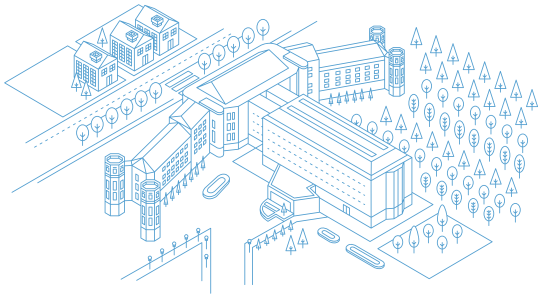
ISSUE 28 - AUGUST 2019

CNIO FRIENDS *newsletter*

Latest news from the Spanish National Cancer Research Centre



COLUMN

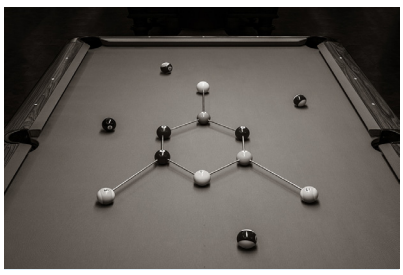
Art as a storyteller of science

Art is one of the things that make humans so unique, because it allows us to embody the world we live in on the basis of our own perspective, curiosity and creativity. This is why I believe there are few better means than art to represent the importance of science for the progress of humanity.

With that aim, we have launched CNIO Arte, whose second edition this year gathers two outstanding participants: quantum physicist Ignacio Cirac, who is working in a research centre in Germany, and the internationally acclaimed photographer Chema Madoz, author of the photograph shown below, who found inspiration in a dialogue with Cirac about the open questions of quantum physics.

Buying one of the thirty numbered photo engravings signed by Madoz, you will be supporting cancer research, since the funds raised will go to CNIO Friends. For more information, please write an email to: **cnioysociedad@cnio.es**

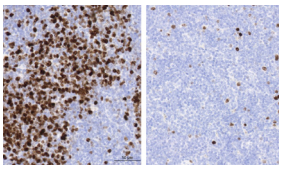
—MARIA BLASCO
Director

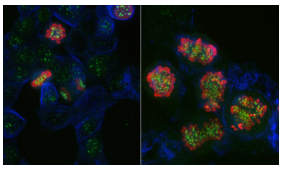


© Chema Madoz, for CNIO Arte

CNIO SCIENCE NEWS

Discovery of a new general pattern in biology: researchers of the CNIO Telomeres and Telomerase Group have compared telomeres in humans and different animal species, and have found that those species species whose telomeres shorten faster have shorter lives. This universal pattern can be used to accurately predict the lifespan of the species solely based on the rate of telomere shortening (+). In addition, the Telomeres and Telomerase Group has found a *butterfly effect* whereby a single change at telomeric chromatin can control the ability of a cell to develop a whole organism. The finding might be of interest for regenerative medicine (+). The Genomic Instability Group found a new method for selecting mammalian cells with half the chromosomes contained in somatic cells. Mammalian haploid have become an important tool to analyse gene function in complex organisms such as mammals, humans included. However, haploid animal cell cultures are unstable as they rapidly become enriched in diploid cells. The method developed at CNIO facilitates the use of this powerful genetic tool that scientists have been trying to establish for fifty years (+). Researchers from the Metabolism and Cell Signalling Group at CNIO found that mutations in the gene RagC, that informs the cell of presence of cellular nutrients via activation of mTOR, promotes the uncontrolled growth of lymphomas. In the study, mice with RagC-mutant tumours treated with the mTOR inhibitor rapamycin, used in clinical practice to treat other types of tumour, lived longer (+).





OUR CENTRE

IBL-300, a group of anti-tumour compounds originated at CNIO and licensed to Irish firm Inflection Biosciences in 2013, will be further developed by Singapore-based biotechnology firm AUM Biosciences.

These compounds are an exclusive multi-target kinase inhibitor series originally developed in the context of the Experimental Therapeutics Programme at CNIO.

The compounds, tested in more than 700 cancer cell lines, have shown potential for clinical development in breast cancer, lung cancer, leukaemia and neuroblastoma.

The agreement between Inflection Biosciences and AUM Biosciences underscores the relevance of CNIO's Experimental Therapeutics Programme, involved in the discovery of innovative drugs.

Also, the agreement indicates the importance of public-private cooperation in the process of translating research findings into commercially viable drugs for the benefit of society. With public-private projects like this one, CNIO transfers technology to patients and gets funding for its research groups.

INTERVIEW

"We might be before a group of follicular lymphomas with positive response to treatment with rapamycin"

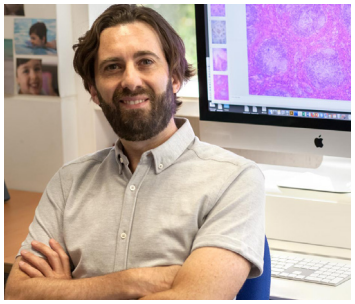


Photo: CNIO

Alejo Efeyan
Head of the Metabolism and Cell Signalling Group, CNIO

We interviewed Alejo Efeyan, Head of the Metabolism and Cell Signalling Group at CNIO. The team has found a connection between nutrients and follicular lymphoma via mutations in the gene RagC.

Why is it important for follicular lymphoma patients that these mutations have been found?

Although we had previously observed these mutations in 15% of patients with follicular lymphoma, we did not know whether they played a role in the origin of the disease or whether they could help to design an effective treatment. Studying genetically modified mice carrying these mutations in RagC, we determined that the mutations were one of the causes of follicular lymphoma in mice, and not the result of the genetic chaos that occurs in tumours. In addition, we observed that when we used a drug called rapamycin in mice with tumours carrying these mutations in RagC, the animals had an extraordinary response and lived longer. Rapamycin inhibits cell functions where RagC is involved.

How did rapamycin extend mice survival?

Rapamycin is a drug that halts cell growth and proliferation by inhibiting the mTOR pathway, itself activated by RagC. Rapamycin is already being used in clinical practice to treat some other tumours, but not lymphomas. Since it has minimal side effects and is particularly effective in cells of the immune system, it is also used as an immunosuppressive agent in organ transplantation. Its strong activity in normal cells of the immune system could also be exploited to target tumour cells derived from immune cells, such as lymphoma cells. Indeed, in our study, rapamycin inhibited tumour growth in all mice with lymphoma, both in mice carrying normal RagC and in those with RagC mutations. However, in more aggressive tumours with RagC mutations, mice had a prolonged positive response and lived longer. This result suggests that the presence of RagC mutations might define a group of tumours that could be effectively treated with rapamycin.

If these results are confirmed by further studies, could a treatment based on rapamycin be transferred over to clinical practice swiftly?

Our results are convincing, but the mouse model must be validated for humans. Rapamycin was approved and is already used to treat patients with other types of tumours. If further studies confirm our findings, rapamycin and other drugs that target the same pathways might be used to treat follicular lymphoma. However, every phase takes time to complete. Preclinical trials help move faster into the clinical stage, learn and test concepts and ideas. Additional work needs to be done before these concepts are applied to patients. We think we found a path that can guide us toward this ultimate goal.

PROFILE

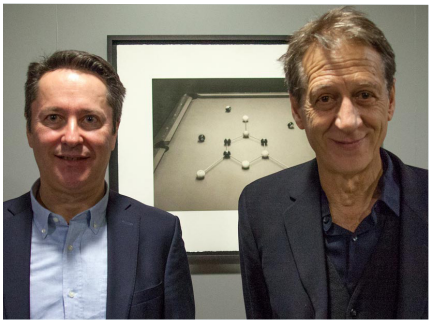


Photo: CNIO

Ignacio Cirac | Chema Madoz
Quantum physicist | Photographer

Ignacio Cirac and Chema Madoz met last year to take part in the CNIO Arte initiative. Cirac is one of the world's leading experts in quantum information. Madoz is known as a craftsman who creates visual poetry. The outcome of their encounter was a photograph by Madoz inspired by Cirac's research in quantum physics. Thirty engravings of the photo have gone on sale; the money raised will go to fund the CNIO Friends programme.

Since the early 1990s, Chema Madoz has been taking photos of ideas embodied in objects he himself designs and builds. In his pieces, irony, humour or quite simply beauty are conceptually highly charged. In his work, surprise is a trigger that activates in the viewer new ways of looking at reality. Among other accolades, he has received the National Photography Award (2000). He is the first living Spanish photographer to whom the Reina Sofía Museum has dedicated a retrospective exhibition. His work also has been internationally acclaimed. Madoz describes the piece he created for CNIO Arte like this: "The billiard table is a pretty magical space where all kinds of possibilities, uncertainties and impossible geometries can happen."

Ignacio Cirac is one of the world's leading experts in quantum information. In 1995, when he was only 30 years old, he co-authored a paper with Peter Zoller that described for the first time how a quantum computer could be built – a goal pursued today by researchers around the world, backed by major corporations. Cirac is Director of the Max Planck Institute for Quantum Optics in Garching, Germany, which he joined in 2001. His accolades include the Blas Cabrera National Research Award, the Prince of Asturias Award, the Wolf Prize in Physics and the Max Planck Medal, among others. In Cirac's words, "we scientists want to understand a world we cannot see, hear or touch. It is this world that art can reach, filling us with the inspiration to ask new questions."