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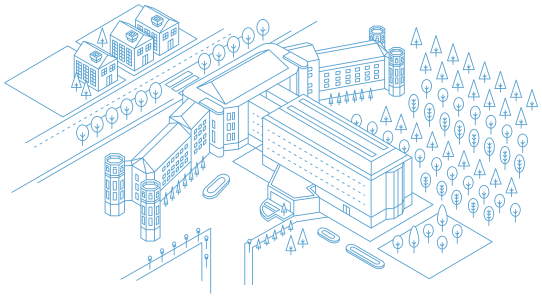
CNIO FRIENDS *newsletter*

Latest news from the Spanish National Cancer Research Centre



COLUMN

We renew ourselves

Over the last few weeks, we have announced the addition of three new group leaders to consolidate the new orientation of the Structural Biology Programme, which will be directed by one of them, Oscar Llorca. The arrival of these researchers has coincided with a period of renewal that can also be seen in our image. A few days ago, we published a new logo, which can already be found on the CNIO website and social media accounts - and that can be seen at the foot of this page. The Centre's Management has always paid special attention to and has tried to take care of our image. At the end of the day, it is another way of transmitting the values and mission of the CNIO, the picture on our passport.

Therefore, we say goodbye to the logo that has served us well since the Centre's inception, and we welcome the new one, which is elegant, clear-cut and faithful to our origins at the Carlos III Health Institute. The renewed graphic symbol of the CNIO matches the leading-edge nature of our research and brings our image into the present. In the coming months, this renovation approach will be extended to other elements to complete the change.

We hope you like it.

—MARIA A. BLASCO
Director

cnio
stop cancer

CNIO SCIENCE NEWS

Patients with Alzheimer's disease have a higher risk of developing glioblastoma and a lower risk of lung cancer. A paper published in *Scientific Reports* by CNIO researchers describes the biological processes that underlie this comorbidity **(1)**. Plk1 inhibitors have recently been acknowledged as an "Innovative Therapy for leukaemia" by the US Food and Drug Administration (FDA). However, a study published in *Nature Medicine* by the Cell Division and Cancer Group suggests that prolonged use of these inhibitors can not only lead to hypertension issues but also to the rupturing of blood vessels and severe cardiovascular problems **(2)**. Half the genes whose alterations confer hereditary susceptibility to develop pheochromocytomas and paragangliomas code for enzymes involved in the Krebs cycle, a metabolic route involved in cellular respiration. A study by the Hereditary Endocrine Cancer Group published in the journal *Clinical Cancer Research* identifies new genes associated with this cycle that are involved in the development of these tumours **(3)**. Human lung adenocarcinomas harbour a number of alterations without obvious oncogenic function, including BRAF-inactivating mutations. Researchers at the CNIO have demonstrated that these mutations are initiating events in lung oncogenesis. The paper appeared in *Nature* **(4)**. Mammalian haploid cell lines have raised great expectations. However, haploidy is unstable and can be lost quickly, hampering the use of these cell cultures. The Genomic Instability Group has offered an explanation of this phenomenon and proposes a way to overcome it. Their work has been published in the journal *Proceedings of the National Academy of Sciences* (*PNAS*) **(5)**.

OUR CENTRE

Last July, the US Prostate Cancer Foundation (PCF) announced its 2017 Young Investigator Awards, which support the first stages in the career of scientists working to find therapies that will improve the life expectancy of men with prostate cancer. Elena Castro, from the CNIO's Prostate Cancer Clinical Research Unit, was granted one of these awards, becoming the only researcher from outside the US to win this year and the second Spanish person ever to receive this prize.

We have also just said farewell to the six students who were on the Summer Laboratory Internship Programme. Before leaving, these young researchers from Spain, Egypt, Peru and the United States presented the work they had been carrying out during these eight weeks at the Centre to their peers. We wish them all the best.

Elena Castro, researcher at the Prostate Cancer Clinical Research Unit.

Some people leave and others arrive. Chiaka Anumudu, a Nigerian researcher and expert in malaria and schistosomiasis, has joined the Genetic and Molecular Epidemiology Group, led by Núria Malats. Anumudu, who will be with us for six months, is part of the *Science by Women* programme of the Women for Africa Foundation.

INTERVIEW

«It is important to enjoy not only the results achieved but also the process»

Óscar Llorca is the new director of the Structural Biology Programme. Llorca will bring one of the greatest revolutions in the study of the structure of proteins to the CNIO: cryo-electron microscopy, a process that uses direct electron detectors to make it possible to view the biological processes involved in cancer or other diseases with almost atomic resolution.

Óscar Llorca
Programme Director

What was the main reason that led you to focus on Molecular Biology?

My doctoral thesis at the National Biotechnology Centre (CNB) was my first contact with Molecular Biology and Structural Biology. The purpose of Molecular Biology is to understand the processes taking place in living beings through the study of the relevant molecules. However, we cannot achieve an in-depth understanding of biological reactions without being aware of the three-dimensional structure of the molecules involved and how they interact with each other; a field known as Structural Biology. Therefore, Structural Biology is part of the essence of the concept and the goals of Molecular Biology. Perhaps the best memory of my doctoral work was the first time I looked at molecules (proteins) I had isolated from some cells through an electron microscope; the beauty of the images and the information that the shape of these molecules provided on the functioning of the proteins that we were studying.

Could you explain exactly what the concept of cryomicroscopy is?

Electron transmission microscopy is a technique that allows the direct visualisation, with a great degree of detail, of very small objects, such as biological molecules (proteins, DNA, etc.). This capacity is due mainly to the use of electrons instead of visible light to observe the molecules. In cryo-electron microscopy (cryo-EM), this capability is combined with the preservation of molecules at very low temperatures (about -175°C), which preserves their structure. The images obtained using cryo-EM can then be applied to computer reconstruction methods to determine the 3D structure of molecules at high resolutions.

After your time at the Institute of Cancer Research in London and the Center for Biological Research (CIB), why the CNIO?

For years now, the group I have been leading has been interested in the study of macromolecular complexes involved in DNA damage repair and in genome instability, important processes in cancer development, using Molecular Biology, Structural Biology and cryo-EM tools. The CNIO has excellent groups working on various aspects of genomic instability, where we are going to find synergies that will allow us to combine the structural studies of the molecules involved in cancer with studies that are more closely related to the disease. In addition, I am convinced that we are going to be able to use new technological developments in cryo-EM to contribute to a multidisciplinary approach to the study of cancer. The CNIO is making a considerable effort to incorporate state-of-the-art cryo-EM equipment, at the highest level in these technologies, and to make substantial progress in defining the molecular mechanisms in cancer, as well as contributing to the development of new compounds of therapeutic interest, in synergy with other Programmes at the Centre.

What advice would you give new generations of scientists?

This profession requires a number of particular qualities, including the ability to recover from partial failures. I think it is important to enjoy not only the results achieved but also the process followed to achieve them; usually years of work in which you constantly have to assess results and experiments that don't work and where the creative process is also about thinking how to solve the problems that arise and having fun doing so. In addition, it is important to learn how to ask yourself the right questions, which requires being familiar with the published literature, having a critical mind, and the ability to enjoy the process.

PROFILE

Raúl Rabadán
Professor at Columbia University

Raúl Rabadán, an expert in Systems Biology, is a professor at the University of Columbia (USA), where he also directs the Center for Topology of Cancer Evolution and Heterogeneity, and has visited the CNIO thanks to the Visiting Scientists Programme funded by the Jesus Serra Foundation. Rabadán's interest in Biology was a rather belated vocation. He had previously worked in the Theoretical Physics Division at CERN (the European Organisation for Nuclear Research), from where he moved to the Institute for Advanced Study in Princeton (USA). Once there, everything changed thanks to Arnold J. Levine, one of the discoverers of the p53 tumour suppressor gene. "I started to collaborate with his group and I realised that this was what I wanted to do with my life." Therefore, he followed his dream and focused on the analysis of biological data, especially on the evolution of systems. First with viruses and then in cancer. His work could be summed up as the search for quantitative responses to biological questions; a field that has progressed and developed significantly in the last 10-15 years and that is going through "a very interesting phase" thanks to the enormous amount of data available to us. Using that data, Rabadán is studying, for example, how cancer genomes evolve at different stages of development, which mutations appear, which are common across different patients, and what they mean...

An essential field in Biology and in the study of cancer, in which Rabadán is one of our leading standard bearers.