



Annual Report Summary 2015

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Annual Report 2015 is
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IRB Barcelona, a decade of discovery in the biomedical sciences



2015 has been a momentous year for our Institute, a year when the extended IRB Barcelona community, including current and former staff and researchers, patrons, supporters, and friends, gathered to celebrate IRB Barcelona's 10th anniversary. Over the past decade, IRB Barcelona has grown from a seedling in the minds and hearts of a handful of visionary people with big dreams to a thriving research institute that has taken up solid footing on the landscape of international research in the life sciences and made vital contributions to the health and well-being of society.

Ten years on, it is a time to reflect on the achievements we have made, but also to look forward to the role that IRB Barcelona will play in future biomedical research. At the end of 2015, **more than 800 talented international researchers had thrived in our labs**. They had published more than **1900 papers** (217 in 2015 alone), and obtained important recognitions. Their research secured **11 ERC grants** (two in 2015), **16 ICREA** positions and **2 ICREA Academia grants**. We launched new innovative training programmes, such as *Crazy About Biomedicine* and *Maths4Life*, and we have also established an Alumni Network, a platform that aims to connect current and former IRB Barcelona researchers and support staff in a lasting framework. In 2015 the Institute also obtained the renewal for four more years of the Severo Ochoa Award for Research Excellence.

"We may be ten years older, but we are as ambitious as we were in 2005."

2015 also saw **the foundation of the Barcelona Institute of Science and Technology (BIST)**, which aims to give valuable impetus to the science conducted in Catalonia, and help leverage its impact. BIST results from the confluence of 6 research centres of excellence, among them IRB Barcelona. BIST will foster increased collaboration in a multidisciplinary setting of scientific excellence, thereby increasing our potential.

Our success depends on the hard work of our scientists and staff. We are keenly aware that this success also depends on continuous support from society. Over the years we have developed a wide range of activities aimed at informing and engaging the public, that we will continue to expand.

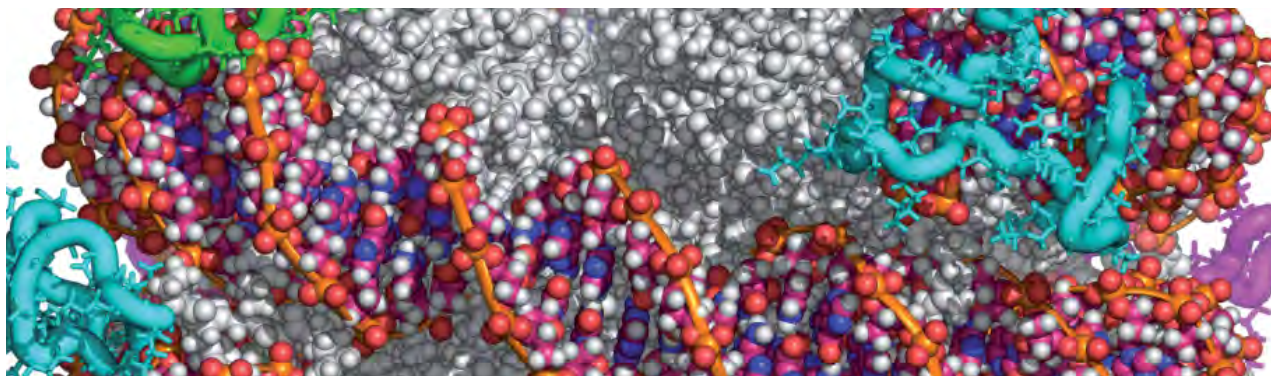
We may be ten years older, but we are as ambitious as we were back in 2005. *The medicine of the future starts here*. We look forward to continuing to work together to make it happen.

Happy Birthday IRB Barcelona, *per molts anys!*

Joan J. Guinovart
IRB Barcelona's Director

On the shoulders of giant... computers

Bioinformatics at IRB Barcelona



Dinucleosome system used to investigate the effect of epigenetic lysine acetylation in histone H4 (H4K16Ac) using molecular dynamics simulations.

Computational biology and simulation of what is not possible to observe directly via experimental means have become essential pillars of biomedical research worldwide. IRB Barcelona scientists are especially prolific in developing theoretical methods to better understand the behaviour of bio-macromolecules, like nucleic acids, on a wide spatial-temporal scale and with a focus on biomedical and biotech applications. In 2015, they conducted a considerable amount of crucial research in this field, which paves the way for future breakthroughs in the design of treatments for many diseases. It is no coincidence that this was the year when IRB Barcelona joined another nine centres and organisations that form the **Spanish node of ELIXIR**, the largest infrastructure of life science data in

Europe and the recipient of 19 million euros of funding through Horizon2020.

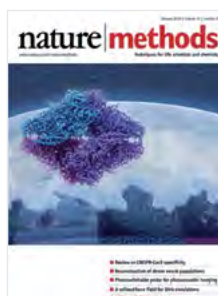
Let's explore some of this year's bio-computational highlights at IRB Barcelona. In February, a team led by Group Leader and ICREA Research Professor **Patrick Aloy** and Research Associate Roberto Mosca developed a versatile web tool that is open-access and free of charge. Allowing mutations to be mapped to the structures and models of human protein-protein interactions, **dSysMap** ("Disease-mutations Systemic Mapping") is especially powerful and useful for the biomedical community in that it provides molecular details about how mutations in certain proteins alter interactions with other proteins, and therefore how they affect cell function. It summarises mutational data in a systemic context, thereby helping biologists to understand the molecular relationships between diseases and to formulate realistic hypotheses about their mechanisms of action. In addition to the precompiled data for thousands of diseases, dSysMap allows scientists from around the world to upload newly discovered mutations. This approach facilitates the inclusion of disease context into primary sequencing studies.



"We place the mutations in a global context of biological processes, which we refer to as systems biology or network biology; by doing this, we provide a more complete view of the effects of known pathological mutations."

Patrick Aloy

"We place the mutations in a global context of biological processes, which we refer to as systems biology or network biology; by doing this, we provide a more complete view of the effects of known pathological mutations," says Patrick Aloy, who describes dSysMap as "a hypothesis-generating system, which, in addition, provides mechanistic details at the molecular level in order to better understand complex diseases of genetic origin, such as cancer, Alzheimer's, and diabetes". The paper that describes dSysMap appeared in *Nature Methods*.



Another key web tool developed at IRB Barcelona in 2015 is called **ParmBSC1**, a so-called "force-field" for DNA atomistic simulations. A force-field is a set of mathematical functions that describe the movement of the atoms that form DNA. "A force-field has never

previously allowed the study of such diverse structures in time-scales relevant for understanding biological phenomena," assures Pablo Dans Puiggròs, IRB Barcelona postdoc in Modesto Orozco's lab and first author of the paper published in December also in *Nature Methods*, together with Ivan Ivani, a PhD student in the same lab.

The technique used by the researchers is called "molecular dynamics," and it allows the simulation of DNA movement, its folding into double, triple or quadruple strands, and even its interaction with proteins and drugs. Molecular dynamics is used to address the processes that occur over time-scales ranging from picoseconds (10^{-12} sec, a trillionth of a second) to minutes, and it can be used for molecular systems of various sizes, from a few nanometres to a meter.

According to the University of Barcelona full professor and Group Leader **Modesto Orozco**, who directed the project, the tool "allows the prediction of DNA properties, which can then be compared directly with experimental results." ParmBSC1 has potential applications in fields ranging from biomedicine to nanotechnology, and it can provide information on mechanisms that underlie DNA regulation and contribute to improvements in the design of drugs that directly or indirectly target DNA.

Bioinformatics can also be effectively used to screen DNA and uncover properties that would otherwise be difficult to perceive. A study published in September, again in *Nature Methods*, described a new and more effective method for the widely extended practice



of tagging proteins. Researchers led by Modesto Orozco proposed the use of two plant protein epitopes, named **inntags**, as the most innocuous and stable tagging tools for the study of the physical and functional interactions of proteins. Epitopes are the specific pieces of the antigen to which an antibody binds.

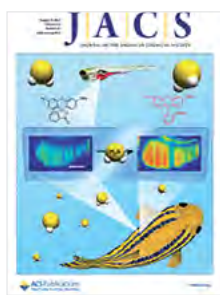
Traditional tagging methods are not very effective because short peptide tags can adopt a variety of conformations, which may facilitate interactions with the target protein and have unpredictable and adverse effects. But thanks to bioinformatics screening methods, researchers analysed the list of peptides with known 3D structures and selected the smallest ones, which both work properly as antigens and cause no undesired effect when fused to other target proteins. *Inntags* maintain their integrity, stability, solubility in cell extracts, and diffusional mobility and do not cause important functional perturbations, unlike other commonly used tags. "Given their structural and functional innocuity and their suitability for in situ analysis, we expect that *inntags* will prove to be valuable tools for studying physical and functional interactions of proteins," they state in the paper.

"Advances in simulation are bringing us closer to being able to simulate key aspects of cell life and thus to realizing the dream of being able to describe the behaviour of organisms based only on the basic rules of physics and chemistry."

Modesto Orozco

Computational methods and simulation also have a direct application in chemistry. Proof of this are three other studies published in 2015. The first one was based on laboratory and computational experiments, which highlighted the tuneable nature of pyridine—a molecule known to unfold DNA and that can change its role and in fact stabilize DNA under acidic conditions. Published in *Angewandte Chemie* in July, this study provides a new means by which to alter the thermal stability of nucleic acids.

On similar lines, and also published a few months before in *Angewandte Chemie*, a study demonstrated, for the first time, that DNA is not a fixed covalent structure but that bond interchanges are possible under stress conditions. This discovery thus opens up avenues to studying DNA chemistry.



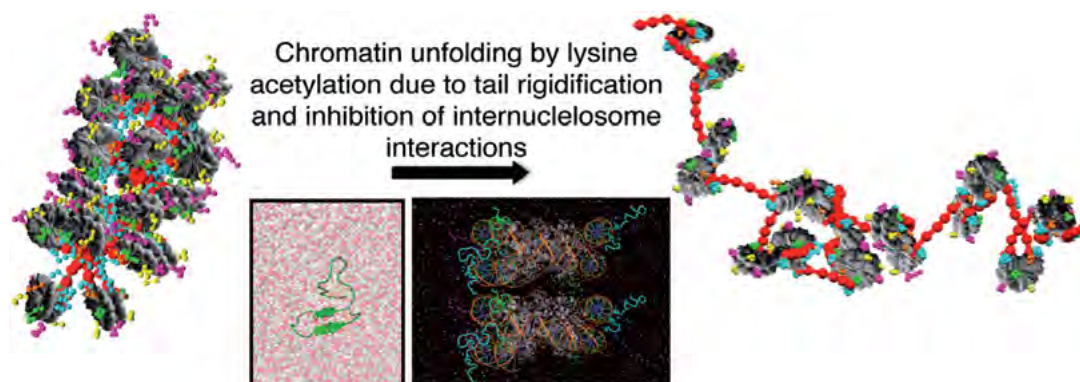
Also, a third study unveiled the mechanics behind the so-called histone-tail acetylation, one of the most common epigenetic phenomena. Acetylation is the name given to the process by which a cell regulates the expression of its genes. According

to the researchers, this is the first mechanical explanation at the atomic level of an epigenetic effect. The study was published in another key journal in chemistry, namely the *Journal of the American Chemical Society*.

Histone tails are loosely structured protein fragments. They are unfolded under normal conditions, and when they move, they can touch other nucleosomes, thereby condensing chromatin—the macromolecule found in eukaryotic cells that consists of DNA, proteins and RNA. Using simulation and nuclear magnetic resonance, the researchers found that the histone tails with lysine acetylation acquire a specific structure and that this structure has an effect on gene expression.

The Structural and Computational Biology Programme is one of the pillars of the science performed at IRB Barcelona. As reflected in this overview of bioinformatics-based science in 2015, many key advances in *in vivo* biology would not be possible without a strong *in silico* backbone.

As Group Leader Modesto Orozco puts it, “Advances in simulation are bringing us closer to being able to simulate key aspects of cell life and thus to realizing the dream of being able to describe the behaviour of organisms based only on the basic rules of physics and chemistry.”



Overcoming the Blood-Brain Barrier, the key to deliver drugs to the brain

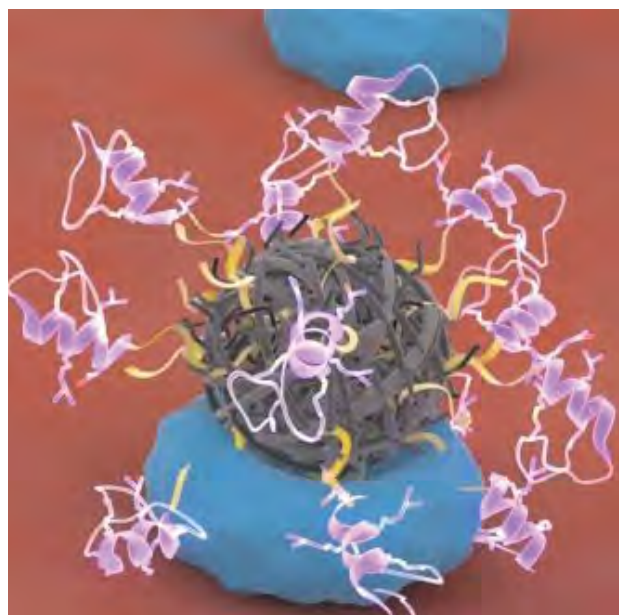
An “ambulance for the brain”

Understanding the molecular, cellular, and physiological mechanisms that allow large molecules to enter the Central Nervous System (CNS), while at the same time defending it from foreign invaders, is fundamental for the development of effective tools by which to deliver drugs to the brain. This is the reason why studying the Blood-Brain Barrier (BBB)—a structure that separates the CNS from circulating blood and prevents infectious substances from reaching the brain—is so important.

IRB Barcelona’s Design, Synthesis, and Structure of Peptides and Proteins Lab is among the leaders worldwide in studying peptides able to cross this barrier. In 2015, University of Barcelona full professor **Ernest Giralt**’s group published two important articles, each one describing a peptide family that can overcome this obstacle (see video: <https://goo.gl/9akqzT>).

Research Associate Meritxell Teixidó explains that one of the methods is based on the retro-enantio approach, which involves introducing non-natural amino acids into the molecule, while the other is inspired in apamin, a natural peptide found in bee venom. Scientists are also looking into how to use peptide shuttles for brain delivery of drugs to fight DIPG, a rare childhood brain cancer, and Friedreich’s Ataxia, a rare degenerative disease of the nervous system, explains Research Associate Macarena Sánchez.

Furthermore, on 2-4 November 2015, together with Tetsuya Terasaki (Tohoku University, Sendai, Japan) and in collaboration with the BBVA Foundation, Ernest Giralt organised the 27th Barcelona BioMed Conference, dedicated to the Blood-Brain Barrier. The group also led the 2015 edition of the “Teachers and science” course, which is dedicated to chemistry and organised in



collaboration with the Catalunya La Pedrera Foundation and the Barcelona Science Park.

Ernest Giralt was one of the speakers in the Barcelona BioMed Prospective series. On 29 September, in a presentation entitled “Ambulances for the brain”, he offered an overview of the research to a very attentive public at the *Centre de Cultura Contemporània de Barcelona*.

The research in this field also received two important awards in 2015. The project “*Gate2Brain, peptide shuttles for protein replacement therapy in Friedreich’s ataxia*” was given funding from the **RecerCaixa** Programme, an initiative of the *Obra Social “la Caixa”* with the collaboration of the *Associació Catalana d’Universitats Públiques (ACUP)*. Also, PhD Student Benjamí Oller won one of the “**Premis Pioner 2015**” for his thesis on the development of minimised apamin derivatives for the brain delivery of antibodies.



Watch video

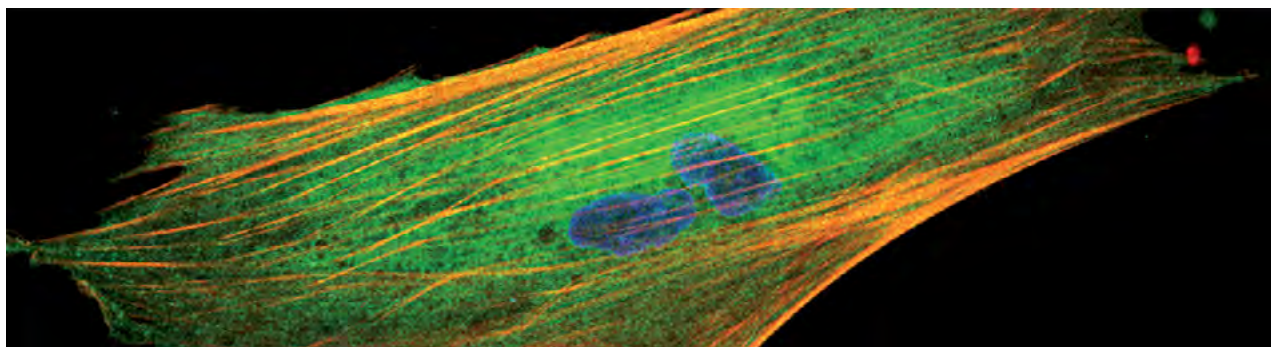


Watch animation



Tackling the genetic bases underlying metastasis

Two promising results for future personalised cancer treatment



Microscopic view of a fibroblast displaying a characteristic flat and elongated shape with numerous membrane extensions (cytoplasmic compartment in green, actin filaments network in red, nucleoli in blue).

Fighting or preventing cancer really means fighting or preventing metastasis—the development of new tumours at a distant site from the primary tumour. The reason for this battle is clear. More than 90% of deaths by cancer are not caused by the primary tumour, but by metastasis. This is why IRB Barcelona’s scientists use their microscopes to dissect not only cancer but also the factors that facilitate the development of new tumours far from the original cancer. The ability to identify the cancers that are likely to metastasise and the site of this process will provide a valuable tool for clinicians, enabling them to intervene early enough to prevent the development of new tumours and at the same time to avoid the unnecessary treatment of patients who are not at risk.

In 2015, two groups at the Institute reported important results in this field. In February, the Colorectal

Cancer Lab, led by ICREA Research Professor **Eduard Batlle**, discovered the “genetic fingerprints” of the cancers that are most likely to relapse, i.e. to form metastasis (usually in the lung or liver for this type of cancer). In a paper published in *Nature Genetics*, Batlle’s team (which also included a number of chemists and bioinformaticians at the Institute) focussed on the stroma, the tissue surrounding the tumour. By examining the genes expressed in the microenvironment of around 1,000 colon tumours from patients from all over the world, these scientists discovered that only the genes expressed in the stroma—and not those in tumour cells, as one could expect—can reliably predict the likelihood of relapse. In this type of cancer, relapse occurs in about half of the cases. However, current methods are not effective in assessing prognosis.

As researchers state in the paper, “these findings pave the way to improve the patient staging system and to identify molecules and signalling pathways associated with colorectal cancer metastasis and disease recurrence that could be targeted therapeutically.”



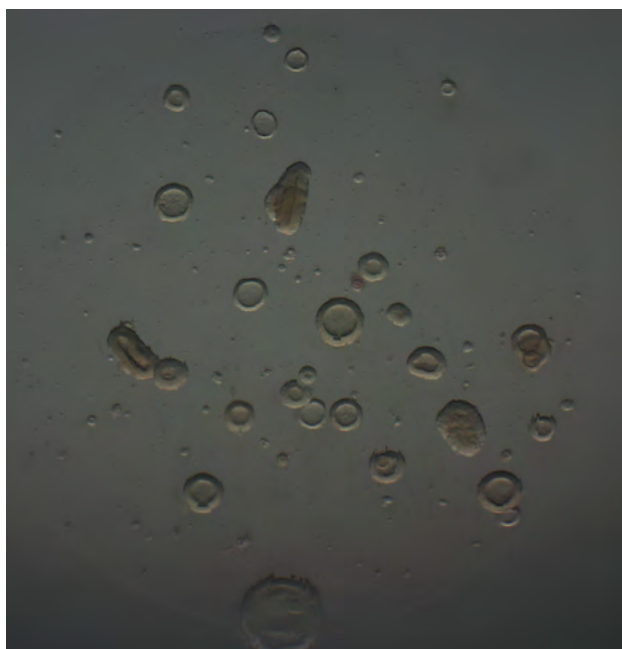
“We confirmed that colon cancer relapse occurs in patients in which tumour cells have the capacity to disrupt the tissue surrounding the tumour.”

Eduard Batlle

“We re-evaluated the classifications under our perspective and confirmed that colon cancer relapse occurs in

patients in which tumour cells have the capacity to disrupt the tissue surrounding the tumour,” says Batlle. The key to the classifications lies in whether the stroma of the tumour is altered or not, and it is precisely the alteration that confers malignancy to colon tumours.”

Cancer communicates with the stroma through the hormone TGF- β . Scientists discovered that this process was enriched in the cancers with poor prognosis. “We propose to explore the possibility of using TGF- β inhibitors to treat colon cancer,” explains Batlle. Several TGF- β inhibitors are being tested for other kinds of tumours.



Patient-derived tumour organoids (mini colon tumours) grown in “in vitro” plates, a technique developed by IRB Barcelona (Alexandre Calon).

To reproduce the behaviour of the original tumour, Batlle’s team used miniature organoids of colon cancer samples taken from patients at the *Hospital del Mar* in Barcelona. This novel technique is proving very promising for future personalised cancer treatment.

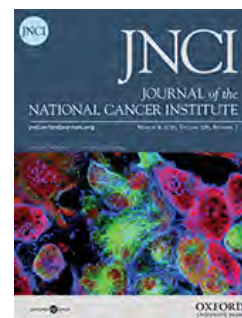
Furthermore, in September 2015, ICREA Research Professor **Roger Gomis**, who heads the Growth Control and Cancer Metastasis Lab, discovered a genetic marker capable of identifying the type of breast cancer most likely to metastasise to the bone. In breast cancer, this process occurs in about 20% of cases. Currently, there

are no biomarkers available for early breast cancer patient populations at risk of bone metastasis.

In a paper published in the *Journal of the National Cancer Institute*, Gomis’ group analyse oestrogen-receptor-positive breast tumours, which account for about 80% of all breast cancers and tend to metastasise to the bone. In this paper, they conclude that the gene MAF “is a mediator of breast cancer bone metastasis.” Basing their research on more than 900 clinical samples and experiments using mouse models, the researchers found that, in the tumours in which this gene was altered, the risk of bone metastasis was more than 14 times higher. According to the researchers, MAF drives the process of bone colonisation and triggers a set of functions in the cell that allow metastasis to take place.

“The next step of our research is to study whether this gene, which reliably predicts metastasis to the bone, is clinically useful. Drugs to prevent bone metastasis might in fact benefit patients under adjuvant therapies, the treatment given after the surgery to lower the risk that the cancer will come back. Our discovery could be highly valuable for clinicians because the unnecessary treatment of patients who are not at risk would be avoided,” explains Gomis.

The discovery has been patented and has led to the creation of the company **Inbiomotion**, founded by Gomis and also involving the participation of ICREA and IRB Barcelona.



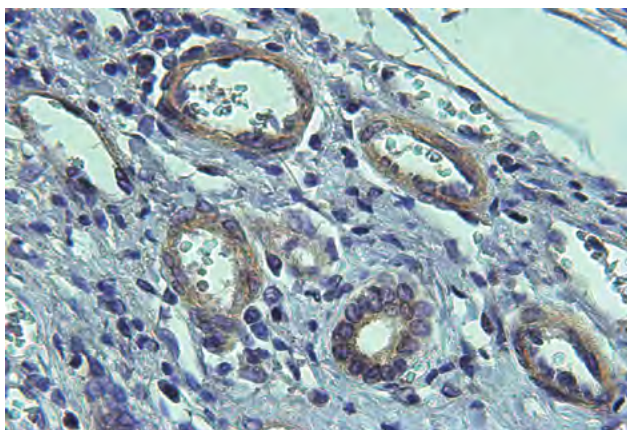
“Our discovery could be highly valuable for clinicians because the unnecessary treatment of patients who are not at risk would be avoided.”

Roger Gomis

Pathological angiogenesis that leads to cirrhosis can be stopped

Inhibition of CPEB4 may prevent the development of abnormal blood vessels

A study published in November 2015 revealed a therapeutic target to prevent the development of the many abnormal blood vessels that cause gastrointestinal bleeding—the main complication in cirrhosis. Cirrhosis is the principal risk factor for liver cancer. The same target may be the key to preventing and treating this condition.



Pathological blood vessels (white circles), with abundant CPEB4 expression in cirrhotic tissue (IRB Barcelona/IDIBAPS).

The accumulation of scar tissue impedes blood circulation in the liver, thus leading to portal hypertension (the portal vein). To relieve the pressure in the vein, collateral blood vessels develop outside the liver. The problem is then two-fold, first because the liver receives even less blood, thereby causing greater damage to the

Scientists headed by **Raúl Méndez**, ICREA Research Professor at the Institute, and Mercedes Fernández, at IDIBAPS in Barcelona, reveal that the inhibition of CPEB4 protein may prevent the development of the abnormal blood vessels associated with cirrhosis.

Pathological angiogenesis is one of the most serious complications in patients with cirrhosis and a key factor in the development and worsening of the disease. Consequently, many research efforts focus on identifying treatments for this condition. The results of the study were published online in *Gastroenterology* in November 2015.

Perverse repairing effect

Cirrhosis is a chronic lesion characterised by the accumulation of scar tissue (fibrous nodules), which alters the normal structure and function of the organ. Chronic hepatic lesions are caused mainly by alcoholism, hepatitis C, and increasingly by obesity.



organ, and second because the blood vessels are of poor quality (pathological angiogenesis).

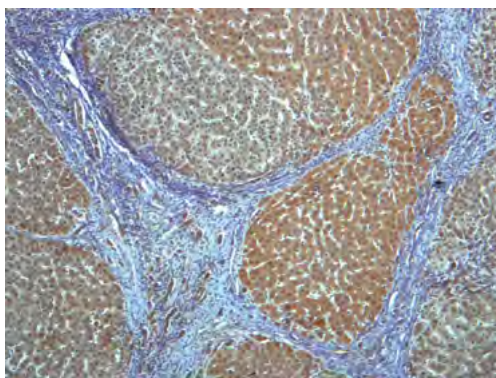
“Hepatic cells try to repair liver lesions, but the way by which they do this turns out to be fatal for the organ. This is a loop that gets bigger and finally threatens the patient’s life. Also, the collateral blood vessels form varicose veins in the oesophagus and stomach of patients with cirrhosis; these veins are fragile and have a high tendency to burst, causing heavy bleeding that is difficult to stop,” explains Mercedes Fernández, co-leader of the study. “This is why a treatment that regresses and/or prevents pathological veins—which is not currently available—would be efficient,” she adds.

A target named CPEB4

VEGF (vascular endothelial growth factor) is the main effector protein in the development of blood vessels. “All current drugs that aim to prevent neovascularisation are based on inhibiting VEGF or VEGF receptors, but the problem is that indiscriminate attack of this protein impairs the normal development of blood vessels, thus causing unbearable adverse effects,” explains Méndez.

In a previous study published in *Nature Medicine*, Méndez, together with researchers at the Hospital del Mar in Barcelona, had already discovered that CPEB proteins are involved in blood vessel development in pancreatic and brain cancer. Given the urgent need to identify new targets for pathological angiogenesis, Méndez and Fernández started collaborating to examine the role of CPEB4 in this process in the context of cirrhosis, a disease characterised by profound neovascularisation.

“The best thing about the study is that we demonstrate that the development of pathological blood vessels can be stopped by interfering with CPEB4 proteins while positive vascularisation remains intact,” says Méndez. The experiments in cells *in vitro*, in animal models, and in samples taken from patients with cirrhosis have revealed the molecular mechanisms through which the increase in CPEB4 favours the overexpression of VEGF in cirrhosis.



Tissue sample of human cirrhotic liver, in which changes in the structure and elevated CPEB4 protein expression can be appreciated in the regeneration nodules. (IRBBarcelona/IDIBAPS).

From cirrhosis to liver cancer

The researchers uphold that the repair cycle that the liver enters worsens the situation to the extent that regeneration nodules, which show high levels of CPEB4, form liver carcinomas. In this context, the Spanish Association against Cancer (AECC) awarded more than €1 million to the Méndez-Fernández tandem, who, together with Jordi Bruix (IDIBAPS-Hospital Clínic), will work in a coordinated manner

to unravel the role of this molecule and to propose a treatment for liver carcinomas.

In parallel, Méndez’s lab is working on a research project on CPEB4 inhibitors. Last year they resolved the structure of this protein at the atomic level—the step previous to the computational design of inhibitors, which is being undertaken in collaboration with Modesto Orozco, at the same centre.

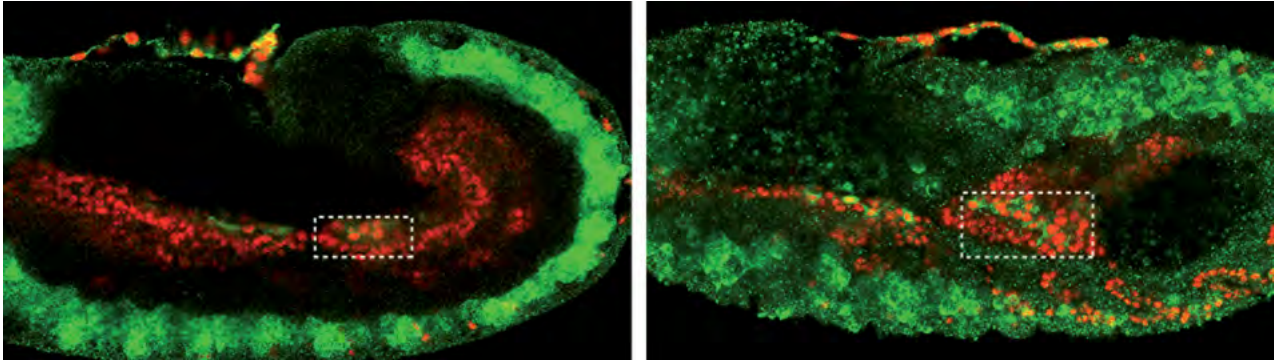
Furthermore, and with the support of the Botín Foundation, Méndez has fine-tuned an assay to test CPEB4 inhibitors, with the aim to speed up the detection of molecules with the greatest therapeutic potential.

“The best thing about the study is that we demonstrate that the development of pathological blood vessels can be stopped by interfering with CPEB4 proteins while positive vascularisation remains intact.”

Raúl Méndez

Fruit fly 'gives a wing' to top research

Research on *Drosophila* moves forward rapidly



Left: position of a group of cells in a wild-type *Drosophila* embryo. Right: mispositioning produced in the same group of cells in a mutant fly embryo for E-Cadherin.

Scientists have been using the fruit fly *Drosophila melanogaster* as a genetic model system in biology since the beginning of the 20th century, and yet it keeps surprising us. In recent years, Barcelona has become home to a powerful cluster of scientists working with this emblematic animal model.

Among them, Group Leaders and ICREA Researcher Professors **Marco Milán** and **Cayetano González**, who in 2015, in collaboration with the BBVA Foundation, celebrated the vigour of research in the field by organising the 26th **Barcelona BioMed Conference**, on *Drosophila* as a model in cancer. The event, held on 15-17 June at the *Institut d'Estudis Catalans* in Barcelona, drew the participation of 150 international fly experts.

"Research on *Drosophila* and cancer is moving forward in a very spectacular way," comments Milán. This model organism has been used for over a century to understand genetics and basic developmental mechanisms. Nowadays, it is used to reproduce some of the most common human tumours, and researchers are confirming that the tumours in flies behave in a similar manner to analogous human cancers.

"The power of fly genetics allows us to rapidly and precisely dissect the molecular mechanisms underlying unlimited

tumour growth, metastatic behaviour, and malignancy to the host at the cellular level," says Milán.

He draws attention to three key elements discussed during the conference. "First, the fly is being widely used to perform drug screening and to identify functional targets for specific types of tumours," he says. "The combination of *Drosophila* genetics and chemical biology helps us to identify the most effective drugs with the lowest number of off-targets."



A second example where flies play a useful role specifically in cancer research is a systemic problem often associated with cancer patients, called cachexia. "Often in the final stages of cancer, the organism succumbs to this general state of weakness and fatigue. This is a very complicated syndrome to study. *Drosophila* is already helping us to identify the molecular mechanisms

underlying cachexia," explains Milán.

Finally, *Drosophila* continues to open new paths for basic research in cancer biology and in other fields. "The fly is one of the best known organisms nowadays. We can use it to study the role of the immune system in cancer development, cancer-associated inflammation, the causal relationship between genomic instability and tumour genesis, cancer metabolism, and the relationship between

diabetes and cancer,” concludes Milán. “Research on flies keeps evolving and contributing to our understanding of diseases. *Drosophila* will keep surprising us for some time to come!”



True to its prowess, the fruit fly has been at the centre of one of this year’s key publications at the Institute. Group Leader and CSIC research professor **Jordi Casanova** and postdoctoral fellow Kyra Campbell authored a study on the protein E-Cadherin, a kind of biological adhesive that keeps cells tightly bound together, thus favouring the organisation of tissues and organs and impeding cell movements.

These two researchers published an article in *Nature Communications* in August 2015 in which they reported that this protein is crucial for the coordinated movement of diverse cell types.

“Cell migration is a common and necessary process for an embryo and also for the correct function of the adult organism. What has been most surprising is the observation that E-Cadherin is a key component in cell movement, when its role was previously assumed to be that of keeping cells static,” explains Casanova.

This new function of the protein may explain why tumours that express intermediary levels of this protein tend to metastasise more and thus have poorer prognosis. E-Cadherin would facilitate highly diverse heterogeneous groups of cells to migrate together from the original tumour. “Our results in *Drosophila* are clinically relevant because they offer an explanation of the role that may be played by E-Cadherin in tumours with metastasis,” says Casanova.

Finally, *Drosophila* has been the protagonist of one of the secondary school teachers courses held in May 2015. Fifteen teachers from schools around Barcelona got up to date with scientific concepts through the third edition of the course “**On the fly**”. The activity focussed on the use of the fruit fly as an animal model for the study of diseases.

The “On the fly” course is part of the **Teachers and Science Programme**, organised by the Catalunya-La Pedrera Foundation. The overall objective of this initiative is to improve science teaching in schools in order to foster scientific vocation among students. In 2015, IRB Barcelona also hosted a similar course dedicated to Chemistry as one of the tools of biomedical research.



The Barcelona BioMed Conference on *Drosophila* as a model in cancer, organised in collaboration with the BBVA Foundation, was held on 15-17 June 2015.

“The combination of *Drosophila* genetics and chemical biology helps us to identify the most effective drugs with the lowest number of off-targets.”

Marco Milán

Breast cancer research targeted with ERC grant for 'p38 Cure'

Angel Nebreda aims to determine whether the five most common breast cancer therapies are more effective when MAPK inhibitors are administered

Last July, Group Leader and ICREA Research Professor **Angel Nebreda** was awarded an ERC Proof of Concept Grant amounting to €150,000 over 18 months. The grant covers the costs associated with verifying the innovation potential of an ERC Advanced Grant-funded project called "p38 Cancer", given to Nebreda in 2011.

Called "**p38 Cure**", Nebreda's Proof of Concept grant aims to determine whether the five most common breast cancer therapies are more effective when MAPK inhibitors are administered to suppress p38.

Nebreda explains that protein p38 helps cells to tolerate adverse conditions, such as when they are

exposed to chemotherapy (see video: <https://goo.gl/eX6r55>).

To study the effects of combining chemotherapy drugs with p38 inhibitors, IRB Barcelona is collaborating with hospitals in Barcelona to collect tumour cells and grow them in mice.

Postdoctoral fellow Ana Igea, who is performing the experiments, explains how some tumours respond better to p38 inhibition than others.

Industrial Liaison Officer Tiago Botelho explains that "p38 Cure" will ultimately benefit breast cancer patients because the results will be made public.



Watch video

IRB Barcelona's expertise in 3D techniques applied to genomic data visualisation

Modesto Orozco coordinates a European project involving six European centres



Multiscale Complex Genomics

In 2015, Group Leader **Modesto Orozco** became coordinator of a European project called “Multi-scale complex genomics”, or **MuG**. Involving six European reference centres in programming, method development, and visualisation techniques for 3D genomics data, the project will be conducted over three years and has a budget of €3 million. The project aims to standardise experiments in 3D genomics and the storage of data and to develop a set of protocols, methods, and processes by which to exploit these data, thus laying the groundwork for an emerging field that lacks organisation.

“It is essentially a methodological project. The techniques used for 3D genomics are very new, they are not mature, and there are huge deficits in data processing. This makes the field unstable, above all with respect to the reproducibility of results,” explains Orozco. MuG puts together expertise from various fields: biologists with an interest in chromatin structure; methods developers; and High Performance Computing facilities with a strong history of helping to solve bio-computational problems.

The objective is now to move from the perspective of amino acid sequences to understanding how chromatin—

the DNA inside cells—folds and how the structure of the folding can provide information about DNA function. “With the 3D vision of DNA, when we observe how the structure changes and adapts, I believe that we will start to find explanations for a lot of statistically relevant information deposited in data bases but that has escaped our understanding until now,” explains Orozco. “We also want to add a fourth dimension, which is seeing how chromatin structures change over time in response to alterations in the external milieu or because of the functional needs of the cell,” he says.

The MuG project aims to standardise experiments in 3D genomics and the storage of data and to develop a set of protocols, methods, and processes by which to exploit these data.

Training future medical researchers

PhD for Medical Doctors (PhD4MD) was launched in 2015



In 2015, the Centre for Genomic Regulation (CRG), IRB Barcelona, the August Pi i Sunyer Biomedical Research Institute (IDIBAPS), and the Vall d'Hebron Research Institute (VHIR)—the last two linked to the Hospital Clínic and Vall d'Hebron Hospital, respectively—joined forces to bridge the gap between research and clinical practice. The programme is called **“PhD for Medical Doctors – PHD4MD”** and seeks to speed up the transfer of results

generated by biomedical research activities to clinical practice—a process commonly known as translational medicine. The call offered fellowships for medical doctors working in Spain who want to be trained in research and to do a PhD. The four participating centres are working on collaborative projects that involve a basic research group and a translational or clinical research team. The programme has already announced its second call in 2016.

Juan Miguel Cejalvo (Valencia, 1984), an oncologist trained at the Hospital Clínico Universitario de Valencia, is the selected student who will do his thesis at IRB Barcelona under the PhD4MD programme. He joined Roger Gomis' Growth Control and Cancer Metastasis group, where he will perform the basic research for his project. Aleix Prat, from IDIBAPS, will lead the clinical part of this project. Both Roger Gomis and Aleix Prat have extensive experience in cancer research, especially breast cancer and metastasis.

Why did you apply for the PHD4MD programme?

This project seemed like a good opportunity to develop translational medicine, which is what helps us answer the questions posed by patients every day. Five years' training in medical oncology makes you realize how important research is. In fact, at the end of my studies, I spent two years doing clinical research into the development of new therapeutic strategies—a project that perfectly combined clinical and basic research. And this experience motivated me.

What attracted you most about the programme?

This programme combines basic and clinical research, which is what interests me. Here I will focus on breast cancer and metastasis, one of the major problems patients face.

We know that between 20% and 25% of them will relapse. Studying the molecular mechanisms that enable metastatic cells to remain dormant for so long and then wake up and generate these macrometastases will allow us to develop therapies to prevent relapse, or, if metastasis occurs, to make it chronic or even stop it from spreading.

What advantages does being a doctor bring to research?

When you treat patients with similar characteristics, they don't all respond the same way. This raises many questions, and to understand what happens we must go to the lab in search for answers. I believe that new knowledge is generated in the laboratory, not at the bedside; this allows us to ask more biologically relevant questions. But in turn, the best way to apply this knowledge is to use a clinical approach. The questions are raised when dealing with patients but are answered in the laboratory. I believe this is key to discovering novel and more efficient therapeutic strategies.

“Questions are raised when dealing with patients but are answered in the laboratory.”

Juan Miguel Cejalvo

Bringing research to the classroom, hand-in-hand with teachers

The TANDEM Project will last until 2018

To use biomedicine to design the teaching programme of a primary school from the first year (ages 5-6) to the sixth year (ages 11-12) and across the full range of subjects. This is the goal and challenge of a three-year project that IRB Barcelona launched in the academic year 2015-16 in collaboration with the school **Mare de Déu de Montserrat**, in Cornellà.

This initiative forms part of the **'Tandem Schools Programme'** and receives counselling, follow-up and funding from the Catalunya-La Pedrera Foundation, with the support of the Department of Education of the Catalan Government.



Tandem Schools are innovative educational projects involving a partnership between a school and a centre of reference. In this regard, the two partners work together to design a school curriculum around a given theme and to boost academic results, the standing of the school, and social cohesion. This is the 9th Tandem Programme to be promoted by the Catalunya-La Pedrera Foundation since 2011, and the first to involve a research centre and a primary school.

"Being the first to undertake such a project is an additional challenge for all those involved."

Helena González

"Being the first to undertake such a project is an additional challenge for all those involved," says Helena González, who coordinated the Tandem Project when she was Public Engagement and Science Education Officer at IRB Barcelona. "A school and a research centre operate in totally different spheres and have different ways of going about things, which means that we will have to make a big effort to adapt to each other," she explains. "Besides being my pet project, I think this is the biggest challenge IRB Barcelona has faced in the outreach area, but I believe we will obtain extraordinary results", she concludes.

Without overlooking the basic skills that students have to acquire, the curriculum of the school will be based upon the project "Discovering biomedicine together," in such a way that pupils end up gaining in-depth knowledge of the topic, while at the same time the general academic results of the school are improved.

The activities undertaken during this initial period are focussing on teacher training. IRB Barcelona is instructing educators about the scientific method and specific concepts of the subjects that will be covered. The teaching programme aims to transfer knowledge to the classroom.

The activity programme for the students has been drawn up taking into account the school's calendar, such as visits to museums or the care of a vegetable plot. The activities will be used to teach the children about diseases such as diabetes, cancer, and Alzheimer's disease, fields in which IRB Barcelona has extensive experience.



IRB Barcelona research continues to receive generous support from grassroots initiatives

In 2015, Carlos Romero swam “against the current” and Xavier Ayala organised wine-tasting events to help research



IRB Barcelona scientists are discovering that an increasing number of people are willing to actively support their efforts in research.

After the launch of the dance video in October 2014, a number of initiatives in favour of IRB Barcelona science sprang up in 2015. One very good example is “**Swimming Against the Current**” (*Nedar contra corrent*), a project led by Carlos Romero, a 43-year-old telecoms engineer who set himself the challenge of swimming the estimated 12,250 strokes it takes to cross the fierce waters of the Strait of Gibraltar on 24 September 2015 in support of IRB Barcelona research into cancer and metastasis.

Carlos’ family has been affected by cancer on various occasions. Since he’s a passionate swimmer, he decided he could help in the fight against this devastating disease by tackling a daunting challenge that only around 700 people have successfully met so far. And he was backed by many people in his hometown, Sant Esteve Sesrovires. They were behind him throughout the year with initiatives such as a community swim-along, where neighbours were invited to the municipal pool to symbolically support Carlos, a *butifarrada* (Catalan sausage barbecue), and the sale of t-shirts and sweets—provided by local businesses—to raise money for research.

Also, throughout the year, the charity initiative **Vi per Vida** organised wine-tasting events headed by the sommelier Xavier Ayala in favour of IRB Barcelona research. In 2015, the organisation, which was founded in 2014, gathered a total of more than 1000 people with the aim to raise awareness about metastasis and to contribute to the work being carried out in this field at the Institute. Also, in Xavier’s case, the charity was founded as a tribute to his father, who died of lung metastasis when Xavier was only 11 years old. The charity is working on the organisation of new wine-tasting events for 2016.

On 1 December 2015, IRB Barcelona also participated in **#GivingTuesday**, a global movement founded four years ago in New York that seeks to promote fundraising and that reached Spain for the first time.

Finally, patients’ associations are also stepping up to help raise awareness about IRB Barcelona’s research. One example is the Spanish Association of Glucogenosis Patients (**AEEG**), which marked International Pompe Day on 15 April by organising activities throughout Spain to bring attention to this rare disease that causes progressive muscle degeneration.



Carlos Romero (top left, in the flask) and Xavier Ayala enthusiastically support research with their philanthropic ideas.

The Alumni Network opens opportunities for the extended IRB Barcelona community

David Vílchez received the first Alumni of Excellence Award

Since IRB Barcelona was founded in 2005, more than **800 scientists, students, and support staff have passed through its doors**. Many of these people have gone on to take the next step in their careers in leading institutes and organisations across Spain and the world. IRB Barcelona alumni have several things in common—they have spent a significant part of their careers at the Institute, and many feel a special connection to it. Upon leaving, many have also found themselves setting up a new life, professionally and personally, in an unfamiliar environment—a task which brings with it challenges and opportunities.

Together, IRB Barcelona alumni represent an important and growing group, armed with invaluable expertise and experience. They have enormous potential to create a useful support network for IRB Barcelona and for science and the scientific community in Barcelona and beyond.

Coinciding with the celebration of its 10th anniversary in 2015, IRB Barcelona launched an **Alumni Network** with

the goal of creating a solid and lasting platform to support the Institute and its extended community.

Membership is open to anyone who has spent at least six months at IRB Barcelona, and all alumni have to do to start taking advantage of the wide range of benefits of staying connected is register.



The first gathering of the Alumni Network took place at the **IRB Barcelona 10th Anniversary Scientific Symposium and Alumni Reunion**, on 26 October. During the celebration, a new **Alumni of Excellence Award** was launched. In January 2016, the prize was presented to **David Vílchez**, group leader at the CECAD-Cluster of

Excellence in Cologne (Germany) “for his great aptitude for ground-breaking science throughout his career, making significant contributions to several fields, such as neurodegeneration, proteostasis, ageing, and stem cell biology.” While at IRB Barcelona, Vílchez was in the Molecular Medicine Programme between 2003 and 2008.



Watch the IRB Barcelona's 10th Anniversary video



David Vílchez received the first Alumni of Excellence Award “for his great aptitude for ground-breaking science throughout his career, making significant contributions to several fields, such as neurodegeneration, proteostasis, ageing, and stem cell biology.”

Awards, Recognitions and Prizes



Angel Nebreda

Received an ERC Proof of Concept Grant



Xavier Salvatella

Received an ERC Consolidator Grant



Raúl Méndez & Isabel García Cao

Received grants from Spanish Association Against Cancer



Roger Gomis

Was awarded funding by Worldwide Cancer Research



Raquel Batlle

Received a grant from the Olga Torres Foundation



Salvador Aznar

Joined the Botín Foundation's Technology Transfer Programme



Joan J. Guinovart

Received the 2015 Gaudí Gresol Prize



Eduard Batlle

Received the *Ciencias de la Salud* prize from the *Fundación Caja Rural de Granada*



IRB Barcelona renewed the Severo Ochoa Award from the Spanish Ministry of Economy and Competitiveness



Awarded funding to **IRB Barcelona's** Strategic Research Commercialisation Plan



IRB Barcelona's **dance video** received the award for the Best Fundraising Campaign and the Jury's Grand Prize from the Spanish Foundation for Fundraising (AEFr). The video also obtained the 2015 Prisma Prize in the category of Best Video

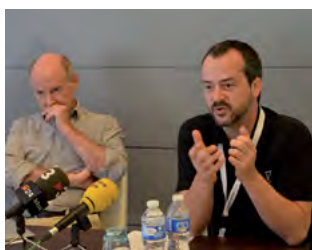
Training at IRB Barcelona



Barcelona BioMed Conferences

Two Barcelona BioMed Conferences, organised in collaboration with the BBVA Foundation, gathered 300 experts from around the world at the *Institut d'Estudis Catalans* to discuss the latest breakthroughs in the following fields:

- *Drosophila* as a model in cancer (15 -17 June 2015)
- Blood-Brain Barrier (2 - 4 November 2015)



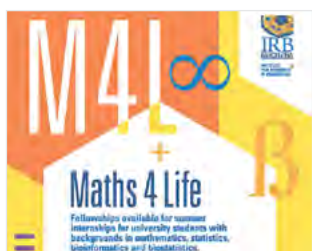
European Light Microscopy Initiative Meeting

More than 400 microscopy experts and users met in Sitges (Barcelona) at the 15th European Light Microscopy Initiative (ELMI) Meeting on 19-22 May 2015, an annual microscopy conference. Advanced Digital Microscopy Core Facility manager **Julien Colombelli** and his CRG counterpart, Timo Zimmermann, organised the meeting that brought together a community of people involved in using, developing or distributing Advanced Light Microscopy techniques for the life sciences.



PhD Students Symposium

The fourth edition of the IRB Barcelona PhD Students Symposium, "Science Fights Back", took place on 12-13 November and saw the participation of around 160 people and 10 invited speakers from all over Europe. Cell stress, ageing and senescence, homeostasis, photopharmacology, chromosome segregation, and small molecule stabilisation were among the topics covered during this 2-day event organised entirely by 14 PhD students at the Institute.



Maths4Life

The second edition of the Maths4Life Programme was held during the summer of 2015. This novel initiative provides opportunities for university students to merge maths, physics and statistics with the life sciences.



A future in biomedicine

In 2015, IRB Barcelona's Academic Office launched a new programme for undergraduate students called "A future in biomedicine," a pioneering activity for outstanding and highly motivated students enrolled in the fourth year of their degree at a local university.

Strengthening Collaborations



**Barcelona Institute
of Science and
Technology**

Top Catalan research centres strengthen links through BIST

In 2015, six top Catalan research centres took a leap forward in their collaboration by constituting The Barcelona Institute of Science and Technology (BIST). The centres involved are the Centre for Genomic Regulation (CRG), the Institute of Chemical Research of Catalonia (ICIQ), the Catalan Institute for Nanoscience and Nanotechnology (ICN2), the Institute of Photonic Sciences (ICFO), the High Energy Physics Institute (IFAE), and IRB Barcelona.

BIST seeks to foster interdisciplinary research, to leverage its scientific impact, and to position itself among leading European institutions. BIST's Board of Trustees includes prominent international scientists, the European University Association, as well as representatives from five major foundations (la Caixa, Banc Sabadell, Catalunya-La Pedrera, Cellex, and Femcat), and from the Catalan Government. Its Director is Monserrat Vendrell.



In July, IRB Barcelona signed a collaboration agreement with the **Center for Integrative Biology of the University of Trento**, to support the exchange of PhD students between the two centres. The agreement seeks to increase contact between the labs at the two institutes by means of PhD student exchanges, facilitating their registration in seminars, workshops and courses of interest to this community and, given the mutual interests of the two research centres, strengthening scientific collaboration.



In June, IRB Barcelona and the **Radboud Institute for Molecular Life Sciences (RIMLS)**, Nijmegen, the Netherlands, signed collaboration agreements on research and training. The agreements pave the way to strengthen current exchanges between the two centres and to explore new collaboration opportunities. Since September 2015, undergraduates and master's students at IRB Barcelona are able to participate in the Master's Programme "Molecular Mechanisms of Diseases", given by RIMLS. PhD student placements are being organised to allow the students to become familiar with the facilities and technology available in the other centre.



In 2015 IRB Barcelona also became one of the members of **BIB, Bioinformatics Barcelona Association**. Formed of dozens of organisations, research centres, hospitals and companies, this association seeks to engage all member organisations in initiatives and dynamic collaborations in advanced research, knowledge transfer, and training, in order to position Barcelona and Catalonia as an international reference in bioinformatics. BIB seeks to set in motion advanced research initiatives in knowledge and tech transfer between research groups, hospital centres, and the biotech, pharmaceutical and agro-food business sectors. Moreover, it aims to implement programmes to train specialists, thus responding to the demands for a range of bioinformatician profiles.

Facts & Figures

Publications



A total of
217
Publications

90.1%

Q1 publications
SJR 2014



nature
INDEX 2015

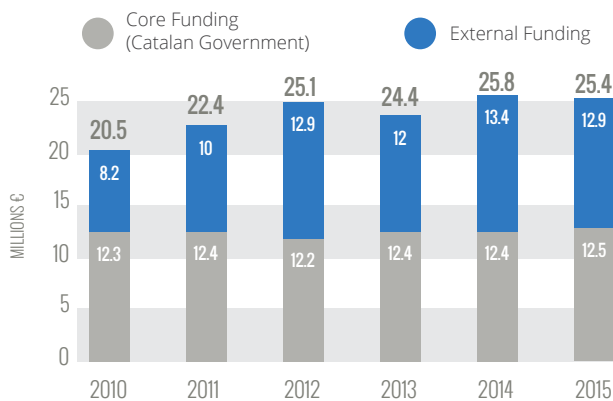
47 of our 217 publications
(21.7%) were published
in the 68 top journals selected
for the Nature Index

64.5%

D1 publications
SJR 2014

Funding

Running budget 2010-2015

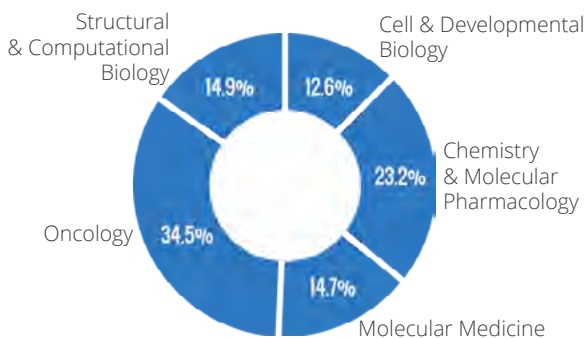


Active projects

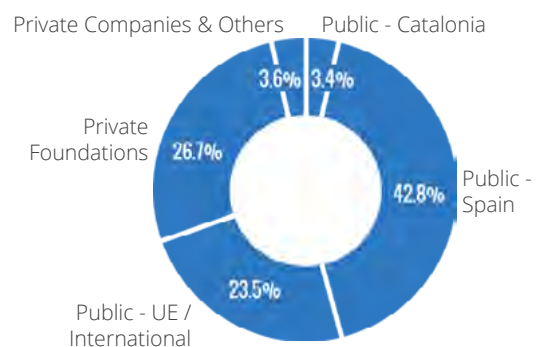


149 National and international
research projects and networks

External funding by research area



External funding by source



Innovation

19

New technologies
identified and
currently under
evaluation

7

New patents
applications and
international patent
extension

20

Agreements
with
private
entities

9

Projects funded
by Proof of
Concept Funds

1

IRB Barcelona Group
Leader joins the
Botín Foundation's
Technology Transfer
Programme

Training

23

PhD theses
defended

11

Complementary
training activities

Facts & Figures

Staff



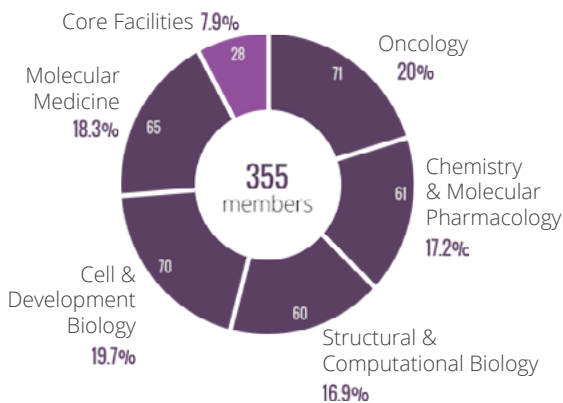
58.5%
Women

41.5%
Men

SCIENTIFIC STAFF



SCIENTIFIC STAFF by Research Programme



SCIENTIFIC STAFF by Professional Category



International



34%

International PhD Student Community



50%

International Postdoc Community



34 Countries

represented at IRB Barcelona

Events

700

Scientists took part in our scientific conferences

136

Seminars

Public Engagement and Science Education

1,402

Primary school students

1,817

Secondary school students

27

Teachers

1,836

Participants from the general public

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