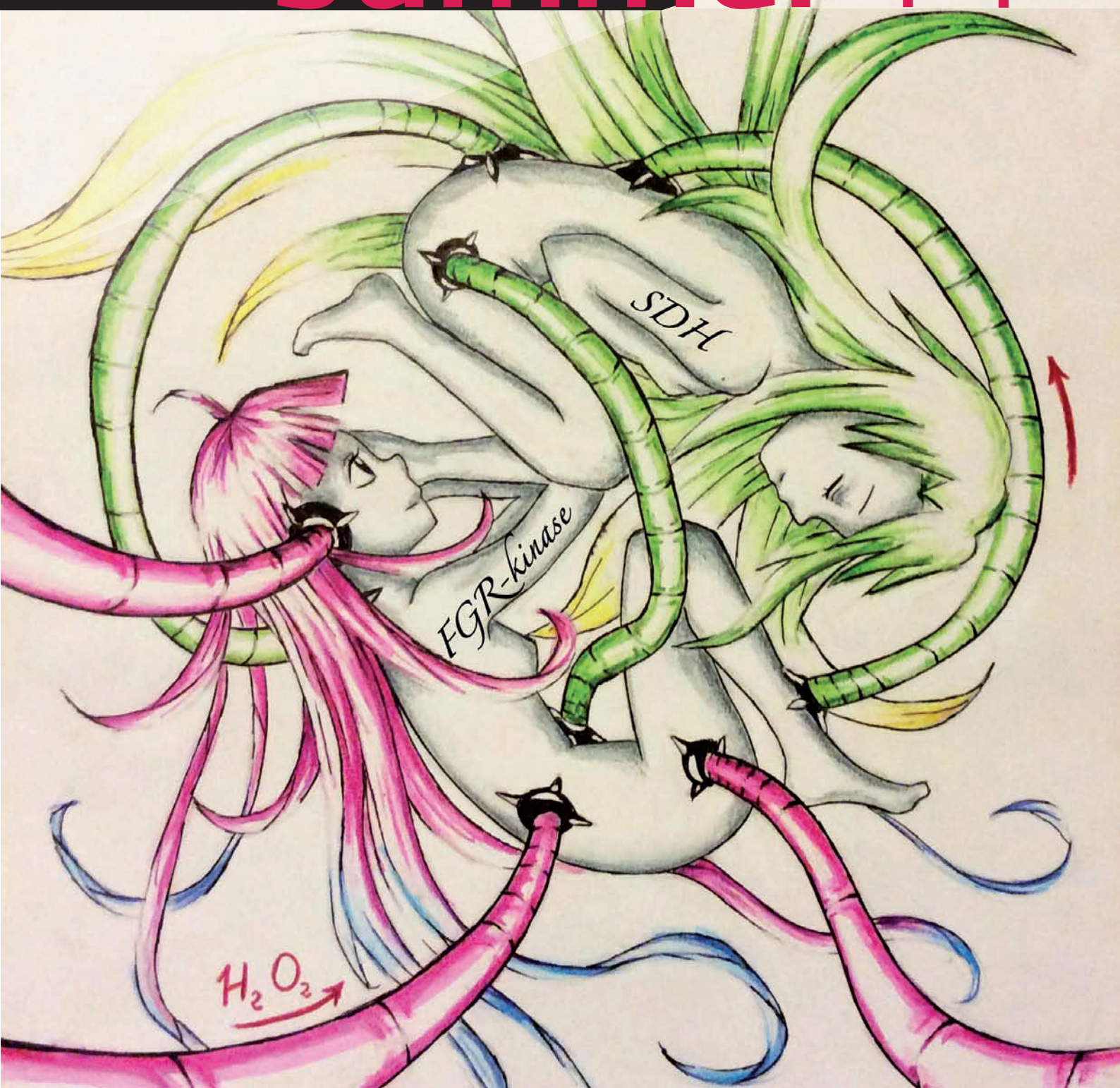


INSIDE SCIENCE
TRAIN2GAIN
WHAT'S ON
CNIC & SOCIETY

... *cnic*PULSE summer'14



contents summer'14



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Fundación proCNIC



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It would make no sense to call this a center of excellence if excellence were not the principal characteristic of the researchers who work here. Valuing talent has of course been a constant from the outset of my professional career, and this philosophy governs the center I now direct. But talent is not a word to be reserved only for acclaimed researchers. Cornerstone goals of the **CNIC** philosophy include capturing talent, providing it with the best training and holding on to it.

This third issue of **CNIC Pulse** amply demonstrates these three tendencies. Attracting talent is the theme of our feature 'Star signings aren't just the stuff of football', which recounts how the **CNIC** attracted two renowned investigators who are sure to make an impact during their time at the center, just as they did in their previous posts. **Jorge Alegre-Cebollada** and **David Filgueiras** bring their enthusiasm and commitment to the **CNIC**, and it is a great pleasure to extend them a very warm welcome.

ATTRACTING, TRAINING AND **RETAINING TALENT**

For training talent, what better than our **CNIC-Joven Training Plan**? In this issue we feature one of the component programs, the **La Caixa-Severo Ochoa CNIC International PhD Program**, in an interview with one of the promising students who has obtained a grant to study for his doctoral thesis at the **CNIC**. Also working toward their doctorates are two young participants in **CardioNext**, an original **Initial Training Network** that combines academic training with hands-on experience in cutting-edge companies.



Dr. Valentín Fuster, Director del CNIC

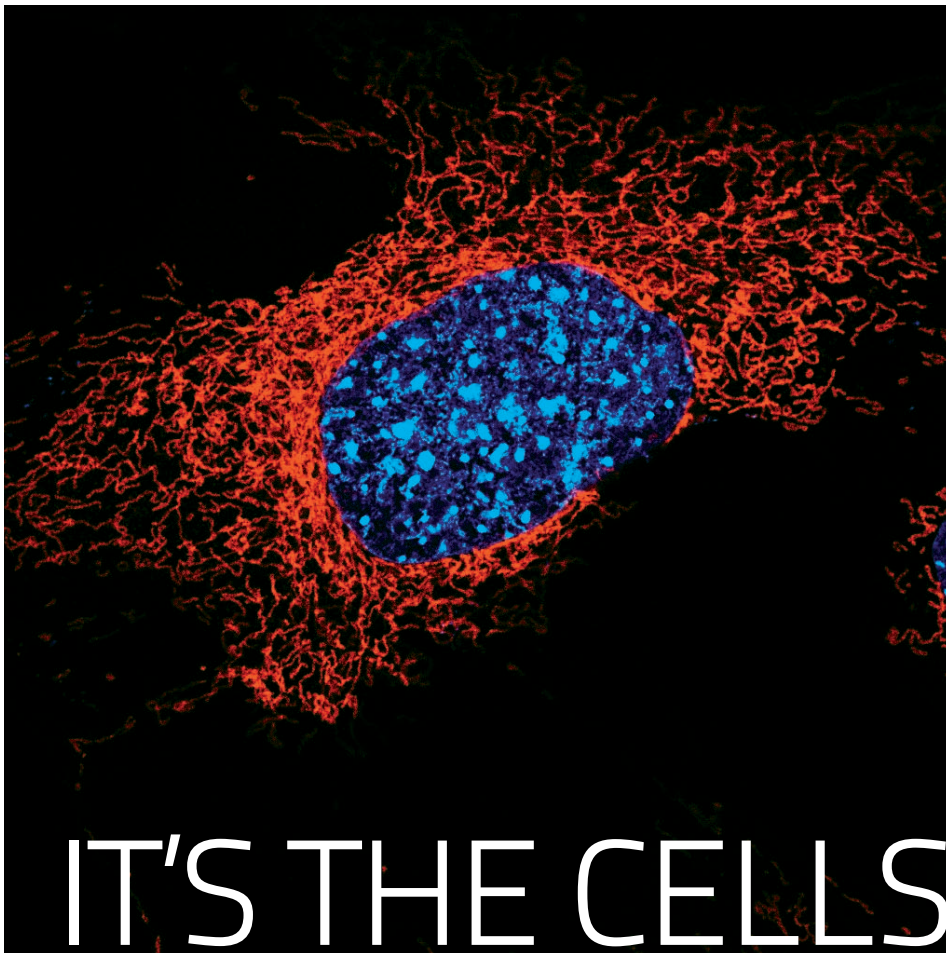
As for retaining talent, one only has to look at our scientific production to see that the **CNIC** also succeeds here. In this issue, we present the latest publication from the group led by **José Antonio Enríquez**, who offers another new and interesting study highlighting the dynamic behavior of mitochondria. The issue also features the **PESA-Banco de Santander** study, which promises to give us crucial information about how to stop cardiovascular disease in its tracks before symptoms appear.

And as well as attracting, training and retaining talented scientists, it's also important to engage with them even if they are not members of our center. Our program of invited speakers is the linchpin here, and in these pages we talk with **Daniel Levy**, director of the **Framingham Study**.

This edition of **CNIC Pulse** is full of good news. Long may it continue.

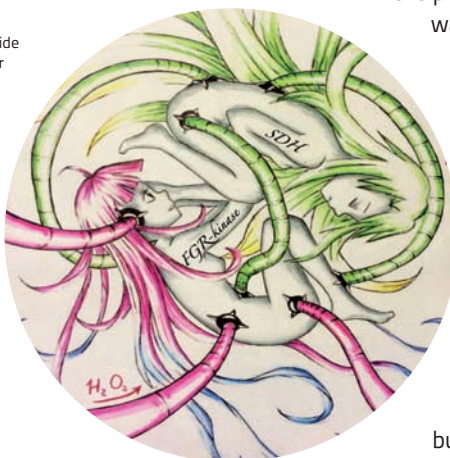
That mitochondria are essential cell constituents in the human body is, by now, no secret. But few know more about this fascinating occupant of the cell interior than the CNIC team led by **José Antonio Enríquez**, which has once again published a study set to change our understanding of these organelles.

BURNING SUGAR OR FAT?



IT'S THE CELLS
THAT DECIDE

The increase in hydrogen peroxide (H_2O_2) activates the sensor Fgr-kinase, which then modifies SDH, one of the mitochondrial 'fuel burners'. This change optimizes mitochondrial activity for the metabolism of fatty acids
(watercolor by Alba Real)



In the latest edition of leading journal **Cell Metabolism**, the scientists led by Enríquez describe the process by which cells optimize and regulate their capacity to use sugars or fats as fuel sources. As José Antonio explains, "the real digestion of foods takes place in all the cells of the body". While some cells preferentially consume sugars, others feed mostly on fats, and others can switch from one nutrient to another.

To guarantee efficient use of nutrients, cells have systems that permit them to capture and transport the available nutrient molecules to their interior. But if several nutrients are available, cells can select those that are of most interest and discard undesired molecules.

Inside cells, nutrients are conducted to the mitochondria, the specialized cell organelles in which nutrients are combusted to release the energy held in their chemical bonds. Both sugars (glucose) and fats (fatty acids) are 'burned' in mitochondria, but these organelles need to adjust their molecular apparatus in different ways depending on whether their main fuel supply comes from sugars or fats. According to José Antonio, "This adjustment can be likened to refitting your boiler to burn natural gas or butane."

The proportion of different food fuels available to cells can be affected by diet, exercise, or a period of fasting, and cells need to be able to adapt to these changes. In some specific situations, for example during the activation of immune cells to defend the body against infection, cells change their activity even if the fuel source is unaltered, and this can be accompanied by changes in the preferential use of glucose instead of fatty acids or vice versa.

In all these cases, mitochondria need to adapt their 'fuel burners', technically known as the electron transport chain (ETC). "The ETC was known to adapt, but the signals that promote this change and the molecules responsible for it were not known."

The **Cell Metabolism** article describes the signals and molecules that regulate this adaptation. Combustion of nutrient fuels in mitochondria requires oxygen, and the process produces, in addition to energy, water (H_2O) and carbon dioxide (CO_2). But when the ETC switches from burning sugars to fatty acids, it is at first not adjusted to burning the new fuel, and additional oxygen derivatives are produced called reactive oxygen species (ROS), among them hydrogen peroxide (H_2O_2).

Production of H_2O_2 activates a molecular sensor called Fgr (Fgr-tyrosine kinase), which raises the alarm that the ETC is not adjusted to burn the fatty acids arriving in the mitochondria. It does this by modifying one of the components of the ETC, adding a phosphate group that makes it more active. This triggers a change in the organization of the ETC so that burns fatty acids more efficiently. The modification, called phosphorylation, is reversible, and the CNIC team believes that another, as-yet-unidentified molecule must trigger the reverse modification (dephosphorylation) when the mitochondrion's fuel burners need to switch back to burning glucose.

The study published in **Cell Metabolism** demonstrates the importance of this mechanism in the adaptation of cells to fasting and a limited oxygen supply (ischemia), and in the activation of cells of the immune system.

To guarantee efficient use of nutrients, cells have systems that permit them to capture and transport the available nutrient molecules to their interior. But if several nutrients are available, cells can select those that are of most interest and discard undesired molecules.

PESA CNIC-SANTANDER: MOVING BEYOND RISK FACTORS



Some people with
risk factors for
disease stay healthy,
while others who
lead a healthy life
are taken by surprise
by a cardiovascular
accident

For now it's science fiction, but it could soon become reality. A blood test for healthy people that accurately predicts who will go on to develop cardiovascular disease. This goal goes way beyond classical assessment of risk factors and if achieved would revolutionize the management of the pandemic that causes most deaths and hospital admissions in the world. This is the most ambitious, but by no means only, goal of the **PESA CNIC-Santander Project**, one of the CNIC's flagship studies, aimed at resolving many of the unknowns about cardiovascular disease, for instance when it starts and what processes occur before the appearance of symptoms.

The **PESA CNIC- Santander Project** certainly does not lack ambition. The project stands out for its originality (it's the only study of its kind to be carried out in healthy subjects), for the number of participants (more than 4000), and for its length, which is set at a minimum of nine years, and could be extended further.

The idea of the project is to monitor this large cohort of healthy subjects—all employees of the Santander Bank and aged between 40 and 54 years—with the aim of identifying subclinical disease: problems in the arteries that haven't yet produced symptoms but which might do over the period of the study.

PESA scientific coordinator **Antonio Fernández-Ortiz**, CNIC researcher and cardiologist at the Hospital Clínico San Carlos, explained to us how the study works. "The participants are first subjected to a series of basic tests, including a full blood test, collection of clinical data, a psychosocial questionnaire, and imaging analysis by coronary CT and vascular ultrasound scanning, all carried out in the installations at the Santander Bank headquarters."

This first phase has been completed, so whatever the future holds **PESA** has already made a breakthrough: compilation of the first database of near-perfect radiography and ultrasound images from a large number of participants who share apparently good health but for whom the real state of their arteries was unknown before this study. The initial findings are of great interest and have been sent for publication to a leading medical journal.

And this initial analysis is just the beginning. Although the participants are outwardly healthy individuals, signs of subclinical atherosclerotic disease have been detected in around 1000. These patients will benefit (in fact, most already have) from one of the most advanced diagnostic imaging tests in the world: hybrid magnetic resonance and positron emission tomography. There is currently only one facility equipped for this technique in Spain, housed in the CNIC's Advanced Imaging Unit.

According to Antonio Fernández-Ortiz, "The results of these scans reveal the characteristics of subclinical atherosclerotic disease: they tell us if the lesions are fibrous, inflamed or have a high lipid content, among other things." But of course the goal goes beyond knowing about the development of these 'invisible' lesions.

The **PESA** study is divided into (at least) three phases: the first evaluation and follow-up studies after three and six years. Some study participants have already undergone the second evaluation, which adds great value to the study. As Dr. Fernández-Ortiz explained, "This design allows us to identify new disease markers before the appearance of symptoms or complications."



Building up a picture of the early development of the disease is important because, as every clinician knows, in cardiology nothing is straightforwardly predictable. Some people with risk factors for disease stay healthy, while others who lead a healthy life are taken by surprise by a cardiovascular accident. "It's an interesting paradox," says Fernández-Ortiz.

The **PESA** scientific director hopes that the study will continue beyond the six-year follow-up, observing this cohort of participants at least until they reach the age of 70, so that this study will be able to "go further than the classical risk factors" and, who knows, produce that hoped-for blood test.

Jorge Alegre-Cebollada



This season's *Liga* has just finished and soon the sports pages will turn their attention to the transfer market. But attracting talent is by no means limited to the world of top-flight sports, and star signings also happen in the seemingly staid world of science. Two of the CNIC's recent signings are sure to get people talking. **David Filgueiras** and **Jorge Alegre-Cebollada** work in different specialties, but they share an enthusiasm to join the center and a commitment to making their time here as productive as possible.

David Filgueiras, originally from Galicia, is a physiotherapist and a clinical cardiologist specializing in cardiac arrhythmias. Since joining the CNIC last November, he has been impressed by the high-caliber personnel at the center. "Across the board the staff here are highly skilled, open, and keen to help, which injects a lot of flexibility in approaching scientific questions."

David first established contacts with the CNIC through a translational project he launched with funding from a Spanish charitable foundation. This initial contact stimulated interest in joining the center to pursue further basic and translational research into cardiac arrhythmias. Joining the

STAR SIGNINGS

AREN'T JUST THE STUFF OF FOOTBALL

CNIC has allowed **Dr. Filgueiras** to establish his research as part of his professional activity, something he had wanted to do since his return from the USA, and something that "is still not that common in Spain". He is now able to combine three days working part-time on patient care with two days full-time and three days part-time dedicated to research.

In contrast, **Jorge Alegre-Cebollada**, a biochemist who will soon join the CNIC from Columbia University, will be dedicated full time to basic research. In the USA, Jorge learned that the search for solutions in science has few limits, and that equipment is not one of them. In a telephone interview, he commented that "In the US I learned that it is possible to design specific instrumentation to address specific questions."

Jorge was attracted to the CNIC by its mission to find cures for disease, a radical change from the basic research he has carried out in the US. After contacting **Miguel Torres** he went through the selection procedure for joining the center, to which he will bring an atomic force microscope of the kind developed for his laboratory in the US.

Within the global aim of curing disease, **David Filgueiras**'s specific goal is to improve procedures for catheter ablation of post-infarction ventricular tachycardia, "to make it more specific and less uncomfortable for the patient". **Filgueiras**, who joined the CNIC as a junior researcher, will continue to work closely with his former boss and mentor at the University of Michigan, **Professor José Jalife**, who can also be considered a new signing for the CNIC, since he will collaborate with David as a senior external advisor.

The heart is also the focus of Jorge Alegre's research. His principal line of research is the role of the protein titin, the largest human protein (the name is a reference to the titans of Greek mythology). Titin plays a crucial role in the elasticity of the ventricular wall during cardiac diastole. **Alegre-Cebollada** thinks that other proteins besides titin are

important for the elasticity of this muscle, the most important in the body. This hypothesis is the spur for some of the research lines he will pursue at the CNIC: "If we see that we can cure disease by modifying the ventricle's natural elastic properties, we will be on course to developing a new way of treating heart disease." For Jorge, the desire to return to Spain was not the deciding factor in his decision to apply to the CNIC; instead he was attracted by the scientific quality of the research carried out at the center.

mechanisms of complex cardiac arrhythmias, and that this would signify "a real benefit for the large numbers of patients affected by atrial fibrillation and ventricular tachycardia".

For his part, **Alegre-Cebollada** would like to be recorded in history for contributing to a new way of understanding the elasticity of the heart that can be applied to the treatment of heart disease.

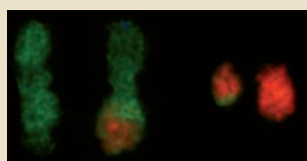


David Filgueiras

This research excellence was also a key factor for **Filgueiras**, who worked for almost two years at the University of Michigan. He is particularly impressed by the CNIC's competitiveness compared with leading centers in the US: "The CNIC is at the same level as the center I worked at in the US, and in terms of infrastructure it might be in some respects superior."

At the end of his scientific career, **Filgueiras** hopes to be remembered for making his small contribution to the understanding of the

"If we see that we can cure disease by modifying the ventricle's natural elastic properties, we will be on course to developing a new way of treating heart disease."



In Nature Communications

KEYS TO THE BATTLE AGAINST CANCER

Two centers of excellence joined forces to produce this study, in which investigators at the CNIO and the CNIC succeeded in reproducing, for the first time in human cells, the chromosomal translocations that underlie certain types of cancer. The authors hope that this achievement will lead to the development of new therapeutic strategies in the fight against the disease.



In J Am Coll Cardiol

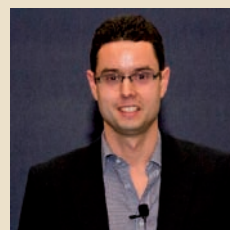
MINIMIZING DAMAGE FROM INFARCTION

Six months follow-up of the patients in the Metocard trial have consolidated the initial findings of this important study: treatment of heart-attack patients with a drug costing less than €2 during hospital transit to hospital significantly reduces the damage to the heart. Next stop: a large-scale trial with more than 4000 patients.

Excellence

RUI BENEDITO, WINNER OF THE PRÍNCIPE DE GIRONA PRIZE

The CNIC has done it again. Rui Benedito, who leads of the Molecular Genetics of Angiogenesis group at the CNIC, has received the *Fundación Príncipe de Girona* Prize for Scientific Research, which recognizes the outstanding careers of enterprising pioneers under the age of 35. He is the third CNIC researcher to win the award, joining Borja Ibáñez and Guadalupe Sabio. Congratulations!



Europe

OFF TO A GOOD START IN H2020

The CNIC has made a good start in the first call for proposals with the European Commission Horizon 2020 Programme, in the 'Health, Demographic Change and Wellbeing' Societal Challenge. CNIC researchers have presented nine applications, three as coordinators. These three and two others have made it to the second phase, which will be completed in August. Now all we can do is wait in hope of good news when the results come out toward the end of the year. The projects that made it to the second round are:

- Age – Well
- Secure
- Move – On
- Sphere
- MyNeDA
- POSTMITAGE

And there's more good news. The CNIC has secured a Cost Action and has presented applications for four ERC Starting Grants and three ERC Consolidator Grants. Go get 'em!





agenda...



CALL CLOSES JUNE 15 FICNIC Program

The CNIC has partnered with the *Fundación Jesús Serra* and the *Fundación Interhospitalaria para Investigación Cardiovascular* to create this new program, aimed at promoting training in translational cardiovascular research. The program offers training fellowships to medical professionals specializing in cardiology or cardiovascular surgery. To be eligible, candidates must be in the final year of their resident intern (MIR) specialization training or have completed their specialization within the three years preceding the application deadline.

Intended for: Medical professionals in the final year of their resident intern physician (MIR) specialization period or cardiologists or cardiovascular surgeons within three years of completing their specialization.

For further information please visit the FIC web and the corresponding call:

<http://fundacionfic.es/>
<http://fundacionfic.es/actualidad/convocatoria-de-una-beca-para-formacion-en-investigacion-cardiovascular-post-residencia/>



CALL CLOSES JULY 17 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, in pursuing their own research projects at their centers within the Spanish National Health System.

A maximum of 5 positions will be awarded for the INVESMIR training programme in the 2014 call.

See our website (<http://www.cnic.es>) for details of host groups and information on their lines of research.



CALL OPENS JULY 2014 RES@CNIC Program

The aim of the RES@CNIC program is to offer medical professionals, during the first years of their specialization period as resident interns, the opportunity to learn about and become familiar with the latest techniques in biomedical research being used in the CNIC's laboratories, under the guidance of a CNIC scientist. Residents participating in RES@CNIC also receive training in theoretical aspects of cardiovascular research through an expert-led taught module.

The Program seeks to create links and partnerships so that these professionals, when they complete their MIR specialization period, will have the chance to undertake research projects in their National Health System centers in collaboration with the CNIC.

The duration of the stay is a maximum of 9 consecutive weeks.

Applicant requirements:

- Applicants must be medical professionals, of any nationality, undergoing MIR specialization in cardiology or cardiovascular surgery at any Hospital in Spanish territory.



OCTOBER 24- 25, 2014 CICERONE Workshop

This group of lectures provides a general introduction to cardiovascular research in Spain, and also gives participants the chance to question key researchers and opinion leaders in the field. Since 2012, the Cicerone Workshop has been run in collaboration with the *Fundación Interhospitalaria para la Investigación Cardiovascular* and takes place in the *Hospital Clínico San Carlos*, Madrid.

The CICERONE Workshop is intended for medical professionals undertaking the first year of their resident specialization internship (MIR) in cardiology or cardiovascular surgery.

Applicant requirements:

- Applicants must be medical professionals, of any nationality, undergoing residency training.
- Training in cardiology or a related specialty will be well regarded.

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

The stay will take place entirely between October 1, 2014 and September 30, 2015.



CALL CLOSES SEPTEMBER 3 BECAS MASTER Program

This grants program provides individual funding for study towards a Master's degree at a Spanish university, with the aim of contributing to the development of human potential in the area of cardiovascular research.

A maximum of 11 grants will be awarded in 2014, each lasting 9 months.

Applicant requirements:

- Applicants must be graduates, of any nationality, in a discipline related to biomedicine, and must hold qualifications sufficient for acceptance on a *Master Oficial* program at a Spanish University.
- Applicants must not be in receipt of any other grant or financial assistance from public or private bodies (Spanish or foreign).
- Applicants must have a formal offer from one of the CNIC's laboratories to carry out the experimental component of their Masters course.
- Applicants must have an average grade of 8.0 or above in their completed credits (scale 0 to 10)

Jaume Agüero y Aleksandra Ronja Binek



RESEARCH, ACADEMIA AND BUSINESS:
HAND IN HAND IN

CARDIONEXT

Many adjectives could be used to define the
CardioNext Program, but certainly innovative
comes top of the list.

“Eventually I would like to be able to treat patients with a truly effective heart failure therapy that I had had a hand in developing during all these years of training,”

This **European Commission Initial Training Network (ITN)** is providing a unique training for 12 researchers from across Europe who, at the end of the four-year program, will leave with much more than a PhD degree on their résumés. **Jaume Agüero** and **Aleksandra Ronja Binek** are two of these lucky students, and their paths to the CNIC couldn't be more different; indeed diverse is another of the adjectives that can be applied to **CardioNext**, a network that integrates and directs this diversity toward an ambitious shared goal: the study of cardiac damage in a model very close to humans as the basis for identifying therapeutic targets and even developing treatments for the diseases that are the leading cause of death in the world..

Aleksandra studied biotechnology in her native Poland and first came to Spain when she was writing up her dissertation. She obviously liked it here, because after completing her degree she returned to interview for the CNIC's Masters' program. “On that visit I learned about the opportunities for PhD training at the CNIC and decided to apply directly for the **CardioNext ITN**”, she explains, as she recalls the difficult admissions procedure, involving several consecutive interviews.

Her application was successful even though on the face of it her profile didn't match the needs of a cardiovascular research center. In her interviews, Aleksandra talked to the tough evaluation committee about her previous research experience in Poland, which was related to *Dickeya solani*, a species of bacteria that attacks potato crops and which has become a major threat in recent years. Aleksandra laughs as she recalls “It had nothing to do with what I do now!”

Although **Jaume Agüero**, a medic, has a background more obviously in keeping with the CNIC's mission, in fact his and Aleksandra's projects complement each other. “**CardioNext** partners researchers with different professional backgrounds, in such a way that each works in a different department and takes on a specific role in the project. So, for example, a clinician and a specialist in an area of basic science work in parallel to identify future treatments and test them in animal models; this gives the project originality in terms of training and complementarity,” explains Jaume, who like the other **CardioNext** fellows has spent most of the last three years working outside Spain

Like all **CardioNext** fellows, Jaume and Aleksandra have outstanding academic and professional records, a prerequisite for inclusion in this training network, which seeks to revolutionize the relationship between research and industry by sending the students to receive part of their training in internships at participating companies.

Another thing the two students have in common is the desire to make a real contribution to reducing the epidemic of cardiovascular disease. Aleksandra, who will complete her training at the CNIC with two company internships working on projects related to proteomics and metabolomics—her areas of specialist training—and a study visit at a university with expertise in these same areas, hopes that in the future her name will be associated with an important advance in the fields of cardiovascular research, proteomics, or metabolomics. Jaume, whose internships will take him to Philips and Mount Sinai Hospital in New York, has similar dreams. “Eventually I would like to be able to treat patients with a truly effective heart failure therapy that I had had a hand in developing during all these years of training,” comments Jaume, who doesn't dismiss the idea of combining research and clinical practice in the future, or even forming part of a CNIC startup.

This openness reflects Jaume's conviction that the industrial sector “can benefit enormously from the research going on at centers like the CNIC, where substantial amounts of money are invested to identify and develop therapeutic targets and treatments, and for its part the pharmaceutical industry can contribute its greater experience to continue with the clinical development of a new line of treatments, a critical step for successful translation from the laboratory to the clinic”. This connection of **CardioNext** with the industrial sector is something that Aleksandra is also keen to stress. “The practical part is extremely attractive, because it offers you the chance to make contacts and open doors to the future while you are still working toward your doctoral thesis, as well as offering highly specific training options, in which you get to choose the training courses that are going to help you most in pursuing your part of the CardioNext project.”

In short, **CardioNext**—so far the only single-center life-sciences ITN in Spain—offers its participants a training opportunity unique in its field. The innovation, diversity and clear practical focus of this endeavor will without doubt make a mark, both on the students and in society.

It's one of the CNIC's star programs and only four or five lucky candidates get to join it each year.

A TOP FELLOWSHIP FOR A TOP CENTER

The **La Caixa – Severo Ochoa CNIC International PhD Program** attracts “exceptional and highly motivated” PhD students. **Iván Menéndez** is one of the young scientists awarded a fellowship in the first year of the program. As Iván recognizes, the fellowship is “very generous economically” and also has other advantages that make it exceptional.

Iván knew this when he applied and was also aware of the high scientific standard at the CNIC, which as a Severo Ochoa center of excellence is one of the few centers that can aspire to train PhD candidates in these conditions. In fact, this young investigator from Asturias had benefitted from the **CNIC Joven Training Plan** before, when he participated in the **CICERONE Program**, establishing contacts with **Dr. Silvia Martín-Puig**, now his thesis advisor.

Menéndez studied Biochemistry at the University of Oviedo, but moved to Madrid to do his **Masters in Molecular and Cellular Biology** at the Autonomous University of Madrid. By coincidence, the funding for his Masters came from the same source as his current fellowship—La Caixa. His previous award meant that Iván could not apply for the general PhD fellowships from La Caixa, but he was eligible to apply to the **La Caixa-Severo Ochoa CNIC International PhD Program**.

Before coming to the CNIC with the **CICERONE Program**, Iván worked on a transporter protein found in neuronal membranes, studying the possible implication of point mutations in the rare disease hyperekplexia. At the CNIC, the focus of his research changed and he began to study the effects of hypoxia (lack of oxygen) with Silvia Martín-Puig. It was during his CICERONE fellowship that he heard about the **La Caixa-Severo Ochoa Program**. He was awarded his current fellowship in September 2013, and remembers that the documentation required for the application was pretty standard for this type of program: curriculum vitae, a letter of presentation, written references, etc. Iván wryly observes, “I don’t remember if they asked for my grade average, but I guess they looked at it”, modestly recognizing that his was good.

One requirement for the fellowship that Iván managed to satisfy “just as the door was closing” was to have previously worked at the CNIC for no more than six months. Once successfully past the first hurdle—an

evaluation of the submitted documentation—Iván was invited to interview with an expert panel. “They asked me about my professional development, the reasons for my interest in the group I had selected and my prospects in the team. I especially remember that they asked me what my options would be in the same group if, for whatever reason, my project didn’t move forward.”


For now, that situation doesn’t look likely, and Iván and his colleagues have a long road of discovery ahead. “We are working on the action of hypoxia during the embryonic development of the heart, because we know that this phenomenon is a normal physiological feature of this process; we know that it is there and that it is performing some function, but we don’t know what or how, and this is what we are trying to discover.”

Iván only has positive things to say about his grant award. Apart from the living allowance, another “good feature” is the separate budget for expenses. “This is really helpful, for example if you need to buy a book, material, attend a scientific meeting, take a course, or whatever.” It also helps the fellow to be “less dependent” on departmental funds, which can be a problem for younger researchers “when times are tough or if the group is large and resources therefore need to be spread more thinly”.

The budget is also easy to manage, as this is done directly in the CNIC. “This is really good because it gives you peace of mind,” says Iván. If Iván has one tiny criticism, it is that there is no budget for study visits. But the fellowship is compatible with others that specifically address this need.

Menéndez believes that the restriction of this kind of fellowship to centers holding the Severo Ochoa award is justified, although he recognizes that “there are very good researchers” in other centers. “But then you see how things work here, with the external evaluations and so on, and it’s very good.”

Iván doesn’t yet have a clear idea about his future beyond preparing to present his doctoral thesis on hypoxia four years from now. But he is clear that he will work outside of Spain when he finishes, not only because this is “necessary”, but also to “experience a different culture”. Asked about a possible eventual return to Spain, Iván prefers to keep his options open; “If I fix on the goal of coming back and then for whatever reason can’t, what a disappointment!”



"We are working on the action of hypoxia during the embryonic development of the heart, because we know that this phenomenon is a normal physiological feature of this process"

Iván Menéndez

Interview

Daniel Levy

director of the Framingham Study

"AS MUCH AS THE SKILLS AND QUALITIES OF OUR RESEARCHERS, WHAT MAKES FRAMINGHAM STUDY TRULY SPECIAL IS THE DEDICATION AND COMMITMENT OF THE PARTICIPANTS"

If there is one study that has more than any other to define the risk factors for cardiovascular disease it is the Framingham Study, which began in 1948 in the small town of the same name, where 5000 of its inhabitants, in a perfect state of health, volunteered to be observed by a team of investigators who aimed to unravel the causes of a disease that already showed signs of becoming the leading cause of death in the world. More than sixty years later, the study is more alive than ever, as current study director Daniel Levy explained during his recent visit to the CNIC.

You have been director of the **Framingham Study** for the past 20 years. What have been the highlights during this period?

During the last 20 years, **Framingham** has gone from a study that merely investigated the epidemiology of cardiovascular disease to one that is now positioned at the cutting edge of genetic and genomic research. In addition, we have a lot of active research in the areas of imaging, biomarkers and other areas that many people don't think of when they think of **Framingham**—research in the areas of cognitive function, dementia, Alzheimer disease, pulmonary disease, to name just a few.

So it's an old study that is at the same time young?

Yes, I would say that is old in its age but new in terms of some of the approaches that we are using.

The third generation study began in 2002. What are the main differences compared with previous generations?

One thing that stands out is that this group of participants comes from all over the USA, and many of them from countries all around the world. They come at their own expense; we don't pay for them to visit us. Since we started the third generation study, every day in the clinic a participant will say to our staff "I've waited my whole life for this day to come" And this has taught me a great deal about the secret of our success in **Framingham**; that as much as the skills and qualities of our researchers, what makes Framingham special is the dedication and commitment of our study participants. These new participants grew up in families where their grandparents and their parents were part of the study. They hear about the study from the time they are children and now was their chance to make a commitment and give up their time to help other people.

If you had to recommend just one measure to reduce the risk of cardiovascular disease, what would it be?

It's very hard to choose just one factor—like choosing which of your children is your favorite [chuckles]. For some people it would be to eliminate cigarette smoking, but for others it might be lipid abnormality, and for others it would be diabetes or blood pressure. The reason there are so many risk factors is that each contributes, and sometimes several risk factors are required to develop real risk.

You helped draft the US clinical practice guidelines on cholesterol and hypertension. These guidelines have attracted criticism from those who say that they unnecessarily increase the numbers of people taking medication. What is your response?

I don't agree. **Framingham's** most important contribution to guidelines is to improve risk assessment, and by doing this we do a better job of identifying high risk and low risk individuals. In this way we can target the intensity of treatment to the patient's level of risk, so that we treat more of the people at high risk, who need treatment, and avoid treating people at low risk who will not benefit from treatment.

You have shown an interest in public policy directed at promoting a healthy lifestyle. What improvements would you like to see in this area?

Cardiovascular diseases, despite the advances we have made in the last 40 to 50 years, remain the single leading cause of death in men and women in the USA. We know that if we could eradicate cigarette smoking, elevated blood pressure and lipid abnormalities we could prevent over 90% of cardiovascular events. We must have a multiple approach that includes lifestyle changes across the entire population, improving the diet of people in our country and all around the world, reducing the intake of trans fat, increasing the level of exercise, reducing the prevalence of overweight and obesity. All these steps will reduce the burden of risk factors that contribute to the risk of cardiovascular disease.

At times it is difficult to understand why, despite the clear messages about cardiovascular prevention, people ignore the recommendations.

That's part of human nature. Young people especially believe in their own immortality even when the data speak otherwise. Probably an education campaign is what is needed to help people understand, because we are working with what are sometimes complex ideas.

An important goal in this type of disease is early diagnosis. Do you think it likely that we will find a biomarker that can be measured in a simple blood test to predict when an individual is likely to develop cardiovascular disease?

The history of medicine is one of incremental improvements in our ability to detect high risk of suffering a disease. Sometimes there are dramatic insights that can come from genetics, blood biomarkers, diagnostic imaging, or a combination of these different measures. There's too much good science going on for me not to be very optimistic.

For more information, visit our website: <http://www.cnic.es/en/eventos/>



October 1, 2014
CNIC Seminar

"Genetic and non-genetic mechanisms contribute to longterm clonal growth dynamics and therapy resistance"

John E. Dick

Princess Margaret Cancer Centre,
University Health Network.
University of Toronto.
Ontario Institute for Cancer Research.
Canada.



November 17, 2014
CNIC Seminar

"Immune-metabolic interactions in atherosclerosis"

Goran k Hansson

Karolinska Institutet
Stockholm
Sweden



October 6, 2014
CNIC Seminar

Title to be announced

Luis Serrano

CRG
Barcelona
Spain



November 7-8, 2015
CNIC Conference

"Energy homeostasis and metabolic disease"

www.cnic-conference.com



October 27, 2014
CNIC Seminar

"Origin and function of tissue dendritic cells and macrophages"

Miriam Merad

Mount Sinai Hospital
New York
USA

The poster features a background image of a modern building with large glass windows. The title "Energy homeostasis and metabolic disease" is prominently displayed in red and black text. Below the title, it states "Abstract submission deadline: September 30, 2014". The location and dates "Madrid, November 7-8, 2014" are listed, along with the website "www.cnic-conference.com". A list of speakers is provided, including E. Dale Abel, Johan Auwerx, Jens Brüning, Barbara Cannon, Ana M. Cuervo, Ronald Evans, Jeff Friedman, Ronald Kahn, Michael Karin, Daniel P. Kelly, David M. Mudd, Catherine Poth, Alan R. Saltiel, Jean E. Schaffer, Steven E. Shoelson, Dominic Withers, and Julien Zierath. Organizers listed are Mercedes Ricse, Gintilipe Sabio, and Antonio Vidal-Puig. Logos for CNIC, Fundación Príncipe de Asturias, and the CNIC National Research Institute are at the bottom.

CNIC WINS THE BACKING OF SPAIN'S TOP-RATED TV NETWORK

It's a familiar and often-repeated public-health message: Cigarette smoking, a diet high in fats and carbohydrates, a sedentary lifestyle—all of these are direct enemies of cardiovascular health. But despite all the berating and coaxing, the message about cardiovascular prevention is still not convincing enough of us to make appropriate lifestyle changes. TV can of course be one the most effective allies in moving an issue to the center of public debate, and the CNIC has enlisted **Spain's top-rated network** to bring its message into people's homes.

The broadcaster in question is **Radio Televisión Española**, the state-run network that shares the CNIC's ethos of public service. The two organizations have forged an agreement to promote cardiovascular health, and are of course joined in this venture by a third partner, the **Pro-CNIC Foundation**—the business-funded non-profit organization that channels private investment to the CNIC.

The goal is both clear and urgent. The CNIC and RTVE are working together to combat what is without question a global pandemic. Cardiovascular disease, in all its manifestations, is the leading cause of death in Spain, above cancer and other diseases.

The immediate practical fallout from the agreement is that RTVE's viewers and listeners are learning about the CNIC's work and mission. All the scientific advances generated through the work and dedication of the CNIC's investigators are gaining public exposure through the radio and TV schedule, and it soon won't be unusual to see white coats and pipettes alongside news stories on politics and sport.

The agreement, ratified in February this year, was signed by RTVE president **Leopoldo González-Echenique**, CNIC managing director **Alberto Sanz** and Pro-CNIC president **Luis de Carlos Bertrán**, in the presence of CNIC director general **Dr. Valentín Fuster**. Through this agreement, these

three organizations have committed themselves to supporting excellence in research, training for young researchers, and the promotion of healthy lifestyle habits.

Leopoldo González-Echenique praised Spain's "pioneering work and leadership in the area of cardiovascular research," while for his part Luis de Carlos expressed his "deep satisfaction" with the agreement: "This partnership will allow us to publicize the CNIC's research and training activities more effectively and to a large and diverse audience, and will also make an important contribution to promoting healthy lifestyle habits and encourage the participation of employers in these activities."



In a suitable start to the partnership, Dr. Fuster spoke directly to network staff as part of RTVE's *Encuentros responsables*, a program of workplace events aimed at keeping staff informed about topics of high interest. The CNIC's director answered wide ranging questions from staff members, who showed great interest in the new initiative.

A few days later, on February 28, the network's viewers had their first opportunity to witness the consequences of the agreement, when Dr. Fuster was invited to appear on the *Los Desayunos* breakfast TV program, which goes out on weekday mornings on RTVE's channel 1. Pundits more versed in political intrigue were keen to ask Dr. Fuster about how to avoid cardiovascular problems and promote wellbeing in this area. This highlighted the importance of health issues for members of the public, even though we often don't give it enough attention.

The **CNIC-RTVE** partnership is certain to ensure greater public awareness of these issues, with a direct impact on the lives of every TV viewer and radio listener.



WEINSTEIN: THE WELL-EARNED TRAVELLING CARPET

Though it's not on display yet, some of the CNIC's researchers have already seen it. And everyone else will soon get used to seeing it in the CNIC auditorium, at least until May 2015, when the **Weinstein Travelling Heart Carpet** journeys to its next destination, Harvard University. This Persian carpet has an original design, made up of separate images depicting different stages in the development of the heart in the embryo. In 2001, **Dr. Nadia Rosenthal**, who commissioned the carpet, donated it to the **Weinstein Conferences** and it has become an unwritten tradition to display it at every meeting since.

The carpet is physical testimony to the holding of this year's **Weinstein Conference on Cardiovascular Development** in Madrid. The event, organized by the CNIC, was held in the Official College of Physicians and attended by 350 scientists from more than a dozen countries. The **Weinstein Conference** has some of the most transparent selection procedures of any scientific event,

because, unlike many other meetings, the speakers are selected through a double-blind system, so that referees don't know the name of the researcher and can thus assess the proposal purely on the basis of quality and novelty. This is one of the characteristics, but by no means the only one, that distinguishes this conference, which celebrated its 21st edition in Spain.

The Weinstein conferences are a forum for discussing research at the cutting-edge of cardiovascular development, ensured by

the exclusive presentation of unpublished studies. But the meetings are also ideal events for forging contacts with other researchers in the field. Many of the younger attendees—at this year's meeting 27% of the participants were predoctoral scientists—take advantage of the meeting to sound out group leaders about future training or employment opportunities.

The holding of the **Weinstein Conference** in Madrid was no chance event, but was rather the fruit of the effort of this year's organizing committee, chaired by José Luis de la Pompa, coordinator of the **Cardiovascular Developmental Biology Program** at the CNIC and 'midwife' to this year's meeting.

All the effort was rewarded by witnessing the satisfaction of the

participants and the commitment of the keynote speakers. This year, these key opinion leaders in cardiovascular research were **Dr. Valentín Fuster**, CNIC director general and Physician-in-Chief at Mount Sinai Hospital in New York, **Dr. Ralph H. Adams** of the Max Planck Institute for Molecular Biomedicine in Münster, Germany, and **Dr. Ángela Nieto** of the *Instituto de Neurociencias* (CSIC-UMH) in Alicante, Spain.

Ensuring the success of this type of meeting requires a strong program, hard work, and of course financial backing. The organizing committee for the Madrid meeting received much-appreciated help from a variety of public and private organizations.

Committee-member **Andy Wessels**, of the Medical University of South Carolina, secured funding from sources in the US that was dedicated exclusively to helping with the travel and accommodation costs of early-stage researchers, who are so important to the success of a conference such as this.

Crossing the Atlantic presented no obstacle for American participants, a fact which speaks volumes about the quality of the program. Around 30% of the attendees travelled from the USA, and visitors also arrived from Japan, China, Australia and elsewhere.

As organizing committee officials explained, "about 90% of the participants stayed through to the end of the conference," a clear sign that the meeting generated scientific interest. "You could see this in people's faces, in the way no-one was in a hurry to end the after-talk question-and-answer sessions, and in many other things."

The **Weinstein Travelling Heart Carpet** remains as a physical testimony to this success. The other legacy, the one that really matters, will be kept in the memories of all the participants and will soon be reflected in the pages of leading scientific journals.