of limited benefit, and the long-term management of the disease is a major cost for health care systems.

The origin of atherosclerosis and its progression to acute myocardial infarction and stroke involve an essential contribution from the inflammatory immune response. However, according to **Francisco Sánchez-Madrid**, of the Hospital Universitario de la Princesa in Madrid, "The relationship between lipid metabolism and the immune response is not

well understood. The established hypothesis is that oxidized low-density lipoproteins (LDLox) induce the recruitment of inflammatory immune cells and their accumulation in the plaque; however, there is also evidence that cells and tissues can respond to LDLox by inhibiting proinflammatory signals."

The new study, published in **Circulation**, was a collaboration between the CNIC research groups led by **Sánchez-Madrid** and **Pilar Martín**. The study identifies the molecule CD69 as a T cell receptor for oxidized lipoproteins that contributes to the control of inflammation and thus prevents the development of atherosclerosis. "Binding of LDLox to CD69 triggers the adoption of an anti-inflammatory profile by T lymphocytes that protects against the development of atherosclerosis in mice and humans," explained Pilar Martín. For this research project, the team used mice lacking the CD69 gene. The project was supported by the Spanish Cardiovascular Disease Research Network (CIBER-CV) as was conducted in partnership with **José Martínez González**, whose group is based at the Instituto de Investigaciones Biomédicas in Barcelona (IIB-Sant Pau).

The results of the Circulation study show that the expression of CD69 in circulating lymphocytes correlates inversely with the presence and extent of subclinical atherosclerosis. Cardiovascular disease is the single largest cause of death in the world, and preventive strategies for this disease are therefore a major priority. ■



Tsilingiri, K., de la Fuente, H., Relano, M., Sánchez-Díaz, R., Rodríguez, C., Crespo, J., ... Sánchez-Madrid, F. (2018). *oxLDL Receptor in Lymphocytes Prevents Atherosclerosis and Predicts Subclinical Disease*. **Circulation**. doi:10.1161/circulationaha.118.034326



CNIC AND QUIRONPREVENCIÓN: AGREEMENT TO PROMOTE CARDIOVASCULAR HEALTH

QUIRONPREVENCIÓN PROVIDES THE CNIC RESEARCHERS **HEALTH INDICATORS FROM MORE THAN 5 MILLION ANONYMOUS CHECKUPS,** UNDER THIS AGREEMENT

Quironprevención has reached an agreement with the CNIC to advance in the knowledge of cardiovascular health. Thanks to this agreement, the CNIC may improve the study of cardiovascular risk prevention and associated diseases, using a database containing the results of 5 million of completely anonymous and untraceable checkups provided by Quironprevención.

This project, from the scientific point of view, analyzes the cardiovascular risk of the active Spanish population, taking into account different variables, from the type of the job (the activity is different for example in office positions than in those where physical effort is required), up to eating habits, consumption of alcohol and tobacco, or the worker's daily physical exercise.

In the words of **Borja Ibáñez**, cardiologist at the Jiménez Díaz Foundation Hospital and Director of Clinical Research

of the CNIC, "the database that we can study thanks to this agreement, is unique. There is no study that has been able to analyze an equal sample size in Spain, with data collected for such a long period, from 2015 to 2018, and with information that allows us to make a comparative analysis by type of activity, eating habits and even environmental-regional setting".

In a preliminary analysis, carried out after signing the agreement, variations in risk of having a heart attack have been detected up to six times higher, according to habits and the geographical area.

This amount of information, which falls into the category of big data analysis, will allow comparisons like this one, with different variables, to be made, and obtain priceless information about the health of the active population of our country and plan the proper health promotion strategies. ■

ALLIANCE BETWEEN THE PRO CNIC FOUNDATION AND HM HOSPITALS



The Pro CNIC Foundation and HM Hospitals signed an agreement at the HM Montepíncipe University Hospital in which both institutions commit to developing initiatives with the purpose of promoting cardiovascular health and healthy habits of the general population.

Dr. Valentín Fuster Carulla, General Director of the National Center for Cardiovascular Research (CNIC) and **Dr. Juan Abarca Cidón**, president of HM Hospitals, attended the signature of this agreement and signed it under the watchful eye of **Mr. Antonio González Terol**, mayor of Boadilla del Monte, and **Mr. Julio Domingo Souto**, Director of the MAPFRE Foundation. The choice of location for the signature of the agreement - HM Montepíncipe University Hospital was no coincidence, as it is the Integral Center of Cardiovascular Illnesses HM CIEC, a unique space of HM Hospitals where the entire cardiac pathology is approached and which integrates specialized patient care with clinical and basic research together with the latest technological resources. Among the initiatives included in the agreement, one that stands out is the development of a Comprehensive Cardiovascular Health Plan for all employees of HM Hospitals, in which the professionals of the Pro CNIC Foundation will provide their information and expertise in this area to specialists of HM Hospitals – a plan of absolute collaboration.

WOMEN FOR THE HEART

Within the spirit of promotion and prevention of cardiovascular health that permeates this agreement, HM Hospitals participates with the 'Women for the Heart' campaign, directed by the MAPFRE Foundation. The main objective of this project is to inform the population about the importance of early warning signs and symptoms of a heart attack in women and the need to maintain a healthy lifestyle that helps reduce the impact of cardiovascular disease in

women. The bus used in this campaign visited the HM Montepíncipe University Hospital to raise awareness among its employees and patients. **Mr. Julio Domingo Souto**, Director of the MAPFRE Foundation, highlighted the importance of this campaign and the positive example of HM Hospitals by joining this initiative, in which a total of 387,000 women from Spain, Brazil, Colombia, Dominican Republic and Panama have already benefited from the campaign.

CARDIOWOMAN

Another one of the main motivations of this agreement is to set a framework of collaboration to sensitize the general public and, specifically women, in order to facilitate the recognition of the early warning signs and symptoms of cardiovascular diseases and encourage healthy lifestyles for the heart. In this sense, the agreement is expected to promote the creation of the Cardiomwoman initiative at HM Hospitals, a specialized consultation in cardiovascular health of women, that will be coordinated by **Dr. Leticia Fernández-Friera**, Director of the Cardiac Imaging Unit of HM CIEC. "According to the World Health Organization (WHO), the main cause of death in the world are cardiovascular diseases. In addition, according to the Spanish Society of Cardiology (SEC), mortality, after a first acute myocardial infarction, is 20% higher in women, especially in countries like Spain. That's why it is important to know exactly what the signals that indicate that a woman is suffering from a heart attack are. A woman does not have to experience the same symptoms as a man, in fact, often women present atypical symptoms and are treated late, which makes the diagnosis more difficult and thus increases the risk of death," says **Dr. Fernández-Friera**. With this agreement HM Hospitals is committed to distributing the contents of the campaign to its more than 4,700 employees and their patients, who make more than 2.5 million appointments annually. ■

AWARDS AND SCHOLARSHIPS



FOUR CNIC PROJECTS WILL RECEIVE 2,5 MILLION EUROS FROM THE CALL "RESEARCH PROJECTS IN HEALTH 2017" OF "LA CAIXA"

Four CNIC projects will receive 2.5 million euros from the call "Research Projects in Health 2017 of "la Caixa". These projects are: "Are leukocyte genes a risk factor for cardiovascular disease?" directed by **Dr. Fuster**; "How does the immune system warn us about the presence of unexpected pathogens?", coordinated by **Francisco Sánchez Madrid**; "Can new biomarkers for cardiovascular disease be found? ", directed by **Almudena Ramiro**, and "Can immune cells be reprogrammed to protect the heart or the brain after a heart attack?", coordinated by **Andrés Hidalgo**.

The investigations are framed within three of the lines of action in the field of research of the "la Caixa" Bank Foundation: post-doctoral scholarships to encourage talent; call for research projects in biomedicine and health, and the CaixaImpulse program, to transfer the results of the research to society. The "la Caixa" Bank Foundation wants to promote leading projects in multidisciplinary research to influence social welfare. The 2016-2019 Strategic Plan includes investment in research as a priority, and plans to triple the budget in this field to up to 90 million euros in the year 2019.

THREE CNIC RESEARCHERS IN THE "SPANISH NATIONAL TEAM OF SCIENCE" OF THE CSIC AND QUO

The Superior Council of Scientific Research (CSIC) and **Quo** Magazine appointed the Spanish scientists and researchers who make up the 2018 Spanish National Team of Science. A team formed by professionals who in recent months have made an outstanding scientific or technological contribution. In this edition two CNIC researchers were selected: **José María Ordovás** and **Pura Muñoz Cánoves**, who combine their activity with their job positions at Tufts University, in Boston (USA) and the Pompeu Fabra University (UPF) respectively. This is the third time that the CNIC has "players" on this team. **Valentín Fuster**,



General Director of the CNIC, already managed to wear the "jersey" in 2014. This is a very special edition for the Spanish National Team of Science.



CNIC PHDAY 2018: SCIENTIFIC GROWTH

With the slogan “Scientific Growth”, a new edition of the CNIC PhDay was held – an event that meets the expectations of any international congress, and that little by little is consolidating itself. PhDay is an open forum for students and graduates, laboratory technicians and post-doctoral researchers who plan to develop their careers as scientists and is based on the exchange of new ideas. This year the theme has revolved around scientific growth, since its aim was to address different aspects presented in the life of a scientist from the early stages of childhood, up until adulthood.

The closing lecture was given by **Dr. Margarita Salas**, who through her speech entitled ‘My research experience’ described in detail her scientific career and shared it with the assistants. In the same way, different workshops were also developed, in which different topics were addressed: the role of social networks in the communication of science; the empowerment of the female scientist; the good work in statistics, or how to communicate science to the little ones through games.

DR. VALENTÍN FUSTER NOMINATED HONORARY DOCTOR BY THE ALFONSO X EL SABIO UNIVERSITY

The Alfonso X el Sabio University nominated **Dr. Valentín Fuster de Carulla** with the Honorary Doctor title, for his extended scientific work in the field of Cardiology and for his strenuous promotion of health, in order to advance in the treatment and prevention of myocardial infarctions.



THE CARDIOVASCULAR POLYPILL, AWARDED THE BEST PROJECT OF MULTIDISCIPLINARY ADHERENCE

The cardiovascular polypill, developed between the CNIC and Ferrer, has been awarded the extraordinary prize of the Best Multidisciplinary Adherence Project, in the first edition of the OAT Awards for the Improvement of Adherence to treatment. These awards are created with the purpose of recognizing all those entities or people that contribute to improve adherence to treatment in patients. This drug, marketed under the name of Trinomia®, has been a great advance in the field of cardiology because it contains in a single capsule three active principles indicated in the prevention of second myocardial infarctions in those people who have already suffered one (atorvastatin, acetylsalicylic acid and ramipril). The advantage of this treatment resides in its simplicity, since patients only need to take one

capsule instead of three, in order to improve adherence to treatment in chronic and high-risk patients, most of whom are elderly people.



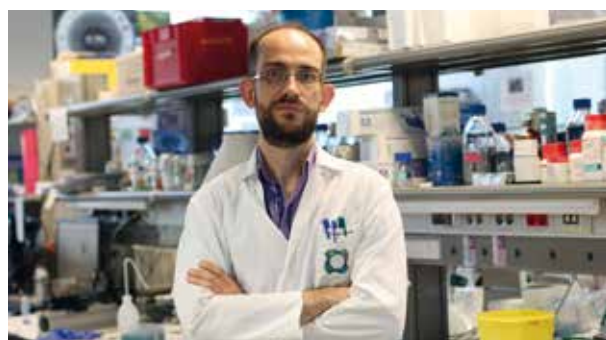


DR. FUSTER RECEIVES THE "OUTSTANDING PERSON IN THE HEALTH CARE FIELD" AWARD

Dr. Valentín Fuster received the recognition of "Outstanding Person in the healthcare field" at the 10th Annual Doctors and Patients Awards held at the Collegial Medical Organization headquarters.

A CNIC RESEARCHER, WINNER IN THE IV YOUNG RESEARCHERS AWARDS OF THE ASTRAZENeca FOUNDATION

Dr. Guadalupe Sabio has been the winner of the IV Young Researchers Awards of the AstraZeneca Foundation, in the category of Type II Diabetes and Obesity for her advances related to the development of obesity and associated diseases. The awards, promoted by the AstraZeneca Foundation, together with the Carlos III Health Institute, encourage the scientific talent of junior researchers under the age of 40 in Spain.



JORGE ALEGRE-CEBOLLADA WILL REPRESENT ARSENIC IN THE PERIODIC TABLE OF YOUNG CHEMISTS OF THE IUPAC

Dr. Jorge Alegre-Cebollada, researcher of the CNIC, was selected to represent Arsenic (As) in the Periodical Table of Young Chemists for the centenary celebration of the International Union of Pure and Applied Chemistry (IUPAC), the global authority of nomenclature and chemical terminology. On the occasion of the centenary celebration of the IUPAC and the International Year of the Periodic Table, IUPAC and the International Network of Young Chemists (IYCN) have created a Periodic Table of Young Chemists who will be paid a tribute in July 2019 during the World Congress of Chemistry and the General Assembly of the IUPAC which will be held in Paris (France). The researchers selected, like **Dr. Alegre-Cebollada**, are part of a group of 118 outstanding young chemists from around the world who embody the mission and the fundamental values of the IUPAC. The resulting periodical table will highlight the career diversity, creativity and dedication of the young chemists of the next century.





IN CARDONA WITH DR. FUSTER

For the second consecutive year the town of Barcelona, Cardona hosted the Master Course "Molecular, Clinical & Population Bases of Cardiovascular Disease and Health", in which the director of the Carlos III National Center for Cardiovascular Research (CNIC) and the Cardiovascular Institute of Mount Sinai Hospital, **Dr. Valentín Fuster**, emphasized the importance of big data and the continuous advances in technology, especially image, in the research of cardiovascular disease.

Dr. Fuster stressed, however that "we should never lose the human side of the doctor-patient relationship. The treatment with the patient is still essential in our work." The Master Course, organized by the Consorci Universitat Internacional Menéndez Pelayo Barcelona (CUIMPB) - Ernest Lluch Centre and the CNIC and sponsored by Ferrer Laboratories, was held on July 16th and 17th, with the objective of updating the latest advances in cardiovascular research and motivating young researchers.

This second edition of the course has been opened to cardiologists from all over the world thanks to its live broadcast via streaming, by the American College of Cardiology, from the website of the **Journal of the American College of Cardiology (JACC)**. More than 300 professionals attend the course, who come to Cardona from 18 different countries.

THE NEW DIRECTOR OF THE CARLOS III HEALTH INSTITUTE VISITS THE CNIC

The new director of the Carlos III Health Institute (ISCIII), **Dr. Raquel Yotti Álvarez**, visited the National Center of Cardiovascular Research (CNIC) accompanied by **Alberto Sanz**, manager of the CNIC, and **Dr. Vincent Andrés** and **Dr. Borja Ibáñez**, Directors of Basic and Clinical Research of the CNIC. The new director of the ISCIII was able to learn more about the main projects of the CNIC at the hand of **Dr. Valentín Fuster**. Then, accompanied by **Alberto Sanz** and **Dr. Andrés** and **Dr. Ibáñez**, she visited some of the CNIC laboratories together with **Margarita Blázquez Herranz**, Assistant General Director of the Networks and Cooperative Research Centers of the ISCIII.



YOUNG AND OLD PARTICIPATE ANOTHER YEAR IN THE CNIC'S "SCIENCE WEEK"

For the seventh consecutive year, the National Center for Cardiovascular Research (CNIC) has participated in a new edition of Science Week. This time, three different activities were scheduled: a conference addressed to the general public, entitled "Cardiovascular research for good heart health. Learn about how we work at the CNIC", the already traditional day 'A day with the family at the CNIC' open to the younger crowd, and the session 'Find your scientific vocation at the CNIC', directed at junior and senior high school students.

SEVENTH EDITION OF THE 'LIVE SEMINAR'

For the seventh consecutive year, the 'Live' Initiative organized an outreach session directed at those who are instilled with the hope of changing the current situation of the cardiovascular epidemic: the young population. Directed at children between 3 and 10 years old, this seventh edition of the 'Live Seminar' was held at the Autonomous University of Madrid, where the little ones could enjoy numerous heart-healthy activities, which started off with a healthy breakfast (fruit and cereal). This year, more than 500 children participated, children of the employees of the 13 companies and entities that make up the Pro CNIC Foundation. ■



TRAIN2GAIN
WHAT'S ON
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CNIC & SOCIETY

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