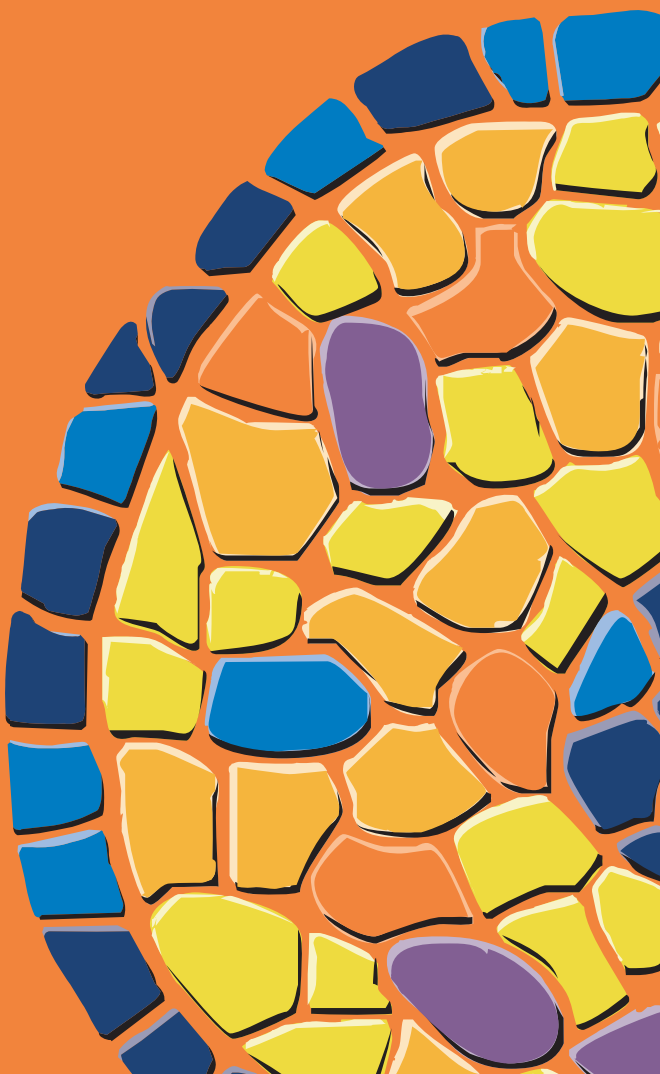
2008 Executive Summary

IRB BARCELONA

INSTITUTE FOR RESEARCH IN BIOMEDICINE



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2008 Executive Summary

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IRB Barcelona: building on a solid foundation

The third edition of IRB Barcelona's Annual Report comprises three volumes: the Scientific Report, which provides a detailed summary of the work carried out during the year by our research groups and core facilities, this Executive Summary, which includes facts and figures about the Institute, and Science Stories from IRB Barcelona, which highlights some of the research currently being conducted and takes a look at the people behind the science at IRB Barcelona. Through these documents, we hope to provide readers with a snapshot of the activities that have taken place over the past year at the Institute. At the same time, we hope they will take away a sense of this unique place and its importance in the landscape of biomedical research.

Not far from the IRB Barcelona premises, construction on the new phase of the Barcelona Science Park (PCB) continues at a steady pace. The PCB, which houses the IRB Barcelona laboratories, is undergoing a massive expansion and is set to grow from 36,800 m^2 to 90,000 m^2 by 2011. The large hole in the ground has been filled and a solid foundation has been laid for the many floors that will house new laboratories and services for the scientific community. The site is a physical testament to the major investment being made into research infrastructures in Barcelona, which is changing the landscape of the city and unleashing the potential for biomedical research in the region.

Something similar is happening at IRB Barcelona and 'construction' on the Institute forges ahead apace with that of its host. Three years have passed since IRB Barcelona was officially founded in 2005 and began its operations. The

foundations of the Institute have been laid and we are building upon them to consolidate IRB Barcelona as one of the foremost research centres worldwide. Over the past year, important steps have been taken by IRB Barcelona to fulfill each of its missions, which include promoting multidisciplinary research of excellence in biomedicine at the interface between structural biology, chemistry and biology, with a special focus on cancer; fostering collaborations with local, national and international research institutes and actively promoting the development of Barcelona as a biomedical cluster; providing a high-level training in biomedical sciences to members and visitors at all stages of their research careers; promoting innovation and technology transfer in the field of biomedicine; and actively engaging in an open dialogue with the public through a series of science and society and education activities.

The foundations of the Institute have been laid and we are building upon them to consolidate IRB Barcelona as one of the foremost research centres worldwide

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Attracting top scientific talent

Efforts to recruit some of the brightest minds in science from across the world continue. In 2008, Jens Lüders (Hannover, 1969) joined IRB Barcelona from Stanford University (USA) in January to lead a group within the Cell and Developmental Biology Programme. His research focus will be on understanding the molecular mechanisms behind microtubule organisation. Xavier Salvatella (Barcelona, 1972) was recruited from the University of Cambridge (UK), and began as a principal investigator in the Chemistry and Molecular Pharmacology Programme in July. He studies the structure and dynamics of biomacromolecules and how they relate to disease. Travis Stracker (Ohio, 1974), previously at The Memorial Sloan Kettering Cancer Center in New York (USA), was recruited to join the Oncology Programme and will start activities in early 2009. His group will focus on genomic instability and cancer and will investigate the role of DNA damage response in tumour suppression.

Serving science with core facilities

A few years ago laboratories often devoted themselves to the functions of just a few genes or molecules in a single model system; today's medically related projects typically involve monitoring the behaviour of the entire genome, in studies that shuttle from the computer, to the test tube, to model organisms and human tissues. No single laboratory can master all the techniques needed to pursue these questions, so we have established several new service units to provide our researchers with state-of-the-art facilities. In addition to the pre-existing facilities

dedicated to Functional Genomics, Mass Spectrometry, Protein Expression and Mouse Mutants, 2008 saw the addition of a Biostatistics and Bioinformatics Unit, led by David Rossell (Barcelona, 1977), recruited from the MD Anderson Cancer Center in Houston, Texas, and an Advanced Digital Microscopy Facility, run in conjunction with the PCB, and led by Julien Colombelli (Paris, 1977), recruited from the European Molecular Biology Laboratory in Heidelberg, Germany. These facilities widen an already considerable palette of platforms established and operated by the Barcelona Science Park and by the Scientific and Technical Services of the University of Barcelona.

Opening doors through collaboration

IRB Barcelona understands that no single institute can effectively tackle the complexities of the molecular life sciences on its own. In order to carry out research that will ultimately lead to benefits for human health, a multidisciplinary approach that draws on the knowledge and abilities of a variety of experts working in different fields is essential. Transforming knowledge into new tools and therapies will require new types of partnerships with research institutes, universities, clinical centres and industry. To this end, IRB Barcelona scientists participate in numerous scientific collaborations and networks, at the local, national and international levels. In addition, a growing number of strategic institutional alliances are being formed.

IRB Barcelona scientists have been highly successful in increasing research resources obtained through competitive grants and private funding

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The joint programme with the Barcelona Supercomputing Center (BSC), launched in 2007, continues on course with the establishment of the Experimental Bioinformatics Laboratory, a group run jointly by principal investigators from IRB Barcelona and the BSC. In addition, researchers from IRB Barcelona and the Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) have begun to plan regular joint meetings as part of the newly-created Institut d'Investigació Sanitària Clínic-IDIBAPS. The initiative aims to foster collaborations between scientists at basic and clinical research centers in order to promote translational research.

Attracting resources

In addition to the core funding provided by the Government of Catalonia (through the Ministry of Innovation, Universities and Business and the Ministry of Health), IRB Barcelona scientists have been highly successful in increasing research resources obtained through competitive grants and

private funding. In 2008, IRB Barcelona was granted the coordination of two new FP7 health projects by the European Commission and chosen as one of the main partners in four other EC-funded projects. IRB Barcelona researcher Eduard Batlle was also awarded in 2008 a starting grant by the European Research Council for his studies on colorectal cancer progression.

Substantial grants for research and related activities were also provided by philanthropic entities. The Banco Bilbao Vizcaya Argentaria Foundation extended and fortified their existing collaboration with IRB Barcelona to fund research activities in the Oncology Programme as well as sponsor Barcelona BioMed activities. The Marcelino Botín Foundation continues to support research groups in the Molecular Medicine and Structural and Computational Biology Programmes. La Caixa chose IRB Barcelona as one of four research institutes in Spain to receive special funding to recruit talented students to join their international PhD programmes. This initiative began with IRB Barcelona's 2008 call for applications, and was an overwhelming success.

In 2008, administrative structures were put in place to assist with grant activities at IRB Barcelona. A grants office began activities in November and will provide support to researchers and guide them through the process of applying for external funding.

An environment for innovation

While the majority of IRB Barcelona research is devoted to basic scientific questions, these areas have been a key source of innovation and new technologies over the past decades. That is most likely to happen in an atmosphere that encourages innovation and makes technology transfer easy for our scientists. In addition to the support offered by the Fundació Bosch i Gimpera, IRB Barcelona has set the groundwork for establishing its own Innovation and Strategic Projects Office, which will become active in early 2009.

Training future leaders: IRB Barcelona's PhD programme

The level of research and the collection of activities at IRB Barcelona provide a unique environment in which students from around the world can do research toward their degrees. Students profit from close mentoring and have access to a wide variety of scientific events, services and networks. The programme that we offer, which has been reinforced this year by the new 'La Caixa'/IRB Barcelona International PhD Programme, goes beyond the bench: PhD students at IRB Barcelona have an excellent opportunity to meet leading researchers in their respective fields through seminars and lectures. Monthly social gatherings, called 'cool-off sessions', provide a welcome opportunity for students from across the Institute to get to know one another in an informal setting. Students have also formed a council that will


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coordinate activities such as a student-run PhD symposium, which will take place in November 2009.

A programme for postdocs

While many funding programmes and incentives exist for researchers at early stages of their careers, and for more experienced scientists starting up their own groups, the needs of postdocs – a major driving force behind science of excellence – are often overlooked. After having consolidated our PhD Programme and achieved excellent results, our aim now is to draw on the strength of this example and enhance structures and resources for researchers at the next stage of their careers. IRB Barcelona provides an exciting and stimulating atmosphere for postdoctoral fellows. They carry out their projects in outstanding research laboratories and facilities working on a diverse range of topics in the biomedical sciences. Like our students, they have access to high-quality seminars, conferences and workshops, as well as to a range of services and networks. IRB Barcelona's goal is to provide an optimal scientific environment for researchers at this critical time in their career and to prepare them on their journey to take up positions as independent scientists in laboratories in Spain, Europe and across the world.

In 2008 we launched a call for Interdisciplinary Postdocs, offering positions for postdoctoral researchers to work on a project led by groups in two different research programmes. The four positions were successfully filled – 3 postdocs took up their positions in 2008, with the

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fourth to begin in 2009. In recognition that postdocs have specific needs in terms of training and career development support, we have begun to implement structures and initiatives that go beyond the bench.

Barcelona BioMed

Today's research is thoroughly international and we will only achieve our aims by staying well informed of world developments throughout the biomedical sciences and by collaborating with other institutes. One mechanism we have put into place is a series of scientific outreach activities called 'Barcelona BioMed'. The series consists of seminars, conferences, workshops and forums, all of which aim to provide an important platform for exchange on topics related to biomedicine among a variety of audiences.

Barcelona BioMed Seminars are weekly lectures where leading international scientists from different areas of the biomedical sciences present and discuss their results and ideas. These seminars allow IRB Barcelona researchers and the local scientific community to learn about the latest developments in the life sciences, and provide an opportunity for direct contact with each seminar speaker. In 2008, more than 100 seminars took place.

Barcelona BioMed Conferences are organised in collaboration with the BBVA Foundation, and are generously hosted at the Institut d'Estudis Catalans in the heart of downtown Barcelona. They provide a new, creative platform where leading researchers can meet and discuss recent breakthroughs in a wide range of fields. The unique formula for these meetings is to bring together a carefully selected group of participants in a think-tank atmosphere. Twenty speakers chosen from among the top international researchers in their field are joined by a limited number of participants for three days of intensive discussions on the state of the art and the future of their fields. Topics for Barcelona BioMed Conferences in 2008 included Targeting and Tinkering with Interaction Networks (April), Metastasis Genes and Functions (May) and Morphogenesis and Cell Behaviour (October).

Barcelona BioMed Conferences provide a new, creative platform where leading researchers can meet and discuss recent breakthroughs in a wide range of fields

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We believe that institutes that have the potential to change society need to discuss their research with the public and help prepare people for those changes. The Barcelona BioMed Forum series brings together members of our scientific community, scholars from other disciplines as well as members of the public for multidisciplinary debate about issues related to biomedical science with the ultimate goal of bringing science and society closer together. This year's Forum event, entitled 'From woman to woman: Practical advice on how to get and stay ahead in science' took a look at the reasons for which women leave science in disproportionately higher numbers than men during the later stages of their academic career and offered practical solutions to help individual women scientists overcome the gender bias and ensure that they have an equal chance at becoming top scientists. Proceedings from the event were published in a special issue of the journal of the Spanish Society for Biochemistry and Molecular Biology and in an IRB Barcelona publication entitled 'Breaking the Glass Ceiling: Proposals to Adjust the Role of Women in Science'.

Building the IRB Barcelona community

IRB Barcelona has directed special efforts at creating opportunities for exchange, both scientific and social. These include the publication of the Institute's quarterly newsletter, *In Vivo*, setting up resources in the Institute's intranet as well as several social activities, including the above-mentioned cool-off sessions, a football club, a Barcelona marathon team, and various social gatherings throughout the year.

2008 has been a year of consolidation and hard work and significant progress has been made in many areas. As the Institute continues to grow, our scientists and support staff look forward to scientific and organisational challenges to ensure that IRB Barcelona secures a prominent place in the landscape of international biomedical research centres.

Joan J Guinovart
Director

Joan Massagué
Adjunct Director

Scientific Summaries

- Cell and Developmental Biology Programme
- Structural and Computational Biology Programme
- Molecular Medicine Programme
- Chemistry and Molecular Pharmacology Programme
- Oncology Programme
- Core Facilities

Cell and Developmental Biology Programme

On a scale stretching from the size of single molecules up to a multicellular organism, the cell lies almost exactly in the middle, and it is the link between the two levels. By transforming information in its genome into proteins and other molecules, a cell knows when to divide, what shape to take on, and how it should behave to build a multicellular organism. Whether that body develops in a healthy way or suffers from disease can usually be traced back to what happens within cells.

The **Cell and Developmental Biology Programme** aims to reveal how these levels are linked by looking deeply into the cell to study how structures arise and contribute to the construction of an organism. Until about two decades ago, these questions were addressed in quite separate disciplines, but have since been drawn together into one which is showing rapid growth. Cell biologists are getting a handle on the processes that enable cells to create larger structures, and developmental biologists are now looking at the cellular mechanisms that underlie the growth of embryos.

Bringing these themes together requires multidisciplinary experimental approaches that stem from modern molecular biology, classical genetics, biochemistry, advanced microscopy and state-of-the-art genomic and proteomic methods. The groups explore topics that include how signals are passed within and between cells, what controls cell migration and intercalation, how boundaries form between tissues during development and how tissue growth is controlled.

Other themes include microtubule organisation, cell division in development and disease, epigenetic regulation and chromatin function, and how controlling the output of genes can be used for biomedical purposes. The research groups that form part of the Programme pursue these questions in several model organisms, among these yeast, *Drosophila*, frogs, mice and human parasites.

Within the nucleus: chromatin structure and function

No cell produces RNAs and proteins from all of its genes all of the time. Part of the reason for this is that the DNA in the nucleus is wrapped around proteins and other molecules in a form called chromatin. These molecules have a crucial role because they help pack a huge amount of DNA into the small space of the nucleus; another function is to make genes accessible (or inaccessible) to the machinery that transforms them into other types of molecules. **Ferran Azorín's lab** studies the molecular processes that structure chromatin and thus control its biological effects. The main question they work on addresses how large blocks of DNA are rendered inactive, also known as 'silencing', and how the cell keeps them that way. Several regions of DNA are almost permanently silenced; others are switched on and off to achieve particular developmental effects. Azorín and his colleagues study both types.

Signals that organise cells into body structures

Building a complex organism requires that cells specialise by changing the way they divide, their shape, and behaviour, such as when and where they migrate. These morphogenetic changes are coordinated by cues from the environment, for instance, molecules secreted by other cells. These must be interpreted properly inside the cell, which means passing information along a pathway of signalling molecules. The same signal may have distinct effects at different times and places in the body. Many of the pathways have been conserved over the course of evolution,

so studies of model organisms, such as the fruit fly, can provide insights into the development of humans and other animals. **Jordi Casanova's lab** focuses on this process using the trachea and the Torso receptor signalling pathway in flies as developmental models.

The basis of cell division

Every cell in our bodies arose when a parent cell divided. Cell division involves the perfect timing of multiple events, and how it happens depends on the context: division works differently in the cells of the early embryo, or as stem cells specialise into blood, neurons and hundreds of other cell types, or within a rapidly growing tumour. Combining genetics, molecular biology, and advanced *in vivo* microscopy, **Cayetano González's lab** follows a multidisciplinary approach to study cell division. As model systems they use *Drosophila* as well as cultured cells from vertebrates. Ongoing projects include the study of the mitotic spindle (an assembly of fibres which pulls chromosomes into two sets), the study of newly discovered proteins that make up structures called centrosomes, and models of cancer development in the fruit fly.

The microtubule cytoskeleton: a matter of organisation

Microtubules assemble the spindles that drive chromosome segregation during meiotic cell divisions leading to the production of egg and sperm, and provide sperm movement by building the flagellum. After fertilisation, microtubules are required for cell proliferation by assembling the mitotic spindle and allowing chromosome segregation and cell division. When cells differentiate, microtubules establish cell polarity, participate in the communication between cells, and are involved in cell migration. To carry out such diverse functions, microtubules are organised into highly ordered arrays of various sizes and shapes. Improper microtubule organisation is linked to cancer and developmental defects. To understand how cells organise their microtubule network, **Jens Lüders' lab** studies the molecular mechanisms that determine where and when microtubules are made. Using tissue cell culture and *Xenopus laevis* egg extract as model systems, the lab focuses on the identification and characterisation of microtubule assembly pathways and on the role of so-called microtubule organising centres, such as the centrosome.

Building limbs: signals, compartments and boundaries

In the embryo, complex structures such as limbs begin as groups of cells that are identical at first, but soon subdivide into smaller territories, called compartments. **Marco Milán's lab** takes advantage of nearly a century of genetic studies on the fruit fly to examine the signals that guide the development of *Drosophila* limbs. Past research has shown that compartments arise because of mechanisms that prevent different types of cells from mixing. This leads to subterritories and clear boundaries between tissues. Cells at the boundary lines secrete signalling molecules such as Wg/Wnt and Dpp/TGFβ, which guide the pattern development and growth of the entire limb. Milán and his colleagues aim to understand how these molecules control complex processes such as the generation of adult limbs with a size, shape and pattern specific to a species.

Gene translation and disease

To survive, cells have to transform information in their genomes into RNAs and then into proteins. Carrying out this latter step, called translation, requires a complicated network of molecules, the details of which scientists are now unravelling. Many interactions extend from the process of protein manufacturing to other regulatory pathways in cells. Imbalances caused by alterations of these interactions are at the root of a number of diseases, and are used by human pathogens during infection. **Lluís Ribas de Pouplana's lab** explores these interaction networks in human cells and in proto-

zoa that infect human beings. Another of the group's interests is the evolution of the gene translation machinery, which underwent significant changes with the emergence of eukaryotic cells such as yeast, plants, and animals. Ribas and his colleagues hope to get a better grasp of how these types of cells evolved by studying molecules related to translation.

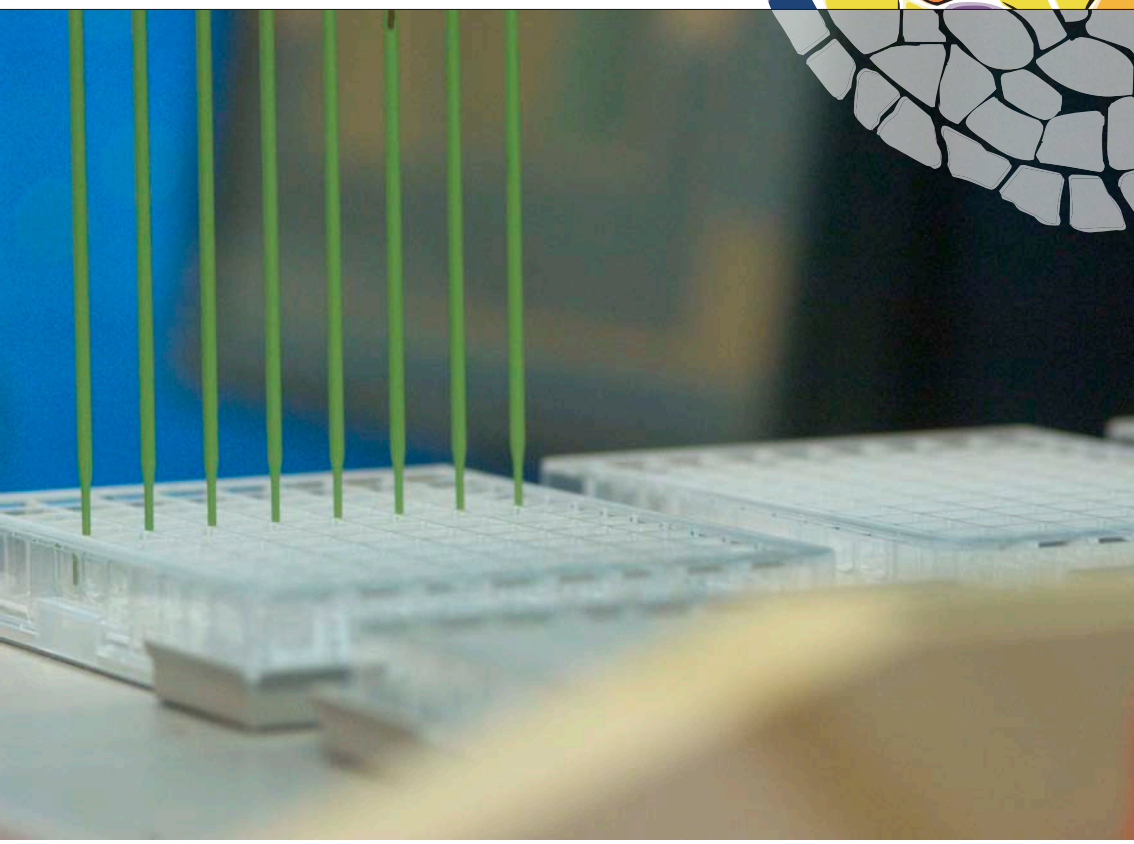
Building and rebuilding the brain

The development of the brain involves several steps: regions have to form, and different types of nerve cells have to develop, migrate to the right places, and properly wire themselves up to each other. They then have to respond properly to stimulation to permit memory and learning. Accomplishing these steps requires that cells activate specific genes at the right time, correctly interpret signalling molecules on the surfaces of other cells (or secreted by them), and respond in the right way. **Eduardo Soriano's lab** focuses on identifying new genes that contribute to these processes. Another topic addressed by the group is the difference between brain cells in the embryo and early childhood, which can develop and repair themselves, and those in the adult, which cannot. Insights into the mechanisms of early brain development may help scientists design new regenerative therapies to repair damage in the adult brain.

Structural and Computational Biology Programme

Physics and life meet at the level of single molecules, the behaviour of which is dictated by their shapes and chemical properties. DNA, RNA, proteins and other molecules interact and transform each other in a complex dance that creates living organisms; a detailed understanding of life requires linking the behaviour of these components to their structures. This knowledge is crucial in research into genetic diseases, which are often caused by small structural changes in molecules. It is also required to improve drugs and develop new ones. A drug is usually a small molecule that functions by plugging itself onto a protein and altering its behaviour. Without a structural picture of this interaction, it is generally impossible to know exactly how pharmaceutical agents work.

The **Structural and Computational Biology Programme** gathers a wide range of expertise to examine these aspects of life. Great advances over the last three decades in techniques like X-ray crystallography and NMR, for which state-of-the-art facilities are available at IRB Barcelona, have provided detailed structural maps of many key biological molecules. But many remain to be explored, and it has also been difficult to get a look at the internal workings of 'molecular machines' comprising many molecules. In many cases it is possible to deduce structural information about new proteins and their interactions by comparing their sequences with those of other known molecules. This approach requires the use of innovative computational tools, the potential of which has grown enormously since scientists have been able to draw on the wealth of information produced in genome projects.



Diagrams of the insides of machines

Genome-sequencing initiatives have provided a nearly complete parts list of the molecules that can be produced by an organism; new post-genomic techniques are steadily revealing which of them are used to build particular machines in the cell. What is missing, however, is a detailed view of the way the pieces snap together. **Patrick Aloy's lab** designs new bioinformatics methods to combine information from genomes (protein sequences) with the parts lists of machines (obtained through mass spectrometry and other techniques) and information about the interactions of single surfaces or parts (from X-ray and NMR studies) into diagrams of the inner construction of complexes. This information can be used to pinpoint specific weak points within a complex that can be targeted in experiments or in the design of new drugs.

Molecules that bind to DNA

Miquel Coll's lab applies several techniques to study how DNA behaves when it is linked to proteins and other molecules. Their main approach is the use of high-intensity X-rays to study molecules in a crystal form. One focus is how proteins link to DNA to control the activity of genes, which is a key step in most biological processes. Another is a phenomenon called horizontal gene transfer, in which cells carry DNA from one to another. This process requires complex mechanisms that can carry DNA across membranes. Other topics include the study of unique DNA structures and novel drugs that dock onto DNA rather than proteins.

Oxidative stress: membrane proteins

Proteins play key roles in most biological processes but seldom act alone. Often a molecule binds to dozens of other proteins, RNAs, or other molecules to perform a particular task. However, it has been difficult to observe details of the inner structures of proteins and in some cases even to discover where they work in the cell. To address these kinds of questions, **Ignasi Fita's lab** uses X-ray crystallography and cryo-electron microscopy to study the structural biology of the peroxisome, one of the smallest, membrane-bound, eukaryotic organelles. The group is particularly interested in complexes that play a role in disease processes and in the proteins that attach to the organelle's membrane. The group also collaborates in the study of the large eukaryotic ribonucleo protein complexes known as 'vaults' and in viruses bound to receptor proteins required for cell entry. Work is also performed on a diversity of enzymes, in particular related to oxidative stress.

NMR and protein purification

A powerful technique for studying three-dimensional structures is NMR, in which intense magnetic fields are applied to protein solutions. Pulse sequences are used to obtain signals that correlate to the distances between atoms, thereby providing a representative family of structures. **Maria Macias' lab** specialises in the use of this technique to study protein structures and their complexes as well as how they fold. Having set up an efficient collaboration process that helps other labs to determine protein structures, the group provides the protocols necessary to produce pure and labelled proteins at the milligram scale, helps and supervises the assignment of NMR data and provides modified protocols for structure determination in solution.

Mining data and modelling interactions

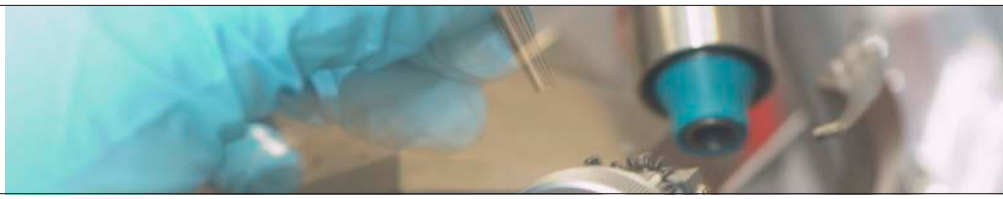
The interactions of proteins and other molecules happen so quickly and at such a small scale that they cannot be observed directly. They have to be studied through models which incorporate information from many sources. **Modesto Orozco's lab** combines a variety of methods —from the automatic mining of biological databases to the adaptation of mathematical calculations from classical dynamics and quantum chemistry— to develop such models in the computer. The long-term goal is to connect the smallest scale of life to the behaviour of cells and larger systems in organisms.

How interactions change structures

NMR is particularly useful in observing very quick changes that occur when proteins interact with each other or with small molecules such as drugs. **Miquel Pons' lab** applies this technique to study what happens during these interactions. A particularly intriguing case is that of intrinsically disordered proteins that hide their interaction potential in an apparent structural chaos. These complicated configurations can be untangled using statistical modelling of NMR and other experimental approaches. In drug development, the complexity of the protein world and protein-protein interactions is matched by the huge variety of chemical structures that constitute the so called chemical space, the size of which is comparable to the estimated number of stars in the universe. Pons and his colleagues develop new computational and NMR screening tools to explore chemical space for small molecules that can restructure protein complexes in a therapeutically promising way.

Integrating computation and experiments

Recent progress in genomics and high-throughput techniques has lead to an explosion of biological data, which in turn has provided a great opportunity to computationally predict, with high accuracy, the complex biological networks in living organisms. Implementation of computational methods in research, however, might raise questions about



the predictive capabilities of computer simulations, thereby making experimental validation required. The **Experimental Bioinformatics Laboratory (EBL)** was created in January 2008 as part of a collaborative programme between IRB Barcelona and the Barcelona Supercomputing Center aimed at pursuing new advances in computational biology. The EBL, managed by Montse Soler, is devoted to integrating experimental information into *in silico* models performed by computational biologists of the Structural and Computational Biology Programme. The lab's main subject areas include the genome mapping of nucleosome positions for a variety of yeast species, and mammalian cell lines to investigate factors that influence positioning in certain regions of the genome, such as DNA methylation. The EBL also analyses the regulatory potential of candidate promoter sequences along the human genome, and aims to describe pathological pathways at the molecular level by combining computational biology and interaction discovery techniques.

Molecular Medicine Programme

The biomedical sciences are standing on the threshold of a new era in medicine that may one day make it possible to cure cancer, diabetes, neurodegenerative conditions, and a variety of diseases that cannot be combated with vaccines, antibiotics, or existing drugs. Scientists have a wide range of new tools available to study the origins of disease and many new approaches to intervene in processes within cells. These tools have already revolutionised medical diagnostics, and the vision for the coming decades is to learn to apply them to directly manipulate the molecules responsible for diseases. The **Molecular Medicine Programme** seeks to further knowledge in these fields and find new ways to put discoveries to use.

The Programme boasts broad expertise in the fields of biochemistry, cell and molecular biology, cell signalling and regulation, genomics, genetics and immunology. Ongoing activities include the study of the molecular bases of diabetes, obesity, inflammation, metabolic syndrome and rare diseases, and research into new treatments for these pathologies.

The Programme also addresses the signalling pathways that control cellular processes, genome-wide investigations of disease processes, the biology of macrophage cells, the molecular basis of inherited aminoacidurias and the structural basis of membrane transporter function.

Understanding signals

Carme Caelles' lab studies the principles that govern cross-talk between some of the cell's most relevant signalling pathways in the context of anti-inflammation. Pro-inflammatory signals initiate the inflammatory response, thereby activating proteins called JNK. In contrast, well-known anti-inflammatory molecules, such as glucocorticoids, block JNK activation, which is crucial to their pharmacological activity. A second focus of the group is the study of signalling proteins of the NIMA family involved in the regulation of the cell division cycle.

Inflammation and macrophages

Antonio Celada's lab studies macrophages, a type of cell that plays a key role in inflammation. At an early stage, these cells have pro-inflammatory activity and eliminate microorganisms (bacteria, parasites, yeast, etc.) present at the site of inflammation. Later, they show anti-inflammatory activity and repair lesions. Macrophages also play a key role in chronic inflammatory processes, such as rheumatoid arthritis, and they induce the formation of blood vessels, thereby promoting the growth of cancer cells. For these reasons, knowledge about how these cells work and how to enhance their beneficial action and prevent their harmful effects is crucial. Celada and his colleagues study the signals induced by molecules that activate macrophages and the regulations of the genes that activate the multiple functions of these cells. Their goal is to find new therapeutic targets to design drugs that alter the activity of macrophages so that they can reproduce, differentiate, or become activated, or die and disappear.

Metabolic engineering and diabetes therapy

Excess glucose is stored in the liver and muscles in the form of glycogen, where it can be converted back to glucose again in situations of high energy demand. The process of synthesis and degradation of glycogen is disturbed in diabetes mellitus. Abnormal glycogen accumulation in neurons has also been described in several pathologies. **Joan Guinovart's lab** aims to further knowledge of glycogen metabolism and how it is altered in these diseases. The group has reported several significant differences in the way glycogen is processed in liver and muscle, which may be relevant to explain the defects observed in diabetes. It has also revealed that neurons have the machinery for glycogen synthesis but keep it blocked by three mechanisms, one of which involves the malin-laforin complex. The demise of the latter mechanism is associated with the neuronal degeneration observed in the devastating Lafora disease. The acquired knowledge will contribute to the development of strategies for the treatment of pathologies related to alterations in glycogen metabolism, such as diabetes mellitus, glycogenoses, Lafora disease and other neurodegenerative conditions. The lab is continuously working on the identification of anti-diabetic compounds. Of note is sodium tungstate, which has been proved to show anti-diabetic and anti-obesity properties. Phase 1 and Phase 2 clinical trials of this compound have been completed.

Supplying and resupplying the body with amino acids

The body needs a constant supply of amino acids to build proteins. Cells are able to produce many of the types of amino acids from simpler building blocks, but others must be obtained through food, and most are recovered through recycling. Obtaining these molecules means drawing them into the cell through the membrane. **Manuel Palacín's lab** studies this system and why it becomes defective in a set of diseases called primary inherited aminoacidurias (PIAs). In these conditions, the kidney, gut, and other tissues may be unable to absorb amino acids. Distinct systems are responsible for different types of amino acids; in some cases, the genes responsible for the defects are still unknown. Over the last 15 years, Palacín's group has identified several members of a new family of membrane proteins called HATs, which are responsible for the transport of several amino acids and are disrupted during PIA diseases. Currently, the lab is analysing the structures of HATs to gain a better understanding of how they carry out their transporter functions.

Insulin resistance and new strategies for diabetes therapies

Our increasingly sedentary lifestyle has created a growing epidemic of type 2 diabetes and associated problems such as obesity, hypertension, and other conditions that lead to increased morbidity and mortality. The combination of these disorders and insulin resistance, a condition known as metabolic syndrome, affects over 40% of people over 60. Recent studies suggest that some of these problems stem from common genetic and cellular mechanisms. **Antonio Zorzano's lab** seeks to identify genes responsible for the development of insulin resistance associated with obesity or type 2 diabetes. The group focuses on genes related to processes that occur in cellular structures called the mitochondria, in the processes that control these and other genes, and the identification of new signals that may be involved. Other goals include understanding how glucose is transported in cells, and identifying new compounds that might be effective in treating metabolic syndrome.

Chemistry and Molecular Pharmacology Programme

The development of novel drugs involves designing new molecules or modifying existing ones in order to achieve a particular effect on cells and organisms. In the past, pharmaceutical science was a matter of trial-and-error finding a substance that helped ease the symptoms of a disease, and then using chemistry to extract and improve it. Often this was done in complete ignorance of how substances really worked. Today scientists have discovered what many drugs do – usually they bind to a particular protein or molecular complex and change its shape or chemistry, thereby affecting how it interacts with other molecules. A wide variety of techniques are now available to study and manipulate these interactions, as well as to find new 'targets' – proteins which play a key role in the development of a disease, and whose manipulation might restore cells to a healthy state.

The **Chemistry and Molecular Pharmacology Programme** includes several types of expertise necessary to carry out this new approach to drug design. The goal is to identify targets, reveal their functions and the nature of their interactions with other molecules, and build or modify molecules that can influence their behaviour.

Researchers in this Programme synthesise a large variety of bioactive compounds, with special focus on nucleic acids, peptides, proteins, peptidomimetics - molecules that resemble or imitate natural peptides - and other chemical compounds. For these purposes, the groups use innovative methods such as enantioselective synthesis, solid-phase synthesis of libraries of bioactive compounds and multi-component reactions.

The ultimate goal is to create substances that might be useful as drugs or tools to study biological systems, and work focuses on studying how drug candidates interact with their targets. The main tools used are NMR, computer studies, and mass spectrometry.

Inventing new compounds

Research at **Fernando Albericio's lab** is based on a robust chemical platform designed to address medicinal chemistry projects with a special focus on cancer. The methodological subprojects have the main objective of feeding the chemistry platform, answering questions and solving problems that arise in research.

Marine ecosystems have demonstrated to be a wide source of biological and chemical biodiversity, which will inevitably lead to new potential drug candidates. The last decade has witnessed a dramatic increase in the number of preclinical lead compounds of diverse marine life entering human clinical trials. The evolution of marine natural products in the drug discovery field may help to identify future avenues that promise to be even more successful. During recent months, the first three marine products have arrived on the market, thereby demonstrating the 'proof-of-concept' that the marine ecosystem is a source of new pharmaceutical compounds.

One of the group's main research topics is the total synthesis of natural products from marine origin with new structures and important bioactivities. Compounds with peptidic or poliheterocyclic structures or a combination of peptide-heterocycle systems are part of the group's research efforts. Another relevant topic addressed is the optimisation of the compounds bioactivity or properties through the preparation of libraries based on natural products. The group's methodological programme aims to facilitate biomedical projects and to answer specific questions that arise in research. The lab also

plans to develop methods to prepare innovative scaffolds and building blocks that, once properly decorated, will be used in medicinal chemistry projects. The implementation of these synthetic goals seeks efficiency, atom economy and structural diversity. In this context, multicomponent reactions are the first option to explore in order to reach these goals. Given that a considerable part of the group's research programmes is based on the use of solid-phase methodology, the lab plans to continue work on the development of resins, handles, coupling reagents and strategies, which will later be applied to the synthesis of drug candidates.

Building artificial DNAs and RNAs

The successful development of the vast majority of scientific projects depends on the capacity of researchers to create small, artificial DNA or RNA molecules. **Ramon Eritja's lab** synthesizes these molecules from their subunits, called nucleotides. The group's activities range from the preparation of complex DNA and RNA molecules as potential drugs to the use of DNA structures for the construction of nanoscale circuits. Recent successful projects include the discovery of non-natural bases that stabilise unusual structures of nucleic acids that may be helpful to design a new class of drugs. A large effort has also been made in the design of new RNA derivatives to control gene expression by the mechanism of RNA interference. The group also pursues the use of nucleic acid derivatives in the organisation of molecules and materials on surfaces that may be of interest on the development of new bioanalytical devices.

Designing and delivering drugs

The ultimate aim of 'rational' drug design is to study the surface of any part of any protein and design a highly efficient, selective ligand – a molecular 'plug' – that will change the protein's behaviour in a desired way. This is still a dream, but **Ernest Giralt's lab** is actively pursuing it by addressing the principles that govern the way molecules recognize and bind to each other. The lab focuses on several issues that have been difficult to resolve: cellular uptake of foreign substances (drugs), ways to break up clumps of proteins that form in Alzheimer's disease and several other neurodegenerative diseases, and the delivery of drugs across the blood-brain barrier. The group has been working to improve the methods required to address these questions: obtaining structural information from NMR, improvements in solid-phase peptide synthesis (a way of artificially designing proteins that do not require cells to produce the molecules) and improving computer algorithms to assist drug discovery.

Developing synthetic methods for bioactive compounds

Antoni Riera's lab develops new synthetic methods required at various stages of drug development. The group has a special focus on asymmetric synthesis. This line of research is crucial because standard processes that synthesise small molecules produce both enantiomers ('left- and right-handed' versions – in other words, molecules that have the same constitution but are mirror images of each other). The reactions of biological molecules to the two types of isomers may differ greatly, so it is crucial to produce and purify only the desired version. Efforts are also devoted to finding ways to scale up synthetic processes of compounds of therapeutic interest, and helping to prepare chemical libraries that can be used for biological screening.

Looking for new bioactive molecules

The preparation of new chemical entities is the first and perhaps the most important step in the drug discovery process. The methodology to design and prepare such compounds in amounts and purities suitable for practical use is crucial for any biomedical project. **Màrius Rubiralta's lab** works on the development of technologies aimed to obtain key bioactive compounds in a pure form. The group develops synthetic procedures to achieve new peptide-like molecules or heterocyclic-containing compounds, structures frequently found in drugs, and also to separate the enantiomers from the

molecules obtained. The group is involved in the description of new multicomponent reactions based on heterocycles, and uses some of the synthetic constructs as a tool in the separation of enantiomers and other products of high-added value by several chromatographic and related technologies. The lab also tackles fundamental procedures and methodological research in this latter field.

Keeping a close eye on misbehaving proteins

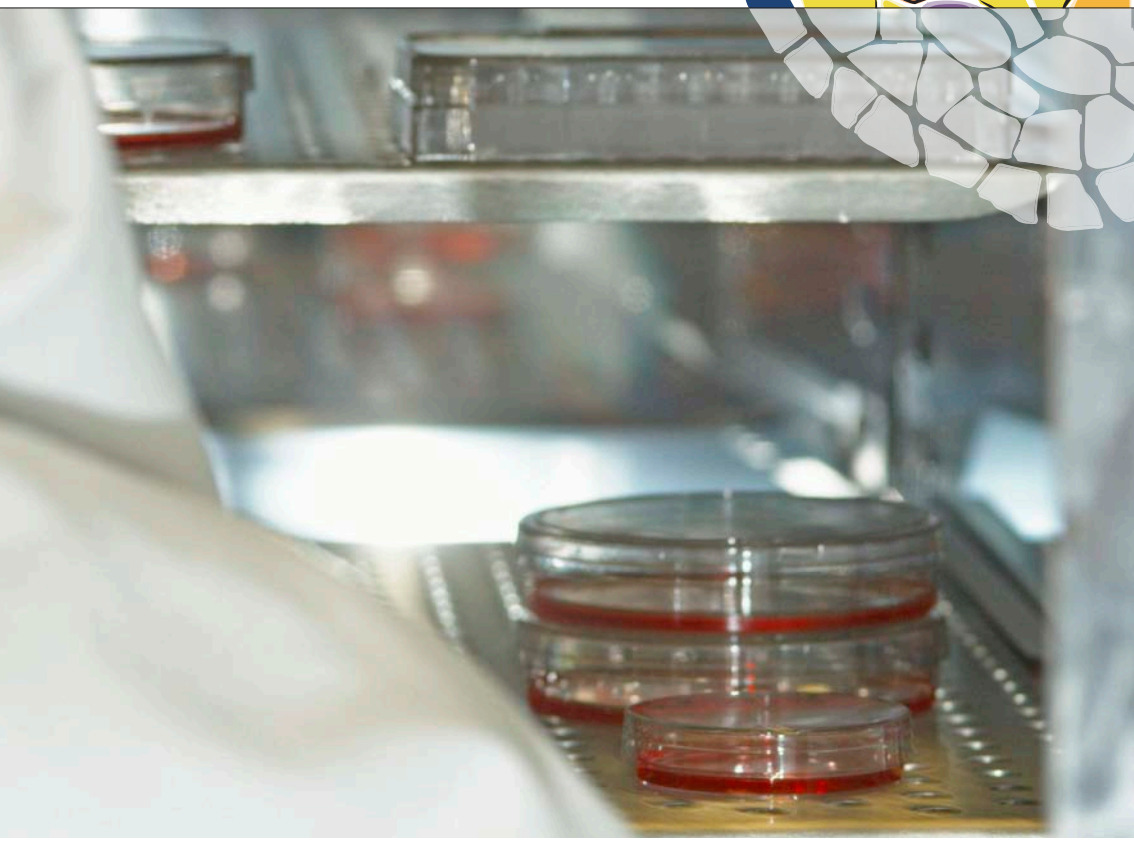
The research carried out in **Xavier Salvatella's lab** aims to describe, in a very detailed manner, the motions of proteins and their involvement in diseases where insoluble protein aggregates accumulate in the tissue of patients such as those with Alzheimer's disease, the systemic amyloidoses and the transmissible spongiform encephalopathies (Creutzfeldt–Jakob disease). Specific questions that the lab is currently addressing include characterising the structural properties of disordered proteins involved in such diseases with innovative methods of analysis that use experimental results to bias computer simulations, as well as establishing structure-toxicity relationships in the aggregates that these proteins form in the tissue of patients. A high resolution description of the events that lead to the onset of disease provides opportunities for the development of novel therapeutic approaches, which is the long-term goal of the group.

Oncology Programme

Cancers arise when fundamental processes that control the reproduction, differentiation, and behaviour of cells go astray. The Oncology Programme aims to improve the prognosis, prevention and treatment of cancer by studying the basic principles of development of this disease.

Research groups in the Programme focus on diverse aspects of how tumours arise and develop. There is a special emphasis on the mechanisms that transform benign tumours into malignant ones, on the relationship between stem cells and cancer, and on the identification of programmes that cause certain types of cancer cells to produce tissue-specific metastasis.

Groups in the Programme need strong ties to the clinical side of cancer research. Collaboration agreements with several oncology and pathology units of hospitals in the metropolitan area of Barcelona will facilitate the translation of basic research into clinically relevant diagnostic and therapeutic tools.



The stages of colorectal cancer

Colorectal cancer is one of the leading causes of death by cancer worldwide. Although most colorectal tumours develop as benign lesions, a small proportion progress to malignant stages because their cells have accumulated mutations in genes that promote cancer or in genes that normally suppress the development of tumours. The final and deadliest step in the development of the disease is the migration of colorectal cancer cells to other organs, where they begin to build new tumours. **Eduard Batlle's lab** studies the initiation of colorectal cancer and its progression from the early stages to the formation of aggressive tumours. They make use of cell and animal models that mimic the human version of this devastating disease. The ultimate goal is to obtain information that permits the design of new therapeutic and diagnostic tools.

Elena Sancho's lab focuses on the cell signalling pathways involved in the different stages of the development of colorectal cancers. The development of a full-blown malignant tumour occurs over a period of several years and seems to follow a precise series of events: particular mutations in cancer-related genes occur in a specific order. The lab is particularly interested in studying the effects of mutations in signalling pathways that affect not only cancer cells but also the tumour microenvironment. Close collaborations with clinical researchers have given the lab access to specimens of colorectal cancer at different stages of the malignancy, thereby permitting an analysis of the cell populations comprising the tumours in each stage of the disease.

The ultimate goal is also to obtain information that permits the design of new therapeutic and diagnostic tools.

The Tumoural Metastasis Laboratory (MetLab)

Intricate signalling networks within cells control their division, differentiation, movement, organisation and death. Cancer cells disobey these signals during tumour progression and metastasis, which is the final step in 90% of all fatal cancers. The main interest of **MetLab**, led by Roger Gomis, is to identify sets of genes and their functions whose abuse by tumour cells make them instruments for metastasis. These functions are responsible for allowing metastatic cells to escape the primary tumour site and enter into the circulation, invade distant organs and finally, form microscopic colonies in these tissues. By means of gene activation or inactivation the group functionally validates pro-metastatic gene candidates. Some of their candidate genes have recently been shown to be affected in tumour samples from patients. By studying how combinations of biological changes facilitate vital organ invasion by metastatic cells, the MetLab will be able to efficiently tackle the disease by using drug combinations against the putative therapeutic targets.

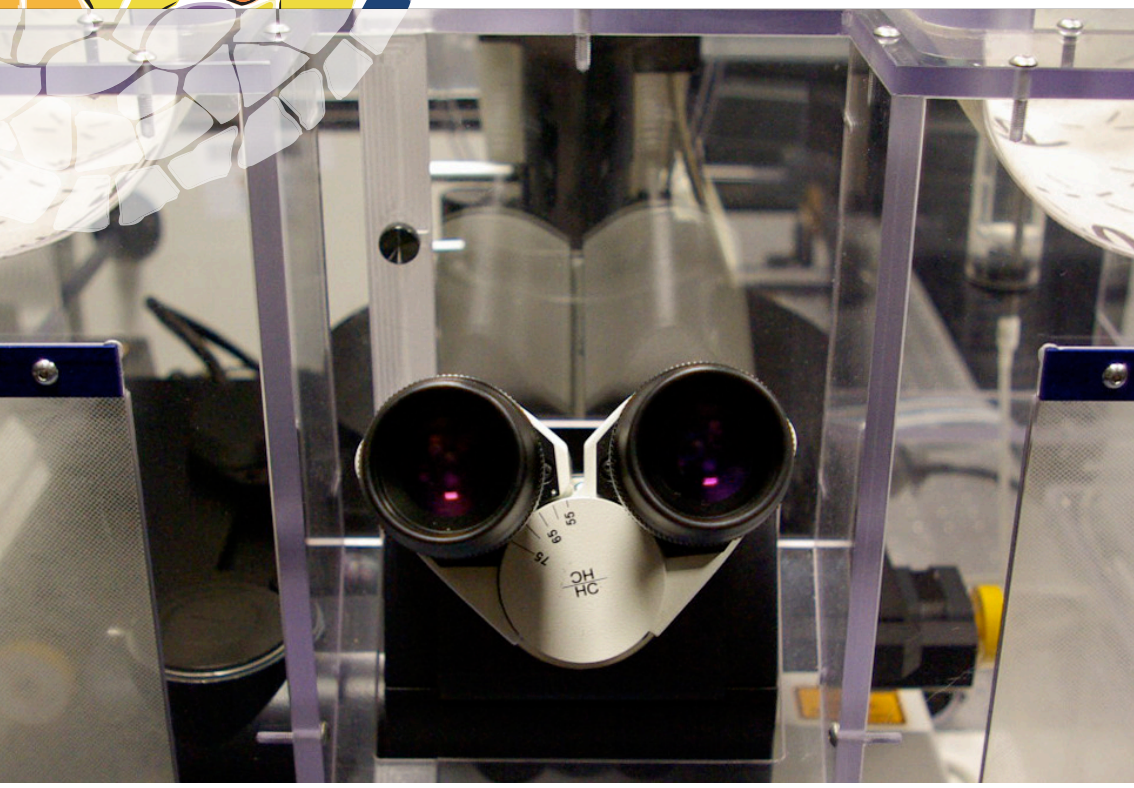
Core Facilities

The research carried out at IRB Barcelona is supported by a wide range of **Core Facilities** that provide technical assistance as well as access to cutting-edge biomedical resources, instrumentation and services aimed to speed up scientific results and conclusions.

IRB Barcelona Core Facilities are equipped with the latest state-of-the-art tools for research, and offer an extensive number of services and techniques in advanced digital microscopy, biostatistics, bioinformatics, functional genomics, mass spectrometry, protein expression and mouse models of disease.

Services provided to IRB Barcelona researchers include cutting-edge genomic techniques to interrogate or alter genes on a genome-wide level, an open-access system to state-of-the-art light microscopy instruments, spectromic techniques to identify a broad range of biological species, software tools to facilitate the interpretation of experimental results, high-throughput protein expression activities to run many parallel variations of an experiment, and development and production of genetically modified mice for research purposes.

These shared facilities are located in the Barcelona Science Park near the IRB Barcelona laboratories to ensure research sinergies and efficiency. In addition to its own Core Facilities, the biomedical research undertaken at IRB Barcelona is also supported by platforms and facilities of the Barcelona Science Park, as well as technical services of the University of Barcelona.



Beyond the limits of conventional light microscopy

The simultaneous advent of fluorescent proteins and lasers has revolutionised light microscopy by allowing tagged-protein specific localisation. Confocal microscopy has tremendously developed to offer the current state-of-the-art instruments, which deliver 3D imaging for high resolution spatial localisation, spectral resolution for multiple fluorophores imaging, highly automatic acquisition for fast live imaging, and multipositioning for medium and high content screening. Beyond mapping multicolour labels in 3D, light microscopy has also accessed the domain of protein dynamics and interactions with techniques of direct laser manipulation to measure biophysical parameters like diffusion, binding and unbinding, interactions, and turnover. Other direct photomanipulation available are photoactivation, which gives the possibility to switch fluorophores at will in a desired location and at a desired time point, or laser surgery for the manipulation or disruption of organs, cells, or even subcellular organelles. Emerging techniques offer the possibility to optically resolve fine fluorescent structures down to several tens of nanometers well below the classical diffraction limit of an optical microscope. On the other hand, a new generation of microscopes based on side-illumination is challenging traditional confocal microscopy by allowing one to perform, with high resolution and contrast, full volume live imaging of large specimens with a size of up to several millimetres.

The **Advanced Digital Microscopy (ADM) Core Facility**, managed by Julien Colombelli, aims to offer access and support to state-of-the-art instruments, from automatic spectral confocal microscopy to emerging techniques for cell manipulation and imaging. The ADM started its activities in 2008 in a new laboratory which offers IRB Barcelona

researchers a wide range of facilities required to perform all the steps of digital imaging, including sample preparation, image acquisition, analysis and interpretation. Optical sectioning in fluorescence is available with spectral confocal, spinning disk and multiphoton microscope systems. Other specific techniques are also being set, such as TIRF, laser nanosurgery, microinjection and automatic widefield fluorescence microscopy. To fill the gap between commercially available systems and cutting-edge research progress, the ADM will also invest efforts in developing instruments in close collaboration with IRB Barcelona research groups such as combined widefield FRAP, laser surgery and photoactivation. The facility staff will also provide teaching activities in advanced microscopy and imaging processing techniques.

Turning data into information

The last decade has popularised a number of technologies that are capable of generating vast amounts of data. High-throughput genomic or proteomic experiments, for instance, produce data from as few as hundreds up to millions of genes or proteins. Nowadays researchers face not only the challenge of obtaining relevant scientific data, but also of extracting as much valuable information as possible. Statistics is the science that transforms data into information. It provides a disciplined and scientifically sound framework to test hypotheses and to learn about the systems and processes that generate biomedical data. The experimental design theory also guides researchers as to the best way to conduct experiments in order to reach their goals.

The **Biostatistics and Bioinformatics Unit**, managed by David Rossell, assists scientists in the design and analysis of biomedical experiments through cutting-edge software tools and innovative methodology. The unit is committed to offering IRB Barcelona research groups a competitive advantage by developing tailored solutions to specific problems. These solutions, which include methodological and software development, are aimed to improve both research quality and speed.

Studying the entire genome in a single experiment

During the last decade, molecular biology has developed from a gene-by-gene analysis into a more comprehensive approach to study regulatory networks involving from dozens to hundreds of interacting partners. For successful performance in this field, researchers require an increasing number of tools to either analyse or alter genes on a genome-wide level. The **Functional Genomics Core Facility**, managed by Herbert Auer, provides state-of-the-art genomic resources for the IRB Barcelona research community and for external organisations. These tools fall into two categories:

- *Genome wide analysis of transcription, DNA polymorphisms, and chromatin immunoprecipitation (ChIP-chip)*. These analyses are performed using microarrays produced by Affymetrix. For all of these analytical methods, the Functional Genomics Core Facility provides a complete service, including initial consultation during the design of the project, quality control of starting material, sample and array processing, initial data analysis, data interpretation, and validation by real-time-PCR.
- *Knockdown of gene expression by shRNAs*. For knockdown of gene expression, the Facility provides a human shRNA library (Sigma), containing approximately 75,000 clones that cover the majority of all known transcripts.

New lights in mass spectrometry

Mass spectrometry has become one of the most important tools in biochemical sciences and has a broad application domain, ranging from small molecule analysis to protein characterisation. Because of this versatility, mass spectrometry is the technology many scientists are turning to. Although still in a relatively new stage, mass spectrometry can now provide an exclusive molecular vantage point for the interrogation of dynamic and non-covalent assemblies that cannot be analysed by other means, thereby shedding new light on the topology of high mass entities that are complicated by weak or fleeting interactions.

The **Mass Spectrometry Core Facility**, managed by Marta Vilaseca, provides modern chromatographic and spectrometric tools to IRB Barcelona researchers for the identification and characterisation of a broad range of biological species. The facility is working to implement intact protein analysis (Top-Down approach) for complete characterisation, and to develop bottom-up proteomic techniques for protein quantitation and determination of post-translational modifications. Moreover, the Facility is using the novel ion mobility-MS coupling to study the macromolecular structure and conformation of proteins and nucleic acid, and their complexes.

Genetically modified mice as research tools

Genetically altered mice represent one of the most powerful models of human disease and development available to the research community. The purpose of the **Mouse Mutant Core Facility** is to facilitate access to this technology. This may entail obtaining pre-generated mice, modified embryonic stem (ES) cells, gene targeting vectors from various public resources or the generation of *de novo* models, for use by the IRB Barcelona research community. The Facility aims to provide a full 'concept to mouse' service and is involved in all stages of development and production of genetically modified mice, from assistance with design and construction of the transgene or gene-targeting vector, and production of genetically modified mouse ES cells, through to injection of purified DNA or ES cells into pre-implantation embryos. An important aspect of the work performed by this service is the adaptation and improvement of current technologies to both increase the efficiency of production and to provide more sophisticated models.

Solving protein challenges the high-throughput way

Traditionally researchers tackle a particular problem with a protein in an iterative process of trial and re-design that can potentially be time-consuming and costly. In contrast, the **Protein Expression Core Facility** concentrates on delivering high-throughput activities where many variations of an experiment (*eg*, truncations or mutations of proteins) are run in parallel. This capacity to perform large numbers (generally up to 96) of experimental variations on a theme in parallel can significantly decrease the time taken to solve a particular protein-related problem, thus bringing experiments to faster conclusions and, more importantly, leading to rapid publication of data. In addition to the time savings offered by high-throughput methods, they are also generally considered economical and can significantly reduce project and laboratory costs.

The Facility, managed by Nick Berrow, has recently issued a first call for projects to IRB Barcelona researchers to use the HTP cloning and *E. coli* expression screening services, and screening in other hosts such as mammalian cells, insect cells or yeasts will be implemented shortly. The facility also plans to offer many high quality reagents including aliquots of competent bacteriophage-resistant, cloning and expression strains of *E. coli*, specialised expression media, and cloning reagents for use by individual researchers.

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Board of Trustees

The Board of Trustees, IRB Barcelona's governing body, consists of 11 members and is chaired by the Minister of Innovation, Universities and Business of the Government of Catalonia. The Board meets twice a year and is responsible for overseeing the Institute's activities, approving the operating funds and ensuring that the annual research goals are met.

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Josep Huguet i Biosca

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First Vicepresident

Marina Geli i Fàbrega

Minister of the Department of Health, Government of Catalonia

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Rector of the University of Barcelona (November 2008–present)

Josep Samitier i Martí

Acting Rector of the University of Barcelona (April 2008–November 2008)

Màrius Rubiralta i Alcáñiz

Rector of the University of Barcelona (October 2005–April 2008)

Members

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General Director for Research of the Department of Innovation, Universities and Business, Government of Catalonia

Joan Roca Acín

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Director of the Research Centres Programme, Department of Health, Government of Catalonia (October 2005- September 2008)

Carme Verdaguer i Montanyà

Director of the Innovation Centre, Bosch i Gimpera Foundation,

Josep Samitier Martí

Pro-rector of Science Policy, University of Barcelona (January 2007-April 2008)

Fernando Albericio i Palomera

General Director, Barcelona Science Park

Roser Artal Rocafort

Manager, Barcelona Science Park

Executive Board

The main responsibilities of the Executive Board are to oversee the Institute's management tasks, to promote research activities, and to ensure that the functions delegated by the Board of Trustees are executed. The Board is currently presided by the Director of the Research Centres Programme of the Department of Health of the Government of Catalonia, and its members are elected for a period of four years.

President

José Jerónimo Navas Palacios

Director of the Research Centres Programme, Department of Health, Government of Catalonia (October 2005-September 2008)

Members

Ramon Moreno Amich

General Director for Research of the Department of Innovation, Universities and Business, Government of Catalonia

Josep Samitier Martí

Pro-rector for Innovation and International Research Programmes and Acting Rector of the University of Barcelona (January 2007-November 2008)

Other Participants

Fernando Albericio Palomera

General Director, Barcelona Science Park

Joan J Guinovart Cirera

Director, IRB Barcelona

Margarida Corominas Bosch

Managing Director, IRB Barcelona

External Advisory Board

Comprised of a panel of 15 distinguished experts in the field of biomedicine, the External Advisory Board of IRB Barcelona is responsible for providing strategic guidance and regularly assessing the scientific work carried out by researchers at the Institute.

Members

Hans Clevers
The Netherlands Institute of Developmental Biology, Utrecht, The Netherlands

Michael Czech
Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, USA

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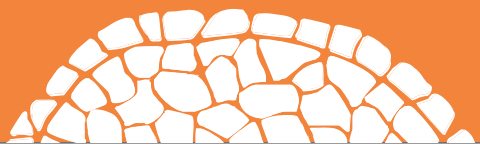

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Funding Sources

The majority of core funding for IRB Barcelona research activities in 2008 was received from the Government of Catalonia through the Ministry of Innovation, Universities and Business, and the Ministry of Health. The Institute also received additional funding through competitive grants obtained, among others, from the Spanish Ministry of Science and Innovation and the European Union, through FEDER funds and the Seventh Framework Programme.

Other entitites that contributed by funding IRB Barcelona scientists through research contracts were the University of Barcelona, the Catalan Institution for Research and Advanced Studies (ICREA), the Spanish National Research Council (CSIC) and several CIBER networks.

Core Funding

Generalitat de Catalunya

Other Funding Sources

GOBIERNO DE ESPAÑA
MINISTERIO DE CIENCIA E INNOVACIÓN

EUROPEAN REGIONAL DEVELOPMENT FUND

Scientific Output Summary

Scientific Publications

Researchers at IRB Barcelona published a total of 159 scientific articles in 2008. From these, 55 were international joint collaborations with partners from industry and academia.

Below is a list of selected publications, representative of the research conducted at IRB Barcelona in 2008.

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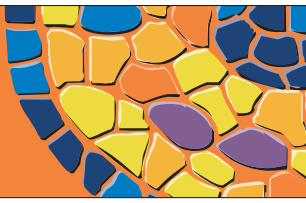

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Stein A, Panjkovich A and Aloy P . 3did update: domain-domain and peptide-mediated interactions of known 3D structure. *Nucleic Acids Res,* **37**, D300-04 (2008)

The BioMoby Consortium, including Orozco M. Interoperability with Moby 1.0--it's better than sharing your toothbrush! *Brief Bioinform,* **9**(3), 220-31 (2008)

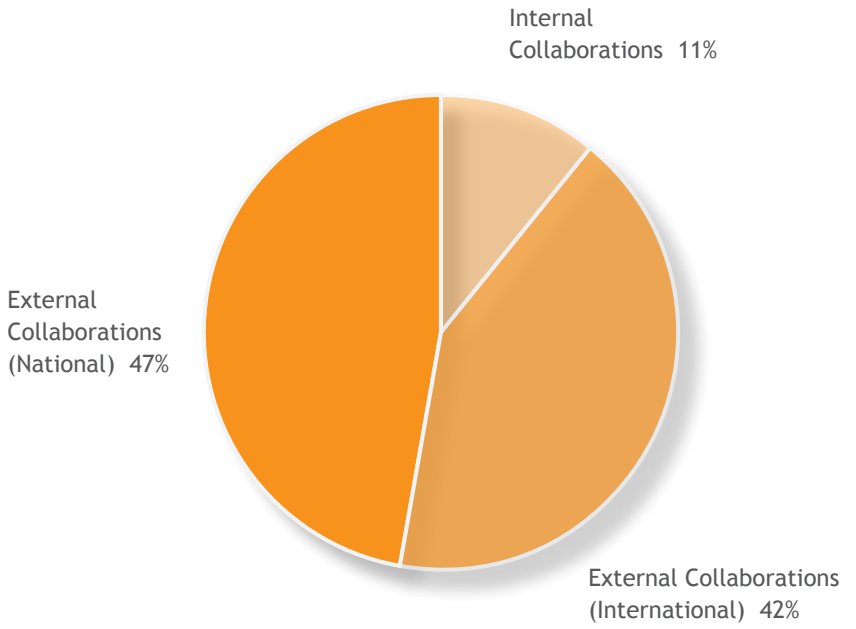
Valledor AF, Arpa L, Sánchez-Tilló E, Comalada M, Casals C, Xaus J, Caelles C, Lloberas J and Celada A. IFN-{gamma}-mediated inhibition of MAPK phosphatase expression results in prolonged MAPK activity in response to M-CSF and inhibition of proliferation. *Blood,* **112**(8), 3274-82 (2008)

Valledor AF, Sánchez-Tilló E, Arpa L, Park JM, Caelles C, Lloberas J and Celada A. Selective roles of MAPKs during the macrophage response to IFN-gamma. *J Immunol*, **180**(7), 4523-29 (2008)

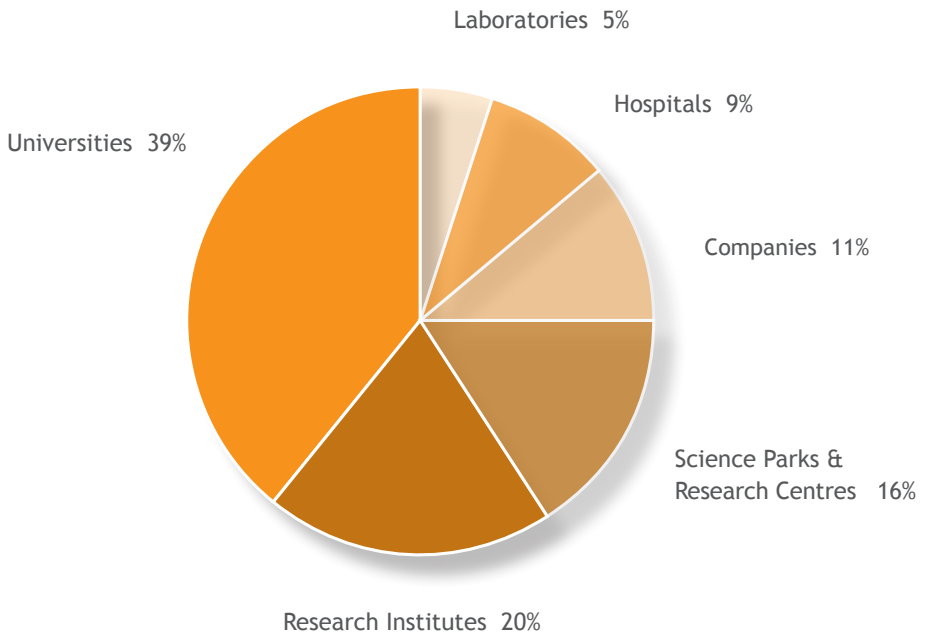
Research Collaborations

IRB Barcelona researchers participated in a total of 190 external collaborations involving national and international partners from industry and academia. Researchers also strengthened joint work among the Institute's research programmes through a further 26 internal collaborations.

Type of Collaborations



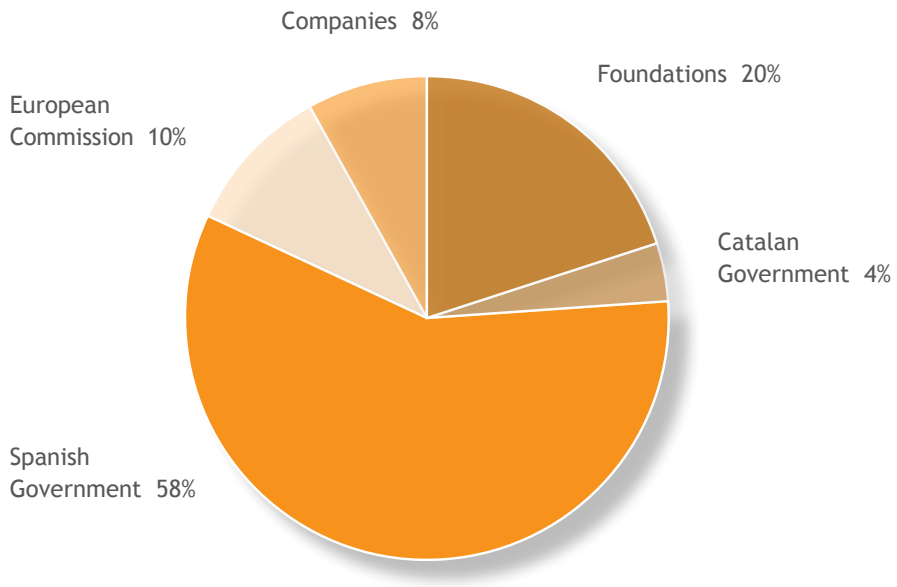
External Collaborations by Sector



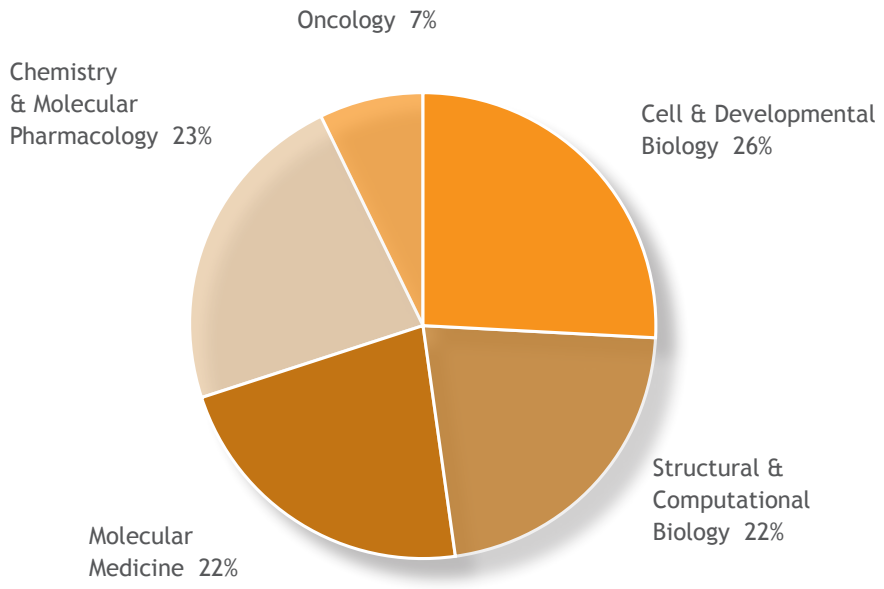
Research Projects and Networks

During 2008, IRB Barcelona researchers participated in a total of 138 national and international research projects and networks. The Institute was chosen by the European Commission to coordinate two European health projects within the 7th Framework Programme. IRB Barcelona researcher Eduard Batlle was also awarded in 2008 a starting grant by the European Research Council to study colorectal cancer progression.

Funding Sources



Research Areas



Research Grants, Networks and Personnel Grants

Research activities at IRB Barcelona were funded by the Government of Catalonia, the Spanish Ministry of Science and Innovation, the European Commission and public and private foundations, institutions and companies. Funding obtained by IRB Barcelona researchers through research grants, networks and personnel grants in 2008 amounted to **€10,246,788**. The following list comprises the institutions that contributed to IRB Barcelona funding through research grants.

Spanish Ministry of Science and Innovation
European Commission
'Marcelino Botin' Foundation
'La Marató de TV3' Foundation
'La Caixa' Foundation
Agency for Administration of University and Research Grants (AGAUR)
'Banco Bilbao Vizcaya Argentaria' Foundation
OncoStem Pharma
Spanish Association Against Cancer (AECC)
Almirall Laboratories
Ferrer Group International
European Science Foundation (ESF)
Spanish Agency for International Cooperation (AECID)
Sylentis
Spanish Foundation for AIDS Research and Prevention (FIPSE)
'Genoma España' Foundation
Palau Pharma
Era Biotech
European Molecular Biology Organization (EMBO)
Ipsen Pharma
Affinity Petcare

The Catalan Institution for Research and Advanced Studies (ICREA) and several research networks (CIBERDEM, CIBERER and CIBERNED) also contributed by funding IRB Barcelona scientists through research contracts.

IRB Barcelona thanks the following private donors:

Dolors Barchino Ricarte, Montserrat Gallofré Bernat, Marta Luz Adalid, Francina Pons Pifarré, Josefina Porras González, Marta Prous (and family) Vilaseca, Vallnord SA.

PhD Theses

The year 2008 saw the launch of a series of new initiatives aimed to provide training and strengthen ties among the more than 150 PhD students doing their practical work at IRB Barcelona. The new initiatives included the creation of an official Student Council to represent the community, a system of lab rotations to promote multidisciplinary interaction among students, the establishment of thesis advisory committees, a five-day introductory course for the newly arriving PhD students, and the launch of a planning group run by students to organise the first IRB Barcelona PhD student symposium, scheduled to take place in November 2009.

During 2008, a total of 27 PhD students successfully defended their theses upon completion of their research project in an IRB Barcelona laboratory.

Activació gènica per la via de Torso i el seu antagonisme amb els mecanismes de repressió transcripcional de la línea germinal a *Drosophila*
José Manuel de la Heras Chanes, University of Barcelona (2008)
Supervisor: Jordi Casanova

Caracterització de la proteïna tirosina quinasa citoplasmàtica Ack1 al sistema nerviós central
Anna La Torre i Vila, University of Barcelona (2008)
Supervisors: Eduardo Soriano García and Jesús Ureña

Caracterització de la proteïna dSAP18 a *Drosophila melanogaster*
Elisabet Costa Cros, University of Barcelona (2008)
Supervisor: Maria Lluïsa Espinàs

Characterisation of the methionyl-tRNA synthetase from mycoplasma penetrans
Thomas Jones, University of Barcelona (2008)
Supervisor: Lluis Ribas de Pouplana

Diseño, síntesis y estructura de dominios helicoidales. Influencia de la introducción de aminoácidos D
Carmen Giovana Granados, University of Barcelona (2008)
Supervisor: Ernest Giralt

Estudio de métodos sintéticos para la preparación de productos naturales con azoles concatenados
Delia Hernández-Romero, University of Barcelona (2008)
Supervisors: Fernando Albericio and Mercédez Álvarez

Estudio de resinas para fase sólida y su aplicación a la síntesis de péptidos antitumorales
Fayna García, University of Barcelona (2008)
Supervisor: Fernando Albericio

Estudio teórico de interacciones moleculares. Aplicaciones al diseño de fármacos
Jordi Muñoz, University of Barcelona (2008)
Supervisor: Modesto Orozco

Estudio teórico del transporte de ligandos en proteínas y de la afinidad ligando receptor
Axel Bidon-Chanal, University of Barcelona (2008)
Supervisor: Modesto Orozco

Estudios de mecanismos de interacción macromolecular
Alberto Pérez, University of Barcelona (2008)
Supervisor: Modesto Orozco

Evolutionary algorithms and *de novo* peptide design
Ignasi Belda, Universitat Politècnica de Catalunya (2008)
Supervisor: Ernest Giralt

Genetic injury and macrophages. Implications in aging and inflammation
Sebastián Muñoz, University of Barcelona (2008)
Supervisors: Antonio Celada and Jorge Lloberas

Identificació de nous elements de la via de senyalització del receptor Torso de *Drosophila melanogaster*
Gemma Ventura, University of Barcelona (2008)
Supervisors: Jordi Casanova and Marc Furriols

Identificación y caracterización de un nuevo mecanismo regulador de la síntesis de glucógeno y su deficiencia en la enfermedad de Lafora
David Vilchez, University of Barcelona (2008)
Supervisor: Joan J Guinovart

La flexibilidad en los ácidos nucleicos. Un estudio de dinámica molecular
Agnes Noy, University of Barcelona (2008)
Supervisor: Modesto Orozco

Les propietats físiques de l'ADN en escala genòmica
Josep Ramon Goñi, University of Barcelona (2008)
Supervisor: Modesto Orozco

Molecular mechanisms that regulate the classical and alternative activation of macrophages
Luis Arpa, University of Barcelona (2008)
Supervisors: Antonio Celada and Annabel Fernández

New protecting groups for the synthesis of complex peptides
Albert Isidro, University of Barcelona (2008)
Supervisors: Fernando Albericio and Mercédez Álvarez

Proteases identification with activity-based proteomics
Eduard Sabidó, University of Barcelona (2008)
Supervisors: Ernest Giralt and Teresa Tarragó

Role of the mitocondrial protein Mitofusin 2 on the hepatic metabolism
José Carlos Paz, University of Barcelona (2008)
Supervisor: Antonio Zorzano

Role and regulation of mitocondrial dynamics in skeletal muscle
Marc Liesa, University of Barcelona (2008)
Supervisor: Antonio Zorzano

Síntesi assimètrica de productes amb interès farmacològic a partir d'epoxialcohols insaturats
Carlos Alegret, University of Barcelona (2008)
Supervisor: Antoni Riera

Síntesis de pseudopéptidos derivados de la miraziridina A
Patricia López, University of Barcelona (2008)
Supervisor: Anna Diez

Structural studies of proteins and protein complexes by mass spectrometry and force microscopy
Stephanie Boussert, University of Barcelona (2008)
Supervisor: Ernest Giralt

Study of the aggregation process of amyloid proteins. Examination of aggregation inhibitors
Dolors Grillo, University of Barcelona (2008)
Supervisors: Ernest Giralt and Francesc Rabanal

The transport of arginine in macrophages and Th1/Th2 susceptibility
Maria Gloria Sans, University of Barcelona (2008)
Supervisors: Antonio Celada and Jorge Lloberas

Use of calix[4]arenes to recover the self-assembly ability of mutated p53 tetramerization domains
Susana Gordo, University of Barcelona (2008)
Supervisor: Ernest Giralt

Technology Transfer Activities

During 2008, IRB Barcelona researchers were involved in a series of inventions that resulted in the publication of patent applications. The scientific work illustrates the intense collaborations between the members of the Institute and the biotechnology and pharma sectors, as well as the industrial interest of the discoveries.

A screening method for identifying new aminoacyl-tRNA synthetase inhibitors
Ribas de Pouplana L, Bori Sanz T, Castro de Moura M and Geslain R
Publication number/date: WO2008028862 (13/3/2008)

A screening method for identifying new drugs
Ribas de Pouplana L and Bori Sanz T
Publication number/date: WO2008000785 (03/01/2008)

Compounds for the treatment of diseases related to insulin resistance
Gumà A, Cantó C and Zorzano A
Publication number/date: WO2008006922 (17/1/2008)

Compounds that act as a vehicle for delivery through the blood-brain barrier and charge delivery vehicle constructions
Giralt E and Teixidó M
Publication number/date: WO2008025867 (06/03/2008)

Inhibition of alpha-synuclein aggregation
Zurdo J, Fowler S, Stallwood Y, Giralt E, Teixidó M and Carulla N
Publication number/date: WO2008003943 (01/10/2008)

Inhibition of beta-amyloid aggregation
Zurdo J, Fowler S, Carulla N, Giralt E and Teixidó M
Publication number/date: WO2008050133 (02/05/2008)

Method and device for the control and analysis of nerve cell growth
Loza P, Amat I, Vathalloor M, Cormack G, Torner Ll, Artigas D, Andres MR and Soriano E
Publication number/date: WO2008043808 (17/04/2008)

Method for obtaining bicyclic peptides
Tulla J, Bayo N and Albericio F
Publication number/date: WO2008040833 (04/10/2008)

Method for peptide synthesis
Giraud M, Albericio F, Quattrini F, Werbitzky O, Senn K and Williner M
Publication number/date: WO2008040536 (04/10/2008)

Polypeptides with the capacity to entrap drugs and release them in a controlled way
Giralt E, Poyatos P, Gulin O and Anglada F
Publication number/date: WO2008071594 (19/06/2008)

Proton acceptor imunium/carbocation-type coupling agents
Albericio F, El-Faham A, Luxembourg Y and Ewenson A
Publication number and date: WO2008139481 (20/11/2008)

P,S-type bidentate chiral ligands and use thereof in the Pauson-Khand reaction
Sola J, Verdaguer X and Riera A
Publication number/date: WO2008046950 (24/4/2008)

Therapeutic agent for treatment of bipolar affective disorder in mammals
Giralt E and Tarragó ME
Publication number/date: WO2008077978 (03/07/2008)

Barcelona BioMed Seminars

Organised by IRB Barcelona principal investigators, the 2008 series of Barcelona BioMed seminars brought together more than 100 international experts in biomedicine to present their current work and latest discoveries to the local scientific community. The seminars served as a platform to keep IRB Barcelona scientists up-to-date on the latest achievements in their field of research.

11 January 2008

Marine sponges as a model system of cellular recognition. Future perspectives in biomedical research
Xavier Fernández, Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

23 January 2008

How telomeres suppress DNA damage signalling at chromosome ends
Eros Lazzerini Denchi, Lange Laboratory, The Rockefeller University, New York, USA

25 January 2008

Nanoscale molecular interactions, dynamics and functional relevance of endothelial adhesive platforms in primary living cells
Francisco Sánchez-Madrid, Hospital de la Princesa, Universidad Autónoma de Madrid, Madrid, Spain

29 January 2008

The IRB Barcelona has a new Biostatistics and Bioinformatics core facility!
David Rossell, Biostatistics Unit, IRB Barcelona, Barcelona, Spain

30 January 2008

Cancer biomarkers and new cancer antigens for vaccine therapy
Robert Rees, Nottingham Trent University, Nottingham, UK

1 February 2008

Control of neuronal cell generation and survival by cannabinoids
Manuel Guzmán, Complutense University, Madrid, Spain

7 February 2008

Analysing stem cells within intact tissue using Drosophila
Allan Spradling, Carnegie Institution, Washington, USA

8 February 2008

Cell proliferation and cell competition: what fruit flies can reveal about growth control
Nicholas Baker, Albert Einstein College of Medicine, New York, USA

15 February 2008

Epidermal stem cells in skin homeostasis and cancer
Salvador Aznar-Benitah, Centre for Genomic Regulation (CRG), Barcelona, Spain

22 February 2008

Metabolic circularity as a guiding vision for systems biology: 'Moonlighting' proteins, a necessity of life?
María Luz Cárdenas, Centre National de la Recherche Scientifique (CNRS), Marseille, France

29 February 2008

Unraveling the host-pathogen interactions in Streptococcus pneumoniae by X-ray crystallography
Juan Hermoso, GCMBE, Instituto Química-Física Rocasolano, Madrid, Spain

7 March 2008

Neurogenic niche in the carotid body and its applicability in cell therapy for Parkinson's disease
José López-Barneo, Hospital Universitario Virgen del Rocío, Seville, Spain

14 March 2008

Structured-based drug design: applications and future perspectives
Celerino Abad-Zapatero, University of Illinois at Chicago, Chicago, USA

26 March 2008

Azaheterocyclic analogues of natural products as lead towards biological activity
Christian Stevens, Ghent University, Ghent, Belgium

28 March 2008

Membrane biology in the genomics era
Stephen Baldwin, Leeds University, Leeds, UK

2 April 2008

Epithelial proliferation and axis specification in Drosophila
Isabel Palacios, Cambridge University, Cambridge, UK

4 April 2008

Complement genes and predisposition to disease. The dark side of innate immunity
Santiago Rodríguez de Córdoba, Centro de Investigaciones Biológicas (CSIC), Madrid, Spain

9 April 2008

Integrating Wnt and Shh signalling during spinal cord morphogenesis
Roberto Álvarez, Institute for Molecular Biology of Barcelona (IBMB-CSIC), Barcelona, Spain

10 April 2008

RNAi therapeutics: Can it move from the bench to the bedside or is it just a flash in the pan?
Sukhendu Dev, IRB Barcelona, Barcelona, Spain

11 April 2008

Interaction of mycobacteria with macrophages: New role of NF–kB in the innate immune response
Maximiliano G Gutiérrez, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany

16 April 2008

Identifying the histone trimethylation role in an in vivo model of neural stem cell maintenance and differentiation
Naiara Aquizu, Institute for Molecular Biology of Barcelona, Barcelona, Spain

18 April 2008

Multifunctional pharmaceutical nanocarriers for therapy and diagnostics
Vladimir Torchilin, Northeastern University, Boston, USA

21 April 2008

The endocytic control of cell-cell signalling and tumor suppression
Thomas Vaccari, University of California, Berkeley, USA

23 April 2008

Spatio-temporal evolution of endocytic subcomplexes during membrane budding: insights from quantitative inmunoelectron microscopy
Fátima Idrissi, Institute for Molecular Biology of Barcelona (IBMB-CSIC), Barcelona, Spain

25 April 2008

Molecular mechanisms of amyotrophic lateral sclerosis (ALS): from in vitro models to cerebrospinal fluid biomarkers
Jacques Borg, Neurochemistry Laboratory, Saint Etienne, France

28 April 2008

Flybase Workshop
Peter McQuilton, Flybase, Cambridge, UK

30 April 2008

Factors that regulate target-cell specific innervations
Sara Rubio, IRB Barcelona, Barcelona, Spain

7 May 2008

Scarface, a novel secreted serine protease-like molecule is a target of JNK signalling required for embryonic dorsal closure in Drosophila
Georgina Sorrosal, IRB Barcelona, Barcelona, Spain

9 May 2008

New approaches towards understanding the cellular basis of embryonic development in the mouse
Miguel Torres, Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain

14 May 2008

Minisymposium: Cell biology meets morphogenesis
Antonio García-Bellido, Centro de Biología Molecular 'Severo Ochoa', Madrid, Spain; Franck Pichaud, University College London, London UK; Markus Affolter, Basel University, Basel, Switzerland

16 May 2008

3D structure and function of macromolecular multi-protein complexes involved in DNA repair using electron microscopy
Óscar Llorca, Centre of Biological Research, Spanish National Research Council, Madrid, Spain

Mechanical constraints pattern cellular

behaviour during dorsal closure in Drosophila
Nicole Gorfinkiel, Cambridge University, Cambridge, UK

19 May 2008

Myosin II and the morphogenesis of the imaginal discs
Luis Escudero, MRC Laboratory of Molecular Biology, Cambridge, UK

21 May 2008

Chemotaxis in Drosophila: Making sense of graded olfactory stimuli
Matthieu Louis, Centre for Genomic Regulation (CRG), Barcelona, Spain

23 May 2008

Is the DNA damage response (DDR) a bona fide tumour suppressor barrier?
Óscar Fernández, Spanish National Cancer Research Centre (CNIO), Madrid, Spain

26 May 2008

Differential regulation of sister chromatid cohesion in female Drosophila germ line stem cells
Rui Martinho, Instituto Gulbenkian de Ciencia, Oeiras, Portugal

28 May 2008

DNA structure and genomics
Juan Subirana, Universitat Politècnica de Catalunya (UPC), Barcelona, Spain

The role of the histone variant macroH2A during cell fate decisions
Marcus Buschbeck, Centre for Genomic Regulation (CRG), Barcelona, Spain

30 May 2008

The oncogenic role of TGF-beta in glioma
Joan Seoane, Vall d'Hebron University Hospital Research Institute, Barcelona, Spain

4 June 2008

Preferential incorporation of adult generated neurons into spatial memory networks
Catia Teixeira, IRB Barcelona, Barcelona, Spain

6 June 2008

Novel strategies to resolve inflammation
Adriano Rossi, University of Edinburgh Medical School, Edinburgh, Scotland, UK

11 June 2008

Graded sonic hedgehog signalling and the control of neural cell fate
James Briscoe, National Institute for Medical Research (NIMR), London, UK

13 June 2008

Neuron-glia metabolic coupling and plasticity
Pierre Magistretti, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland

17 June 2008

Unveiling novel regulators of senescence using genetic screenings
Jesús Gil, Imperial College Faculty of Medicine, London, UK

18 June 2008

Role of the Wnt pathway during planarians regeneration
Teresa Adell, University of Barcelona, Barcelona, Spain

20 June 2008

TRAIL, apoptosis and autophagy in normal and transformed cells
Abelardo López Rivas, Centro Andaluz de Biología Molecular y Medicina Regenerativa, Seville, Spain

25 June 2008

A permissive role of Notch in maintaining the DV affinity boundary of the Drosophila wing
Isabelle Becam, IRB Barcelona, Barcelona, Spain

27 June 2008

Identification and characterisation of Lynch syndrome: contributions of the EPICOLON project
Antoni Castells, Gastroenterology Service, Hospital Clínic, Barcelona, Spain

2 July 2008

The necrotic serpin, a protease inhibitor which controls the innate immune response in Drosophila
David Gubb, CIC bioGUNE, Derio, Spain

3 July 2008

Regulation of self-renewal, proliferation and differentiation in a stem cell lineage
Minx Fuller, Stanford University School of Medicine, Stanford, USA

4 July 2008

Translation in time and space: Sequential waves of polyadenylation and deadenylation define a translation circuit that drives meiotic progression
Raúl Méndez, Centre for Genomic Regulation (CRG), Barcelona, Spain

9 July 2008

Intra-cytoplasmic lumen formation during terminal branches elongation of the Drosophila tracheal system
Louis Gervais, IRB Barcelona, Barcelona, Spain

11 July 2008

Synthetic peptides for specific DNA recognition
José Luis Mascareñas, University of Santiago, Santiago de Compostela, Spain

14 July 2008

miRNA in stem cells
Hannele Ruohola Baker, Washington University, Washington, USA

15 July 2008

Generation of patient-specific iPS cells
Ángel Raya, Centre of Regenerative Medicine in Barcelona (CMRB), Barcelona, Spain

16 July 2008

Thermostabilisation and structure determination of a b1 adregenic receptor

María Serrano Vega, MRC Laboratory of Molecular Biology, Cambridge, UK

25 July 2008

Mitochondrial dysfunction increases oxidative stress and decreases chronological life span in fission yeast
Elena Hidalgo, Pompeu Fabra University, Barcelona, Spain

28 July 2008

Toward carbohydrate-based drug discovery
Shin-Ichiro Nishimura, National Institute of Advanced Industrial Science and Technology, Sapporo, Japan

3 September 2008

The unicell-to-multicell transition: A functional and comparative genomics approach
Iñaki Ruiz, University of Barcelona, Barcelona, Spain

8 September 2008

Molecular imaging of angiogenesis: Peptides, proteins and nanoparticles
Weibo Cai, University of Wisconsin, Madison, USA

10 September 2008

Bioinformatics characterisation of protein variability
Xavier de la Cruz, IRB Barcelona, Barcelona, Spain

17 September 2008

Cell polarity and tissue morphogenesis in Drosophila
Kyra Campbell, Cambridge University, Cambridge, UK

19 September 2008

The mammalian 'hipo' pathway: signal trasduction through the Rassf1/Nore1-Mst1/2 tumor suppressor complexes
Joseph Avruch, Harvard Medical School, Harvard University, Boston, Massachusetts, USA

22 September 2008

Targeted genome editing in mammalian cells using engineered zinc finger nucleases
Phil Simmons, Sigma Aldrich, St. Louis, USA

25 September 2008

Discovery of novel potent, selective and orally efficacious A2B adenosine receptor antagonists
Bernat Vidal, Almirall Laboratories, Barcelona, Spain

26 September 2008

Structural characterisation of MuB helical filaments by electron microscopy
Santiago Ramón-Maiques, Institute of Biomedicine of Valencia (IBV-CSIC), Valencia, Spain

1 October 2008

Skeletal muscular formation and fibrosis; new insights about the role of TGB-beta and CTGF
Enrique Brandan, Universidad Católica de Chile, Santiago, Chile

Quantitative proteomics of the intra-erythrocytic life stages of the malaria parasite Plasmodium falciparum
Bernardo Foth, School of Biological Sciences, Nanyang Technological University, Singapore

Host cell invasion by hemorrhagic arenaviruses
Stefan Kunz, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

8 October 2008

Polyploidy In colon carcinoma cells is modulated by mithramycin Sk
Marc Bataller, Institute for Molecular Biology of Barcelona (IBMB-CSIC), Barcelona, Spain

9 October 2008

Brain tumor supressors and neural stem cell self-renewal in Drosophila
Hongyan Wang, Duke-NUS Graduate Medical School, Singapore

Towards rational intervention in Parkinson's disease: structural studies of intrinsically disordered α-synuclein and associated protein complexes
Carlos Bertoncini, Cambridge University, UK

10 October 2008

Regulation of pre-mRNA splicing in budding yeast
Josep Vilardell, Centre for Genomic Regulation (CRG), Barcelona, Spain

15 October 2008

The cytosolic kinase Ack1 in the developing nervous system
Anna La Torre, University of Barcelona/IRB Barcelona, Barcelona, Spain

17 October 2008

Looking for the Kepler's laws of drug discovery
Celerino Abad-Zapatero, University of Illinois at Chicago (UIC), Chicago, USA

22 October 2008

Regulatory particle of the proteasome: a nanoprocessor controlling cellular pathways
Bernat Crosas, Institute for Molecular Biology of Barcelona (IBMB-CSIC), Barcelona, Spain

Spatio-temporal evolution of endocytic subcomplexes during membrane budding: insights from quantitative immunoelectron microscopy
Fátima Idrissi, Institute for Molecular Biology of Barcelona (IBMB-CSIC), Barcelona, Spain

24 October 2008

Biogenesis of a transport carrier during protein secretion
Vivek Malhotra, Centre for Genomic Regulation (CRG), Barcelona, Spain

27 October 2008

Mysteries in growth control and the hippo pathway
Georg Halder, University of Texas, MD Anderson Cancer Centre, Houston, USA

Oscarella lobularis, an emerging sponge model in comparative developmental biology

Eve Gazave, Centre d'Océanologie de Marseille, Marseille, France

28 October 2008

A role for the p53 tumor suppressor protein in metabolism
Karim Bensaad, Cancer Research UK, Beatson Laboratories, Glasgow, UK

A role of Stardust in morphogenesis and function of the Drosophila eye
Natalia Bulgakova, Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

29 October 2008

Towards a theory of biological networks
Natasa Przulj, University of California, Irvine, USA

Mechanisms of dendrite differentiation and remodeling
Gaia Tavosanis, Max Planck Institute of Neurobiology, Martinsried, Germany

31 October 2008

Understanding and manipulating protein-protein interactions in G protein signalling: one step beyond GPCRs
Alan Smrcka, University of Rochester Medical Centre, Rochester, USA

3 November 2008

Lipochaperones: lipids as molecular chaperones and topological determinants
Mikhail Bogdanov, University of Texas, Houston, USA

5 November 2008

JmjC+N histone demethylases in Drosophila melanogaster
Marta Lloret, Institute for Molecular Biology of Barcelona/IRB Barcelona, Barcelona, Spain

7 November 2008

Mechanisms of structural plasticity at the vertebrate neuromuscular junction
Rüdiger Rudolf, Karlsruhe Institute of Technology, Karlsruhe, Germany

12 November 2008

Force sensing in actin bundles: a model system to seek mechanosensors involved in cell adhesion and contractility
Julien Colombelli, IRB Barcelona, Barcelona, Spain

14 November 2008

Protein misfolding and disease: mapping the triggering event
Mikael Akke, Lund University, Lund, Sweden

19 November 2008

Dissecting Reelin functions in the adult brain by conditional transgene expression
Lluís Pujadas Puigdomènech, IRB Barcelona, Barcelona, Spain

24 November 2008

ER to nucleus communication relies on HAC1 mRNA targeting
Tomás Aragón, University of California, San Francisco (UCSF), San Francisco, USA

28 November 2008

Alteration of mitochondrial form and function in metabolic diseases and cancer
Rossignol Rodrigue, Université Victor Segalen, Bordeaux, France

3 December 2008

Drosophila as a model to identify new human genes
Álvaro Tavares, Instituto Gulbenkian de Ciéncia, Oeiras, Portugal

Identification of proteins that interact with cyclophilin A, cyclophilin B and FKBP12 and their implications in CsA
Guillermo Suñé, Institut de Recerca Vall d'Hebron, Barcelona, Spain

5 December 2008

The function of the intermediate compartment in pre-Golgi trafficking involves its stable connection with the centrosome
Jaakko Saraste, Bergen University, Bergen, Norway

10 December 2008

Investigating the molecular mechanisms of Myo5p recruitment to endocytic sites in Saccharomyces Cerevisiae
Jonathan Giblin, Institute for Molecular Biology of Barcelona (IBMB-CSIC), Barcelona, Spain

12 December 2008

Transcription factors Foxc2 and Prox1 in lymphatic vascular development and cancer
Tanya Petrova, CePO, CHUV and University of Lausanne, Epalinges, Switzerland

15 December 2008

A blow of fresh air: An unexpected role of NF-kB and JNK pathways in the response to hypoxia
Jordi Rius, University of California, San Diego, USA

16 December 2008

Tumor microenvironment: Effect on tumor metastasis and cancer stem cell maintenance
Xiao-Fan Wang, Duke University Medical Centre, Durham, USA

18 December 2008

The two-component system DesK/DesR: A general mechanism of signal transduction?
Pedro Alzari, Institut Pasteur, Paris, France

19 December 2008

Genomics of complex diseases
Jesús Sainz, Instituto de Biomedicina y Biotecnología de Cantabria (IBBTEC), Cantabria, Spain

Barcelona BioMed Conferences

The Barcelona BioMed Conference series brought together leading experts to present and discuss the latest breakthroughs in several fields of the biomedical sciences. Organised by IRB Barcelona, made possible thanks to the BBVA Foundation, the 2008 lineup included top international speakers in cell and developmental biology, oncology, and structural and computational biology. Generously hosted by the Institut d'Estudis Catalans in downtown Barcelona, the conferences succeeded in drawing hundreds of participants from industry and academia from around the world.

6-8 October 2008

MORPHOGENESIS AND CELL BEHAVIOUR

Organisers: Jordi Casanova (IRB Barcelona/IBMB-CSIC) and Marco Milán (IRB Barcelona)

19-21 May 2008

METASTASIS GENES AND FUNCTIONS

Organisers: Tyler Jacks, Massachusetts Institute of Technology (Cambridge, USA) and Joan Massagué, Memorial Sloan-Kettering Cancer Center (New York, USA)

14-16 April 2008

TARGETING AND TINKERING WITH INTERACTION NETWORKS

Organisers: Patrick Aloy (IRB Barcelona) and Rob Russell (European Molecular Biology Laboratory, Heidelberg, Germany)

The 2008 series also brought together leading female researchers for a Barcelona BioMed Forum aimed to raise awareness and provide tips to overcome the gender bias in science.

21 July 2008

Barcelona BioMed Forum

FROM WOMAN TO WOMAN: PRACTICAL ADVICE ON HOW TO GET AND STAY AHEAD IN SCIENCE

Organiser: IRB Barcelona

Outreach Activities

IRB Barcelona researchers set time aside in 2008 to participate in a series of outreach activities organised by the Barcelona Science Park. Open to the general public and targeting primary and secondary school students, IRB Barcelona's involvement in these educational activities was aimed to raise awareness of the research carried out at the Institute as well as to motivate students to take up careers in science.

10 January-24 April | 25 October-29 November 2008

RESEARCH!

A hands-on series of weekly workshops for students and the general public

IRB Barcelona participants: Elisabeth Castellanos[1], Consol Farrera[2], Ana Janic[1], Leire Mendizábal[1] and Maria Serra[2]
[1]Cell Division Laboratory, [2]Macrophage Biology: Regulation of Gene Expression

Topics: DNA analysis to track down a criminal, flies with cancer

January-December 2008

RESEARCH IN PRIMARY SCHOOLS

A bimonthly research activity to bring science closer to students through active involvement in projects and experiments

IRB Barcelona participants: Carme Cortina and Elisa Espinet
Colorectal Cancer Laboratories I and II

Topics: Introduction to the scientific method, DNA extraction, stem cells, microscope analysis

10-11 April 2008

LIVE RESEARCH FAIR

A science fair to show the latest research taking place in Barcelona

IRB Barcelona participants: Carme Cortina and Sergio Palomo
Colorectal Cancer Laboratories I and II

Topics: What is colon cancer and what can we do about it?

7-8 June 2008

FESTA DE LA CIÈNCIA 2008

A research festival with live demonstrations at the Ciutadella Park in Barcelona

IRB Barcelona participants: Elisabeth Castellanos and Ana Janic
Cell Division Laboratory

Topic: DNA extraction from saliva

1 July-30 September 2008

SPEND THE SUMMER AT THE PARK!

An internship programme for undergraduate students involving active participation in research projects performed by groups at the Barcelona Science Park

IRB Barcelona participants (student tutors): Fernando Albericio[1], Carme Caelles[2], Albert Canals[3], Antonio Celada[4], Ernest Giralt[5], Joan Guinovart[6], Jens Lüders[7], Marco Milán[8], Cristina Minguillón[9], Lluís Ribas de Pouplana[10] and Antoni Riera[11]

[1]Combinatorial Chemistry for the Discovery of New Compounds, [2]Cell Signalling, [3]Structural Biology of Proteins, Nucleic Acids and their Complexes, [4]Macrophage Biology: Regulation of Gene Expression, [5]Design, Synthesis and Structure of Peptides and Proteins, [6]Metabolic Engineering and Diabetes Therapy, [7]Microtubule Organisation, [8]Development and Growth Control Laboratory, [9]Bioactive peptidomimetic and heterocycles (Biosyner), [10]Gene Translation Laboratory, [11]Research Unit on Asymmetric Synthesis

July 2008-March 2009

RESEARCH IN SECONDARY SCHOOLS

A mentoring activity to assist secondary school students in their research projects

IRB Barcelona participants (student tutors): Maria Isabel Arévalo[1], Elisabeth Casstellanos[2], Ana Janic[2], Irene Martín[3], Carles Martínez[4], Laura Nocito[4], Neus Rafel[5], Lidia Ruiz[6], Isabel Saez[4], Pablo Sirkin[7], Jordi Vallès[4] and Dèlia Zafra[4]

[1]Cell signalling, [2]Cell Division Laboratory, [3]Design, Synthesis and Structure of Peptides and Proteins, [4]Metabolic Engineering and Diabetes Therapy, [5]Development and Growth Control Laboratory, [6]Biomolecular NMR Spectroscopy, [7]Chromatin Structure and Function

18-20 November 2008

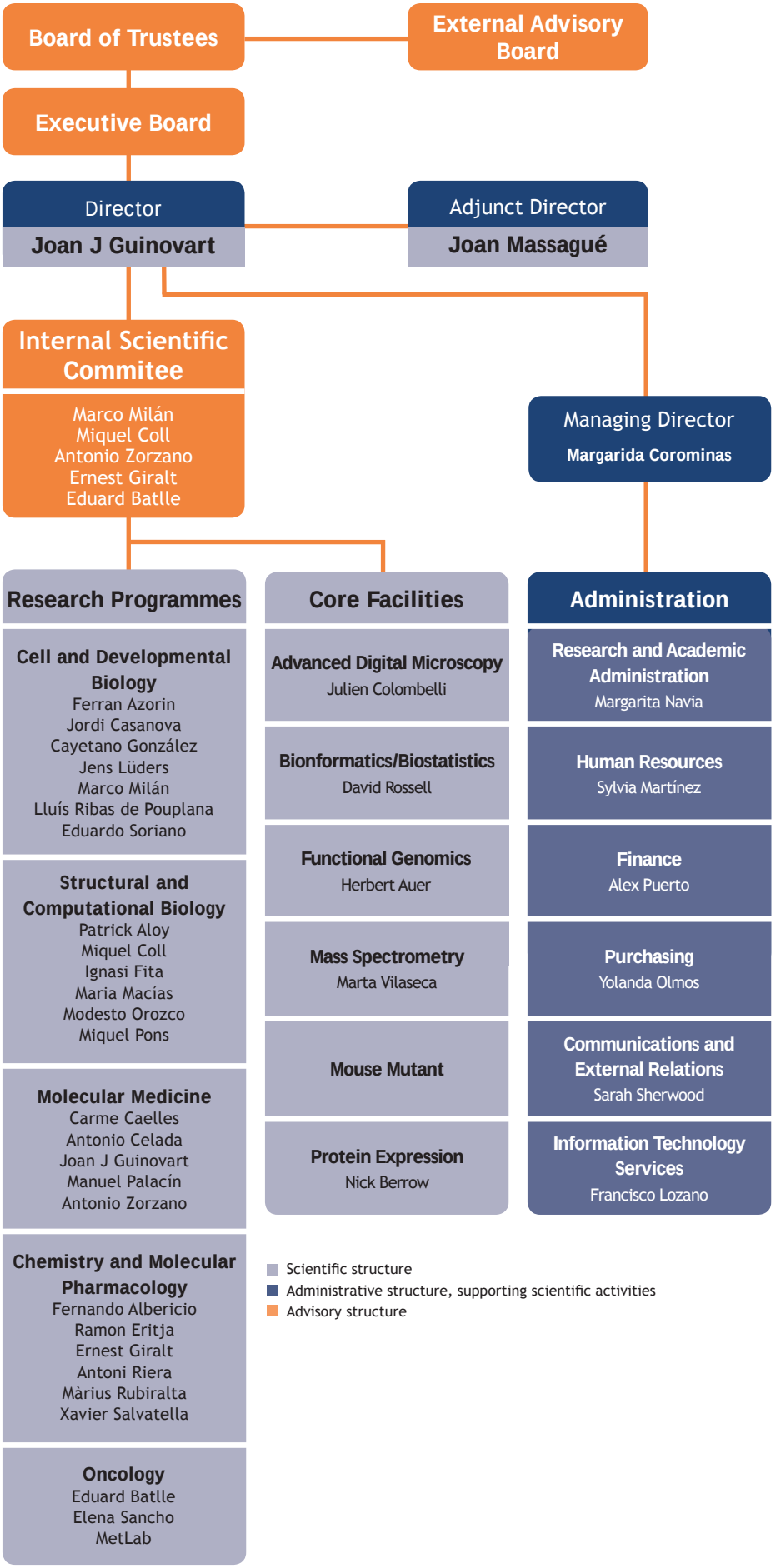
OPEN DAY: WHAT IS THE BARCELONA SCIENCE PARK? WHAT IS RESEARCH ABOUT?

A one-day event to bring science closer to secondary school students

IRB Barcelona participants: Carme Cortina and Elisa Espinet
Colorectal Cancer Laboratories I and II

Topics: RNA extraction, cell visualisation, *in vitro* cell culture, RNA analysis from tumoural cells, separation of benign and malignant tumoural cells

Organisation Chart



Directorate & Administration Staff

Directorate

Director
Joan J Guinovart

Adjunct Director
Joan Massagué

Managing Director
Margarida Corominas

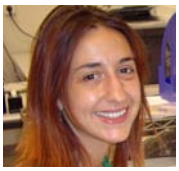
Directorate Secretary
Maria Estévez

Research Programmes

Coordinator, Cell & Developmental Biology
Marco Milán

Programme Secretary
Martha Brigg

Coordinator, Structural & Computational Biology
Miquel Coll



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Vanessa Llobet

Coordinator, Molecular Medicine
Antonio Zorzano

Programme Secretary
Natàlia Molner

Coordinator, Chemistry & Molecular Pharmacology
Ernest Giralt

Programme Secretary
Eva Poca

Coordinator, Oncology
Eduard Batlle

Programme Secretary
Sara Martorell

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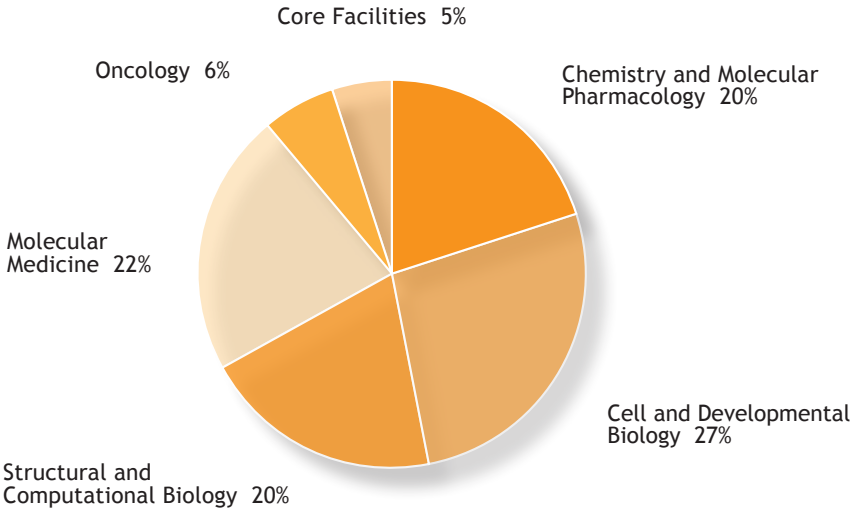
Research and Academic Administration Margarita Navia (Head), Clara Caminal (Academic Officer), Sònia Saborit (Project Officer), Adriana Grosu (European Project Manager) **Human Resources** Sylvia Martínez (Head), Silvia Aguadé (Personnel Management Technician), Maria Rovira (Human Resources Technician) **Finance** Alex Puerto (Head), Elisava de la Hoz (Accounting Officer), Stel·la Serra (Project Technician), Dan Maldonado (Accounting Officer), Silvia Ramírez (Accounting Officer, until September 2008), Cristina Coletas (Finance Assistant) **Purchasing** Yolanda Olmos (Head), Xavier López (Purchasing Officer), Sara López (Purchasing Administrative), Eric González (Purchasing Administrative Assistant), Mª Jesús López (Purchasing Administrative Assistant, until October 2008), Carles Coarassa (Head of Former Finance and Purchasing Department, until May 2008) **Communications and External Relations** Sarah Sherwood (Head), Sònia Armengou (Press and Media Relations Officer), Anna Alsina (Information and Publications Officer), Meritxell Gavaldà (Conference/Event Coordinator), Tanya Yates (Editorial Support) **Information Technology Services** Francisco Lozano (Head), Roberto Bartolomé (Systems Architect), David Villanueva (Systems Administrator), Jesús Sánchez (Systems Administrator)

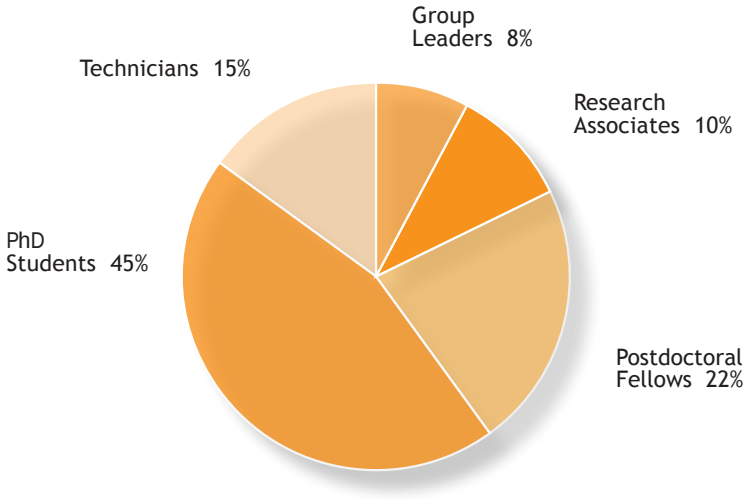
Human Resources Statistics

IRB BARCELONA MEMBERS	
Laboratories	362
Core Facilities	17
Administration	28
Total	**407**

Scientific staff by research programme



Scientific staff by professional category



Researcher Affiliations

University of Barcelona (UB)

Principal Investigators
Fernando Albericio
Carme Caelles
Antonio Celada
Ernest Giralt
Joan J Guinovart
Modesto Orozco
Manuel Palacín
Miquel Pons
Antoni Riera
Màrius Rubiralta
Eduardo Soriano
Antonio Zorzano

Other Researchers
Mercedes Álvarez
Ferran Burgaya
José Antonio del Río (until December 2008)
Anna Diez
Annabel Fernández
Josep Lluís Gelpí
Rodolfo Lavilla
Jorge Lloberas
Albert Martínez
Cristina Minguillón
Jesús Ureña
Xavier Verdaguer

Catalan Institution for Research and Advanced Studies (ICREA)

Principal Investigators
Patrick Aloy
Eduard Batlle
Roger Gomis
Cayetano González
Maria Macías
Marco Milán
Lluís Ribas de Pouplana
Xavier Salvatella

Other Researchers
Natàlia Carulla
Elena Casacuberta (until July 2008)
Alfred Cortés
Xavier de la Cruz (until September 2008)
José Luís Vázquez Ibar

Consejo Superior de Investigaciones Científicas (CSIC)

Principal Investigators
Ferran Azorín
Jordi Casanova
Miquel Coll
Ramón Eritja
Ignasi Fita

Other Researchers
Maria Lluïsa Espinàs
Rosa Pérez Luque
Maria Solà
Cristina Vega

A project in expansion

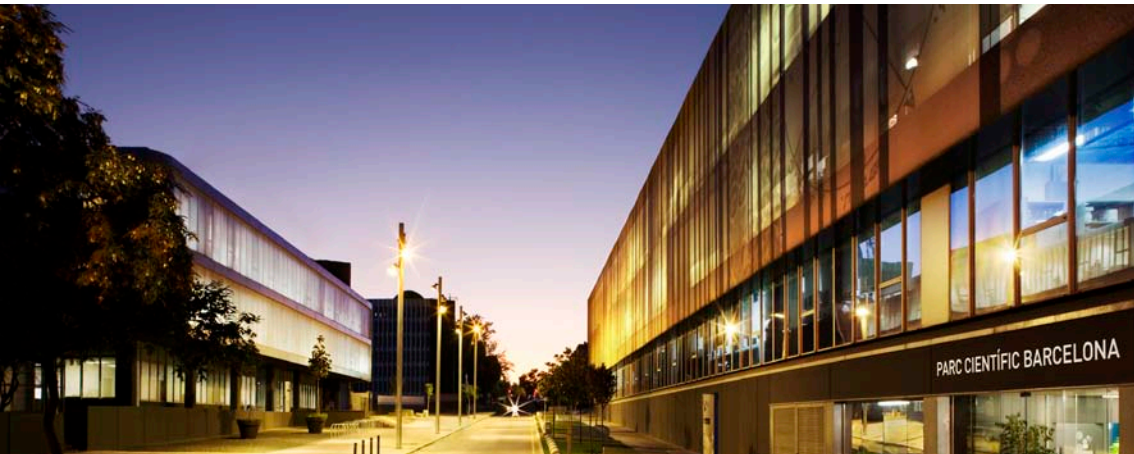
During 2008, the Barcelona Science Park (PCB) has pursued its objectives through several activities in the fields of research, innovation and the dissemination of science, and has experienced a considerable increase in surface area and infrastructures as well as in the number of people, enterprises and organisations working in its facilities. At the end of December, the Park hosted 2,200 professionals, almost 50 companies, and 25 scientific and technological units, in addition to more than 70 research groups.

As part of the PCB expansion plans, the year 2008 saw the opening of the Helix Building, which provided the Park with additional space of more than 6,500 m^2, the completion of the refurbishment of the Administration building, which hosts the management and administration departments of the main research institutes located at the Park, and the move of the main entrance to Baldiri Reixac street, which allowed the grouping of receptions and security services for the Modular and Administration buildings. The renovation work on the Research and Innovation Towers, which will become operational in 2009, was also completed in 2008, thereby providing around 10,000 m^2 of additional space.

The year also saw the set up of the Drug Discovery Platform, which offers public and private organisations, whether hosted at the Park or elsewhere, a consultancy service during the drug dicovery process. Other developments included the extension of the Core Scientific Services of the University of Barcelona devoted to research into *Drosophila*, and the completion of the renovation work on the Animal Research Centre (SEA-PCB), which allowed it to increase its housing capacity from an initial 15,000 to up to 35,000 animals, and to set up an area devoted to aquatic organisms.

In the field of innovation, special mention is given to the opening of the PCB-Santander Bioincubator. Promoted jointly by the Park and by the Bosch i Gimpera Foundation, with the support of the 'Banco Santander', this initiative seeks to facilitate the set up and growth of technology-based enterprises. At the end of December 2008, the bioincubator hosted 13 companies, together employing more than 80 people. This is the second generation of companies that has participated in this project.

The second phase of the Park's construction project, which continued throughout 2008, will be completed in 2011 and will allow the park to increase four-fold its initial surface area.



IRB BARCELONA

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Parc Científic de Barcelona

With the collaboration of

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