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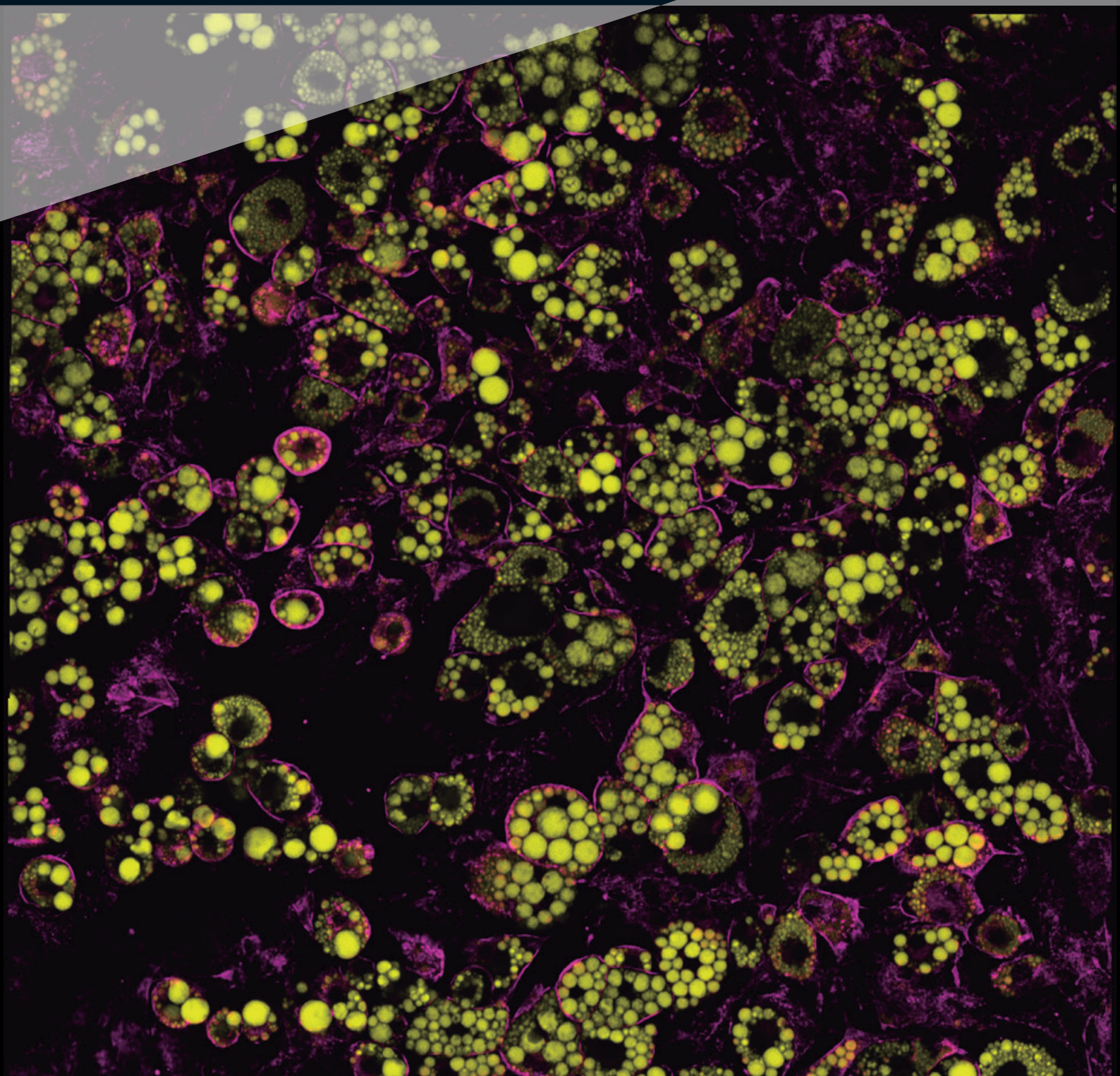

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CNIC: A TALENT INCUBATOR CENTER

The CNIC has established itself as a benchmark in training young scientists through its scholarship and biomedical training programs. Since 2006, these initiatives have supported the careers of more than 600 students, granting them access to cutting-edge research and fostering their professional development in the scientific field.

The CNIC's commitment to training young researchers is reflected in its various programs tailored to different stages of a research career.

Talent drives scientific progress. As Albert Einstein once said, *"Genius is made up of 1% talent and 99% hard work."* Perseverance and training are essential to transform potential into meaningful contributions to knowledge.

The CNIC embodies this philosophy through its training programs, which provide opportunities for young scientists to develop their talent and project it onto the world stage.

Researchers trained at the CNIC offer advice to future scientists—simple but often overlooked aspects due to daily routines. They recommend trusting oneself, being proactive and persistent, expanding professional networks, and, above all, enjoying the scientific process. They also emphasize the importance of passion, collaboration, and continuous learning in achieving leadership in research. They advise reading extensively, designing experiments meticulously, sharing knowledge with colleagues, stepping out of one's comfort zone through international stays, and surrounding oneself with excellent mentors.

A scientific career is a challenge filled with uncertainty, but also with opportunities.

At the CNIC, we strive to ensure that future researchers have access to the most advanced techniques and technologies, such as those available through the Distributed Network for Biomedical Imaging (ReDIB), a key infrastructure for biomedical research in Spain. Coordinated by the CNIC and funded as a Singular Scientific and Technical Infrastructure (ICTS), ReDIB celebrates its 10th anniversary, having facilitated access to advanced biomedical imaging technologies. Its infrastructure is essential for scientific and technological progress, justifying its availability to the R&D&I community.

Dr. Valentín Fuster, General Director of the Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC)

Additionally, this year the CNIC has strengthened its leadership in the fight against cardiovascular diseases with the REACT project, which promotes precision medicine for the early detection and personalized treatment of atherosclerosis. This initiative aims to revolutionize prevention and reduce the socioeconomic impact of these conditions. REACT reinforces the CNIC's role at the forefront of science and highlights the importance of investing in innovation to address major medical challenges.

CNIC: EXPORTING TALENT AROUND THE WORLD

CNIC is a center of excellence that has consolidated its role as a reference in training young scientists, through its scholarship and training programs in biomedicine. Since 2006 its initiatives have enhanced the careers of more than 600 students, facilitating their access to cutting-edge research and professional development in the scientific field.

Cicerone Program:
The first access to research

The Cicerone Program, aimed at university students, has counted on the participation of 431 young people, since its creation in 2006. This initiative offers an immersion experience in research laboratories during the summer months, allowing students to have their first contact with biomedical science in a setting of excellence.

Master's Scholarships: A bridge to specialization
Since 2008, the CNIC has awarded 159 Master's scholarships, providing financial support for studies in biomedicine. In addition to theoretical training, the beneficiaries do their internship and develop their thesis project at the CNIC, acquiring key experience for their professional future.

Impact on doctoral training and professional development
The CNIC's commitment in the training of young researchers is reflected in the 247 doctorates that were completed between 2006 y 2024. The long-term impact of these programs can be appreciated in the fact that the 102 people who participated in the Ciceron Program obtained a Master's scholarship at the CNIC. Of these 102, 71 of them (71%) continued a career as predoctoral researchers at the center. Furthermore, 47 of them, have already successfully defended their doctoral thesis and 24 of them are still working on them.

Additionally, the CNIC has followed-up on 232 doctors trained at the center, all of whom, have achieved promising results in the job market. 162 have continued their career in research, 19 have obtained job positions as professors or group leaders and 70 have taken their talent to the biomedical industry, contributing to the development of new solutions in this sector.

This data confirms the CNIC's key role in the training and consolidation of a new generation of scientists, ensuring the continuity of talent in biomedical research and its impact on society.

Amelia Escolano, group leader in Vaccine & Immunotherapy at the Wistar Center in Philadelphia (USA): "Day after day, I keep on applying everything I learned at the CNIC"

Amelia Escolano completed her pre-doctoral studies at the CNIC, in Juan Miguel Redondo's laboratory, which was "essential in order to develop my career as a researcher". There she acquired the necessary knowledge in molecular biology, biochemistry and immunology for the next steps of her training, but also to "acquire the scientific independence and maturity needed to confront my post-doctoral training".

Amelia recognizes how much she learned from Dr. Redondo's team, and how it benefited her scientific career, learning about professional ethics and what it means to have a good mentor.

It was during the COVID-19 pandemic when she started her independent laboratory, a period in which she had the opportunity to prepare herself for that transition. She says the new position "involves new activities and responsibilities". She remembers that the most difficult thing was "the responsibility of knowing that my team and its future professionals depended on me, financially and scientifically. The pressure to obtain funding is something that worries us all."

Amelia continues collaborating with many people who were or are at the CNIC, like Dr. Almudena Ramiro.

Her laboratory is currently working on the design of vaccines for HIV. "We work with molecular biology, animal models, structural biology and AI. Although I now focus on vaccines and immune response, I continue applying and sharing what I learned at the CNIC."

From her experience, Amelia advises new researchers to "trust themselves and their training, fight and be proactive in order to find their place and not be intimidated. Work hard, to keep at it even though they may think about quitting sometimes, to expand their network of collaborators and connections and above all, to never stop enjoying science."

Rosario Fernández Godino, director of the Target Screening and Validation area at the MEDINA Foundation:

"The techniques of cellular biology that I developed at the CNIC were the basis for the advanced models of my postdoctoral studies"

Rosario, who has directed the Target Screening and Validation area at the MEDINA foun-

dation since 2022, states that her first real contact with a research center was at the CNIC.

The step from leading her own group or developing a new line of independent research she recalls that the "most difficult thing is to obtain funding, but also to find competent people. When you are an emerging researcher, you have to do it all: be at the laboratory, write projects, write articles, etc., and it's very stressful".

Rosario is currently working on discovering new pharmaceutical drugs, targeted towards cancer, neurodegenerative diseases, and new antibiotics. Nonetheless, she claims that "the techniques of cellular biology that I developed during my PhD at the CNIC were the seed for the advanced models that I created afterwards during my postdoc".

To those who want to dedicate themselves to research, she advises them to "have innovative ideas", but also "know how to transmit them and be able to establish objectives and the experimental design in a clear way. This is the best way for the projects to receive funding."

In her opinion, "having experience abroad is essential; it's important to see how work is done abroad and to broaden horizons beyond the place where the thesis was carried out".

Rafael Mayoral Monibas, Associate Director, Translational Science, R&D Corcept Therapeutics: **"The path to research leadership requires time, dedication and continuous learning"**

The CNIC was essential for the development of my scientific skills, says Rafael. "Thanks to my mentors – Paloma Martín-Sanz and Lisardo Boscá Gomar, I developed critical thinking and scientific rigor which are essential in my research". At the CNIC, I experienced the transition to open spaces, promoting collaboration, which is crucial in research today".

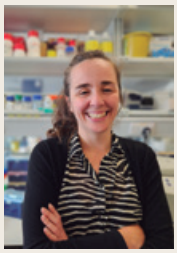
His transition from researcher to leading and developing a line of research, as well as coordinating the development of a PhD thesis or managing a team, has presented him with many challenges "I had to develop management, leadership and strategic decision-making skills, which are essential, but not frequently taught in scientific training. This experience has helped me grow and expand my vision of research."

Rafael has continued to collaborate with CNIC researchers throughout his career, participating in CIBERehd projects and maintaining contact with CNIC staff, like Andrés Hidalgo.

He is currently developing a line of research in the field of MASH (metabolic dysfunction-associated steatohepatitis). "My work connects preclinical research and clinical trials, focusing on the miricorilant compound, a selective modulator of the glucocorticoid receptor. My predoctoral experiences at the CNIC, which focused on hepatic inflammation and metabolic diseases, were essential for my current job."

Rafael comments that the path to leadership in research requires time, dedication and continuous learning. "It's crucial to choose an area that generates passion, because a scientific career demands long-term commitment and the capacity to overcome several obstacles. Collaboration and teamwork are key in leading scientific projects. During training, international stays broaden perspectives and promote valuable connections. To build a solid career, it's essential to apply critical thinking, scientific rigor and focus on long-term objectives. Furthermore, skills such as communication, project management and mentoring are essential when leading a team or research project.

Teresa Rayon, leader of the Comparative Stem Cell Dynamics Laboratory at the Babraham Institute: **"My training at the CNIC was key to becoming the scientist I have become"**



Teresa started her PhD at the CNIC in 2008 in "Vertebrate Developmental Biology", under the direction of Miguel Torres, and finished it in 2014 in "Regenerative Biology", in the program that was directed by Miguel Manzanares. "My training at the CNIC was key to becoming the scientist I have become and has influenced how I direct my own group of research. In addition to establishing my scientific skills, the collaborative work structure and access to resources were also essential."

She remembers the department's Friday seminars from her training period; "they were a key experience, where I could present and discuss my results with colleagues and group leaders. During those years I learned what it meant to "do science" and the importance of scientific integrity, reproducibility, and experimental rigor. The training seminars taught by Simon Bartlett, on how to revise scientific articles and do presentations in English, were also essential".

She chose an Institute that maintains the same philosophy and culture of excellence as the CNIC or the Francis Crick Institute: "my laboratory shares space in a large laboratory and the PhD students participate in a PhD program that includes seminars about integrity and replicability, among others".

The biggest challenge for Teresa was going from being responsible for one or two projects to being the supervisor of many. "You stop becoming the person who carries out the experiments and analyzes the data, and your role becomes that of supporting your group members in the daily development of the projects, maintaining their interest, helping them analyze, interpret and put the new results in perspective in order to design the next step. I will never forget the first time that I saw one of my group members present and carry out a project he made his own; a project which originally only existed in my head. It was a very emotional experience".

Furthermore, there is a great deal of management work that group leaders need to do, something that she had no idea about when she first started out. "This part of the job

is crucial, but it often goes unnoticed. At first, you feel like you don't know how to manage these aspects, because you've never been trained for them. Luckily, most of these tasks can be accomplished with common sense, and decisions are rarely taken on an individual basis.

Despite not having any direct collaborations with the CNIC, Teresa maintains direct contact with former colleagues of the CNIC. "A very high proportion of the PhD students from my time have gone on to forming their own independent research groups, and the training and common interests that we share allow us to keep on collaborating on our projects".

"My passion is mammalian developmental biology, and I learned a lot about it at the CNIC. Moreover, it's where I started working on mouse stem cells (embryonic stem cells), which allowed me to develop my postdoctoral project at the Francis Crick Institute in London in James Briscoe's laboratory".

In his laboratory, "Comparative stem cell dynamics", they try to understand the molecular mechanisms that measure time in animals and find out if they are the same as those that determine life expectancy.

To future researchers, she recommends "reading a lot", and that they dedicate "time to design the best experiment to answer their questions, and that they try to answer the questions that they consider important, regardless of the techniques or trends". She also advises them to "speak a lot about the results and experiments with colleagues, and help others with their experiments, because science cannot be done in isolation".

Bárbara López Terán, Xaira Therapeutics:

"The scientific career is a marathon, and enjoying the race makes it easier to reach the finish line"

Barbara completed her Master's and Doctoral studies at the CNIC, where, surrounded by high-level scientists and with access to top notch facilities and the latest technologies, she was able to develop her career as a scientist at an internationally competitive level. She highlights the support of the center's management in initiatives promoted by the PhD students themselves, such as the opportunity she had to coordinate the first edition of CNIC's PhD Day, which allowed her to cultivate leadership skills. "The combination of a high-quality scientific training and the promotion of leadership was key to helping me become a competitive figure in international science."

Bárbara, who currently works at Xaira Therapeutics, had to make the transition from purely academic research to the adjustment of doing science in the industry, at a start-up, where, although the techniques are still the same, the strategy of how to do science is completely different. In an environment such as this, she says "you need to obtain results in a much shorter time frame, focusing on very concrete objectives, which can constantly change according to factors that are not exclusively scientific, like the market needs or investments available".

Moreover, she says that moving from being a researcher to leading her own group, involved taking on new responsibilities in managing the team and resources, which also challenged her to balance the scientific part with the administrative part. "I had to learn how to make strategic decisions quickly, adapt to a more dynamic environment, and manage expectations, both within the team as well as with the external stakeholders. These challenges made me grow as a leader and establish my own line of independent research".

Currently, her team is part of the Early Discovery division, where they focus on using the most advanced technologies available in genomics and proteomics, alongside more standard experimental techniques, to study the mechanisms of action of therapeutic targets of interest. "The objective is to generate data which can support the decision of whether or not these targets should enter the company's drug development pipeline"

Her experience at the CNIC, especially in the study of cardiovascular diseases, using cellular and animal models, together with the rigorous scientific training she received there, have been key to being able to support and interpret the results of these projects. "The deep understanding of molecular mechanisms that I acquired at the CNIC has allowed me to apply this knowledge to a research context that is more oriented towards therapy, where the challenge is to translate basic discoveries to clinical applications".

She advises those researchers who are training at the CNIC to focus on a scientific topic that they really enjoy. The scientific career is a marathon, and enjoying the race makes it easier to reach the finish line. Working at other laboratories and getting out of your comfort zone allows you to learn and to grow. There are many ways to have a successful career, both in academia and in industry, the important thing is to keep an open mind".

José Ángel Nicolás, Cardiovascular Research Institute of the UCSF:

"Nobody is born a leader, nor does one become one overnight"

For Jose Ángel Nicolás, his training at the CNIC was essential for his development as a scientist. "I came to this institution in 2013, just after completing my Degree in Biology, to complete a stay through the CICERONE program. There I met Andrés Hidalgo's group, with whom I continued my training through a CNIC Master's degree and a doctorate funded by a FPI Severo Ochoa scholarship".

Each one of these stages at the CNIC have allowed him to acquire the experience, knowledge and skills necessary to do high-level science. Moreover, he highlights that the interaction with leading researchers of various subjects has broadened his scientific perspective and has taught him the importance of collaboration and critical thinking. Additionally, "the access to advanced technologies al-

lowed me to address innovative questions with unique depth and efficiency".

In terms of leadership, he asserts that his progressive career at the CNIC allowed him to develop key skills, like project management, mentoring students, and effective scientific communication. "I learned from great mentors, both inside and outside of my group, who guided me through each transition as a researcher in training, and they became role models for my professional growth. The opportunity to apply and perfect these skills in a natural and progressive way throughout my years at the CNIC, has been essential in my evolution to become the leader of my own group".

After leaving the CNIC for the Cardiovascular Research Institute of the UCSF, defining an independent line of research was the least of his problems; "there are many questions that I am passionate about and that I feel comfortable and motivated to work on. However, the most drastic change has been in my daily work dynamic".

Ángel says that the transition from researcher to group leader has been a "significant challenge, sometimes even frustrating, but also an opportunity to grown on multiple levels".

One of the biggest challenges, he adds "has been balancing scientific tasks with administrative and management responsibilities. As a leader, I discovered that obligations such as bureaucracy, management and meetings take up a lot of time, which makes it harder to be in the laboratory and miss those moments that make us fall in love with science".

Even so, leading a group has enormous rewards. "Making decisions about the direction of the research, strategically managing resources and contributing to the development of the team is extremely gratifying. For me, being a good leader isn't only about managing projects, it's also about inspiring confidence, promoting the professional growth of each member and creating an environment where everyone finds the motivation to give their best".

His laboratory researches the role of the immune cells in the function of healthy tissues, with a particular focus on cardiac macrophages. "These projects emerged from studies that I conducted at the CNIC". This project, he adds "was made possible thanks to the chance I had to develop myself in a highly interdisciplinary environment at the CNIC, where I was able to integrate knowledge of immunology, cardiology, metabolism and cellular biology to address completely new questions about the role of macrophages in tissue health."

Nobody is born a leader, nor does one become one overnight, Ángel warns. To those who are currently at the CNIC, he says "you are lucky to be in an exceptional center where you can grow, train and develop yourselves as scientists. Take advantage of this opportunity: ask for advice, learn from the great researchers who surround you and work towards your goals progressively, with foresight and determination".

Macarena Fernández Chacón, Vice Dean of the Faculty of Health Sciences and Coordinator of the Degree in Biotechnology and Department of Health and Biomedical Sciences of the University of Loyola (Seville): **"I'm in the process of finding the right balance between the administrative tasks and research"**

Macarena acknowledges that the training at the CNIC was key to her scientific and professional development. She says that working in an environment of excellence "allowed me to learn from international leaders, understand the importance of multidisciplinarity and address complex research questions with innovative approaches". Moreover, thanks to the CNIC's Units and Services, she was able to receive training in the use of advanced technologies, essential for the development of her research projects.

But she also points out that the CNIC was key to reaching her current position as group leader, from managing projects to organizing teamwork, to communicating ideas effectively and making strategic research decisions. "All of this was essential for me to lead my own research group at the University of Loyola Andalucia, where I apply not only the knowledge I acquired, but also the values of rigor, innovation and collaboration that I internalized at the CNIC".

In her new job position, Macarena assures that one of her biggest challenges has been designing long-term research strategies, but managing resources and searching for funding are also important challenges. "I'm in the process of finding the right balance between the administrative tasks and research".

She maintains collaborations with researchers from the CNIC or those who trained there and are now in other centers or countries. In fact, she states "many of my international collaborations are former CNIC colleagues who now have their own research groups".

Her team is focused on understanding the role of the endothelium in the calcification of the aortic valve, a serious problem in cardiovascular health, for which there are still no effective therapies. "This line of research comes from my training and experience studying endothelial heterogeneity in Dr. Rui Benedito's group, as well as from my current collaboration with Dr. Antonio Ordoñez, professor and cardiovascular surgeon at Virgen del Rocio Hospital (Seville).

From her time at the CNIC she recalls the unique environment there. "It's a privilege being able to train there", she says. That's why she advises those who are now starting their career in research to "make the most of this environment at the CNIC, which offers exceptional resources, a collaborative work environment and the possibility to learn from top notch scientists". She also recommends "developing critical thinking, learning to formulate relevant questions, and above all, not being afraid to step outside your comfort zone".

And, while considering that the career of a researcher is full of challenges and moments of uncertainty, she affirms that every obstacle is a learning opportunity. "It's important to be perseverant, stay motivated and surround yourself with good mentors and collaborators".

Juanma González-Rosa, Assistant Professor at Boston College and Affiliated with Harvard Medical School
"My doctoral training at the CNIC was the most important and influential phase in the development of my career"

For Juanma, his doctoral training at the CNIC represented the most decisive phase in his professional career. "It has also been, by far, the most gratifying and stimulating."

His connection with the CNIC started in 2008 as a student of the Cicerone Program and he later became Nadia Mercader's first doctoral student in the Department of Cardiovascular Developmental Biology. "During this period, I was exposed to high-level science in a collaborative and dynamic environment. I learned from seminars with leading researchers and discussed my work with them. The most influential aspect was the atmosphere of excellence, which has shaped my way of working, a decade later."

Juanma considers that joining the CNIC was one of his best decisions. "I feel very lucky: this experience was essential to launch my career as a scientist and take off with an extraordinary foundation."

However, he highlights that the transition from researcher to group leader involves significant challenges. "Going from being focused exclusively on your research to leading a group is a very difficult transition. After years of preparing to be a researcher, you suddenly need to take on duties that you were not trained for, like managing a team, resolving conflicts and ensuring funding. You become a leader and a promoter of your science. It's an exciting challenge, but the transition is difficult."

Although, he is currently in contact with some CNIC researchers, he'd like to strengthen these collaborations further. "I firmly believe that there are many synergies and collaborations left to explore, and I feel very attached to the center, as my alma mater."

Juanma's work is closely linked to his studies at the CNIC, focusing on identifying the mechanisms that enable the regeneration of the heart in zebrafish. "We want to learn from nature and evolution on how to regenerate the heart, especially by eliminating the fibrotic tissue. This was an observation from my thesis at the CNIC and it's still key in our projects. We are interested in understanding the role of the immune system and its communication with the fibroblasts in this process."

Moreover, his scientific approach is based on a quote from Nobel prize winner Sydney Brenner: "Progress in science depends on new techniques, new discoveries and new ideas, probably in that order." With this premise, his laboratory constantly seeks to overcome technical barriers.

For new scientists, Juanma emphasizes that research is "a long-distance race, extremely tough, but also very gratifying, at times." He'd like to remind his students that being a researcher is a vocation for discovery. "I would advise them to build a network of mentors that guide them, and to enjoy the whole process, not just the end goal, as daily effort is the key to success."

Yamilee Hurtado Roca, Scientific University of the South, Lima. "The CNIC was a fundamental pillar in the development of my scientific abilities and in my evolution as a research leader"

For Yamilee, the training at the CNIC was a fundamental pillar in the development of her scientific abilities and in her evolution as a research leader. "I had the opportunity to work in a highly-specialized environment, where I could strengthen my abilities in the design and execution of biomedical research projects."

Furthermore, the CNIC's methodological rigor and innovative approach, allowed her to perfect her capacity to interpret results and find solutions to complex scientific problems.

From a leadership point of view, the training she received a the CNIC provided her with the tools needed to coordinate multidisciplinary teams, manage research projects and promote effective communication within a collaborative environment.

After her time at the CNIC, Yamilee has expanded her focus towards public health in Peru, leading management departments in research, development and innovation in the health sector. "I have taken on strategic responsibilities, like defining national health research priorities for Peru by 2030, thus contributing to health research in my country".

Her main lines of research focus on maternal health, women's health, non-communicable diseases and environmental health, with a focus on both clinical and public policy development. "These areas of interest emerged mainly from my experience at the CNIC, where I acquired an integral vision of the risk factors and the importance of health prevention", she assures. Although she currently does not have any active collaborations with the CNIC, she acknowledges that the experience and learning she acquired there have been vital in her development as a researcher. She has created a network of contacts with national and international researchers with whom she collaborates on projects aimed at finding innovative solutions for public health challenges. To the young researchers at the CNIC who aspire to lead projects and teams, she recommends that they focus both on strengthening their scientific foundation, and developing their management and leadership skills. She highlights the importance of combining rigorous training in public health, clinical research and advanced methodologies with the ability to work in multidisciplinary and international environments.

She also emphasizes the need to take advantage of every opportunity to learn from the experts, seek mentorship and fearlessly take on new challenges. "Developing skills in communication, teamwork and project management is essential to transform innovative ideas in initiatives that have a real impact on public health". ■

DISTRIBUTED BIOMEDICAL IMAGING NETWORK (REDIB): A DECADE PROMOTING SCIENTIFIC RESEARCH

In the last ten years, the Distributed Biomedical Imaging Network (ReDIB) has consolidated its position as a vital infrastructure for biomedical research in Spain, offering access to advanced technologies in biomedical imaging to national and international researchers. This initiative, coordinated by the National Center of Cardiovascular Research (CNIC) and financed by the Ministry of Economy and Competitiveness as a Unique Science and Technology Infrastructure (ICTS), has made it possible to overcome the barriers and allow access to expensive and specialized technology, promoting the advancement of science in several fields.

ReDIB was created in 2014 in response to the scientific community's increasing need to access advanced biomedical imaging tools. When it first started, it was made up of two founding nodes: the CNIC in Madrid, with its Advanced Infrastructure for Translational Imaging (TRIMA-CNIC) and the CICbiomaGUNE in San Sebastian, with its Molecular and Functional Imaging Platform. Later, in 2018, the Complutense Bioimaging Center (BioIMAC) of the Complutense University of Madrid and the PREBI-GIBI230 (La Fe Imaging) of the La Fe University Hospital of Valencia also joined. (https://www.redib.net/redib)

The CNIC's scientific-technical biomedical imaging infrastructures are indispensable for the development of a scientific and technological research that is unique and exceptional in its kind, with a very high cost of investment, maintenance and operation. Their importance and strategic nature justify their availability to the whole Research Development and Innovation group.

The creation of these infrastructures facilitates the collaboration and cooperation of their capacities among them. In many cases they are geographically spread out in Spain, this allows their critical mass to increase, improve the competitiveness of the group, and avoid duplications and redundancies.

ReDIB works under a single-window model, with a coordinator from the CNIC who manages its operation. Each node has its own structure of self-management, with a node manager and highly trained specialists and technicians who use state-of-the-art technologies.

Currently, ReDIB has 16 strategic facilities hosting 49 advanced technologies. These include tools for molecular, functional, multi-modal, and sequential imaging studies, as well as advanced microscopy, manufacturing of nanoparticles, radiochemistry and clinical and preclinical tests. The nodes also have infrastructures for animal-testing, certified laboratories and specialized operating rooms.

The importance of biomedical imaging studies was demonstrated by Dr. Valentín Fuster, General Director of the CNIC, President of Mount Sinai Heart and Medical Director of Mount Sinai Hospital of New York, through projects like Bioimage and PESA CNIC-Santander, which are some of the most representative in clinical research and have proven the usefulness of imaging techniques for the detection of the atherosclerotic disease, long before the appearance of clinical symptoms. The TRIMA@CNIC node, as the founding node of ReDIB, has provided advanced technologies, both in clinical and preclinical imaging, through its basic and translational units; it has also described new study and interpretation imaging techniques that allow for more precise and efficient evaluations.

ReDIB does not establish limitations on the acceptance of potential users, as it responds to national and international requests in all the sectors, especially the medical and pharmaceutical ones, but also in the agriculture and industry sectors, among others. It offers services to public and private entities, from non-governmental organizations, universities, research centers and hospitals. Users have access to the biomedical imaging facilities of ReDIB through an easy access protocol, with different service offering modalities, depending on the requesting user´s profile and the complexity of the studies requested.

Competitive Open Access

ReDIB is considered an ICTS because it possesses three fundamental characteristics: it is publicly owned, its facilities have unique technology, and these facilities are open to the research community by competitive access. The infrastructures that are considered to be essential are those that contribute significantly to the uniqueness of the network. At least 20% of its total capacity is offered to the users of the scientific and technologic community in competitive open access (COA) calls.

During the last 10 years ReDIB has offered COA calls (https://www.redib.net/convocatorias) to researchers from different countries, through a defined and public access protocol. The applications are evaluated on the basis of scientific-technical excellence criteria and technical viability, regulated by a protocol which establishes the frequency of the COA calls. This protocol is applied by an Access Committee that is external to the ICTS, that can count on the support of experts that belong to the infrastructure. https://www.redib.net/upload/secciones-publicas/redib-02-pda-protocolo-acceso_original.pdf

The COA mechanism is easy and includes: 1) review of the technical viability of carrying out the presented project at one of the network facilities; and 2) evaluation of the relevance and scientific quality of the application by an expert advisory committee. After the review and evaluation of the proposals presented, the accepted applications are classified in two categories according to the score that they have obtained in the review with the advisory committee: 1) with the assigned usage time and, 2) on hold. This way a prioritized waiting list can be created which can minimize the risk of overdemand of the facilities.

In these last 10 years, ReDIB has acquired new infrastructures and updated others so as to offer better features and capabilities to the scientific community. For example, for preclinical studies it is worth mentioning the purchase of a PET/SPECT/CT system, a 9 4T MRI and the upgrade of 7 T and 11 T MRI system components.

For the clinical studies, it is worth mentioning the purchase of a new spectral CT device, a PET-CT, and a 3T MRI; as well as the upgrade of existing 3T MRI and PET/MRI facilities. The modernization of these infrastructures has been carried out using proper funding from each node or through European aid funding: FEDER funds or

In these last 10 years, ReDIB has acquired new infrastructures and updated others so as to offer better features and capabilities to the scientific community

specific programs for ICTS funding through the Recovery, Transformation and Resilience Plan.

Furthermore, the COA calls not only give access to optimized state of the art imaging services at subsidized prices, they also allow: 1) Access to certified facilities, that guarantee high-quality reproducible quantitative data; 2) Access to scientists and technicians experts in imaging who can address the full potential of the facilities; 3) Access to new applications and new protocols for image acquisition and data analysis; 4)Access to new collaboration opportunities among researchers and imaging networks; and 5)Communication with technical staff that can offer ongoing orientation and short response time to users.

Since its creation, ReDIB has launched 14 COA calls, in which 166 projects have been presented, and 161 have been accepted, which represents an acceptance rate of 96,9%. The proposals are evaluated according to criteria of scientific excellence, technical viability and potential impact, and are reviewed by an external committee of experts.

Regarding the sector of origin of the 166 projects, 69% are from the academic sector of universities and research centers, and only 2% are from companies or societies of the industrial sector. This may be related to a lack of permeability of ReDIB in these sectors, in terms of communication and applicability. Regarding the subject matter of the proposals, of the 161 approved projects, 142 (88%) are from the subject matter of Biomedicine, 13 (8%) from Bioscience and Biotechnology and the other 6

from other scientific knowledge areas (energy and transport, environmental science and technologies and material technologies). Regarding the country of origin of the international proposals presented in the COA calls during the above-mentioned period, there were 10 projects approved from 5 different countries: four from France, two from Portugal and Great Britain, and one from Ireland and another one from Australia.

The projects supported by ReDIB have generated a significant impact on scientific research. Between 2020 and 2024, 144 competitive accesses were granted, which resulted in the publication of 103 scientific articles in journals classified with impact factor, 36 conference presentations and 3 technical reports.

The average impact factor of the journals has displayed a constant increase, growing from 5.01 in 2020 to 8.81 in 2023. In addition, 69.7% of the publications were issued in high-impact journals (Q1), and these investigations have summed up a total of 927 citations, proving their relevancy in the scientific community.

The 103 scientific articles were published in 83 different journals, and the average impact factor of the journal (year of publication) varied from 5,01 to 8.81. The journals with greater impact factor, and which show results obtained from the use of the network infrastructures, were Cells, European Heart Journal, Circulation, Neurotherapeutics and Journal of the American College of Cardiology. In these 5 years, on average 69,7% of all the articles were published in the Q1 journal of its field and have been cited by other authors a total of 927 times.

During the last decade, ReDIB has significantly invested in the acquisition and upgrade of technologies that allow them to stay at the forefront. Among these acquisitions, some that stand out are the PET/SPECT/CT systems, high-field MRIs (9.4 T and 7T) and clinical equipment like PET-CT and 3T-MRI. These improvements have been financed through European funds (FEDER) and national programs, which have made it possible to expand the network capacity, in order to handle more ambitious and complex projects.

In its 10 years of existence, the ReDIB has proven to be an essential infrastructure in Spain which facilitates the access to advanced biomedical imaging technologies, especially in clinical and preclinical research. Since its creation in 2014 and the incorporation of new nodes in 2018, ReDIB has expanded its service capabilities and increased its scientific impact, with the increase in the quantity and quality of scientific publications. Its management model, which includes a single-window model and an Access Committee for the evaluation of proposals, has contributed to a high acceptance rate of applications, the optimization of the use of available resources, and the allocation of these in a transparent manner.

Despite its success, ReDIB also faces challenges in terms of outreach. Although most of the applications come from academic and research institutions, the interest from the private sector is still limited, representing only 2% of the applications received. This highlights the need to strengthen the communication with technological and pharmaceutical companies, as well as promoting the internationalization of the network.

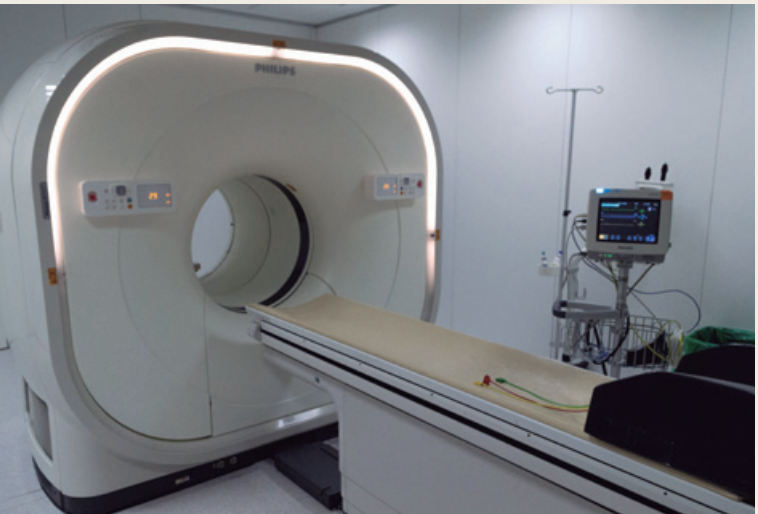
Furthermore, the growth of demand to access the infrastructures demonstrates the importance of continuing to optimize the management of resources and guaranteeing the long-term sustainability of the network.

Impact on Biomedical Research

The impact of ReDIB is reflected in the scientific advances that have been achieved thanks to its support. Emblematic projects like PESA CNIC-Santander and Bioimage have demonstrated the usefulness of imaging technologies in the detection of diseases such as atherosclerosis in early stages, long before the appearance of clinical symptoms. These initiatives have proven how valuable the network is as a strategic tool for translational research.

In its 10 years of history, ReDIB has established itself as an essential infrastructure for scientific research in Spain, offering access to state-of-the-art biomedical imaging technologies. Its efficient management model, combined with the continuous modernization of its facilities, have permitted a notable increase in the quantity and quality of scientific results.

Nonetheless, the potential of ReDIB has not yet been completely exploited. Expanding its reach to the private sector and internationalizing its impact will be key steps to guarantee that this network continues being a motor of innovation and development in the next decade. ■



CNIC CONFERENCE
"UNDERSTANDING IMMUNITY IN CARDIOVASCULAR DISEASE"

In recent years, we have observed how important the role of the immune system is in the development, structure and function of the cardiovascular system, which opens up new treatment possibilities that were unknown of up until now.

The objective of the CNIC Conference 'Understanding Immunity in Cardiovascular Disease', which brought together the leading experts in the field of immunology and cardiovascular disease in Madrid, is to promote state-of-the-art science in the fields of immunology, vascular biology and cardiology. All the participants of this event were given the opportunity to learn how immune cell dysregulation affects the cardiovascular system, as well as its role in the development and progression of cardiovascular diseases, like atherosclerosis, heart failure and inflammatory cardiomyopathies.

The deregulation or alteration of the normal control of cellular processes of the immune system is key in atherosclerosis and other cardiac pathologies, like inflammatory cardiomyopathies or myocardial infarctions, which are normally associated to an immune response to repair damage or fight against infection. However, an exaggerated inflammatory response or an autoimmune response against cardiac or vascular tissue can result in mid or long-term damage. Understanding how these processes work and intervening using the tools that immunotherapy offers us can improve the life expectancy and quality of life in these patients.

During the CNIC Conference, organized by researchers Almudena Ramiro, David Sancho, and Pilar Martín from CNIC; Andrés Hidalgo from Yale University; and Klaus Ley from Augusta University, recent advances in these crucial areas were presented:

- Regulation of the immune response in heart repair.
- Mechanisms that control cardiovascular inflammation.
- Autoimmunity in heart disease.
- New mechanisms of inflammatory cardiomyopathies.
- Immune responses in atherosclerosis.
- Immune cell-cell interactions in cardiovascular diseases.

Director of the Medical Research Center and the Institute of Immunobiology at the Kantonsspital St. Gallen (Switzerland)

Burkhard Ludewig:

"PERSISTENCE IS KEY IN SCIENTIFIC DISCOVERY"

Burkhard Ludewig is the director of the Medical Research Center and the Institute of Immunobiology at the Kantonsspital St. Gallen (Switzerland). His work focuses on the interaction of viruses with the innate and adaptive immune systems. Additionally, his laboratory has developed a transgenic mouse model for the in vivo targeting of stromal cells. He is a member of the editorial boards of the Journal of Immunology and the European Journal of Immunology.

Can you summarize the relationship between inflammation and cardiovascular disease?

The cardiovascular system is incredibly complex, encompassing the heart and blood vessels. It is fascinating scientifically because it involves physical, metabolic, and inflammatory processes. Over the last 20-30 years, we have learned that the immune system plays a crucial role in these processes, particularly in conditions like atherosclerosis. Our challenge is to distinguish causes from consequences in these diseases and develop targeted therapies. Heart failure, for example, is becoming increasingly common, and we urgently need new treatments. Understanding the role of immune processes in the heart is the next frontier in addressing heart failure.

What are you focusing on in your research on heart failure and the immune system?

Our research centers on the interactions between cardiomyocytes (heart muscle cells) and the immune system. While cardiomyocytes cannot regenerate themselves once lost, we aim to identify early processes that lead to their damage and explore ways to maintain their function. We believe that immune cells and fibroblasts support cardiomyocyte resilience, and we are working to understand how to preserve and restore their homeostasis.

Immunotherapy is complex and can have side effects. How do you address these challenges?

Balancing the immune system is always challenging. Immune therapies, like those for cancer or inflammatory diseases, show promise but require precision to avoid unwanted side effects. We are learning from other fields, like oncology, where approaches like immune checkpoint inhibitors and anti-inflammatory therapies have been transformative. Our goal is to adapt these insights to

cardiovascular diseases while respecting the unique characteristics of the heart.

How far are we from applying immunotherapy to cardiovascular diseases like we see in cancer?

It is a complex road, as balancing immune reactivity in the heart is crucial. For example, myocarditis—whether autoimmune or caused by immune checkpoint inhibitors—shows how delicate this balance can be. We are in the early stages of integrating immune-based treatments into cardiology, but progress is happening. Like cancer immunotherapy, this will take years to develop, but the potential is transformative.

What inspired your focus on cardiovascular diseases?

I started as a veterinarian, working on viruses and the immune system. During my postdoctoral fellowship, I became fascinated with how immune reactions around blood vessels affect heart health. I was advised to be patient, as developing models and insights in this field could take a decade or more. It has been over 15 years, and now we are seeing significant progress. Persistence is key in scientific discovery.

Balancing the immune system is always challenging. Immune therapies like those for cancer or inflammato-ry diseases, show promise but require precision to avoid unwanted side effects

You have participated in the CNIC Conference: Understanding immunity in cardiovascular? What stood out for you?

The conference is an incredible opportunity to meet world-leading experts in inflammation and cardiovascular disease. The lineup of speakers is fantastic, the quality of the talks is exceptional, and most importantly, the interactions are very productive. The event's design and planning have been outstanding.

How do you view the CNIC?

It is an excellent institution with outstanding infrastructure and talent. The Spanish government's investment in research is impressive, and I hope the CNIC continues to attract top researchers globally. Mobility within Europe and beyond is essential to fostering collaboration and innovation. ■

Group leader at the Francis Crick Institute in London and the John Curtin School of Medical Research in Canberra

Carola Vinuesa: "SCIENCE OFFERS MANY OPPORTUNITIES TO REINVENT YOURSELF, TO TRAVEL, TO WORK IN DIFFERENT ENVIRONMENTS, AND TO MEET NEW PEOPLE"

Carola Vinuesa is a Group Leader and Assistant Director of Research at the Francis Crick Institute in London (UK). Dr Vinuesa has discovered new T cell subsets that control B cell responses (follicular helper T cells [Tfh] and follicular regulatory T cells [Tfr]), as well as the mechanisms by which they regulate antibody responses and limit autoimmunity. Her recent discoveries are connecting genetic variation in humans to autoimmune diseases such as lupus, and shedding light on disease pathogenesis. . Her name became famous in Australia, and then throughout the world, following a long judicial process in that country, in which this Spanish immunologist managed to free Kathleen Folbigg from prison, a woman who was imprisoned for twenty years accused of having killed her children, by proving that her four deceased children were not murdered, but carried genetic mutations that would explain their premature death.

Your laboratory has been researching the factors that contribute to the development of autoimmunity for many years.

Over the past 10 years, we have focused on discovering new or very low-frequency genetic variants in patients with severe immunodeficiencies, especially in children. The genetic architecture of these diseases covers a very wide spectrum, from highly polygenic diseases with many contributing variants, to a narrower monogenic spectrum where only one variant can cause the disease. Identifying these variants in monogenic diseases offers us valuable information about the pathogenesis or mechanisms of the disease. Even though these severe and rare mutations are found in few children, understanding how they cause the disease can give us bigger clues to help understand autoimmune diseases, which in many cases are not understood well.

Our team is also working on linking human genetic variation to autoimmune diseases to identify more specific treatments. By sequencing the DNA of patients with various forms of autoimmunity, such as lupus, we have identified new and rare variants that highlight the role of specific genes in immune tolerance. This is helping us create different disease models that we can use to better understand disease development, improve diagnosis, and test new treatments.

For example, in my lab we have found a central pathway in lupus. We have designed a model that replicates the human disease, introducing the mutation from a girl with lupus into a mouse model that develops severe lupus, similar to the patient's. By adding two more sophisticated models, that we have developed ourselves, we can finally answer questions that previously had no answer. Where do the cells that produce antibodies come from? Are they new cells from the bone marrow, or are they autoimmune cells that were generated by some viral trigger and have survived for decades? We can research whether these cells are in a specific tissue or in the bone marrow. This has been very exciting for us, as these models allow us to address fundamental questions that used to prevent us from better understanding these diseases.

Your research has also had an impact on forensic medicine, at least in Australia.

Thanks to the genomic work that we carried out in the Kathleen Folbigg case, we have started to understand the

differences between clinical genomic analysis and forensic genomic analysis. Unfortunately, there are many cases today where a genomic diagnosis adapted to medical forensics is not being applied. That is, the level of certainty required for a clinical diagnosis is different from that needed to establish reasonable doubt in a trial. However, up until now, the genomic framework we have used, that of the American College of Medical Genetics and Genomics, is rigid because it needs to be so, in order to be useful in the clinic. But we are seeing that it has limitations in medical legal cases and that it needs to be adapted, for example, to look more closely at variants of uncertain significance (VUS).

While working on the Folbigg case, I suppose you faced many obstacles in explaining your discoveries to the judges and the judicial system.

Part of the obstacle was getting the legal system to understand it, and the other part of it was due to the disagreement between two groups of geneticists. I'm not saying that one was right and the other was wrong, because we were all trying to do our best. However, the framework used in court was very rigid. This approach, although suitable for use in the clinic, did not allow for the exploration of unknown genetic variants, which are often more lethal, precisely because they are severe, and therefore studied less. Because they are so severe, these mutations often prevent individuals from reaching reproductive age and are therefore not transmitted to offspring. That's why, it is possible that they may only be detected once in a lifetime. Due to their rarity, it is difficult to classify them as likely pathogenic or non-pathogenic variants, but that does not mean that they should be excluded from study, especially in a legal context, such as in cases of sudden infant death.

Unfortunately, this is not the only case. Since we have been working on this case, we have received other similar ones, in which women have been accused – some possibly wrongly – of causing harm or death to their children. In many of these cases, rare diseases are involved. We know that there are already around 10,000 rare genetic diseases affecting 400 million people, and it is not unusual for a child to have two genetic diseases at the same time. However, it is impossible for a pediatrician to have all these diagnoses in mind or have direct experience with them. Many of these diseases manifest themselves in unusual ways, and sometimes accusations against mothers are made when they insist that something is wrong with the child, or when they make complaints against a doctor, ask for a second opinion, or seek multiple consultations. It is at these times that, unfortunately, they are unfairly accused.

But we are seeing that it has limitations in medical legal cases and that it needs to be adapted, for example, to look more closely at variants of uncertain significance (VUS)

My laboratory has received some of these cases and by conducting more in-depth genetic studies, we have discovered variants that were at first considered uncertain. However, by analyzing the family tree, we can see that some mutations are new. These are things that are not researched in routine laboratory diagnostics. Even though diagnostic laboratories do a good job, they may not have the appropriate resources or methods to approach these complex legal cases

Aren't you worried that you have become a reference for these types of legal cases?

We can't do very much about this. Of all the things that have been mentioned to me, I have only been able to help in a few cases because I do everything in my free time and without remuneration. We are talking about a group of people concerned about this problem, trying to create a foundation. The problem is that now there is no money to pay geneticists, pediatricians or lawyers who want and can analyze these cases in depth. It is a very big setback, because there are hundreds of mothers - mostly women, although also some fathers - accused of having caused harm, when in many cases it seems that they are dealing with rare genetic diseases.

We can't do everything, so it is necessary to educate and explain the need to conduct a broader and more in-depth diagnosis, including variants of uncertain significance (VUS). I'm not saying that we shouldn't aim for certainty that the variant is pathogenic, that is what we aim for. What we have observed is that, as soon as you contact experts, analyze the family tree, and obtain more samples from the family, in some cases functional tests are performed and those variants are reclassified. However, it is important to incorporate them into the genetic study from the start, and not to limit yourself to gene panels only, as many times the mutation occurs in a gene that was not previously anticipated, but which makes more sense later.

Your approach to genomics seems to be more dynamic, not as fragmented as in other fields.

Current genomics is fragmented, routine, and focused on the clinic and on actionable variants, for which, it is true, a very high level of certainty is required. However, in many of these cases of sudden death, the cause can be very different pathologies, which is sometimes diffi-

cult to anticipate. From sudden death related to epilepsy, to cardiac death, or even to mitochondrial or metabolic diseases. Therefore, it is necessary to address these cases in a much broader way, without restricting ourselves to gene panels only, and with more inclusive entry criteria.

Many of these variants, precisely because they are so pathogenic, lethal, and rare, have not been seen before, which makes their initial classification as pathogenic variants difficult.

Do you think your medical vocation influences your approach to research?

I think that those of us who practice medicine, in general, do so because we are attracted by the idea of being able to solve problems. It is a vocation of service. At first, I thought that I wanted to be a Doctor Without Borders and go to work in some country in Africa, for example. But then I changed direction a little because I was very interested in research and I saw that through it, large-scale problems that affect many people could be resolved, and that was very gratifying for me.

Why do I dedicate myself to this? I am very affected by injustice. When I see cases in which there have been accusations and, from the start, it seems obvious that it is a medical problem, it worries me. I have a medical background and, for example, in the case of Kathleen Folbigg, the mother accused of murdering her four children, when they tell you that the children died, and that one of them had epilepsy with blindness and another myocarditis, it is natural to think that something does not add up. Furthermore, all the evidence was circumstantial, because no one had seen this woman harm her children, which is very different from other cases.

You immediately think it makes sense to do a more in-depth investigation, and currently genetics has provided us with tools that we did not have 10 years ago. We were already doing this type of work, so why not apply it, if it can help other people. I was contacted after they tried to speak to several people who for various reasons, could not or did not want to do it. So, I thought: "well, if we can help, and they can't find anyone else to do it, why wouldn't we?".

There are researchers who are more motivated by pure knowledge, discovering a gene or a specific pathway. In your case, it seems that you are not only interested in the knowledge itself, but also on its applicability, like in this case where it served to defend a person, or for example, in the lupus case.

I have always been motivated by knowledge. I love asking important and difficult questions, and facing the challenge of solving important

I think that those of us who practice medicine, in general, do so because we are attracted by the idea of being able to solve problems

dilemmas in science. However, it is true that when you come across cases like these and you get involved, even though it is very satisfying, it can also be very painful and difficult. In fact, in this case that we discussed earlier, I felt quite attacked; anyone who has undergone a judicial process knows that. You are criticized, and during these years, I felt very stressed out. But looking back, I think it has been one of the things that has given me the most satisfaction in my life. Being able to help a person, prove their innocence... and it is not just one person. This has also led to a review of the legal system in Australia.

This case was recognized as the biggest miscarriage of justice in Australian history: 20 years in jail, plus 5 previous years, arrested and charged. It was a huge mistake, with multiple trials, many judges involved and numerous legal reviews. This has caused Australia's legal system to consider the need for an independent criminal case review commission, which did not exist up until now. Before, it was a politically elected figure who decided whether a case was reviewed or not.

It is gratifying to think that a legal system can be improved. Cases like this exist all over the world, and there is now a greater awareness of how easy it is to give a wrong verdict or diagnosis. There are 4 or 5 diseases within this spectrum where, without proper genetic testing, it is very difficult to conclude that the child has been harmed, and not recognizing that it could be a rare disease. We already know that there are 10,000 rare diseases, and sadly, many of the children we see have more than one. For example, a mutation that causes chronic pain syndrome and, at the same time, a mutation that causes aphasia, intellectual disability or epilepsy.

In the past, when a child had seizures and pain, it was considered a possible sign of abuse. But nowadays, we must consider the possibility of rare diseases. I think this is positive, because it means there is a lot of potential for change, both in medicine and in justice, and in how mothers are treated, who are 90% of the defendants in these cases. This is because they are usually the caregivers.

If you could change something in the judicial system, what would it be?

I would like to change two things. Firstly, to establish clear guidelines on who should be consulted when statistics or probabilities

are used in court, because the misuse of statistics has contributed to many wrongful convictions. If the court needs to use statistics to back up a conviction, it should consult impartial expert entities such as the Royal Society of Statistics in London.

Secondly, before accusing a father or mother of harming or killing a child, when there is no strong evidence or history of abuse, a thorough genomic investigation should be conducted, including variants of uncertain significance, and that are not part of routine clinical genomic diagnosis.

In some ways, you got rid of the pressure of living in Australia.

It wasn't because of this case, although yes, I went through a hard time because of it. However, it made sense for me to go back to Europe; I had been at the same university for 20 years and my family is in Spain. I liked life in Australia, and I have very good memories.

It was the time of the transition. I started with the case in 2018. The first interview was between 2018 and 2019, and in 2021 we requested the petition of forgiveness, because we published the article in 2020. In August 2021 I came to England, and in2022 they called me for the second consultation. We had the second interview between 2022 and 2023. In fact, I went to Australia twice, in November 2022 and in February 2023.

How does someone go from wanting to be a Doctor Without Borders to studying immunology? It's quite a big change.

My residency years in the United Kingdom were very hard. I think the health system had very few resources: there were few doctors and we suffered a high level of pressure and lack of supervision, which was very stressful for me. In addition, I was always interested in understanding diseases better and how they work. I like asking questions. So, I asked myself what I would be interested in studying if I could choose a field to research. Despite my experience in India and Ghana, where the biggest problems are infections, I must say that I have very fond memories of my immunology teachers during my degree. For me, it was one of the subjects I liked the most. Both Eduardo Ortiz de Landázuri and Francisco Sánchez Madrid were my teachers at La Princesa Hospital, where I studied the last three years at the Autonomous University. I have wonderful memories of how they taught us immunology, which nowadays, we know is at the root of many diseases, such as inflammation, autoimmunity or immunodeficiencies. I found it to be a very attractive field, and that's why I decided to pursue it.

Do you transmit this passion for research to the young generations in your laboratory?

We are lucky to continue having very motivated students. Science is still a vocation, and those who come to do doctorates or postdocs are really interested. I think it's easy to spread passion and interest when you have them yourself. I love seeing how they fall in love with research, how they begin to formulate their own hypotheses. It's a wonderful process, and one of the things I enjoy most is working with young people and watching them grow and get excited about important questions, although to some they may seem a little dark.

Mentoring is not something that is formally taught, it's more a question of trial and error. What advice do you give your students?

I think the best advice I can give them, and I see it with my daughters too, is that they believe in themselves. If I can get them to finish their PhD or post-doctorate believing in their capacity to generate good hypothesis, I will have done my job. Giving them space to ask questions, to design their own experiments and believing that they are good and capable, is an art. If they reach that level, they don't need any more advice. If they believe in themselves, they will have a good career ahead of them and they will be good researchers. And it is hard, because it is a competitive career and sometimes you receive negative criticism. The scientific articles are always harshly reviewed, and everything is very competitive. But, if despite that negative atmosphere, they believe in themselves, they can succeed.

If you could say something to your 20-year-old self, what would you say?

Maybe I would tell her not to worry so much about the future. Deciding whether to leave medicine or go into research was very stressful for me. Over time, you realize that life takes you down paths you never imagined before, and you end up finding things that you are passionate about. Don't worry, life takes many turns, and change is good. I would tell myself to allow me to be guided by my own instinct. Many of my decisions were coincidental. I never went to do job interviews; opportunities just came up randomly. That's life, and change is positive. You learn from everything, and there is no experience that I look back on and think was negative. I'm sure I learned something important from all my experiences. Science gives you many opportunities to reinvent yourself, to travel, to work in different environments and meet new people. I would tell myself: take advantage of the positive side in every situation and learn from your mistakes. Don't stress out about not knowing which way to go. Life is full of changes and opportunities, and you never know what lies ahead. ■

Group leader at the Neuromaternal research group at the Gregorio Marañón Hospital in Madrid

Susana Carmona:

"MY PRIMARY INTEREST IS TO ASK QUESTIONS, TRY TO ANSWER THEM AND COMMUNICATE WHAT I LEARN"

In 2017 Susana Carmona's team demonstrated for the first time that the anatomy of the brain in postpartum mothers 3 months after birth was different than what it was before they got pregnant for the first time. Her team explained what mothers already sensed: motherhood transforms us. Carmona, Psychologist and Neuroscience Doctor, directs the Neuromaternal research group at the Gregorio Marañon Hospital in Madrid, this group researches the brain changes that come with pregnancy and motherhood. In her book Neuromaternal, she gathers scientific information about this process and asks and answers many important questions about pregnancy, a condition that nearly 85% of women experience at some point in their life.

What happens in a woman's brain during pregnancy?
Our studies strongly prove how a woman's brain changes dynamically and persistently during pregnancy, modulated by hormones. These changes are directly connected to the endocrine, immune and cardiovascular systems. They are crucial and require more attention. What do pregnancy, menopause and adolescence have in common? They are all periods where abrupt hormone changes take place, which make the body and the brain readapt themselves, thus increasing vulnerability. That's why pregnancy, adolescence and menopause are periods with a high incidence in diseases in women, those such as anxiety and depression.

Why do changes occur in pregnant women's brains?
We are trying to identify the different mediating factors. In animal models, the hormones, especially estrogens, play a crucial role, along with others like prolactin, progestins and oxytocin. Estrogens are important in humans, but they are not the only ones. These interact with the cells from the immune system and the blood flow which increases up to about 50%. Identifying just one causing factor is impossible due to the complexity of the process.

In your book «Neuromaternal» you affirm that new neurons are generated in the brain.
In mice models, yes. In the subventricular part of the brain, cells that are influenced by prolactin, are generated and these migrate toward the olfactory bulb before the birth, helping the mother recognize the smell of her child. Verifying this in humans is very difficult.

Does personality change during pregnancy?
The idea that personality changes during pregnancy is related to the concept of matrescence. The book relates experiences from many mothers and theoretical psychological data. Neuroimaging techniques show changes in parts of the brain involved in the perception of the self, but it is a very complex issue.

·How are the changes in the brain during pregnancy?
In humans, we have not been able to test it completely. In animal models, during the first pregnancy strong changes are produced, and then there are readjustments in successive pregnancies. Cross-sectional studies in middle aged women suggest that pregnancy has cumulative effects on the brain. Machine learning models estimate that women who have had children have younger brains, with a limit of up to 3 years.

Most of the people who lead these types of researches are women. Certainly, you have been asked about female empowerment in science.
It's not just about empowerment or social justice. We have contributed perspectives that perhaps men don't consider relevant. Processes like menopause, the menstrual cycle or birth control are usually ignored in traditional medical research.

That's because the medical research conducted by men didn't see it as a priority.
I don't know if it's malice or ignorance, probably a mix of both. They have not gone through these processes, thus don't understand their impact on mental and physical health

in women. It seems like it's more lack of interest than malice, a bit like "This doesn't affect me, I have bigger problems to deal with". However, problems such as breast cancer have evolved a lot because time was invested in them. If we have sent a man to the moon, we have resources to research this. Yes, it's a question of priorities. And also, of representation. There's a saying that I like a lot, which is: "I don't worry as much about geniuses like Einstein as I do about those brains that got lost on the way." The absence of women in key positions limits what is considered important to research.

It is contradictory. In centers that praise themselves about being inclusive, the majority of the senior directors are men, despite there being more women on staff than men.

That happens in a lot of places. The data from the Carlos III Health Institute shows a clear "scissor effect": more women at the bottom and a lot less in the high positions. The increase in the number of women in science and in positions of power to decide what is relevant to study, has influenced in the research of processes related to women. Bias in clinical studies has been resolved, and processes like pregnancy or menopause, which in the past were forgotten, are now starting to be studied more thoroughly. These processes involve big hormonal fluctuations. The hormones, that have receptors in the brain cells, induce neuroplasticity. Therefore, during pregnancy and menopause, the brain cells have to readapt themselves and work in a different way. It was almost obvious. The weird thing was that nobody had studied it before.

How did you become interested in science?

I have always been very curious. I remember being in the kitchen with my mother, asking strange questions or playing with food as if it were part of an experiment. Even with the cat, I thought, "If I put something here, will it change color?" Things like that, but it wasn't that I wanted to pursue science.

You also draw.

Yes, drawing is my passion. Actually, at first, I thought about studying Psychology so I could then pursue Fine Arts as a hobby. But then I received scholarships, and opportunities, like a stay in the United States, and I ended up immersing myself in all of this. Though, deep down, I'm still passionate about Humanities.

Your explanations are very visual, and your book (Neuromaternal) also reflects this, with images that allow one to better understand what is happening.

Yes, I think it has to do with my inclination towards art. Although I like science very much, I don't consider myself to be a "pure" scientist. My main interest is to ask questions, try to answer them and communicate what I learn.

Do you think there is a dichotomy between Science and Humanities?

That's right, they make us choose, and it's too bad. I think there is a wonderful bridge between both areas. Science is essential, but there are other types of knowledge equally valuable. My book tries to connect these perspectives: science, psychology, art, human experiences. It's a way of looking at a phenomenon, from different angles, and I love that.

It's obvious that you are interested in communicating.

Exactly. I started communicating to recruit participants for my studies. I created an Instagram account, initially for that purpose, and little by little, I realized how important it was to explain what we do and give something back to those who participate.

Have you had any "crazy" research idea that you haven't been able to do yet?

I think I've already done it. We evaluated women before and after pregnancy, something that was quite innovative at the time. It was risky because some women don't end up getting pregnant, and it took us almost 10 years to publish. Though it's quite known now, at that time, nobody spoke about the maternal brain.

Do the great ideas usually arise outside the laboratory?

Totally. I believe that the best ideas come up when we are relaxed, like when you are reading something from another field. For example, mixing medical anthropology with neuroscience made me ask myself if brain changes during pregnancy could be compared to those of adolescence.

And speaking of great ideas, if you had an unlimited budget, time and resources, what project would you work on?

I would love to create a database about women, to study how pregnancy affects risk and resilience on a long-term basis. We could provide answers to questions like if the risk of Alzheimer and cardiovascular diseases varies depending on the number of pregnancies. It would be a multidisciplinary job, combining biology, communication, and even public policies. To make it accessible, I'd invite the public to participate using an app where they'd record information about their health and receive personalized updates according to the findings. This project could change our understanding of feminine health and its impact on global health policies. ■

Professor at the Nell Hodgson Woodruff School of Nursing (USA)

Britanny Butts:

"THE CNIC REMINDS ME OF THE NIH IN THE U.S."

Dra. Britanny Butts is a professor at the Nell Hodgson Woodruff School of Nursing (USA). Dr. Butts earned her Ph.D. at Emory University, focusing on cardiovascular diseases, immunology, and exercise. She received her Bachelor of Science in Nursing from Georgia State University and her Bachelor of Science in Biology from the University of the Virgin Islands. Her translational research centers on the connection between cardiovascular diseases and Alzheimer's disease, encompassing areas such as immune cell subsets, the renin-angiotensin system, vascular and cognitive function, with a special emphasis on social determinants of health and patient-reported outcomes, such as symptoms and quality of life. Her main areas of interest include inflammatory pathways in cardiovascular diseases, the heart-brain connection, pathophysiological mechanisms associated with symptoms in heart failure, oxidative stress, the impact of the renin-angiotensin-aldosterone system on brain health, and biological aging in heart failure.

Your talk is titled "What is good for the heart is good for the brain." Could you share the connection and what you'll be discussing today?

Today, we'll explore how cardiovascular disease can lead to cognitive changes, including cognitive impairment and dementia. We'll discuss the mechanisms linking cardiovascular health with brain health, such as inflammation, vascular changes, and blood flow regulation. For instance, reduced blood flow due to conditions like atherosclerosis can damage brain cells, leading to cognitive decline. We'll also delve into neural and hormonal mechanisms, such as the roles of the sympathetic nervous system and the renin-angiotensin system. These are central in cardiovascular disease but also influence brain health and cognitive function. Additionally, we'll review how cardiovascular drugs, like ACE inhibitors, beta-blockers, and ARBs, might impact brain health, with emerging evidence suggesting that ARBs could offer unique cognitive benefits.

I've read that you studied nursing and biology. Could you tell us more about your background?

I initially studied biology and began a PhD in Immunology. However, my biology training focused more on evolutionary aspects, leaving me without sufficient knowledge of human health to conduct research on human subjects. I decided to attend nursing school to deepen my understanding of human health and disease. This shift allowed me to transition from basic science and animal models to researching human health. During this time, I also gained valuable experience working in the emergency room before completing my PhD.

You transitioned from biology to working directly with patients and focusing on quality of life. You also emphasize social determinants of health. Could you elaborate?

My experiences shaped my focus on social determinants of health. In my research, we aim to capture a representative sample by recruiting from both clinical settings and communities. In Atlanta, where I work, we focus on Black

and African American populations due to higher rates of cardiovascular conditions like hypertension and heart failure. Social factors such as housing, education, food security, and racism significantly influence cardiovascular and brain health. By understanding these lived experiences, we can better assess how social determinants impact health outcomes.

You mentioned these challenges specifically affect Black populations in the US, how can we address these disparities?

It's a systemic issue that requires multifaceted solutions. Change can begin at the community level, where resources, healthcare, education, and social support can be provided. For example, immigrant communities might benefit from spaces for social interaction and support, which can mitigate feelings of isolation. However, broader systemic changes, such as equitable healthcare policies, are essential for long-term solutions.

Your research focuses on both cardiovascular disease and Alzheimer's disease. How did you become interested in these connections?

It started with the immune system, which is involved in nearly every disease. Cardiovascular risk factors, often evident in midlife, are linked to cognitive impairment and dementia later in life. I became interested in inflammation as a key connection between cardiovascular and brain health. Damage to the heart and blood vessels can disrupt the blood-brain barrier, allowing inflammation to harm the brain. I also study the renin-angiotensin system (RAS), a fascinating system that links cardiovascular health with cognitive outcomes.

Your research seems to integrate two approaches: biological pathways like inflammation and social factors. How do you manage this complexity?

Integrating these approaches is challenging, especially when it comes to funding and logistics. In our studies, we collect biological data, such as blood and cerebrospinal fluid samples, alongside social data like lived experiences and neighborhood deprivation. For example, we use the Area Deprivation Index to measure factors like access to schools and green spaces, which correlate with cognitive function. This combined approach helps us understand how biological and social factors jointly impact health.

Change can begin at the community level, where resources, healthcare, education, and social support can be provided

Broader systemic changes, such as equitable healthcare policies, are essential for long-term solutions

Do you face challenges involving families and caregivers in communities with limited healthcare access?

Engaging communities requires effort and presence, but it's not necessarily difficult. We participate in community events—at Black churches, veteran gatherings, and LGBTQ+ events—to build trust and raise awareness about our research. Many participants have personal connections to Alzheimer's disease, motivating them to contribute to research that could benefit their communities.

Did you have mentors who guided you in your research journey?

Mentorship has been pivotal to my career. I've been fortunate to have excellent mentors at every stage, from my undergraduate work in coral genetics to my current focus on cardiovascular and brain health. Now, I collaborate closely with Dr. Whitney Wharton, an expert in minority health and sex hormones, while I specialize in cardiovascular health.

It's inspiring to hear how mentorship shaped your career. Are you mentoring students now?

Yes, and it's been incredibly rewarding. I believe in giving back, as I've benefited greatly from the guidance of my mentors. Supporting the next generation of researchers is an essential part of advancing science.

Is this your first visit to the CNIC? What are your impressions?

Yes, this is my first visit. The CNIC reminds me of the NIH in the U.S., with its multidisciplinary collaboration across specialties. It's inspiring to see such innovative work happening here.■

Director of the Cardiovascular Research Center of the Clinical Science Center at the University of Wisconsin

Héctor Valdivia: "WHAT DOESN'T KILL US, MAKES US STRONGER: EXPLORING THE BENEFITS OF"

Dr. Héctor Valdivia is a leading cardiologist and researcher in the field of cardiovascular medicine, with special interest in the physiology of the heart, ion channels and the regulation of intracellular calcium. He is a professor at the Clinical Science Center of the University of Wisconsin, where he also directs the Cardiovascular Research Center, coordinating the efforts of more than 130 members. Additionally, he leads the MATRIX program, focused on improving the success rates of young researchers in obtaining funding.With more than 25 years of experience, Dr. Valdivia has published more than 130 articles on the dynamics of calcium and ion channels in the heart. His laboratory has discovered a new family of ryanodine receptor ligands with therapeutic potential to treat cardiac arrhythmias. Throughout his career he has received many prestigious awards such as the Fulbright-Tocqueville Distinguished Chair Award and has been a Fulbright specialist on several occasions. He is a member of the editorial board of Frontiers in Bioscience, Journal of Molecular & Cellular Cardiology, and Circulation Research.

What doesn't kill us makes us stronger.

The phrase "What doesn't kill us makes us stronger", by Friedrich Nietzsche, refers to how we develop resistance to situations that can harm us, which makes us stronger. My laboratory works with scorpion peptides. When we think of scorpions, the first thing that comes to mind is something dangerous or toxic. In fact, its toxins are very well known. However, the peptides we researched are not toxic to people, but rather have beneficial effects in certain clinical contexts. For example, we work with a syndrome called CPVT, which causes calcium intoxication. The heart needs calcium to contract, but in this syndrome, there is excessive accumulation due to a mutation in one of the proteins. The peptides we studied regulate calcium output in a controlled manner, which reduces cardiac arrhythmias in patients with CPVT. This syndrome is not very common, and only affects about 1 in 10,000 people, mainly children and adolescents, and can cause sudden fainting or, in more severe cases, sudden death. Although its incidence is very low, it is a wonderful model to study the effects of calcium within the heart cell. This way we learn what happens in more common diseases, such as atrial fibrillation, which is very common especially in older people, heart failure, which is also a very frequent process in developed countries, and other genetic diseases, such as congenital cardiomyopathy

How do you obtain scorpion poison and manipulate it to use in treatments?

Scorpion poison is a very complex mixture of toxins, almost like a Molotov cocktail. It has toxins that block sodium and potassium channels, among others, which paralyzes its prey. The peptides we studied represent a tiny fraction of the poison, only 0.001%. At first, we had to milk scorpions to extract these peptides, which requires stimulating the animal to release the poison. Now, that we know the composition of the peptide, we can chemically synthesize it in the laboratory, which is much more efficient. Currently, we are in the testing phase with animal models, such as mice and rabbits. Our objective is to pass on this treatment to clinical trials, but first we must ensure that there are no toxic effects on animals. The use of animal poisons in medicine is not new. For example, the drug Captopril, which is widely used in patients with heart failure, is derived from snake poison. It inhibits the angiotensin-converting enzyme and is a powerful vasodilator. Another example is Exenatide, a peptide from the Gila monster poison, which is currently used for the treatment of diabetes and weight loss, under the trade name Ozempic. Both are examples of how poisons can be converted into beneficial drugs when synthesized in a controlled manner

In recent years, more cases of arrhythmias are being discovered than ever imagined. What is this due to?

Thanks to the improvement in diagnostic techniques, we are detecting more cases of arrhythmias. Our laboratory focuses on arrhythmias related to calcium. The heart beats thanks to an electrical system in the cell membrane and a calcium system that transmits the electrical signal to the myofilaments for contraction. We study the second phase of this process. There are several diseases that are due to calcium disorders, and by understanding these mechanisms, we can apply what we learn to other more common conditions, such as atrial fibrillation and heart failure, which are frequent problems in older people.

Did you always know that you wanted a career in medical research or was it a decision you made later on?

It wasn't something I knew from the beginning. When I was studying medicine at the University of Mexico, I really enjoyed biochemistry and I was an instructor of that subject. That's when I discovered research, thanks to professors who introduced me to this world. Before that, I thought my career would be in the operating room or attending patients. However, once I entered a laboratory, I knew that was what I really wanted to do. I started working in this field thanks to a toxinologist who invited me to his laboratory, where I became fascinated by the study of poison receptors and ion channels.

Peptides from scorpion poison, far from being toxic, can regulate calcium in the heart and reduce fatal arrhythmias in patients with CPVT.

It seems that your medical training gives you a different perspective when it comes to research. How do you think this influences your work?

It's true, I think doctors have an advantage in scientific research because we understand the systemic impact of what we study better. Doctors don't just focus on a disease, but on the patient as a whole. This holistic approach allows us to see how different systems in the body interact and how research can directly benefit patients. Although some biologists, biochemists, etc. might disagree, I think doctors have a slight advantage in this sense.

Speaking of the interaction between subjects, do you think collaboration between researchers from different fields is important?

Absolutely. At our research center we work in a very similar way to the CNIC in Spain, where the laboratories are open and encourage collaboration between cardiologists, biologists, biochemists and engineers. This interaction between different subjects is crucial to advance in research. No group can do it alone, and the synergy among different fields allows us to discover more complete solutions.

> The peptides we researched are not toxic to people, but rather have beneficial effects in certain clinical contexts

You lead a mentoring program called Matrix. What led you to create this project?

The Matrix project emerged to support young researchers at the start of their careers, since, in the United States, new researchers are at a disadvantage when competing for funds from the National Institute of Health (NIH). This mentoring system, which I adopted from the University of Michigan, has been demonstrated to significantly increase the success rate of these young people in obtaining funds. In this program, we pair experienced mentors with up to three mentees, and for nine months they guide them on how to formulate hypotheses, write proposals, and present projects effectively. It is very difficult for the mentor to know everything about the mentee's field; however, they do know how to propose a hypothesis, how to write it, how to sell it, etc., and these are precisely the types of things that a person who is just starting out, does not know how to do well. During those 9 months they start by doing the most basic things, what are you going to propose, how are you going to say it, up until the final review in which, sometimes, they tear the poor person to pieces. Additionally, all of this, also helps in some ways, create future mentors.

Do you plan on returning to Mexico one day or continue collaborating from the USA?

Although I have not returned to Mexico permanently, I still have a strong connection with my country. Every year I travel to collaborate with Mexican researchers and receive students in my laboratory. It is my way of giving back to what Mexico gave me, since all of my academic training, except the final part of my doctorate, was done in Mexico. It is a shame that there isn't more financial support for research in the country, but I always try to maintain this connection and help as much as I can. ■

Dr. Gonzalo del Monte-Nieto manages his own laboratory at the Australian Regenerative Medicine Institute at Monash University (Australia)

Gonzalo del Monte-Nieto: "TRAINING AT THE CNIC IS VERY HIGHLY VALUED AND OPENS UP MANY DOORS"

Dr. Gonzalo del Monte-Nieto received his PhD in 2011 from the Autonoma University in Madrid (Spain). He received training in Developmental and Molecular Biology by Professor José Luis de la Pompa and in 3D Image Analysis by Professor Antoon Moorman (Netherlands). In 2011 he joined Professor Richard Harvey at the Victor Chang Cardiac Research Institute (Sydney, Australia) to do his postdoc. In 2018 he founded his own laboratory at the Australian Regenerative Medicine Institute at Monash University (Melbourne, Australia). Throughout his career, he has made important discoveries about the mechanisms that are behind the formation of cardiac chambers, valves, epicardium, and coronary vessels during embryonic development. His research has led to important breakthroughs to better understand cardiovascular diseases such as noncompaction cardiomyopathy, atrial septal defects, coronary artery disease, gestational hypoxia, as well as pancreatic cancer. His laboratory focuses on the study of molecular mechanisms and developmental processes that orchestrate heart development and the transfer of that knowledge to congenital and adult heart diseases, as well as cardiac regeneration. His laboratory is also developing innovative methods to analyze 2D and 3D images so as to optimize the morphological and molecular characterization of cardiac development and disease.

What is a Spanish researcher doing in Australia?

I studied Biology at the Autonoma University of Madrid and during that time, I was part of José Luis de Pompa's team at the National Center for Biotechnology (CNB-CSIC). After a short stay in Amsterdam, I finished my PhD at the CNIC, also on Jose Luis' (de la Pompa) team. After finishing my PhD, I received an offer from Richard Harvey, a cardiovascular researcher in Sydney, and that's where I finished my postdoc. I'm currently in charge of the laboratory at ARMI (Australian Regenerative Medicine Institute) at Monash University.

What does your research consist of in Australia?

My work focuses on cardiovascular development, especially the integration of not only the communication among tissues, but also the space between them, that is, the extracellular matrix. We have discovered that the extracellular matrix plays a fundamental role in the formation of the heart. We are trying to understand how those processes permit the correct formation of the heart during embryonic development. If we are able to understand how the heart is formed in the embryo, we can identify the critical processes, that, when not working correctly, can generate cardiovascular disease, like congenital malformation that affects babies. Furthermore, we also work on adult cardiovascular diseases that recapitulate certain embryonic processes, but in pathological conditions. Understanding those processes could help us identify new therapeutic targets. Another important aspect of our research is understanding how the myocardium, the heart muscle, is formed and also what structure it has. Learning about the proliferation of the cardiac muscle cells in the embryo can help us reactivate this proliferation in adults, a process that is lost in adult life. This is relevant, for example, for regeneration after a heart attack.

In mammalian embryos, the heart can regenerate itself, but this regenerative capacity is lost in the first days of life and an adult heart, affected by, for example, a myocardial infraction, cannot be repaired. What is the difference between those cells and those of the adult?

We are investigating the differences. One of the hy-

potheses that we are tracking in my laboratory is that the extracellular matrix of an adult is very restrictive, whilst that of the embryo is much more permissive, which allows the cells to move more freely. We believe that, if we can create a more permissive environment in the adult, with the help of mitogens, such as neuregulin for example, we can improve cardiac regeneration. We know there is no "pool" of stem cells in the heart of an adult, which is why the cardiomyocytes, the cells of the heart muscle, differ and participate in regeneration.

Do you think this is the most plausible way to regenerate the heart or are there other alternatives?

It's just one of the possible ways. I don't believe there is just one single solution, but rather a combination of various ones. There is research in the immune system that suggests that certain immune cells can prevent the formation of scars, and this is important when the heart suffers a myocardial infarction. When there is a wound, if the heart cells cannot proliferate and regenerate themselves, the body forms fibrous tissue to "close" the wound and maintain cardiac function, but at the cost of losing contractility. If we could reduce the formation of scars and activate proliferation of the cardiac muscle cells in a more permissive environment, we could offer a more effective alternative treatment.

Does all your research have a translational focus, intended for clinical application?

In my laboratory, we work with not only with congenital diseases but also with other fundamental aspects. The first step is always trying to find out what is happening at a basic level. For example, if we identify genes related with a congenital cardiovascular disease, we can understand the process behind the defect and determine what is being altered. Although, the early diagnosis of cardiac defects in fetuses through echocardiography is not viable at this moment, we are advancing in that direction. The more we know about the processes involved in this, the better we can identify therapeutic targets to improve the results and avoid having to do a transplant.

Are you working on complete organ models? Can you explain what this consists of?

Yes, unlike classic developmental biology, we are starting to study complete organs rather than just sections. We use embryonic hearts, and we are developing automated image analysis protocols. The key is to train artificial intelligence systems to learn to identify patterns in the images, something that is quite difficult for the human eye due to the complexity of the parameters involved. This technology allows us to work with complete tissues and conduct specific quantitative analyses.

What does your role as student supervisor involve?

I started supervising during my postdoc, and since I started my research group, I try to apply the best practices that I learned from my previous experiences. I formed my research group almost while the COVID-19 pandemic started, so it was a hard year to establish the laboratory. The Australian borders were closed for two years and we had to work in shifts. It was a challenge, especially because I lost most of the senior researchers whom I worked with. However now, looking back, it was useful because it allowed me to develop automations and methodologies. I currently have a team of 10 people, including PhD students, one post doc student, one laboratory technician and two image analysis specialists.

What is the scientific community in Australia like?

The scientific community in Australia is a little smaller, which allows one to find their own niche and become an expert in their area. This encourages collaboration and allows for a more relaxed work environment, with less competitiveness than in other countries. Nonetheless, what I miss most is the interaction with scientists from other parts of the world. Australia is quite isolated, and although the virtual conferences are useful, they lack that personal contact that you get from the in-person events.

What is the perception of the CNIC in Australia?

The CNIC is a very internationally well-known center. When one says they've done their PhD there, everyone acknowledges it as a leading center, a reference in biomedical research. Training at the CNIC is very highly-valued and opens up many doors. ■

THE PESA CNIC-SANTANDER STUDY CONSOLIDATES ITSELF AS THE MOST IMPORTANT STUDY IN THE WORLD IN THE DIAGNOSIS AND PREVENTION OF CARDIOVASCULAR DISEASES

The findings of this study have been key for the development of REACT, a new research project, that will count on the collaboration of Santander Bank, and will expand the study of the age group for the prevention of cardiovascular diseases, which will include 8,000 new participants.

The PESA CNIC-Santander study, led by Dr. Valentín Fuster, and with the collaboration of Santander Bank, consolidates itself as a world reference in the prevention and diagnosis of cardiovascular diseases. With a 15-year track record, this project has analyzed the health of more than 4,000 employees at Santander Bank, between the ages of 40 to 54, using advanced imaging technology and blood biomarkers to detect silent atherosclerosis in its early stages.

Among its findings, the study highlights that 63% of asymptomatic participants show signs of atherosclerosis in its early stages, a process that can be reversed with lifestyle changes. Moreover, it's been shown that this disease not only affects the big arteries, but also microcirculation, potentially affecting mental health and the risk of diseases such as Alzheimer.

Dr. Valentín Fuster, General Director of the National Centre of Cardiovascular Research (CNIC), and Ana Botín, President of Santander Bank, presented the main conclusions of the PESA CNIC-Santander study to employees of the bank and members of the CNIC. This study has become a unique worldwide database for the prevention and treatment of cardiovascular diseases, marking a scientific milestone for the promotion of health.

The PESA CNIC-Santander study has allowed for the expansion of knowledge in how atherosclerosis develops in its early stages. Thanks to the use of advanced imaging technology and the analysis of blood biomarkers, the study has been able to detect this silent disease before the appearance of symptoms and has laid the foundation for developing new prevention and treatment strategies.

During the event, Ana Botín highlighted: "Public-private collaboration is essential to approach the big challenges of our society, especially in the field of scientific and medical research. The PESA CNIC-Santander study is a clear example of how joining forces can generate significant advances that benefit all of society. These types of alliances not only allow innovation and leadership in the scientific field, they also show our commitment to contribute to the health and well-being of people".

On his part, Dr. Valentín Fuster highlighted: "The PESA CNIC-Santander study has not only transformed our understanding of the cardiovascular disease, it also lays down the groundwork for developing more effective prevention and treatment strategies, that are beneficial to all of society. We have laid the foundation for demonstrating that, with appropriate and timely interventions, not only is it possible to prevent the progression of these diseases, but also reverse them.

The PESA CNIC-Santander study reveals that 63% of the asymptomatic participants between the ages of 40 and 55 show signs of atherosclerosis, a systemic condition that affects large arteries as well as the microcirculation of the heart and the brain. Although

historically considered irreversible, it can improve with healthy habits and early control of risk factors like high cholesterol, hypertension, obesity, insulin resistance and high triglycerides. Moreover, atherosclerosis speeds up biological aging and is linked to cerebral hypometabolism and the risk of Alzheimer. Sustained lifestyle changes can prevent its progression and reduce cardiovascular and cognitive risks.

The event also served to announce the start of the project: REACT, a new study that has its roots in the advances of the PESA CNIC-Santander study. This project, led by the CNIC and Rigshospitalet of Denmark, will analyze 16,000 people between the ages of 20 and 70, 8,000 of these in Spain, with the aim of implementing a precise medical approach in the prevention of atherosclerosis. The study intends to collect a representative sample of the Spanish population, hence including people from different social and geographical strata.

For this purpose, of the 8,000 participants, a significant proportion will be selected among Santander Bank employees, their family members and the banks' service providers, who show interest in participating, in this way reaffirming the bank's commitment to research in the cardiovascular field. Santander Bank will also collaborate with REACT, by making the facilities of their medical center available for this study.

Among its findings, the study highlights that 63% of asymptomatic participants show signs of atherosclerosis in its early stages, a process that can be reversed with lifestyle changes

REACT will have two phases: in the first, non-invasive imaging studies of different arterial territories, including the coronary arteries and the retina, and the blood biomarkers will be analyzed with the most sophisticated technology to detect the disease in a more precise way. The impact of lifestyle (diet, exercise, sleep, etc.) on the appearance of this silent disease will also be evaluated. In the second phase, new personalized strategies will be developed to intervene in the initial phases of atherosclerosis and reduce the impact of the disease on the population.

With this new collaboration, the CNIC and Santander Bank, continue a nearly 20-year collaboration that keeps on generating scientific breakthroughs with a global impact on cardiovascular health. ■

CNIC PARTICIPATES IN AN INTERNATIONAL LEDUCQ FOUNDATION PROJECT INVESTIGATING THE CONNECTION BETWEEN THE PLACENTA AND THE HEART DURING EMBRYONIC DEVELOPMENT

The new project, 'The Placenta in Maternal and Fetal Cardiovascular Health and Disease', aims to understand how the placenta influences cardiovascular health in mothers and their children, promising improvements in the prevention and treatment of related diseases.

The group at the Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC) led by José Luis de la Pompa, a member of the Spanish cardiovascular research network (CIBER CV), is participating in an ambitious project funded by the Leducq Foundation. Titled "The Placenta in Maternal and Foetal Cardiovascular Health and Disease", the project aims to understand how the placenta influences cardiovascular health in mothers and children and to improve the prevention and treatment related diseases, increasing global well-being.

The project is coordinated by Ananth Karumanchi at Cedars-Sinai Medical Center (USA) and Didier Stainier at the Max Planck Institute for Heart and Lung Research (Germany). The total of $8 million dedicated to the project over five years includes an allocation of $1,078,000 to the CNIC. This innovative study is one of four projects selected in the 2024 edition of the prestigious Leducq Transatlantic Networks of Excellence Program.

Other internationally renowned scientists participating in this international consortium include Zoltan Arany and Mark Kahn (University of Pennsylvania, USA), Myriam Hemberger (University of Calgary, Canada), and Abigail Fraser (University of Bristol, UK).

The placenta is a vital organ during pregnancy, essential for fetal development and for adapting the mother's body to the demands of gestation. The role of the placenta extends beyond nourishing the fetus, and its activity has profound impacts on maternal and fetal and infant cardiovascular health during and after pregnancy.

As Dr. de la Pompa explained, "Failure of placental function can give rise to severe complications, such as cardiovascular disease in the mother and congenital heart defects in the baby. While there is evidence linking these conditions to placental dysfunction, the specific causes remain poorly understood and are often overlooked in clinical practice."

The PlacHeart network is dedicated to unravelling the molecular and cellular mechanisms that link the placenta to the cardiovascular health of mothers and children.

Researchers on the project will use advanced genetic tools in mouse and zebrafish models, alongside the analysis of human tissues and genetic data. "This approach will help to identify new pathogenic pathways underlying the placental alterations that can lead to cardiovascular disease and congenital defects," said de la Pompa, whose group consists of D. MacGrogan, B. Flores-Garza, T. González-Costa, V. Sebastián-Serrano, J.L. de la Pompa, L. Méndez-Peralta, A. Pau-Navalón, A. Galicia-Martín, J. Santos-Cantador, C. Relaño-Ruperez, and M. Siguero-Álvarez.

The multidisciplinary team comprises experts in placental biology, developmental biology in mice and humans, maternal heart failure, congenital heart defects, and epidemiology, and the consortium members will work collaboratively to translate the findings into new therapeutic strategies.

The PlacHeart network is dedicated to unravelling the molecular and cellular mechanisms that link the placenta to the cardiovascular health of mothers and children

De la Pompa concluded that, "The ultimate goal is to improve the prevention and treatment of cardiovascular disease associated with placental dysfunction, improving the health of mothers and children worldwide."

Through this research project, the CNIC and its international partners are reinforcing their commitment to scientific excellence and the advancement of global cardiovascular health.

The Leducq Transatlantic Networks of Excellence Program fosters global collaboration among leading scientists in cardiovascular and neurovascular research. Since its inception in 2004, the program has funded 80 research networks, involving more than 500 investigators working in 130 institutions across 21 countries. ■

CNIC OBTAINS ISO 9001 CERTIFICATION IN ITS 11 TECHNICAL UNITS

CNIC has obtained ISO 9001 certification in its 11 technical units, a remarkable milestone that reinforces its commitment to the quality and excellence of the services it provides. This achievement highlights the CNIC's commitment to the quality in the management and provision of scientific and technological services, consolidating itself as both a national and international reference.

The 11 Technical Units of the CNIC - Genomics, Proteomics, Advanced Imaging, Bioinformatics, Flow Cytometry, Transgenesis, Pluripotent Cells, Viral Vectors, Microscopy, Clinical Trials Unit and Comparative Medicine – have obtained this certification, which guarantees that the operations and services offered meet international quality standards. This recognition guarantees the reliability of its results and facilitates collaboration with external institutions, which is key for its mission in leading cardiovascular research.

Furthermore, this level of integral certification positions the CNIC as a pioneer in quality management in the scientific field.

"The ISO 9001 certification is especially valuable in a context where not all research centers have these certifications, which places the CNIC in a competitive position to attract external financing and research calls", assures Beatriz Álvarez Flores, Technological Development Coordinator at the CNIC.

In this way, she adds, the ISO 9001 certification ensures that all of the center's units meet the international quality standards, an element that could become obligatory for all research centers in the future.

The success of the process also highlights the center's investment in quality, from hiring a quality manager to improving computer and statistical systems. These efforts reflect an institutional commitment with excellence and ongoing improvement, guaranteeing its users that the services provided meet high standards.

The certification of a research center's services, like the CNIC, under the ISO 9001 standard is very important, both nationally and internationally.

▪ **Guarantee of quality and excellence**
The ISO 9001 certification assures that the services meet international quality standards. This proves that the processes are efficient, reproducible and oriented towards ongoing improvement. It reinforces the trust of collaborators, funders and partners in the center's capacity to produce reliable and high-quality results.

▪ **Optimization of internal processes**
The implementation of ISO 9001 certification imposes the standardizing of procedures and reducing errors. This not only increases operational productivity, but also optimizes the use of time and resources. It promotes an environment of continuous improvement, essential in a field as competitive as research.

▪ **Credibility to Society**
The certification reinforces transparency and accountability. This is crucial for institutions that depend, in part, on public funding.

▪ **Assures that the results of scientific research and services are trustworthy and can be applied for the benefit of society.**
▪ **Greater International Competitiveness**
In a globalized environment, the certification allows the center to compete on equal terms with other institutions of international prestige.

It opens doors to international collaborations, as many of the partners demand certified standards as a requirement for working together.

▪ **Attraction of talent and resources**
Having certified systems of quality makes the center more appealing to high-level researchers that are looking to work in institutions of excellence.

Makes it easier to obtain funding and scholarships from organizations that value the quality of management.

▪ **Regulatory Compliance and Security**
The ISO 9001 certification promotes compliance with the legal and ethical regulations, reducing risks related to mistakes, negligence or failures in the quality of services.

Guarantees that the biological samples, clinical data and sensible data are managed properly.

The complete certification of the CNIC under the ISO 9001 standard, places the CNIC as a leader in the field of technological and scientific research in Spain. This recognition not only strengthens its ability to compete at an international level, but also ensures a positive impact on society through the development of innovative solutions for cardiovascular health. ■

JACARDI GENERAL ASSEMBLY: MORE THAN 200 EXPERTS FROM 21 EUROPEAN COUNTRIES UNITE TO IMPROVE CARE FOR CARDIOVASCULAR DISEASE AND DIABETES

More than 200 public health experts from 21 European countries, including Ukraine, met in Paris from 16-18 October for the second General Assembly of the Joint Action on Cardiovascular Diseases and Diabetes (JACARDI) to address some of the most pressing challenges in public health: the prevention and control of cardiovascular diseases (CVD) and diabetes. This European initiative is being developed through the implementation of 11 work packages and 142 pilot projects. JACARDI is coordinated by the Italian National Institute of Health (ISS) and has received funding of 53 million euros from the European Commission.

The General Assembly reviewed the achievements of the first year of this European strategy. They also delved into the pilot projects led by 76 partner institutions, each designed to improve health outcomes across Europe. A decisive step in this collective effort to reduce the burden of CVD and diabetes and improve the lives of millions of people in Europe.

Through coordinated efforts among Member States, JACARDI focuses on evidence-based strategies and best practices to effectively prevent and manage NCDs and diabetes. The 142 pilot projects aim to provide evidence-based information to enable policy makers to make informed decisions to improve public health in this area.

In the framework of the General Assembly in Paris, side events on 17-18 October were dedicated to specific working groups, such as health literacy, integrated care pathways, data accessibility and patient self-management.

Our participation in JACARDI

The National Center for Cardiovascular Research (CNIC), a center under the Carlos III Health Institute (ISCIII), an entity attached to the Ministry of Science, Innovation, and Universities, and the Health Research Institute of Hospital 12 de Octubre (i+12), representing SERMAS, co-lead one of the JACARDI working groups, aimed at data availability, quality, accessibility and exchange.

The aim of this group is to design and implement pilot projects that will provide information on existing data on CVD and diabetes, standardise and harmonise data collection methods, and improve data exchange mechanisms to create a dedicated network of CVD and diabetes registries in Europe. Some of the projects being developed by the CNIC and the i+12 - SERMAS address relevant issues such as gender differences in cardiovascular health or support for self-care in patients with CVD.

'In today's dynamic and changing world, paying deep and thoughtful attention to gender differences in CVD and diabetes is essential to drive progress and raise awareness,' says Héctor Bueno, co-director of the working group, coordinator of the clinical area of hospitalisation and research at the Cardiology Service of the Hospital 12 de Octubre and leader of a research group at the CNIC.

For Fátima Sánchez-Cabo, head of the CNIC Bioinformatics Unit, 'it is essential that the data are of high quality and consistent, so that the impact of JACARDI is significant. Only then will we be able to perform analyses that truly contribute to improving clinical outcomes and developing more effective prevention strategies across Europe'. ■

SEVERAL STUDIES LED BY THE CNIC, INFORMED RECOMMENDATIONS INCLUDED IN THE NEWLY RELEASED 2024 ESC CLINICAL PRACTICE GUIDELINES (CPG)

In the framework of the ESC Congress 2024, which is being held these days in London, up to 12 clinical studies led by the Spanish National Cardiovascular Research Centre (CNIC) are considered of such relevance that are cited in support of practice recommendations in 3 Guidelines: 'Guidelines for the management of chronic coronary syndromes', 'Guidelines for the management of high blood pressure and hypertension', and 'Guidelines for the management of peripheral arterial and aortic diseases'.

ESC Congress 2024 London

Among the CNIC-led studies informing clinical practice guidelines are PESA, TANSNIP, Focus, AWHS, SECURE, and Reboot.

These recognitions underline the CNIC's influence and excellence in cardiovascular research, consolidating its leadership in promoting best clinical practices worldwide.

THE CNIC WILL RECEIVE €4 MILLION TO DEVELOP THE AI TRAINING PROGRAM

CNIC is leading the AI and Big Data Training Plan for Cardiovascular Health (cardiotrAIning), coordinated by Dr. Borja Ibáñez and Dr. Fátima Sánchez Cabo. The program's objective is to attract professionals from the ICT field (computer scientists, engineers, mathematicians, physicists, etc.) and train them in the use of AI and Big Data applied to cardiovascular health.

Thanks to this initiative, the CNIC will train 15 new specialists in artificial intelligence for cardiovascular research, consolidating itself as a reference in the integration of advanced technologies in biomedicine.

This call is part of the Talent Attraction and Retention Programs of the National Digital Skills Plan and the Artificial Intelligence Strategy. Red.es has allocated 120 million euros for scholarships and contracts in AI, of which nearly 4 million will be directed to the cardiotrAIning program.

SEC-CNIC CARDIOVASCULAR PHYSIOPATHOLOGY COURSE

The CNIC and the Spanish Society of Cardiology (SEC) organized the XVII Physiopathology Cardiovascular Course "From Symptoms to Genes". The objective of this course is to offer a translational vision of cardiology, bringing resident doctors closer to the study of physiopathology and basic research by showing them the molecular and genetic backgrounds of cardiac disease and, at the same time, giving them a more modern vision of cardiac physiology.

EXCELLENCE IN THE SCIENCE COMMUNICATION

JACC: The sooner the better: teaching healthy habits in elementary school reduces abdominal fat

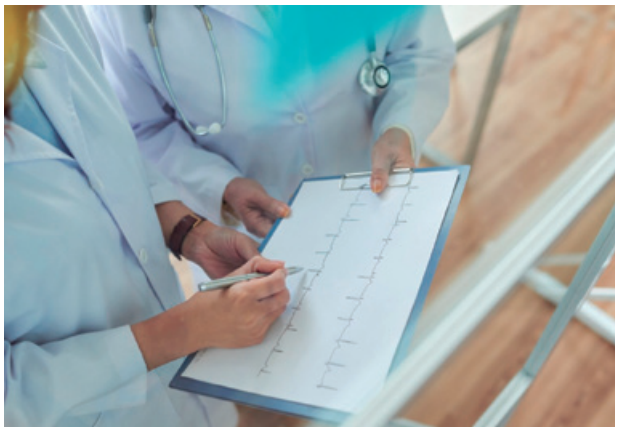
A study by the CNIC and Fundación SHE, supported by "la Caixa" Foundation demonstrates that teaching healthy habits through classroom activities helps to prevent the accumulation of abdominal fat during the first school years. The study, published in the *Journal of the American College of Cardiology* (JACC), is one of the largest contemporary school-based health promotion studies and has one of the most extensive participant follow-up schedules.

The study included 1771 boys and girls attending 48 public elementary schools in the Comunidad de Madrid. The schools were divided into 4 groups. One group of 12 schools conducted a health-promotion intervention throughout the six years of elementary school; the intervention covered emotions management, acquisition of healthy eating habits, active living, and knowledge of the body and heart (SI! Program–Comprehensive Health). Another two groups conducted the same intervention but only for three years, one group during the first three years and the other group in the final three years. The fourth group did not conduct any specific health-related intervention.

Excess weight affects almost 1 of every 3 children in Spain, especially those in more vulnerable social groups. The results of this study suggest that interventions promoting healthy lifestyle habits can be more effective at reducing childhood obesity if implemented early, in the first years of elementary school.

Santos-Beneit G, Bodega P, de Cos-Gandoy A, de Miguel M, Rodríguez C, Orrit X, Carral V, Haro D, Carvajal I, Peyra C, Martínez-Gómez J, Fernández-Alvira JM, Fernández-Jiménez R, Fuster V. Effect of Time-Varying Exposure to School-Based Health Promotion on Adiposity in Childhood. J Am Coll Cardiol. 2024 Aug 6;84(6):499-508. doi: 10.1016/j.jacc.2024.04.065. PMID: 39084824.

JACC Clinical Electrophysiology: Genetics would explain a large number of cases of young adults with a pacemaker without an identified cause



A study led by CNIC cardiologists Juan Pablo Ochoa and Pablo García-Pavia, published in the *JACC Clinical Electrophysiology*, revealed that rare genetic variants increase the risks of cardiac conduction disorders in young adults who need to use a pacemaker. According to the study, 15% of cases have a direct genetic mutation, and an additional 30% have relevant genetic alterations. This underlines the importance of genetics in the diagnosis and management of these disorders.

Detecting genetic mutations not only allows for a more precise diagnosis and early treatment to prevent future complications, it also benefits the patient's family members by identifying if they have inherited the mutation and are at risk.

The study analyzed 150 patients under the age of 60 who used pacemakers due to an unknown cause, comparing their genetic profile with that of a reference population. The results support the need to perform genetic tests in young patients with unexplained cardiac conduction disorders in order to improve treatment and family management. This is the biggest analysis about genetics and cardiac conduction disorders that has been done up until now.

Ochoa, J, Espinosa, M, Gayan-Ordas, J. et al. Rare Genetic Variants in Young Adults Requiring Pacemaker Implantation. J Am Coll Cardiol EP. null2024, 0 (0). doi: 10.1016/j.jacep.2024.05.008

Science Advances: Why physical exercise stimulates the desire to stay active: the molecular relationship between the muscle and the brain is revealed

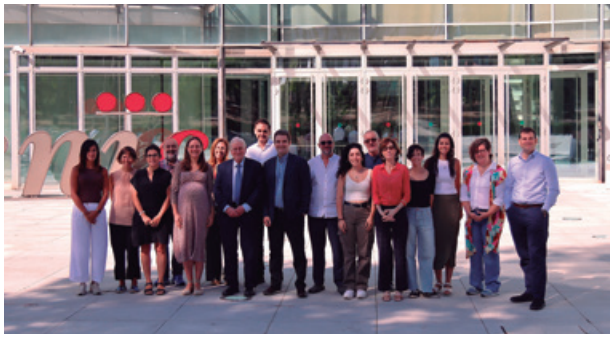
A study led by Guadalupe Sabio, currently at the CNIO, with the participation of the CNIC, discovered a mechanism between the muscle and the brain that regulates the desire to do exercise. During exercise, the muscles activate the p38γ protein, which increases the secretion of the interleukin 15 (Il-15) protein. This protein stimulates the brain's motor cortex, which increases the motivation to exercise, according to data obtained in animal and human models.

The study shows that constant exercise boosts this effect, even in cases of obesity, improving metabolism and reducing the risks of diabetes and liver fat accumulation, without significant adverse effects. In humans, the levels of IL-15 increase with exercise, but they are lower in obese people, which could convert this into an interesting marker because of physical activity.

This discovery opens doors to designing more personalized workout programs and to possible treatments, such as a drug derived from the IL-15 protein for those who have more difficulty staying active, as well as for obese people. The next steps include researching the relationship between exercises, longevity and cancer, and exploring how different exercises affect this mechanism.

Folgueira C, Herrera-Melle L, López JA, Galvan-Alvarez V, Martin-Rincon M, Cuartero MI, García-Culebras A, Dumesic PA, Rodríguez E, Leiva-Vega L, León M, Porteiro B, Iglesias C, Torres JL, Hernández-Cosido L, Bonacasa C, Marcos M, Moro MÁ, Vázquez J, Calbet JAL, Spiegelman BM, Mora A, Sabio G. Remodeling p38 signaling in muscle controls locomotor activity via IL-15. Sci Adv. 2024 Aug 16;10(33):eadn5993. doi: 10.1126/sciadv.adn5993. Epub 2024 Aug 14. PMID: 39141732.

Nature Medicine: CNIC scientists discover a new cardiovascular risk factor and identify a drug able to reduce its effects



A new study published in *Nature Medicine* and carried out by researchers at the CNIC resolves this critical debate by establishing clonal hematopoiesis as a new risk factor for atherosclerosis—the formation of lesions in the arterial wall that underlies most cardiovascular disorders. In a second study, published in the European Heart Journal, the CNIC scientists propose the ancient medication colchicine as the central plank of personalized strategies to alleviate the effects of clonal hematopoiesis associated with acquired mutations in the TET2 gene. The results of these important studies will be presented today at the European Society of Cardiology meeting in London, UK.

Both studies highlight the potential of personalized strategies to prevent cardiovascular diseases by targeting these mutations.

The PESA study is cofunded by the CNIC and Santander Bank. The two studies were additionally funded by the Spanish Ministerio de Ciencia, Innovación e Universidades (PLEC2021-008194), the Spanish cardiovascular research network (CIBERCV), Fundación "la Caixa" (LCF/PR/HR17/52150007; LCF/PR/HR22/52420011), and Fundación 'La Marató TV3' (202314-31).

Díez-Díez M, Ramos-Neble BL, de la Barrera J, Silla-Castro JC, Quintas A, Vázquez E, Rey-Martín MA, Izzi B, Sánchez-García L, García-Lunar I, Mendieta G, Mass V, Gómez-López N, Espadas C, González G, Quesada AJ, García-Álvarez A, Fernández-Ortiz A, Lara-Pezzi E, Dopazo A, Sánchez-Cabo F, Ibáñez B, Andrés V, Fuster V, Fuster JJ. Unidirectional association of clonal hematopoiesis with atherosclerosis development. Nat Med. 2024 Aug 30. doi: 10.1038/s41591-024-03213-1. Epub ahead of print. PMID: 39215150.
María A Zuriaga, Zhi Yu, Nuria Matesanz, Buu Truong, Beatriz L Ramos-Neble, Mari C Asensio-López, Md Mesbah Uddin, Tetsushi Nakao, Abhishek Niroula, Virginia Zorita, Marta Amorós-Pérez, Rosa Moro, Benjamin L Ebert, Michael C Honigberg, Domingo Pascual-Figal, Pradeep Natarajan, José J Fuster, Colchicine prevents accelerated atherosclerosis in TET2-mutant clonal haematopoiesis, European Heart Journal, 2024;, ehae546, https://doi.org/10.1093/eurheartj/ehae546

Circulation: A new mechanism of early-onset atherosclerosis in a premature aging syndrome

Scientists at CNIC have identified the process of endothelial-to-mesenchymal transition (EndMT) as a novel mechanism in premature atherosclerosis in progeria. The study, published in the journal *Circulation*, also proposes a new therapeutic target for this disease. The study was led by Dr. Vicente Andrés, leader of the Molecular and Genetic Cardiovascular Pathophysiology group at the CNIC and a principal investigator in the Spanish cardiovascular research network (CIBERCV), and Dr. Magda Hamczyk, a research fellow at the University of Oviedo and a CNIC visiting scientist.

Atherosclerosis is marked by the accumulation of cells and cholesterol in arterial walls, leading to plaque formation that can obstruct arteries and cause life-threatening cardiovascular events. Research in this field is crucial for improving patient outcomes, as emphasized by Dr. Vicente Andrés.

Hutchinson-Gilford progeria syndrome (HGPS) is a rare genetic disorder characterized by premature aging and accelerated atherosclerosis, leading to early death from cardiovascular complications. Previous studies by Dr. Andrés and colleagues identified smooth muscle cell death as a key factor in this process.

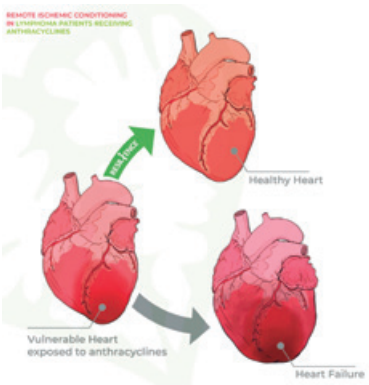
The study explored how smooth muscle cell loss affects endothelial cells, leading to immune cell recruitment and increased LDL permeability, which accelerates plaque formation. The most significant discovery was the hyperactivation of endothelial-to-mesenchymal transition (EndMT), a process that exacerbates atherosclerosis.

The research also identified the hyperactivated TGFβ1–SMAD3 signaling pathway as a potential therapeutic target. Inhibiting this pathway with SIS3 alleviated vascular disease symptoms in progeroid mice. Dr. Andrés highlighted that studying rare diseases like progeria can contribute to treatments for broader conditions like atherosclerosis, a major global health concern.

The study was funded by the Ministerio de Ciencia, Innovación y Universidades (MICIU)/Agencia Estatal de Investigación (AEI) (/10.13039/501100011033) and ERDF/EU (PID2022-141211OB-I00). The CNIC is supported by the Instituto de Salud Carlos III (ISCIII), the MICIU, and the Pro CNIC Foundation and is a Severo Ochoa Center of Excellence (grant CEX2020-001041-S funded by MICIN/AEI/10.13039/501100011033).

Hamczyk MR, Nevado RM, Gonzalo P, Andrés-Manzano MJ, Nogales P, Quesada V, Rosado A, Torroja C, Sánchez-Cabo F, Dopazo A, Bentzon JF, López-Otín C, Andrés V. Endothelial-to-Mesenchymal Transition Contributes to Accelerated Atherosclerosis in Hutchinson-Gilford Progeria Syndrome. Circulation. 2024 Aug 29. doi: 10.1161/CIRCULATIONAHA.123.065768. Epub ahead of print. PMID: 39206565.

The RESILIENCE trial: preventing heart injury caused by anticancer drugs



The RESILIENCE clinical trial has been designed to explore the effectiveness and safety of remote ischemic conditioning (RIC) used to prevent the cardiotoxic effects of anthracyline-based chemotherapy in patients with lymphoma. As described in a recent *European Journal of Heart Failure* editorial this international double-blind clinical trial promises to generate new knowledge and provide possible treatments for this major clinical challenge.

RESILIENCE is financed by the European Commission (H2020 Programme), and its goal is to reduce the prevalence of heart failure in cancer survivors and thus improve their quality of life. The trial is coordinated by the CNIC under the leadership of Dr. Borja Ibáñez, and among the key project partners is the European Society of Cardiology, which will lead one work package and participate in several other activities within the consortium.

Cancer patients are a vulnerable population at risk of developing cardiovascular complications. Some of these adverse cardiovascular effects are caused by drugs used to treat cancer. Anthracyclines are highly effective against many types of cancer, including the various forms of lymphoma, breast cancer, leukemia, melanoma, and uterine and gastric cancers. However, these drugs have a potential toxic effect on the heart that can lead to chronic heart failure.

Another unique feature of the RESILIENCE trial is the use of the latest generation CMR technology to investigate the effect of RIC on heart function and composition. Study participants will be randomized to receive weekly RIC or a dummy procedure throughout their chemotherapy treatment. The patients will be examined by multiparametric CMR at three key time points: at the start of the study, halfway chemotherapy (i.e. after the third chemotherapy cycle, intermediate CMR), and two months after the end of the chemotherapy treatment. These CMR scans will monitor changes in heart function, with particular focus on left ventricular ejection fraction (LVEF).

The RESILIENCE trial represents a significant advance in the development of cardioprotective strategies for cancer patients with a high risk of anthracycline-induced cardiomyopathy. "All the patients included in the trial have some characteristic that places them at high risk of this cardiac complication secondary to cancer chemotherapy," concluded Dr. Ibáñez.

The RESILIENCE trial is funded by the European Commission (H2020-HEALTH, grant number 945118).

Moreno-Arciniegas A, García A, Kelm M, D'Amore F, da Silva MG, Sánchez-González J, Sánchez PL, López-Fernández T, Córdoba R, Asteggiano R, Camus V, Smink J, Ferreira A, Kersten MJ, Bolaños N, Escalera N, Pacella E, Gómez-Talavera S, Quesada A, Rosselló X, Ibanez B; RESILIENCE Trial Investigators. Rationale and design of RESILIENCE: A prospective randomized clinical trial evaluating remote ischaemic conditioning for the prevention of anthracycline cardiotoxicity. Eur J Heart Fail. 2024 Aug 30. doi: 10.1002/ejhf.3395. Epub ahead of print. PMID: 39212445.

Cell: Scientists at the CNIC discover an unexpected involvement of sodium transport in mitochondrial energy generation

The GENOXPHOS (Functional Genetics of the Oxidative Phosphorylation System) group at the CNIC has discovered a crucial role of sodium in the generation of cellular energy. The study, led by GENOXPHOS group leader Dr. José Antonio Enríquez, and published in the journal *Cell*, reveals that respiratory complex I, the first enzyme of the mitochondrial electron transport chain, possesses a hitherto unknown sodium transport activity that is crucial for efficient cellular energy production

The discovery of this activity provides a molecular explanation for the origin of the neurodegenerative disease Leber's hereditary optic neuropathy (LHON). First described in 1988, LHON is linked to defects in mitochondrial DNA and is the most frequent mitochondrially inherited disease in the world. The new study shows that the hereditary optic neuropathy in LHON is caused by a specific defect in the transport of sodium and protons by complex I.

Led by CNIC scientists José Antonio Enríquez and Pablo Hernansanz, the research team used an array of mutants and diverse genetic models to demonstrate that mitochondrial complex I exchanges sodium ions for protons, thus generating a gradient of sodium ions that parallels the proton gradient. This sodium gradient accounts for as much as half of the mitochondrial membrane potential and is essential for ATP production.

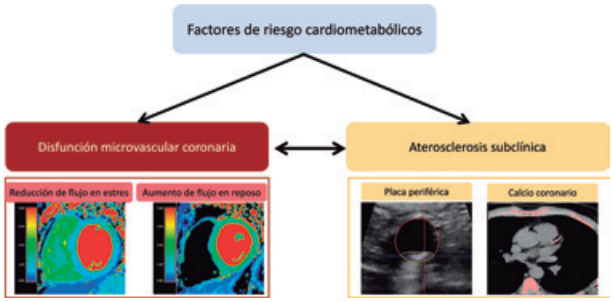
Discussing possible treatments for LHON, José Antonio Enríquez commented that while drugs are available that successfully replicate sodium transport across the inner membrane of isolated mitochondria, clinical use of these drugs is hindered by their toxic secondary effects on sodium transport in the cell membrane. "The challenge now is to design drugs that act specifically in mitochondria without effecting other parts of the cell," said Dr. Enríquez.

The researchers also believe that defects in sodium–proton transport may play a role in other, more frequent neurodegenerative diseases such as Parkinson's, in which an involvement of complex I has been detected.

The study was supported by the Ministerio de Ciencia e Innovación (MCIN) RTI2018-099357-B-I00, and CIBERFES (CB16/10/00282), the Human Frontier Science Program (grant RGP0016/2018), and Leducq Transatlantic Networks (17CVD04).

·Hernansanz-Agustín P, Morales-Vidal C, Calvo E, Natale P, Martí-Mateos Y, Jaroszewicz SN, Cabrera-Alarcón JL, Acín-Pérez R, López-Montero I, Vázquez J, Enríquez JA. A transmitochondrial sodium gradient controls membrane potential in mammalian mitochondria. Cell. 2024 Sep 19, 187: 1-15. doi: 10.1016/j.cell.2024.08.045

JACC: Cardiovascular Imaging: Cardiometabolic risk factors in apparently healthy individuals are linked to altered coronary microcirculation



A study from CNIC reveals how risk factors and subclinical atherosclerosis affect heart microcirculation in asymptomatic middle-aged individuals. The research, published in *JACC: Cardiovascular Imaging*, highlights the importance of assessing the heart vessels' ability to regulate blood flow and predict future cardiovascular risk. The study highlights the importance of assessing coronary microvascular function in individuals with no known cardiovascular disease in order to improve the prediction of atherosclerosis progression and future cardiovascular risk.

The results demonstrate that impaired coronary microvascular function is directly associated with the presence of cardiometabolic indicators such as metabolic syndrome, insulin resistance, and diabetes, as well as with subclinical atherosclerosis (the presence of fatty lesions in artery walls before the appearance of symptoms) in peripheral or coronary arteries.

Dr. Borja Ibáñez, who is the Scientific Director at the CNIC emphasized the value of examining PESA study participants: "The PESA population covers a crucial age group for the early detection of cardiovascular disease. By assessing microvascular function in this population, we were able to iden-

tify patterns that might have been hidden in other groups. Focusing on this age group gives us a unique window of opportunity for the implementation of primary prevention strategies, before the appearance of clinical symptoms."

Over a three-year follow-up, atherosclerosis progression was less pronounced among participants who had better coronary microvascular function at the start of the study. This result underlines the potential of microvascular function as a key marker in the stratification of cardiovascular risk and the prevention of future events.

Overall, the study shows that, in a large cohort of asymptomatic middle-aged individuals with no ischemic heart disease, the presence of cardiometabolic risk factors and systemic atherosclerosis is associated with altered coronary microvascular function. The higher the burden of cardiometabolic risk factors and the greater the extent of subclinical atherosclerosis, the stronger the impairment of coronary microvascular function. Moreover, preserved coronary microvascular function is associated with a lower risk of atherosclerosis progression.

The PESA study is funded by the CNIC and Banco Santander. The study also received financial support from the European Commission (ERC-CoG 819775 and H2020-HEALTH 945118), The Spanish Ministerio de Ciencia e Innovación (PID2019-110369RB-I00), and the Red Madrileña de Nanomedicina en Imagen Molecular - Comunidad de Madrid (S2017/BMD-3867 RENIM-CM).

Devesa A, Fuster V, García-Lunar I, Oliva B, García-Alvarez A, Moreno-Arciniegas A, Vazirani R, Pérez-Herreras C, Marina P, Bueno H, Fernández-Friera L, Fernández-Ortiz A, Sanchez-Gonzalez J, Ibanez B. Coronary Microvascular Function in Asymptomatic Middle-Aged Individuals With Cardiometabolic Risk Factors. JACC Cardiovasc Imaging. 2024 Aug 31:S1936-878X(24)00342-5. doi: 10.1016/j.jcmg.2024.08.002. Epub ahead of print. PMID: 39269413.

JACC: Progression of subclinical atherosclerosis predicts all-cause mortality risk

A study carried out at Mount Sinai Fuster Heart Hospital in New York in collaboration with the CNIC provides important new information about atherosclerosis, a disease in which lipids (cholesterol) and other substances accumulate in plaques on the arterial wall, causing the vessels to harden and narrow, and increasing the risk of severe cardiovascular conditions.
The study shows that both the burden of atherosclerosis and its progression (growth of plaques or the spread of the disease to new arteries) in asymptomatic individuals is independently associated with the risk of death from any cause
The goal of the new study was to determine the independent predictive value of the burden and progression of subclinical atherosclerosis above and beyond prediction based on established cardiovascular risk factors

The study included 5716 asymptomatic adults with an average age of 69 years (56.7% women) who were examined from 2008 to 2009 as part of the BioImage project, which examined a US population to evaluate factors implicated in atherosclerosis progression.

BioImage, led by Dr. Fuster, was the first study to demonstrate the value of 3D echocardiography and other advanced imaging technologies to detect atherosclerotic disease of the large vessels long before the appearance of symptoms. "The long asymptomatic phase of the disease presents a window of opportunity that has not been exploited in the younger population," said Fuster, who is the lead author on the *JACC* study.

The study, concluded Dr. Fuster, demonstrates that detecting subclinical atherosclerosis early and monitoring its progression can improve the prediction and prevention of death from any cause, offering a valuable tool for clinical practice

"Vascular ultrasound is a noninvasive and affordable test, and the valuable prognostic information it provides can be used to improve risk stratification and to target lifestyle recommendations for the control of cardiovascular risk factors", underlined Dr. Borja Ibáñez, CNIC Scientific Director, a cardiologist at Fundación Jiménez Díaz, and a member of the Spanish cardiovascular research network (CIBERCV).

The study, concluded Dr. Fuster, demonstrates that detecting subclinical atherosclerosis early and monitoring its progression can improve the prediction and prevention of death from any cause, offering a valuable tool for clinical practice.

Fuster V, García-Álvarez A, Devesa A, Mass V, Owen R, Quesada A, Fuster JJ, García-Lunar I, Pocock S, Sánchez-González J, Sartori S, Peyra C, Andres V, Muntendam P, Ibanez B. Influence of Subclinical Atherosclerosis Burden and Progression on Mortality. J Am Coll Cardiol. 2024 Oct 8;84(15):1391-1403. doi: 10.1016/j.jacc.2024.06.045. PMID: 39357937.

EUROPACE: A new image processing strategy for cardiac magnetic resonance

The, methodology validated in a multicenter study led by the Hospital Clínico San Carlos and the CNIC, enables preoperative planning based on a cardiac magnetic resonance imag-

ing strategy that avoids the biases intrinsic to conventional image analysis

The study has described and validated a new strategy for guiding ablation procedures in patients with complex tachycardias. Ablation procedures use energy—usually heat or cold—to eliminate small areas of heart tissue that cause pathological cardiac arrhythmias, thereby restoring normal heart rhythm. This type of procedure is frequently used to treat ventricular tachycardias originating in areas affected by scarring after a myocardial infarction.

The new approach uses advanced methods for processing cardiac magnetic resonance (CMR) images to identify the areas that maintain ventricular tachycardia in heart regions affected by postinfarction scarring. The method allows images to be processed systematically, avoiding the biases that can arise when CMR imaging parameters are selected manually. This systematic image processing increases the sensitivity for the detection of the regions responsible for these types of arrhythmias; moreover, the new strategy supports preoperative planning by allowing operators to accurately detect these regions before starting the ablation procedure.

The study used a swine model of myocardial infarction to analyze how variability in image processing parameters impedes accurate detection of the cardiac tissue circuits that maintain complex ventricular tachycardias. Using this animal model, the researchers designed a strategy that avoids this problem, and the method was later validated in patients in a multicenter study conducted between 2013 and 2022 and involving leading national and international experts.

The simplified planning of ablation procedures with the new method is especially useful in patients for whom conventional invasive catheter mapping is contraindicated due to the risk of inducing more severe tachycardias and circulatory collapse. In place of these risky procedures, the new method uses cardiac images obtained before the ablation procedure to identify target areas without the need to induce tachycardia during the procedure, reducing risk without reducing efficacy.

The study helps to avoid gaps in image integration when planning the ablation of complex ventricular tachycardias and is especially useful in patients with poorly tolerated episodes

Ramos-Prada A, Redondo-Rodríguez A, Roca-Luque I, Porta-Sánchez A, Ter Bekke RMA, Quintanilla JG, Sánchez-González J, Peinado R, Merino JL, Cluitmans M, Holtackers RJ, Marina-Breysse M, Galán-Arriola C, Enríquez-Vázquez D, Vázquez-Calvo S, Alfonso-Almazán JM, Pizarro G, Ibáñez B, González-Ferrer JJ, Salgado-Aranda R, Cañadas-Godoy V, Calvo D, Pérez-Villacastín J, Pérez-Castellano N, Filgueiras-Rama D. Novel systematic processing of cardiac magnetic resonance imaging identifies target regions associated with infarct-related ventricular tachycardia. Europace. 2024 Sep 19:euae244. doi: 10.1093/europace/euae244. Epub ahead of print. PMID: 39298664.

The new strategy is highly applicable in the clinic and can be easily implemented in commercial systems currently used to guide the ablation of postinfarction ventricular tachycardias.

The study was supported by the Spanish Ministerio de Ciencia e Innovación (MCIN) and the Pro-CNIC Foundation in relation to the CNIC's status as a Severo Ochoa Center of Excellence (CEX2020-001041-S). The study was also supported by grants from the MCIN (PID2019-109329RB-I00), the Asociación de Ritmo Cardiac of the Spanish Society of Cardiology, the Fundación Interhospitalaria para la Investigación Cardiovascular, and the Fundación Fundación Eugenio Rodríguez Pascual

JCI: A new study reveals a key mechanism driving atherosclerosis in Hutchinson-Gilford Progeria Syndrome

A team of scientists from the CNIC and the CSIC has identified a key mechanism in the development of atherosclerosis in patients with the rare genetic disease Hutchinson-Gilford progeria syndrome. The researchers has made a significant breakthrough in understanding the underlying causes of cardiovascular disease in patients with Hutchinson-Gilford progeria syndrome (HGPS), an ultra-rare genetic disorder that accelerates the aging process. The most serious consequence of HGPS is the early onset of cardiovascular disease, leading to premature death at an average age of 14.5 years.

In the study, the researchers identify the activation of the YAP/TAZ pathway in endothelial cells as a major contributor to the development of atherosclerosis in HGPS. The discovery, published in The Journal of Clinical Investigation, sheds light on the vascular problems faced by HGPS patients and opens up potential new avenues for treatment.

HGPS is caused by a mutation in the LMNA gene that leads to the synthesis of a toxic protein called progerin. This mutant protein disrupts normal cell function and accelerates cell aging. Children with HGPS typically show signs of rapid aging in the first two years of life, and by the time they reach their early teens most patients develop severe atherosclerosis—a condition in which the arteries stiffen and narrow—leading to heart attack, stroke, or heart failure, the main causes of premature death in HGPS patients. Despite the severity of this disease, the precise mechanisms underlying the cardiovascular problems in HGPS patients have remained poorly understood.

The authors explored how endothelial cells—the cells that line blood vessels—are affected in HGPS. Using advanced single-cell RNA-sequencing technology, they analyzed gene expression in the multiple cell types present in the arterial wall in a mouse model of HGPS and in healthy control mice. This approach allowed the researchers to examine the behavior of individual endothelial cells in unprecedented detail.

In addition to its significance for HGPS, the study has broader implications for understanding cardiovascular disease in the general population. Atherosclerosis is a leading cause of death worldwide, and many of the processes identified in this study—such as vascular stiffening and the activation of inflammatory pathways—also occur in the arteries of older adults.

The insights we've gained from studying HGPS can help us gain a better understanding of the aging process in general and of the factors that contribute to cardiovascular disease in older individual. By targeting the molecular pathways that drive vascular aging, we may be able to develop new therapies that extend healthy lifespan and improve quality of life.

The study was supported by grants from the Spanish Ministerio de Ciencia, Innovación y Universidades (MICIU) and Agencia Estatal de Investigación (AEI) (MICIU/AEI/10.13039/501100011033), ERDF/EU and "NextGenerationEU"/PRTR (PID2022-141211OB-I00, PID2022-137111OA-I00, RYC2021-033805-I), and the Comunidad de Madrid with co-funding from the ESIF/EU (2017-T1/BMD-5247, 2021-5A/BMD-20944).

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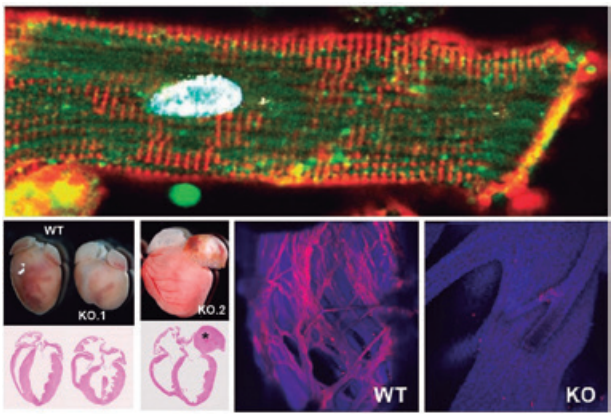
Nature Communications: A key mechanism in the development and functioning of the conduction cardiac system is discovered



A study published in by a research team from the Carlos III Rare Diseases Research Institute (ISCIII), CIBER, CNIC Pompeu Fabra University (UPF) and Severo Ochoa Center for Molecular Biology (CBM, CSIC-UAM) has identified the Dhx36 protein as an essential regulator for the development and functioning of the heart, particularly in the conduction cardiac system.

This breakthrough, led by scientists Pablo Gómez del Arco (ISCIII), Pura Muñoz-Cánoves (UPF and Altos Labs), and Juan Miguel Redondo (CBM, CSIC-UAM), has shown that Dhx36 modulates gene networks that control the cardiomyocyte differentiation, through the resolution of G-quadruplex structures in the promoters of key genes of the cardiac conduction system. This function is crucial for the formation of specialized cells that make up the conduction system that transmits and controls the heart's electric impulses.

The study also demonstrated that the absence of Dhx36 in the mouse cardiomyocytes during embryonic development and in adulthood provokes severe cardiac problems, including dilated cardiomyopathy and blockage in the transmission of the electrical impulse between the chambers of the heart, particularly between the atria and ventricles. These findings suggest that Dhx36 is essential for maintaining heart health, especially after birth, and that defects in this protein could be related to heart diseases that affect the electrical activity of the heart and cause dilated cardiomyopathy.

The study also identified the genes and signaling pathways involved in cardiac cell differentiation and in the development of the specialized fiber system of the Purkinje system, essential for the synchronization of ventricular contraction. The results suggest that transcriptional regulation plays a crucial role in cardiac function and opens new perspectives for the development of therapies to treat disorders in the cardiac conduction system, like those associated with heart failure.

Pablo Gómez-del Arco, Joan Isern, Daniel Jimenez-Carretero, Dolores López-Maderuelo, Rebeca Piñeiro-Sabarís, Fadoua El Abdellaoui-Soussi, Carlos Torroja, María Linarejos Vera-Pedrosa, Mercedes Grima, Alberto Benguria, Ana Simón-Chica, Antonio Queiro-Palou, Ana Dopazo, Fátima Sánchez-Cabo, José Jalife, José Luis de la Pompa, David Filgueiras-Rama, Pura Muñoz-Cánoves and Juan Miguel Redondo The G4 Resolvase Dhx36 Modulates Cardiomyocyte Differentiation and Ventricular Conduction System Development. Nature Communications, 2024. doi: 10.1038/s41467-024-52809-1.

Science Advances: A new CNIC study describes a mechanism whereby cells respond to mechanical signals from their surroundings

A study conducted at the CNIC, led by Dr. Jorge Alegre-Cebollada, has revealed the fundamental role of tissue viscoelasticity—a property still largely unexplored—in cellular function. The extracellular matrix (ECM), a network of proteins that supports and connects cells, influences processes such as cell migration, proliferation, and differentiation through its mechanical properties, including stiffness and viscoelasticity.

Until now, research on the mechanical properties of the ECM has primarily focused on stiffness, especially in the context of diseases like myocardial infarction and certain types of cancer. However, the cellular response to viscoelasticity has not been fully understood, particularly in stiffer tissues. The study, published in *Science Advances*, demonstrates for the first time how tissue viscoelasticity plays a crucial role in the process known as cellular homeostasis, which is the ability of cells to maintain an adequate internal balance for proper function.

According to Dr. Carla Huerta-López, who led the study, viscoelasticity regulates the time cells need to respond to mechanical stimuli. Using the example of a viscoelastic mattress that takes time to return to its shape after being pressed, Huerta-López compares this process to how cells require time to recover from mechanical alterations, such as a handshake or a blow.

The research team developed protein-based biomaterials that mimic the mechanical properties of the ECM to study how cells respond to viscoelasticity. Using these biomaterials and a computational model, the researchers discovered a mechanism in which tissue viscoelasticity counteracts the cellular response to stiffness in an unexpected way. This finding contradicts previous models and provides new explanations about how cells react to the mechanical properties of their environment, which could have implications for improving artificial tissues and treating diseases associated with changes in tissue viscoelasticity, such as certain types of cancer and cardiovascular diseases.

The study was made possible thanks to funding from the Ministry of Science, Innovation and Universities, the European Research Council (ERC), and the Community of Madrid through the interdisciplinary consortium Tec4Bio-CM. Notably, four principal investigators from Tec4Bio-CM directly contributed to this work from CNIC, ICMM-CSIC, and the Polytechnic University of Madrid..

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CNIC scientists discover a key mechanism in fat cells that protects the body against energetic excess

A team at the (CNIC) led by Professor Miguel Ángel del Pozo Barriuso, who heads the Mechanoadaptation and Caveolae Biology group at the CNIC, has identified an essential mechanism in fat cells (adipocytes) that enables them to enlarge safely to store energy. This process avoids tissue damage and protects the body from the toxic effects of accumulating fat molecules (lipids) in inappropriate places. The results, published in *Nature Communications*, signify a major advance in the understanding of metabolic diseases. Moreover, this discovery opens the door to the development of new therapeutic strategies to combat diseases related to chronic energetic excess, such as overweight, obesity, lipodystrophy, and metabolic syndrome, and their grave cardiovascular and metabolic complications. The team analyzed the role of caveolae, small invaginations in the cell membrane that act as sensors and shock absorbers of these stresses. "When an adipocyte accumulates fat and its surface is

under increased tensile stress, the caveolae flatten, releasing a 'reservoir' of membrane that allows the cell to enlarge without breaking apart. Conversely, when fat reserves diminish, these structures regroup to reduce the excess membrane and restore cellular stability," explained study first author Dr. María Aboy Pardal. The CNIC study highlights the key role of the caveolae protein caveolin-1 (Cav-1). For caveolae to flatten correctly in response to fluctuations in mechanical tension in the cell membrane, Cav-1 needs to be chemically altered by the addition of a phosphoryl group to a specific amino acid, a process called phosphorylation. For the study, the researchers developed a transgenic mouse that expresses a genetically altered version of Cav-1 that cannot be phosphorylated.

The study was funded by the Ministerio de Ciencia, Innovación y Universidades (MICIU) through the Agencia Estatal de Investigación (AEI) and with funding from the European Regional Development Fund "A way to make Europe" (SAF2017-83130-R, IGP-SO grant MINSEV1512-07-2016, BFU2016-81912-REDC, and SAF2020 (PID2020-118658RB-I00)) and by the Fundación "la Caixa" (AtheroConvergence, HR20-00075), the Community of Madrid regional government (Tec4Bio-CM, S2018/...), Fundació La Marató de TV3 (201936-30-31), and the Asociación Española Contra el Cáncer (PROYE20089DELP).

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Nature Methods: CNIC presents iFlpMosaics, an innovative genetic toolkit for the study of gene function

A team at the CNIC, led by Dr. Rui Benedito, has developed a comprehensive set of innovative genetic tools and mouse lines, called iFlpMosaics, designed to enhance the study of gene function and its implications in health and disease.

The groundbreaking study, published in *Nature Methods*, presents a pioneering approach that overcomes critical limitations of existing methods for generating genetic mosaics. These innovations will enable scientists to more accurately investigate the effects of somatic mutations on cellular biology and disease.

The study highlights the iFlpMosaics toolkit's utility across different experimental setups, detailing how it allows scientists to track the effects of single or multiple gene deletions within the same tissue. This advance opens the way to deeper insight into the function of genes in cell biology, regeneration, and disease.

The iFlpMosaics toolkit is unburdened by these shortcomings and allows researchers to induce genetic mosaics with high throughput and precision, making it easier to study cell-autonomous gene function directly within the same organism.

The toolkit not only enhances the understanding of genetic mutations in tissue development and disease processes, but also facilitates the study of complex interactions between cells within their microenvironment.

"iFlpMosaics offers a big step forward for researchers studying diseases caused by somatic mutations, such as cancer and vascular malformations" said Dr. Rui Benedito. "It's precision and versatility provide an important resource for anyone seeking a better understanding of gene function in normal organ development and function, as well as in disease settings."

The study was funded by the European Research Council (ERC) through Starting Grant AngioGenesHD (638028) and Consolidator Grant AngioUnrestUHD (101001814), the Spanish Ministry of Science, Innovation, and Universities (SAF2017-89299-P y PID2020-120252RB-I00), and the "la Caixa" Foundation (HR19-00120 and HR22-00316 AngioHeart).

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AWARDS

Valentin Fuster, wins prestigious award from the International Atherosclerosis Society

The International Atherosclerosis Society has awarded Dr. Valentín Fuster, the Antonio M. Gotto Jr. Prize in Atherosclerosis Research in recognition of his outstanding contributions to the understanding and treatment of atherosclerosis. The award was presented by Peter Libby, President of the International Atherosclerosis Society, during the opening ceremony of the International Atherosclerosis Society's Annual Symposium in Oman. This award honors Dr. Fuster's outstanding contributions to the understanding of the progression, prevention, and treatment of atherosclerosis, also known as hardening of the arteries.

Héctor Bueno receives the ESC President's Awards 2024 at the Congress of the European Society of Cardiology

Dr. Héctor Bueno, principal investigator of the Multidisciplinary Translational Cardiovascular Research group at the Spanish National Cardiovascular Research Centre (CNIC), Coordinator of the Clinical Hospitalization Area and Research of the Cardiology Service at the 12 de Octubre Hospital, leader of the i+12 Multidisciplinary Translational Cardiovascular Research Institute, has received the ESC President's Awards 2024 from the European Society of Cardiology (ESC) at the ESC Congress 2024 in London. This award recognizes Héctor Bueno·s outstanding individual contribution to the ESC. According to Professor Franz Weidinger, President of the ESC, Dr. Bueno´s years of selfless service to ESC have made ‹a profund impact in many ways, to members of the ESC but also for our patients›.

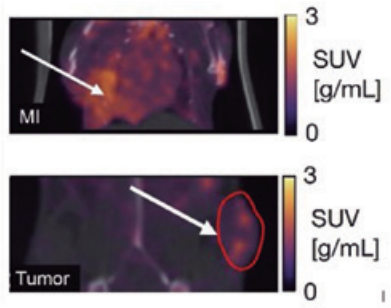
Prof. María Ángeles Moro Joins the Royal National Academy of Pharmacy

Prof. María Ángeles Moro Sánchez, PhD in Pharmacy and expert in Neurovascular Pathophysiology, has been appointed as a Full Member of the Royal National Academy of Pharmacy (RANF). During her inauguration, she emphasized her commitment to the institution's objectives: promoting scientific knowledge in health, advancing research in innovative treatments, and fostering continuous education for healthcare professionals.

CNIC receives the Severo Ochoa Center of Excellence Award from the Ministry of Science and Innovation, granted in 2021

The CNIC received the Severo Ochoa Center of Excellence 2021 distinction, awarded by the State Research Agency, in recognition of its scientific impact and international leadership, as well as its collaboration with the social and business environment. This prestigious recognition, which CNIC first received in 2011, aims to accredit and fund research centers of excellence in Spain.

CNIC study named Nature PJ Imaging Article of the Year for 2024



A study coordinated by Dr. Carlos Pérez Medina from the Centro Nacional de Investigaciones Cardiovasculares (CNIC) in Madrid has been named by the journal npj Imaging as its Article of the Year for 2024 (npj Imaging). The article, 'Macrophage PET imaging in mouse models of cardiovascular disease and cancer with an apolipoprotein-inspired radiotracer', describes an innovative probe for the noninvasive detection of macrophages—immune cells that play a key role in the inflammatory response—by positron emission tomography (PET). The study, published in May 2024, was carried out by scientists at the CNIC and Mount Sinai Hospital in New York.

ACTIVITIES

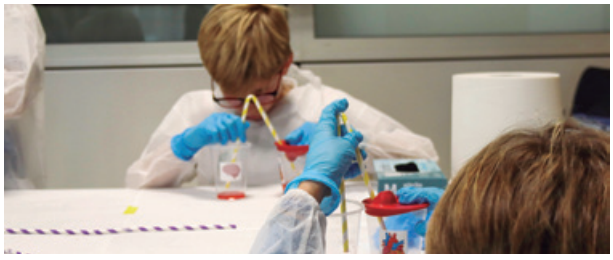
European Researchers' Night 2024 at CNIC

Through eight activities open to both adults and children, attendees of the 15th European Researchers' Night in Madrid, hosted by CNIC, participated in seminars and workshops that brought them closer to the research conducted at the center. This event offers an exciting opportunity to dive into the world of science and innovation. From fascinating experiments to inspiring talks, CNIC provides a glimpse into the latest discoveries and technological wonders.

Eight Top High School Students in Spain Join CNIC's ACÉRCATE Program

Eight high school students from across Spain participated in CNIC's ACÉRCATE program, part of the CNIC-Joven Training Plan led by Dr. Valentín Fuster. This program, aimed at fostering young talent in cardiovascular research, selected five female and three male students from over 50 candidates hailing from regions such as Catalonia, Murcia, Castile and León, Valencia, and Andalusia.

CNIC at the 2024 Science Week



From November 7 to 15, CNIC organized 11 activities during the 24th Science and Innovation Week, welcoming participants of all ages. Attendees engaged in practical workshops and had the chance to visit CNIC's state-of-the-art laboratories.

CNIC PhDay 2024: "Learning from the Past for a Better Future"

The 10th edition of CNIC PhDay was held on November 29, 2024, organized by doctoral students and postdoctoral researchers. Under the theme "Learning from the Past for a Better Future," the event focused on the impact of science on the environment and society.

CNIC Joins the 2024 Heart Race

CNIC took part in the 15th Popular Heart Race organized by the Spanish Heart Foundation, promoting cardiovascular health and fitness through community participation.

Sammy Basso, the Longest-Living Progeria Patient, Passes Away

Sammy Basso, the world's longest-living patient with progeria, has passed away, leaving a legacy of resilience and inspiration for those affected by this rare condition.

TRAIN2GAIN
WHAT'S ON
INSIDE SCIENCE
CNIC & SOCIETY

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