INSIDE SCIENCE
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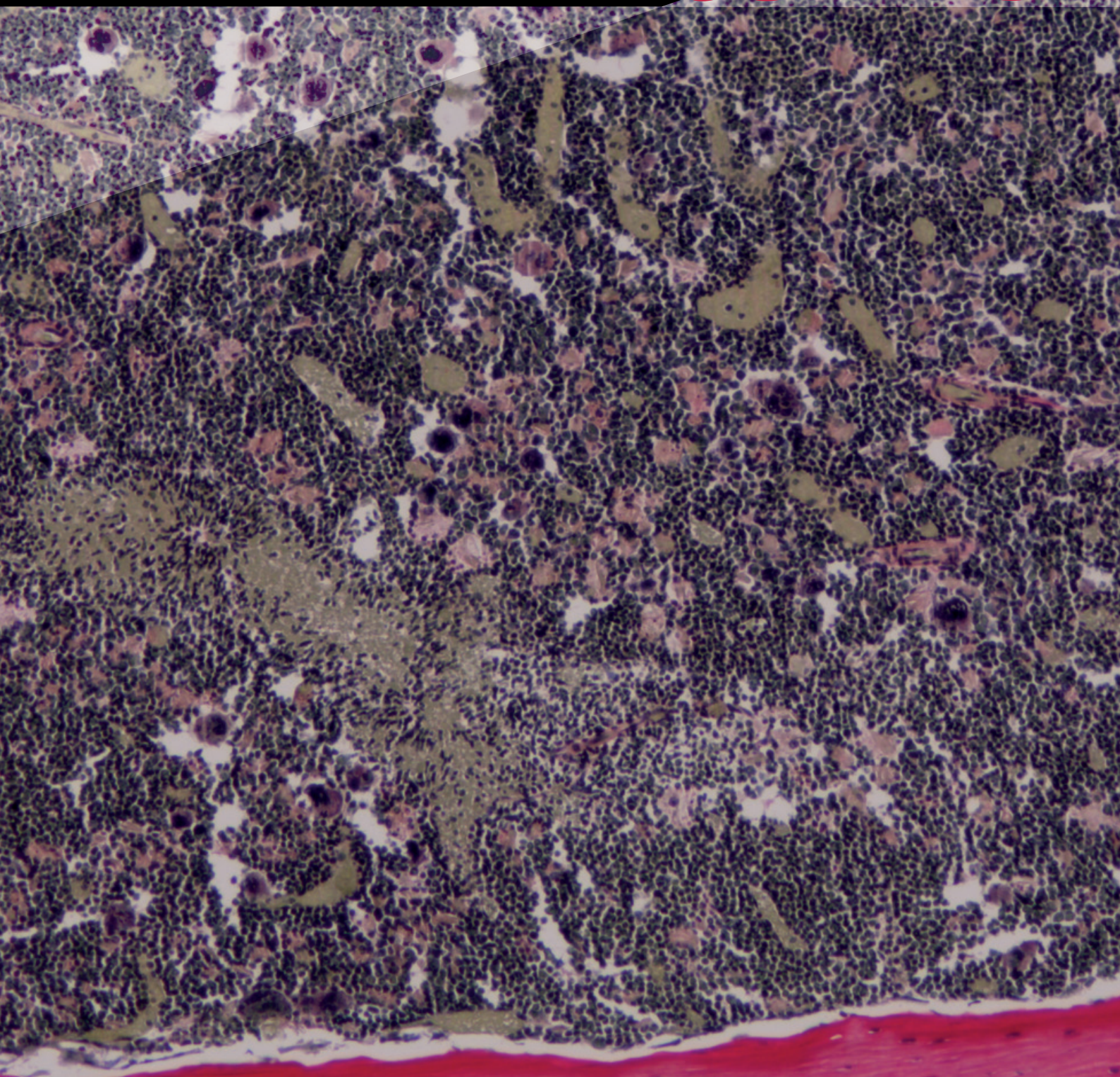
WHAT'S ON
CNIC & SOCIETY

cnic PULSE

winter'15



contents winter'15

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More on the CNIC at www.cnic.es
Please send any comments or suggestions to flois@cnic.es

Dr. Valentín Fuster, Director of the CNIC

The academic and medical sectors always appear to be at loggerheads. Academia is associated in the popular imagination with the ivory tower of isolated study, while the clinical world is concerned with more immediate problem solving. Of course this division ceased to hold true a long time ago, and at the CNIC we are very committed to ensuring that these two sectors work together.

In this issue of CNIC PULSE we once again turn attention to our support for training, this time in direct relation to the academic sector. Every year the CNIC hosts several students working toward their Master's degree, that crucial stage that for many confirms their dedication to a career in research.

WITH THE UNIVERSITY AND FOR THE PATIENT

Two programs, the Master Program and the Cardiovascular Diseases Module, part of the Master's in Biomolecular Medicine run by the Autonomous University of Madrid, provide high-level training that benefits both the participants and the research effort at the CNIC.

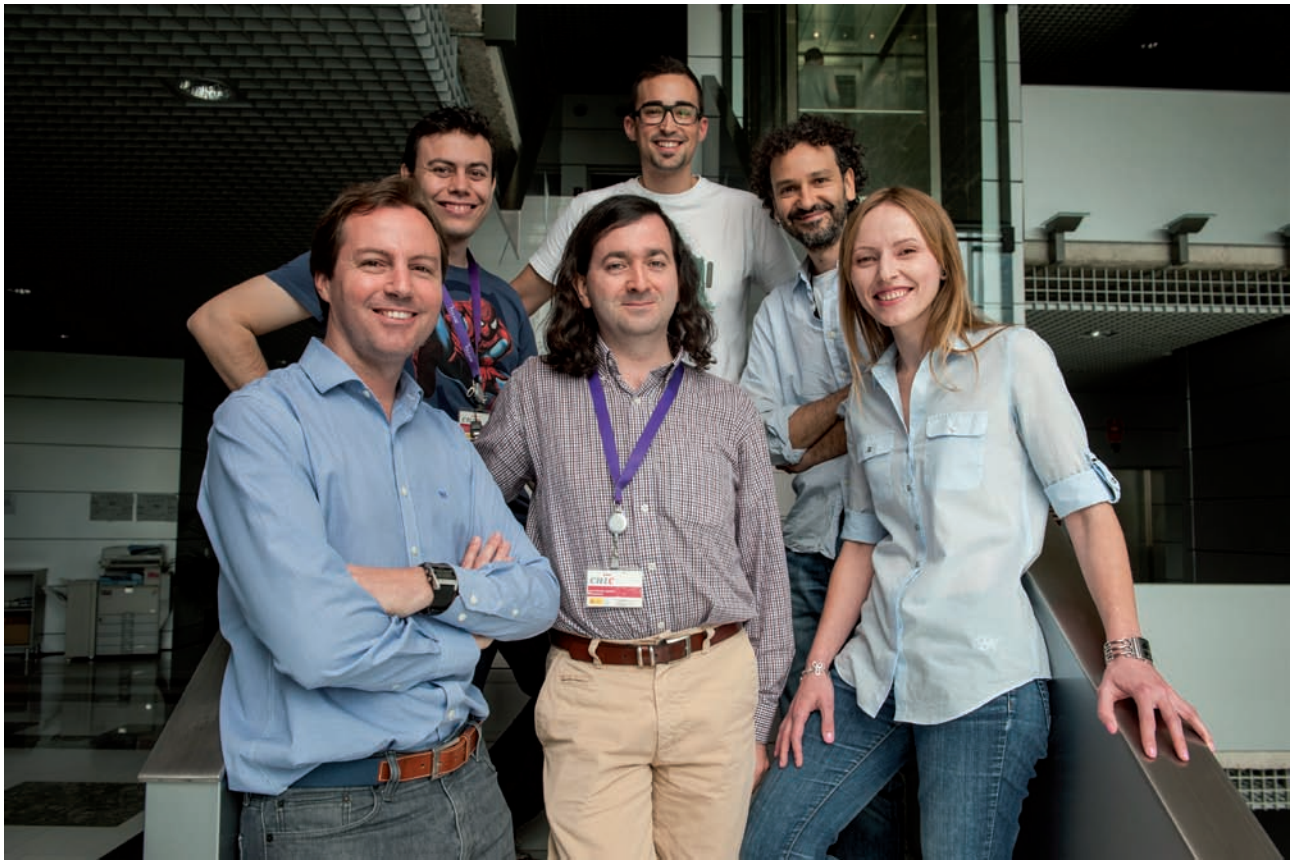
We also highlight another success of our training program, Cardiojoven, one of whose alumni has been awarded a prize by the European Society of Cardiology.

We continue to benefit from the input of leading scientists who come to the Center to share their research findings. A case in point was the recent visit of **Luis Serrano**, director of the CRG, a center that shares many qualities with the CNIC, and we took the opportunity to interview him for CNIC PULSE.

But we don't only receive visits from scientists. In June Spanish President **Mariano Rajoy** came to the CNIC and praised our model of scientific management.

This new edition of CNIC PULSE not only confirms that there is still plenty to say about our center but also shows that the new generation of researchers is set to ensure that this momentum never falters.

THE MICROENVIRONMENT THAT CONTROLS HEMATOPOIETIC STEM CELLS IS A POSSIBLE THERAPEUTIC TARGET FOR MYELOPROLIFERATIVE DISORDERS



The discovery of a new therapeutic target for certain kinds of myeloproliferative disease is, without doubt, good news. This is precisely the discovery made by the Stem Cell Physiopathology group at the CNIC, led by **Dr. Simón Méndez–Ferrer**. The team has shown that the microenvironment that controls hematopoietic stem cells can be targeted for the treatment of a set of disorders called myeloproliferative neoplasias. The research team studied a type of myeloproliferative neoplasia called polycythemia vera.

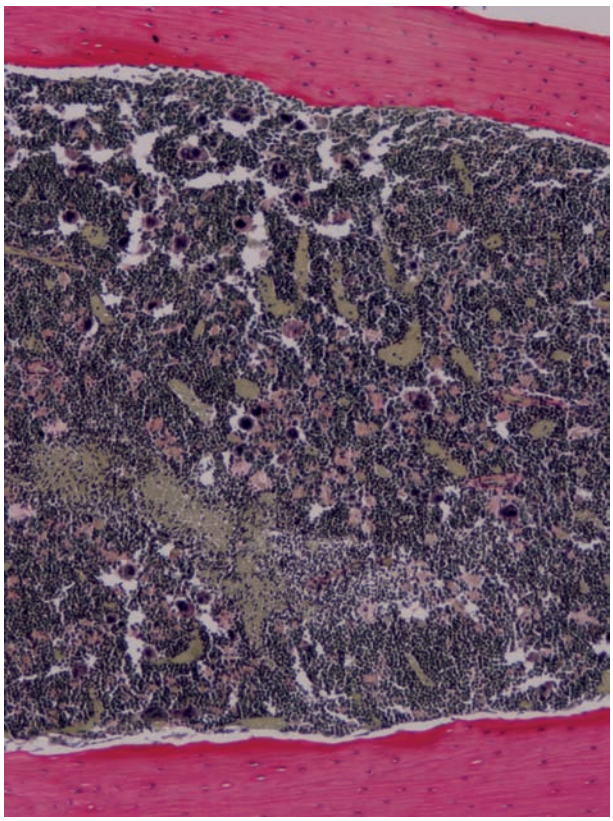
The findings, published in ***Nature***, demonstrate that these myeloproliferative neoplasias only appear after damage to the microenvironment that sustains and controls the hematopoietic stem cells—the cells that produce the cells of the blood and the immune system. Protecting this microenvironment, or niche, has thus emerged as a new route for the treatment of these diseases, for which there is currently no fully effective treatment.

"In normal conditions, the microenvironment is able to control the proliferation, differentiation and migration of the hematopoietic stem cell. A specific genetic mutation in these cells triggers a cascade of events that lead to myeloproliferative disease. However, the disease develops only when the mutated cell is able to damage the local microenvironment that normally regulates it, thereby escaping the control this microenvironment exerts on cell proliferation. What we have found is that the mutated cell produces an inflammatory injury to the microenvironment, resulting in the breakdown of this control. But our team has also demonstrated that this damage can be prevented or reversed by treatments that target the niche." explained **Dr. Méndez-Ferrer**.

This last finding takes the work beyond basic research, and is good news for patients. Indeed, the same team of researchers has demonstrated the efficacy of a possible new treatment, which has been patented through the CNIC. The treatment involves an innovative use of clinically approved treatments for other diseases, so that, according to the authors, "it shouldn't be associated with adverse side effects".

The new treatment route has been tested in animals and has received financial backing for a multicenter phase II clinical trial. "This study has a very strong translational and clinical potential", emphasized study first author **Lorena Arranz**, who added that "current treatment for myeloproliferative neoplasias is largely symptomatic and directed at preventing thrombosis and fatal cardiovascular events".

The only real cure available today is a bone marrow transplant, which is not advisable in patients over 50 years old. "This makes it important to identify new therapeutic targets for the development of effective treatments," the investigators conclude.



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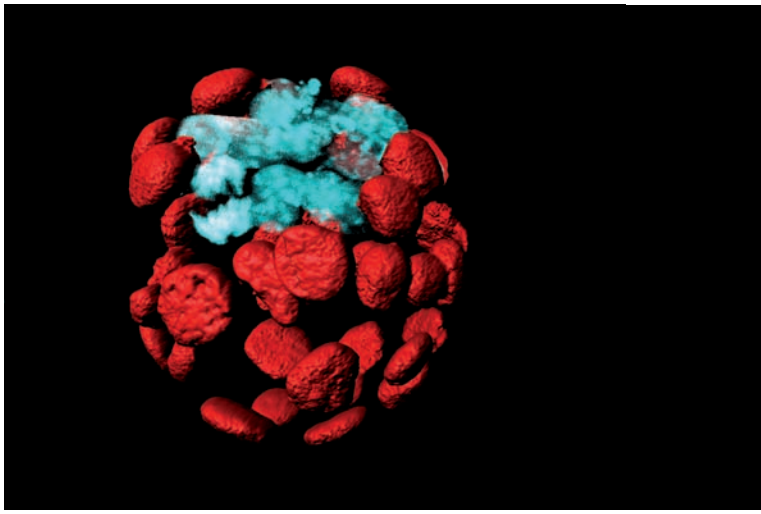
WHEN DO MAMMALIAN CELLS BEGIN TO DIFFERENTIATE?



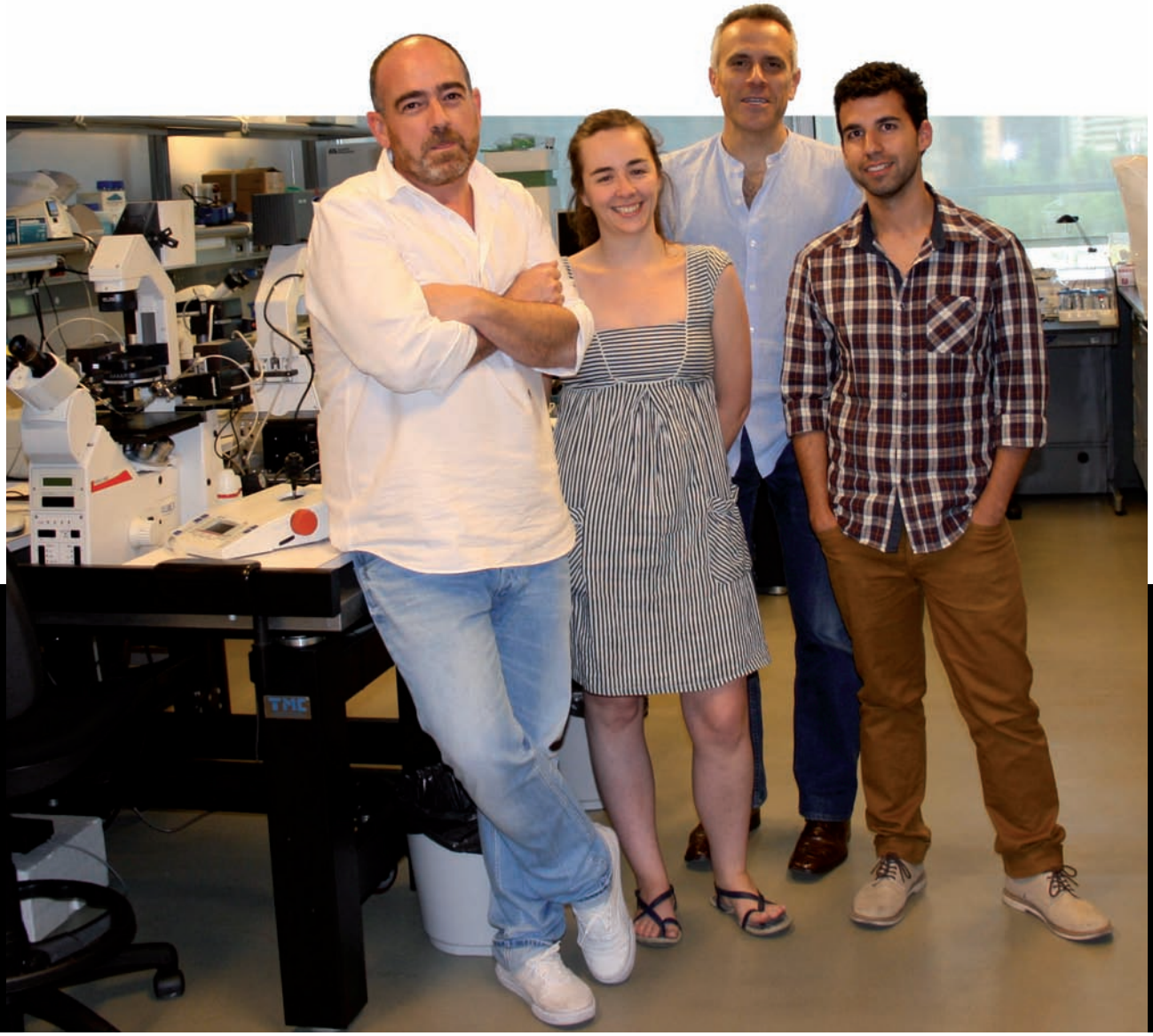
3D reconstruction of an embryo at the blastocyst stage. The nuclei on the outside (in red) correspond to the cells of the trophectoderm, the first extraembryonic tissue to form. The interior cells (marked in blue) form the inner cell mass, which will give rise to all the tissues and organs of the adult.

CNIC researchers have identified one of the key factors regulating the appearance of the first differentiated cell types in mammals. This event takes place even before the embryo implants in the mother's uterus, during a stage when the embryo is a ball of cells called the blastocyst. This important discovery has been recognized by the editors of the journal ***Developmental Cell***.

The CNIC team did not work alone, and the author list includes investigators from the Sickkids Hospital in Toronto, the Sloan-Kettering Institute in New York, and the University of Kumamoto in Japan. Together, this international team identified a regulatory element implicated in the function of a gene that plays an important role in the first cell differentiation event in mammals: the generation of the embryonic and extraembryonic cell types.

The blastocyst is an embryonic structure present in the early stages of mammalian development, before the embryo implants in the uterus, and consists of a ball of between 64 and 100 cells surrounding a central cavity. Before this stage, all the cells of the embryo are equivalent and totipotent, meaning that they are capable of contributing to all structures of the embryo.

But with the formation of the blastocyst comes the first distinction between different cell types. Errors during this



process can result in failed pregnancy, generally due to the formation of defective embryonic structures that impede development.

This first lineage decision in the blastocyst establishes two populations of cells: those that will go on to form the trophectoderm, the origin of the future placenta, and those that will form the inner cell mass, the origin of the embryo proper and all the tissues of the new organism.

According to lead author **Miguel Manzanares**, "This segregation is crucial because it is through this process that embryonic cells lose their totipotency and at the same time generate the trophectoderm, a tissue characteristic of mammals." The trophectoderm develops into the trophoblast, which, after differentiating into various cell types, forms the placenta and the amniotic membranes. In this process a fundamental role is played by the gene Cdx2, which is essential for the segregation of the trophectoderm from the inner cell mass.

Dr. Manzanares's team, with **Teresa Rayón** (first author on the study) and **Sergio Menchero**, working together with the other study authors including the CNIC group led by **Dr. José Luis de la Pompa**, has identified a specific DNA sequence—called a regulatory element—that regulates the function of Cdx2 by acting as a switch for the activity of this gene.

Teresa Rayón explains that "the element we discovered directs the restricted expression of a marker gene in the trophectoderm, and this helps us to understand how Cdx2 receives and processes information in order to be activated and carry out its function.

The team also discovered that the formation of the trophectoderm involves signaling via the receptor protein Notch acting in concert with Tead4, a gene recently implicated in this lineage decision and which forms part of another signaling pathway called Hippo. The researchers found that the Notch and Hippo pathways act in parallel on the newly identified Cdx2 regulatory element. This combined action helps to ensure the correct development of the embryo by providing compensatory mechanisms at these developmental stages that favor embryo viability.

"The essential features of the early specification of the trophectoderm are conserved between humans and mice, so knowledge of lineage differentiation in the mouse can give us a better understanding of what happens in humans and also help to improve assisted reproductive technology," emphasizes **Dr. Manzanares**. "This knowledge will also help to advance research into the genetic influences on early trophoblast differentiation, both in normal and pathological conditions."

A TOUCHSTONE IN IMAGING RESEARCH

Translational research is a distinctive characteristic of the Centro Nacional de Investigaciones Cardiovasculares (CNIC). Indeed, doing everything possible to move knowledge obtained in basic research into new patient treatments is almost an obsession for all the researchers at the CNIC, starting with Center director **Dr. Valentín Fuster**. **Borja Ibáñez**, the Center's head of imaging in large animal models and humans, explains that since the refounding of the CNIC the aim has been to use the most advanced imaging technology "as the tool for moving from small to large animal models and from there to humans."

For this reason, one of the first steps taken after the inauguration of the Center in its current phase was to set up an international competition to select the best provider of the latest in imaging technology. The winner was Philips. **Dr. Ibáñez** fills in the background: "Until recently, the state-of-the-art in cardiac magnetic resonance was 1.5 Tesla. 3-Tesla scanners, which give better resolution, were available in other fields but were seldom used in cardiology." This was simply a consequence of normal cardiac physiology: the extensive movement of the beating heart. "To resolve this and other problems," continues **Ibáñez**, "Philips developed a new patented tool in which the radiofrequency is distributed across two independent excitation sources, instead of the classical approach with just one excitation source". "This new technology produces more homogeneous images with improved contrast between cardiac structures, allowing us to take full advantage of the potential of 3T machines in cardiovascular studies."

But this was not the only reason for selecting Philips. The company's proposal did more than offer the CNIC the best imaging equipment available; the package also included an agreement for a scientific development partnership. This agreement assures the CNIC priority access to revolutionary updates and prototypes in cardiovascular imaging. **Borja** emphasizes that "this brought us the first 3 Tesla multi-transmitter MRI scanner for large animal work to be installed in the world, and the second in the world for humans." He goes on to remark that "A researcher from Philips, **Dr. Javier Sánchez-González**, works with us and a second researcher will be joining the team through this partnership." This arrangement has already borne fruit in the form of a patent to be filed jointly by the CNIC and Philips. "The patent covers a new method for capturing cardiac magnetic resonance images," says **Borja**, adding that a full cardiac magnetic resonance imaging study takes at least 45 minutes. "Any procedure that can reduce the time needed for image acquisition is a spectacular advance and will promote the routine use of this innovative technique."

Very few centers in the world boast the advanced equipment found at the CNIC, and centers where such equipment is dedicated exclusively to research form an exclusive elite. Highlights include the hybrid scanners: a PET/CT scanner for exclusive use with large animal models and the PET/MRI equipment for human studies. "These scanners are designed for clinical use, and very few centers have this equipment dedicated exclusively to research."

And, in imaging research, the CNIC has its own jewel in the crown: the CNIC-Santander PESA Project. "What is impressive is that, until now, the largest series of hybrid PET/MRI scans for atherosclerosis included at most 30 people; we have already scanned more than 1000 participants in the PESA study." **Dr. Ibáñez** explains that "this is only possible when you have the right equipment and dedicate it exclusively to research," adding that "the information coming out of this study is amazing."

The CNIC, far from keeping an exclusive hold on its imaging equipment, actively seeks to share its imaging infrastructure with top-flight researchers, wherever they are based. **Dr. Ibáñez** explains: "This can benefit hospitals throughout Spain, and especially those in Madrid. Access to the equipment is overseen by a committee formed by representatives of the CNIC and hospitals within the Madrid region, allowing any high-quality research team that needs to use this unique imaging equipment to carry out its project in these installations."

The studies with this technology are carried out a few hundred meters from the main CNIC site, in the Human Cardiovascular Imaging Laboratory, a source of great pride for those who work there. Opened in December 2011, the laboratory is the product of an agreement with the Madrid regional government, which provided the site for the construction of this pioneering center as part of its commitment to promoting translational medicine. This is an advance that will without doubt contribute to the improved health of everyone.

Europe

STARTING GRANT FOR RUI BENEDITO

The resolution of the Horizon 2020 call was eagerly awaited throughout Europe because of the prestige and sheer economic value of these awards from the European Research Council. CNIC researcher **Rui Benedito** is one of the 20 lucky researchers from Spain to be awarded a Starting Grant. Congratulations!

Excellence

CRISTINA CLAVERÍA, PREMIO FUNDACIÓN PFIZER

New recognition for a job well done, on this occasion by CNIC researcher **Cristina Clavería**, who has won the Premio Fundación Pfizer in the Basic Research category for a study published in the journal ***Nature***.

Future

DE LA POMPA, SELECTED BY THE FUNDACIÓN BBVA

CNIC researcher **José Luis de la Pompa** has recently received funding from the highly competitive Ayudas Fundación BBVA for projects in basic research. Just six of the 589 submitted projects secured this significant economic injection of €150,000.

In JACC

A POLYPILL FOR BETTER TREATMENT ADHERENCE

It should be easy, but experience shows that it isn't. People who have survived a heart attack find it difficult to take all the medications they need in order to prevent a second attack. The polypill, which combines three drugs in a single pill, makes it easier to adhere to the recommended treatment. Great news for patients!

agenda...

OPEN FROM FEBRUARY 2015
CNIC International Postdoctoral Program: CNIC IPP

In February 2015 the CNIC will launch the fourth call of its International Postdoctoral Program, supported by €1.6 million from the European Commissison through the COFUND Programme, within the Marie Curie Actions theme in FP7.

The CNIC IPP supports transnational mobility of postdoctoral researchers with the aim of broadening and deepening their individual competences, particularly in terms of acquisition of complementary skills needed to become an independent group leader in the future. The program is open to researchers who hold a PhD degree at the time of the application deadline.

Successful applicants are hired on 3-year contracts.

Researchers on the CNIC IPP program receive additional funding for travel and a benefits package that includes full social security cover, a flexible salary package, life insurance for death or permanent disability, civil liability insurance, work and family-life balance, assistance with nursery care, and language training (English and Spanish).

OPEN FROM FEBRUARY 2015
CICERONE Program

The CICERONE Program is open to advanced undergraduate students studying toward a biomedicine-related university degree. Participants extend their scientific training through hands-on experience of laboratory-based biomedical research during the summer recess. In addition to carrying out a supervised research project, the students also attend CNIC seminars.

The aim of the program is to give university students first-hand knowledge of biomedical research so that they can make more informed choices about the possibility of pursuing a scientific career in the future.

OPEN FROM MARCH 2015
INVESMIR Program

The INVESMIR program offers medical professionals, during their specialization period as resident interns, the opportunity to further their training through a research project in one of the CNIC's laboratories, under the supervision of a CNIC scientist.

An important aim of the program is that participants will establish contacts and collaborations in the CNIC that will support them, after completion of their MIR specialization training, in pursuing their own research projects at their centers within the Spanish National Health System.

The duration of the stay is flexible (between 4 and 6 months) in accordance with the regulations laid down in the program for resident intern training at the participant's home center.

IN PARTNERSHIP WITH HIGHER EDUCATION

No one is born a great scientist. Everyone passes through various phases of training. And successful researchers tend to be fired by a curiosity common among professions with a strong vocational element, and that in many cases starts in early childhood. If there is one key stage in the making of a scientist it is, without doubt, the university training, a period with which the CNIC is very closely involved. Two of the CNIC's training programs are specifically targeted at students studying Spanish Masters courses, a "critical phase during which students must decide if they want to continue with a research career or pursue other options," says **David Sancho**, one of the group leaders participating in the CNIC MASTER Program.

The program recruits young university postgraduates with a strong interest in a research career, and is "essential to maintaining a dynamic influx of new predoctoral researchers to the CNIC's research groups," comments **Sancho**, who believes that these programs "increase the competitiveness of the CNIC by recruiting the best students."

Students enrolled on the CNIC MASTER Program spend nine months at the Center. While here, they work closely with their assigned group leader and participate actively in life at the CNIC. So much so, as **Sancho** points out, that most of the students go on to continue their scientific training at the CNIC; "I think that this is a testament to the quality of training and scientific research at the CNIC." This year 11 students are participating in the program.

The other CNIC program directed at Masters students is the module on Cardiovascular Diseases, better known as BMM9, which is taught as part of Madrid Autonomous University's Masters in Molecular Biomedicine. The module is a jewel in the predoctoral training offered by the CNIC, and students who take the course do not forget their time at the Center.

Enrique Lara, one of the coordinators of BMM9, feels that the module addresses an important need. As he points out, with the exception of medical degrees, "there is a lack of training in cardiovascular research" in life science

If there is one key stage in the making of a scientist it is, without doubt, the university training, a period with which the CNIC is very closely involved.

degree courses, which form the academic background of the students enrolled on BMM9. "The course ensures that students entering the CNIC receive a solid basic training in this area."

Jesús María Ruiz-Cabello, another BMM9 coordinator, highlights that the two-month module provides students with "access to unmatched scientific installations and the opportunity to interact with leading research groups in the cardiovascular area. With the depth and breadth of the theoretical and practical course material, students receive a unique and exclusive training that it would be hard to find in another academic or research center."

But while BMM9 is an unrivalled opportunity for the student, it also brings great benefits to the CNIC. **Ruiz-Cabello** emphasizes that the module "allows CNIC research groups that have no regular contact with students to meet and get to know research partners."

Echoing this viewpoint, **Lara** affirms that the module offers a means for the CNIC to "participate in university education," and also "increases the Center's profile." It is also, in his opinion, a way for researchers to "provide an additional service to society."

Although they spend only two months at the CNIC, the 14 students, who start the course in January, receive a very full training. "The module is of extremely high quality, and the balance of theoretical and practical components gives the students a well-rounded training in cutting-edge cardiovascular research," summarizes **Ruiz Cabello**. **Lara** agrees, and highlights the three "pillars" of the module: basic, clinical and translational research.

But the BMM9 and the MASTER Program both bring an additional advantage. In addition to confirming a research vocation in the participants, another aim of these programs—and one they achieve—is that the best students continue at the CNIC to study for their doctoral degrees. This is a win-win situation for students and teachers, and an excellent connection with the university sector.

Ana García Álvarez

"PULMONARY HYPERTENSION REQUIRES PHARMACOLOGICAL ATTENTION"

Ana García Álvarez isn't scared of a challenge. Indeed, she admits that she centered her interest in pulmonary hypertension—a very prevalent but not widely known condition—because it was one of the most complicated diseases to study. Her perseverance won her a Young Research Award from the European Society of Cardiology, presented to her at its latest annual conference in Barcelona.

How and why did you come to be awarded this important prize?

These prizes are awarded to the four best studies presented at the European Society of Cardiology conference on pulmonary hypertension, and are given to young researchers up to the age of 35. My work is directed at testing a new treatment for pulmonary hypertension that acts by stimulating beta-3 adrenergic receptors.

How does the treatment work?

Right now we are testing the active compound in preclinical studies, but this drug is already licensed for use in another context, for the treatment of patients with overactive bladder syndrome. In that setting, the drug works by relaxing the bladder muscle. We are testing the ability of the same drug to relax the smooth muscle of the pulmonary artery to dilate the vessel and reduce pulmonary hypertension.

Will this facilitate the translation of this treatment to humans?

Yes. From the point of view of the jump to research in humans, at least we already have the drug formulation, which has already passed all pharmacodynamics and toxicity tests, etc.

How far have you got?

Here at the CNIC we have completed an experimental study in a large animal model, and we've tested the active compound in pulmonary artery samples from human patients. We have also submitted a proposal to the Horizon 2020 program of the European Commission, requesting funding for a pilot clinical trial to assess the safety and efficacy of this drug for the treatment of pulmonary hypertension. This will be a phase II trial, in patients with the condition. I am coordinating this project from the CNIC with the involvement of the Hospital Clínic in Barcelona and other partners across Europe.

What does the European Society of Cardiology prize consist of?

The award consists of a diploma and a cash payment of €4000.

Can you give us a brief summary of your professional development to date?

I studied medicine in Salamanca, and then did my residency in Cardiology at the Hospital Clínic. In my last year there I applied to an ambitious program at the CNIC, called Cardiojoven. The program provides a translational training in cardiology, covering not only clinical aspects but also basic research and epidemiology. As part of the program I spent a year in Baltimore at the Johns Hopkins Bloomberg School of Public Health doing the equivalent of a Master's, with a special focus on epidemiology, statistics, and epidemiological genetics. After this training, program participants spend a year working at a hospital of their choice. I went to Mount Sinai in New York, where I learned how to use and apply advanced imaging techniques in cardiology, mostly magnetic resonance and computed tomography.

The last part of the program consisted of 15 months at the CNIC. What did you do here?

I joined **Borja Ibañez**'s group. In New York I had already started to work on pulmonary hypertension and when I arrived here I asked **Dr. Ibáñez** if I could do some experiments to develop models of this condition. This was challenging because his group mostly specialized in myocardial infarction, and so we had to start up a new line of research. But he supported me and that's how it all got started. I began by generating two models of pulmonary hypertension in pigs, one simulating chronic thromboembolic pulmonary hypertension and another simulating pulmonary hypertension secondary to cardiomyopathy. Both models work very well and have been very fruitful in a number of projects.

Is pulmonary hypertension a rare disease?

Pulmonary hypertension is more of a condition than a disease, a condition in which the blood pressure in the pulmonary circulation is elevated. This high blood pressure is similar to systemic hypertension, but restricted to the pulmonary circulation. The condition has different types and causes. The first type is rare, occurring in young people, mostly women, and has a very poor prognosis, with high mortality within three years of diagnosis. But there are other very common causes of pulmonary hypertension, including cardiomyopathy and chronic obstructive pulmonary disease (COPD), which usually results from tobacco smoking. And these conditions are very prevalent indeed. Approximately 50% of people with cardiomyopathy have pulmonary hypertension. The incidence is very high and right now there is no specific pharmacological treatment; the cardiomyopathy or COPD is treated, but patients receive no treatment for the pulmonary hypertension because nothing works. So it's a disease that requires attention.

Are you working with the pharmaceutical company that developed the drug for its original use?

The medication we are testing is commercialized by Astellas for overactive bladder, and while we have had some contact with them for the moment our research is not closely linked to industry. **Dr. Fuster**, **Dr. Ibáñez** and I have applied for a patent for the use of this drug in pulmonary hypertension. Demonstration of its success in patients would be very exciting because in addition to this compound there are several other beta-3 adrenergic agonists. So we would not be restricted to using the specific formulation we've been working with so far.

What got you interested in pulmonary hypertension?

All over the world, cardiologists tend to focus their attention on the left ventricle and the aorta, the systemic part of the circulation. Very few people pay attention to the right ventricle and the pulmonary circulation, and this neglect was something that attracted me. The anatomy of the right ventricle makes its study more of a challenge because it is structurally much more complex. Magnetic resonance imaging allows a very good evaluation of the right ventricle, and my training in this technique also stimulated my interest in this area. The right side of the heart is less known.

DIRECTOR OF THE CENTER FOR GENOMIC REGULATION

Luis Serrano

"TO GET FUNDING FROM THE ERC YOU SIMPLY HAVE TO DO EXCELLENT SCIENCE, PUBLISH VERY WELL AND WRITE A BOLD PROJECT"

Luis Serrano (Madrid, 1959) directs a center that has a lot in common with the CNIC. Like the CNIC, the Center for Genomic Regulation (Centro para la Regulación Genómica; CRG), located in Barcelona, is a center of excellence, and this adjective also aptly describes the work of its director, who was recently invited to present a seminar at the CNIC.

How would you describe your group's work and what practical applications might it have?

The group has two lines of research. The first is on signal transduction in human cells, where we are trying to gain a quantitative understanding of how these signal transduction networks operate and how they become dysregulated in cancer, with the obvious intention of finding new treatment strategies. The second research line is the study of a very small bacterium, *Mycoplasma pneumonia,* which has just 689 genes. We are interested in this organism for two reasons. The first is that it provides a model in which to try to gain the first quantitative understanding of a living organism. The second is related to synthetic biology: we are modifying this bacterium for use in the treatment of lung damage, the generation of vaccines, and several other applications.

Do these research lines have the potential to reduce the number of studies needed for approval of new medication?

I think so. An example directly related to cardiovascular research is provided by the heart models generated by **Denis Noble**. These models have been around for many years now, and are used extensively in the pharmaceutical industry to test medicines before moving to animal and patient studies. This was one of the first successful applications of computational biology. This approach allows you firstly to avoid work with animals and secondly to test a huge number of conditions that you couldn't test experimentally.

In time, could this lead to a reduction in the costs of developing therapies?

This is the final goal, but we're not there yet. At this stage we're something like the Wright brothers, working with wooden airplanes. It'll take five or ten years, but it's a development that will come. The problem will with such a development is what it will mean for the role of the physician, when we have a computer program that can reach a diagnosis and identify a treatment better than a doctor.

The CRG is a center of research excellence with a proven track record in securing competitive funding. Just this year you were awarded a Synergy grant. What advice would you give people about obtaining this type of support?

At the beginning of the year we were awared the Synergy grant from the European Research Council (ERC). Unlike other ERC awards, the Synergy grant simultaneously finances several researchers in the same; in our case, the award has gone to two of the most senior research groups. To get funding from the ERC you simply have to do excellent science, publish very well and write a bold project. I think that the ERC has been a game changer for research in Europe, where for the first time there is open competition among researchers from all countries for very solid funding. The funding can be as much as €3 million over five years, or up to €16 million in the Synergy grants, albeit shared among four groups.

What is your opinion of the current situation of research in Spain?

I think the new centers, like the CNIO, the CNIC and the center I direct, have in general escaped the worst of the economic crisis. Of course we have had to put some projects on hold, but by making an effort to contain costs we have avoided serious problems. But the problem is that a country cannot maintain a position in international research with seven centers of excellence. We need what I call the 'second line': the very good scientific research carried out in many institutes and universities in Spain. It is these centers that are really suffering with the crisis. We used to have a more robust pyramid structure, where we had the centers of excellence supported by many centers of the national research council and the universities. What we are seeing now is that structure changing to something more like a cylinder, with a handful of centers at the top and most of those lower down being starved of funding. In the long term this situation is not sustainable; a country cannot maintain a research base with seven centers.

So what would be your recipe for improving this situation?

At a time when we are seeing cutbacks in hospitals, education, etc., we can't expect unlimited funding for science. I do, however, think that there's been a failure to take the opportunity to put some order into the system and improve the management of the resources we do have. Someone should have had the guts to make some brave decisions: closing some institutes and concentrating researchers in a smaller number of centers; converting the CSIC (the Spanish research council) into something modeled on the Max Plank Society, with each center having financial autonomy; launching a revolution in the universities so that rectors would be elected by an international external committee and not by students of teaching staff. I think we have lost an opportunity to come out of the horror of the crisis stronger and with a more ordered scientific system. And that's a great pity.

January 26, 2015
CNIC Seminar

"Nuclear Control of Cholesterol Metabolism"

Peter Tontonoz
Howard Hughes Medical Institute
& Laboratory Medicine University of California
Los Angeles
USA

February 9, 2015
CNIC Seminar

"Antibodies in HIV Vaccine and Therapy"

Michel Nussenzweig
Howard Hughes Medical Institute,
The Rockefeller University
New York
USA

March 23, 2015
CNIC Seminar
Edward E. Morrisey
Perelman School of Medicine,
University of Pennsylvania
Philadelphia
USA

April 13, 2015
CNIC Seminar

"Transcription, Circadian Rhythms, and Metabolism: Two-Way Streets"

Mitch Lazar
Institute for Diabetes, Obesity, and Metabolism /
Perelman School of Medicine, University of Pennsylvania
Philadelphia
USA

April 27, 2015
CNIC Seminar
Matthias Nahrendorf
MGH Center for Systems Biology,
Harvard Medical School
Boston
USA

CNIC, THE FIRST SCIENTIFIC RESEARCH CENTER VISITED BY PRESIDENT RAJOY

The government's support and recognition for the work of the Pro-CNIC Foundation and the Centro Nacional de Investigaciones Cardiovasculares (CNIC) is confirmed by the continued joint financial backing given year after year, showing solid commitment to cutting edge cardiovascular research.

But it's certainly a sign of additional recognition that President **Mariano Rajoy** chose the CNIC as the venue for his first visit to a scientific research center since taking office. The visit took place in June, on the occasion of a meeting of the Pro-CNIC Foundation's governing council. Rajoy took advantage of his attendance at the meeting to learn about the center and the mood among its researchers.

He was accompanied by Health Minister **Ana Mato** and Secretary of State for Research, Development and Innovation **Carmen Vela**. And of course, the meeting was also attended by representatives of the 14 companies and institutions that, through the Pro-CNIC Foundation, have helped the CNIC since 2006 to become a world leading research institute, recognized by its award of the status as a Severo Ochoa Center of Excellence. The meeting was chaired by **Valentín Fuster** in his capacity as CNIC General Director.

Pro-CNIC Foundation president **Luis de Carlos** underlined that the contribution of the business community signals not only a clear commitment to research and development, but also "a firm commitment to an issue of great social interest: the health and quality of life of all Spaniards."

Dr. Fuster presented data attesting to the strong scientific health of the Center, demonstrated by the doubling of the impact factor of CNIC publications. He also highlighted some of the Center's key characteristics: the practice of applied medicine, the commitment to motivating young people, and the Center's many strategic alliances.

All those attending the event were eager to hear about the impression the Center had made on President **Rajoy**, who said that the CNIC is an example of the "best of Spanish talent" and a reflection of the aspirations Spain needs to have as a country of innovation. He also underlined the value of the Center's mixed funding model and affirmed that it is "imperative" that the private sector support centers like the CNIC, which he defined as "a pragmatic model" of public-private partnership.

EFFORT AND EXCELLENCE TAKE THE PRIZE

You get a double benefit! In the first place, you get to study for your PhD degree without having to worry about expenses. And in second place, you carry out your doctoral research at a Severo Ochoa center of excellence, an accreditation awarded to the CNIC in the inaugural year of the La Caixa–Severo Ochoa program and enjoyed by a handful of other select Spanish research institutes.

So it was no surprise to witness the party atmosphere last July in the Caixaforum in Madrid, at an event organized for the formal presentation of the diplomas for the first fellowships of the program.

The goal of this program is clear: to promote excellence in the research carried out in Spain in all fields of science. And what better way to do this than by supporting the accreditation of the Severo Ochoa Centers of Excellence, a subprogram of the Department of State for Research, Development and Innovation within the Ministry of Economy and Competitiveness. In other words, the program provides fellowships to help the best graduates study for their doctoral thesis in the best research institutes in Spain: a win-win recipe that's assured of success.

As one of the first Spanish centers with Severo Ochoa accreditation, the CNIC has benefitted from these fellowships, together with five of the 40 fellows funded by La Caixa in the first edition the program. The first call was launched in 2012, and after an extremely competitive selection process, fellowships were awarded to these five students, who have been working on their projects with maximum enthusiasm since 2013.

The story was repeated the following year, with the selection of four students, who have also integrated seamlessly into the life of the CNIC. And next year another group of excellent students will be selected in the third call of this program.

The formal presentation of the fellowships was attended by the Secretary of State for Research, Development and Innovation, **Carmen Vela**, who underlined that this program is training students who are "competitive at an international level." The CNIC's experience bears this out.