IRB BARCELONA

INSTITUTE FOR RESEARCH IN BIOMEDICINE

2007 Executive Summary

Centres de recerca de Catalunya

Credits

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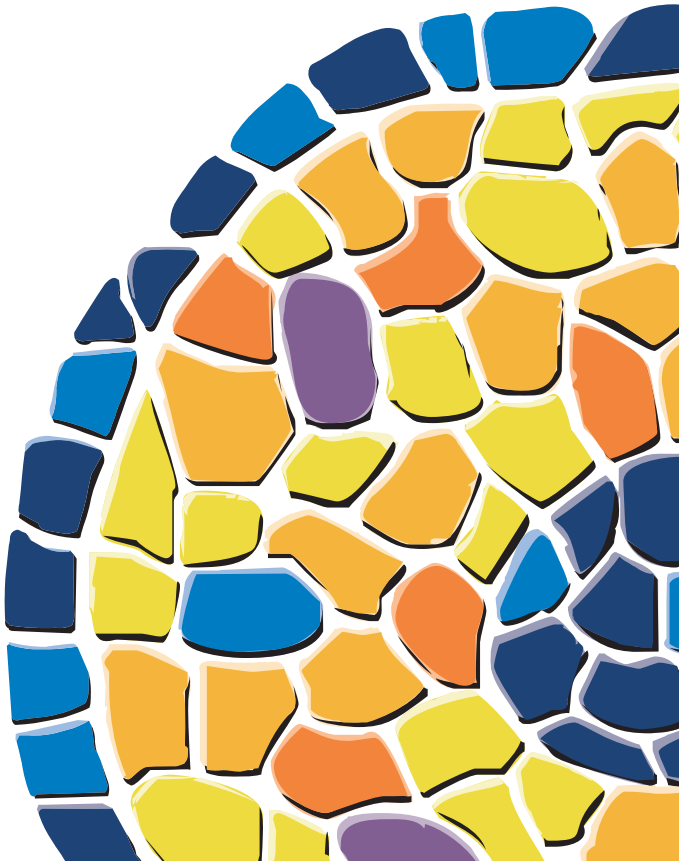
2007 Executive Summary



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Foreword

IRB Barcelona moves forward in the landscape of biomedical research

This is the second Annual Report of IRB Barcelona, a vibrant young research institute in the capital of Catalonia. It is composed of 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, the Executive Summary, which includes facts and figures about the institute, and Science Stories from IRB Barcelona, which highlights some of the research conducted over the past year and takes a look at the people behind the science at IRB Barcelona. The main goal of these documents is to provide a snapshot of the activities that have taken place at the Institute over the past year. Along the way, we hope readers will get a feeling for this unique new place and its importance in the landscape of biomedical research.

Long recognised as a lighthouse for the arts, architecture and music, Catalonia is now making major investments in the cultivation of its scientific resources

Setting the stage for research of excellence in a city of excellence

An institute's character is shaped by many things. First and foremost are its vision, the personalities of its scientists, and the quality of their research. It is also formed by the physical setting in which it is found, its research infrastructures, and the scientific and political climate which surround it. Long recognised as a lighthouse for the arts, architecture and music, Catalonia is now making major investments in the cultivation of its scientific resources. Those who have not visited Barcelona recently would likely be amazed at the city's new scientific profile. IRB Barcelona is an important engine of this change as the Catalonian and Spanish governments, the city of Barcelona, a host of industries, and some key individuals transform

the region into an internationally recognised focal point for science.

We have a challenging, forward-looking vision: to carry out research in the molecular life sciences that will lead to benefits for human health. The past decade has seen a boom in new concepts in biotechnology that have already had a major impact on the practice of medicine. The result has been powerful new diagnostic tools and the first 'rationally designed' drugs. These changes only scratch the surface of what is likely to happen in the near future. Taking advantage of them will require new, flexible ways of doing research.

We have a challenging, forward-looking vision: to carry out research in the molecular life sciences that will lead to benefits for human health

The last great revolution in medicine started in the late 19th century and carried on through the next with the identification of the microbes that cause infectious diseases and the development of vaccines, antibiotics, and other drugs. This knowledge and its products changed society. It expanded lifespans and the quality of life in the developed world and, increasingly, in the developing world.

Today's major causes of death in most parts of the industrialised world – cardiovascular disease, cancer, and neurodegenerative diseases – stem from a different source: from defects in human genes and complex biological processes. Learning to diagnose and treat them will require a new type of medicine based on a deep, molecular view of cells and organisms. Yet knowledge alone is not a cure; it has to be transformed into new tools and therapies. Doing so is a major challenge that an institute like IRB Barcelona cannot accomplish on its own, so we are establishing new types of partnerships with universities, clinical centres, and industry.

Joan Massagué, Adjunct Director (left) and Joan J Guinovart, Director, IRB Barcelona

This vision must be pursued in a new, interdisciplinary way. Scientific groups used to concentrate on a small number of molecules and processes, usually in one model organism. Today they may follow a process across the whole genome, in experiments that go from the computer to the test tube to mice and even human tissue. This requires a palette of techniques that cannot be mastered by a single group. So alongside the Institute's research, this report describes the establishment of cutting-edge platforms. It also presents other areas of activity such as training and our public information activities, which play an important role in supporting IRB Barcelona science.

A year of consolidation and growth

IRB Barcelona, formally founded just two years ago, has made a grand entrance onto the scientific scene, at the local, national and international levels. Over the past year we have recruited talented new researchers, established a number of core facilities and implemented administrative procedures in support of the scientific work done here. It has been a year of consolidation and growth and we are well on our way to establishing IRB Barcelona as one of the foremost biomedical research institutes worldwide.

A good measure of our progress can be seen in the list of publications authored by IRB Barcelona scientists, listed in the Scientific Report and summarised on page 42 of this volume, achieved in the short time that they have been working here.

We have also been able to recruit highly talented scientists to set up their research groups at IRB Barcelona. Jens Lüders (from Stanford University) was recruited to the Cell and Developmental Biology Programme and will focus his research efforts on understanding the molecular mechanisms behind microtubule organisation. Xavier Salvatella (from the University of Cambridge) will join the Chemistry and Molecular Pharmacology Programme to work on the structure and dynamics of biomacromolecules and how they

relate to disease. Both will take up their positions in 2008. In addition, managers were recruited for the Functional Genomics (Herbert Auer, from Ohio State University), Protein Expression (Nick Berrow, from the University of Oxford) and Mutant Mouse Core Facilities in 2007. Activities in the Mass Spectrometry Core Facility also began under the leadership of Marta Vilaseca (from the University of Barcelona).

IRB Barcelona, formally founded just two years ago, has made a grand entrance onto the scientific scene, at the local, national and international levels

In September, IRB Barcelona and the Barcelona Supercomputing Center (BSC) signed an agreement to set up a joint research programme, which comprises a team of researchers from the Department of Life Sciences at the BSC and the Structural and Computational Biology Programme at IRB Barcelona. Its main goal is to strengthen research in computational biology and favour collaborations between the two institutes. Through this initiative, IRB Barcelona researchers have direct access to the formidable computational resources of the BSC, and BSC researchers have access to the laboratory facilities at IRB Barcelona.

November 2007 saw the first meeting of the External Advisory Board, which comprises 15 leading international researchers in biomedicine. The main task of the Board is to provide guidance in shaping our research and related activities. Initial feedback on progress made so far was extremely positive and has provided valuable insight into focusing IRB Barcelona's future.

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, both at the level of individual researchers and for special programmes, such as Consolider and CIBER of the Spanish Ministries for Education and Science and Health and Consumer Affairs, respectively, and in EU-funded programmes. Participation in research networks and grants received are summarised

on page 45 of this Executive Summary, while full details for each group can be found at the end of their entry in the Scientific Report volume.

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 will begin with IRB Barcelona's 2008 call for applications.

Research at IRB Barcelona

Our groups are organised into five programmes. Each has a core area of focus but includes themes and projects which overlap with the rest:

Cell and Developmental Biology studies how information in the genome is used to create structures within the cell, to guide the formation and regeneration of tissues, and to create a whole organism. High-throughput methods are used to watch the global activity of genes and proteins during these processes in healthy and diseased organisms.

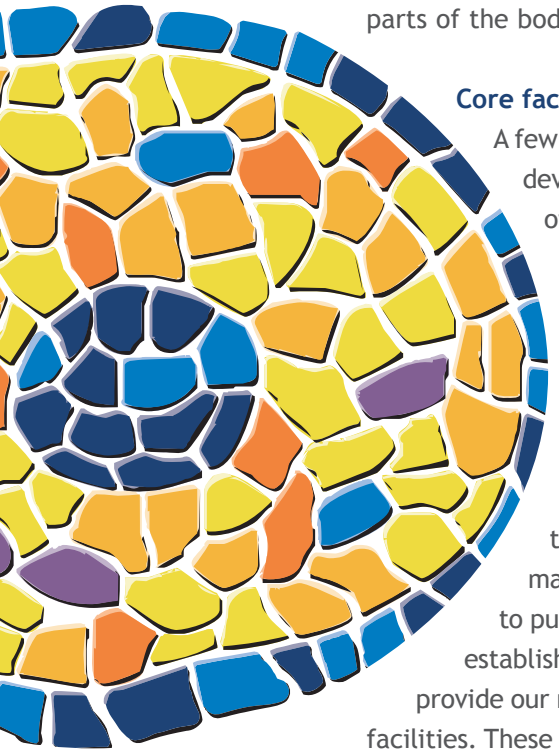
Structural and Computational Biology begins at the molecular level, studying the structure of single molecules and their interactions. The chief methods that are used derive from physics and computational science: X-rays, NMR, electron microscopy, macromolecular biophysics, bioinformatics and molecular modelling.

Molecular Medicine probes the molecular bases of metabolic and genetic diseases, searches for diagnostic or therapeutic targets, and studies the behaviour of the entire genome and proteome during diseases.

Chemistry and Molecular Pharmacology specializes in the design and synthesis of small

molecules and macromolecules that can be used to probe proteins and other biological molecules. The programme has a special emphasis on combinatorial chemistry. One focus involves building libraries of substances and optimising methods to produce them; a second involves understanding how drugs affect molecules and how they can be modified in order to better control their effects.

Oncology studies diverse aspects of how tumours arise and develop, the relationship between stem cells and cancer, and the identification of cellular programmes that cause particular types of tumours to spread and metastasise in specific parts of the body.



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. These 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.

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 which encourages innovation and makes technology transfer easy for our scientists. Here IRB Barcelona is ideally situated in the Barcelona Science Park complex and can draw on close ties to the Innovation Centre of the Bosch i Gimpera

Foundation and the Agency for Assessing and Marketing Research Results of the University of Barcelona.

Training future leaders: IRB Barcelona's PhD Programme

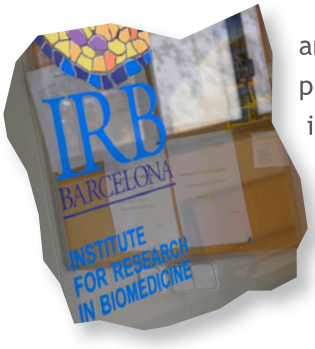
The level of research and the collection of activities and platforms at IRB Barcelona provide a unique environment in which students from around the world can do research toward their degrees. Students profit from close mentoring and have access to a wide variety of scientific activities, services and networks. The programme that we offer 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. Events are organised several times a week and ensure that PhD students keep abreast of the latest advances in biomedicine. 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. In addition to setting the stage for friendships among students, they also help to foster the spirit of collaboration right from the outset of their scientific career. Students have already taken steps to form a council that will coordinate activities such as a student-run PhD symposium.

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

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



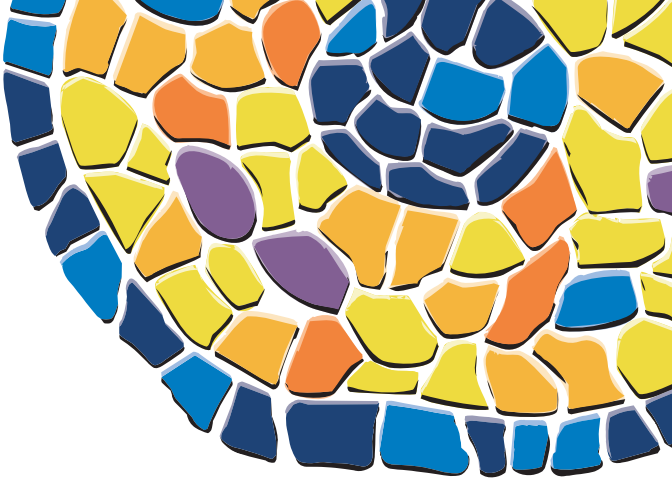
areas of the biomedical sciences present and discuss their results and ideas. These seminars allow IRB Barcelona researchers and the local scientific community to learn about the latest developments in the life sciences, and provide an opportunity for direct contact with each seminar speaker.

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 2007 included The Regulation of Chromatin Functions (March), Inflammation and Chronic Disease (June) and Stem Cells and Cancer (October).

With 27 independent research groups, a large contingent of core facilities, and nearly 400 members, IRB Barcelona has rapidly coalesced into a significant presence in the landscape of biomedical research institutes

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. In 2007 we launched the **Barcelona BioMed Forums**, events open to the public and aimed at increasing awareness and encouraging a better understanding of progress in the biomedical sciences and its implications for society. The first Barcelona BioMed Forum, entitled 'Science, Economy and Society: Invest in Oncology Research,' was held in April and brought together representatives from science, economy and society to discuss the measures and strategies needed to limit the social and economic impacts of cancer.

With 27 independent research groups, a large contingent of core facilities, and nearly 400



members, IRB Barcelona has rapidly coalesced into a significant presence in the landscape of biomedical research institutes. Yet, IRB Barcelona has much growth ahead and, most importantly, much potential to be realised. To this end, we plan in the upcoming year to fortify our efforts to recruit top international scientific talent to head up new research groups and core facilities, to embrace initiatives of our PhD community to strengthen activities and opportunities available to our students, and to expand on our outreach activities in order to bring the biomedical research carried out at IRB Barcelona closer to the public.

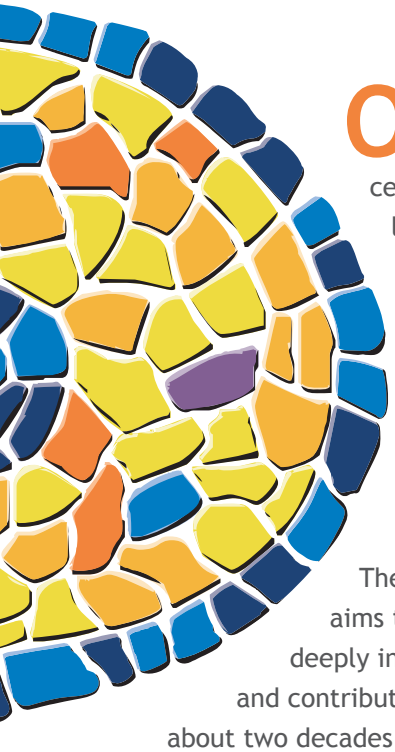
Joan J Guinovart
Director

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, and 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

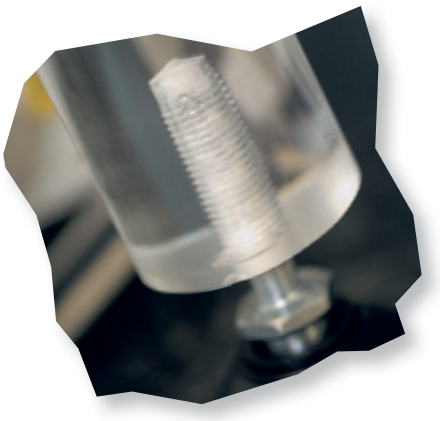
No cell produces RNAs and proteins from all of its genes all of the time. Part of the reason for this is that the DNA in the nucleus is wrapped around proteins and other molecules in a form called chromatin. These molecules have a crucial role because they help pack a huge amount of DNA into the small 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 organize cells into body structures

Building a complex organism requires that cells specialize 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 example, 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 specialize 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.



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/TGF□, 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 protozoa 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 group** 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 group 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 J Macias' lab** specializes 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

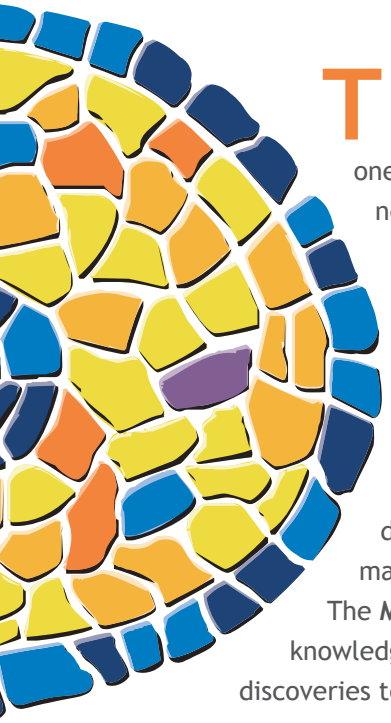
The interactions of proteins and other molecules happen so quickly and at such a small scale that they cannot be observed directly. They have to be studied through models which incorporate information from many sources. **Modesto Orozco's group** combines a variety of methods —from the automatic mining 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, referred to as chemical spaces, which can be compared 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.

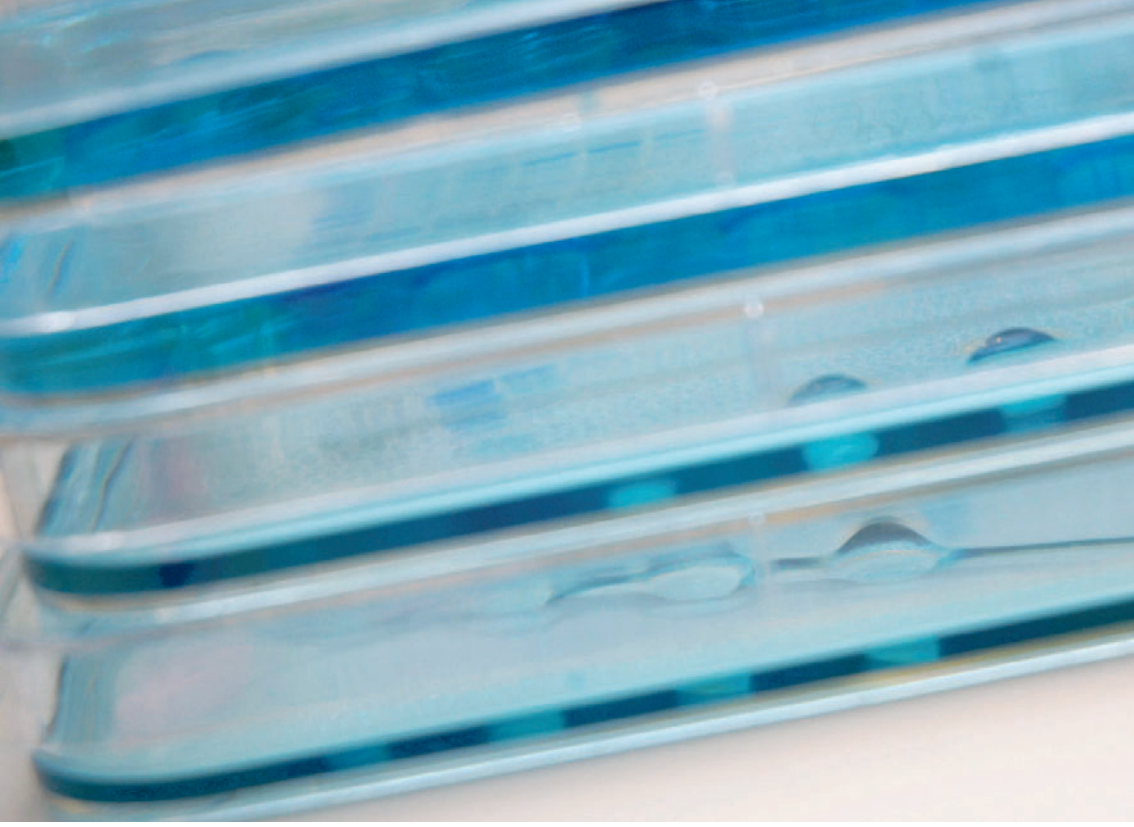
Molecular Medicine Programme



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 revolutionized 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 following fields: 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 group studies macrophages, cells that play 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 J 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 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 clinical trials of this compound have been completed, and Phase 2 anti-obesity trials are in course.

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 analyzing 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 is called metabolic syndrome, which 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 in particular 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 synthesize 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

Fernando Albericio's lab aims to discover and synthesize new compounds that might be useful as therapies against central nervous system disorders and cancer. The group takes an integrated approach based on peptides and small molecules, which are studied in joint collaborations with industrial partners.

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 group** 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.

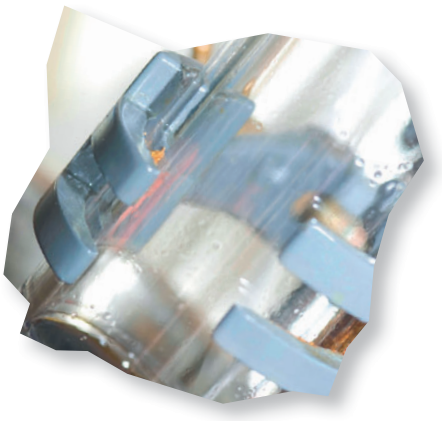
Designing and delivering drugs

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 group** 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 focus is crucial because standard processes that synthesize small molecules produce both enantiomers ('left- and right-handed' versions – in other words, molecules that have the same properties but are mirror images of each other). The reactions of biological molecules to the two types of enantiomer may differ greatly, so it is crucial to produce and purify only the desired version.

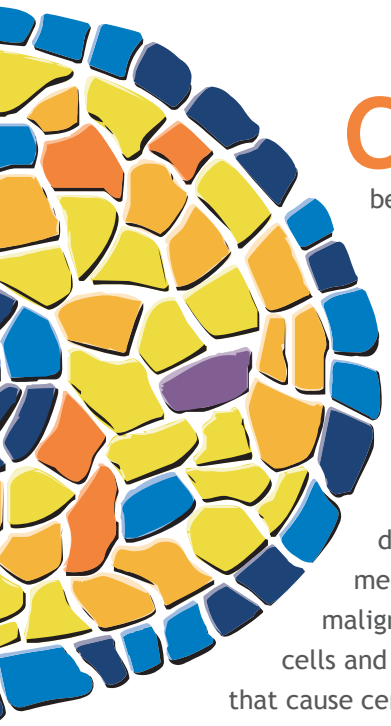
Other efforts are devoted to finding ways to scale up synthetic processes of compounds of therapeutic interest. Finally, the group helps to prepare chemical libraries that can be used for biological screening.



Looking for new bioactive molecules

Màrius Rubiralta's group works on the development of technologies addressed to obtain key bioactive compounds in a pure form. Thus, synthetic procedures are developed 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.

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

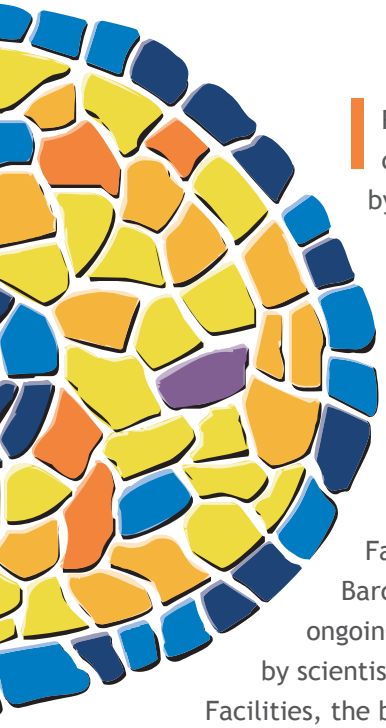
Colorectal cancer is one of the leading causes of death by cancer worldwide. Most colorectal tumours develop as benign lesions but a small proportion progress to more malignant stages because their cells have accumulated mutations in genes that promote cancer or in genes that normally suppress the development of tumours. The final and deadliest step in the development of the disease is the migration of colorectal cancer cells to other organs, mainly the liver, 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 group 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 **MetLab**'s main interest 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



IRB Barcelona has a series of **Core Facilities** devoted to assisting researchers in their work by providing technical support, state-of-the-art technologies and scientific services. These shared resources are essential for cutting-edge research in biomedicine and play a crucial role in increasing research efficiency and bringing experiments to faster conclusions.

Equipped with the latest technologies and staffed with qualified personnel, the Core Facilities offer a wide range of services to IRB Barcelona researchers and also participate in ongoing funded projects and activities conducted by scientists at the Institute. 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.

Located in the Barcelona Science Park near the IRB Barcelona laboratories, the Core Facilities support biomedical research through a range of new technologies and services in protein expression, high resolution mass spectrometry, functional genomics and mouse models of disease. Research tools to analyse or alter genes on a genome-wide level, high throughput protein expression activities to run many variations of an experiment in parallel, development and production of genetically modified mice for research purposes, small molecule analysis and protein characterization are some of the services provided to IRB Barcelona researchers.

The number of shared Core Facilities will continue to increase in the future in order to broaden services and provide a strong research infrastructure to the IRB Barcelona scientific community.

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 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** provides state-of-the-art genomic tools for the IRB Barcelona research community and for external organisations. These tools fall into two categories:

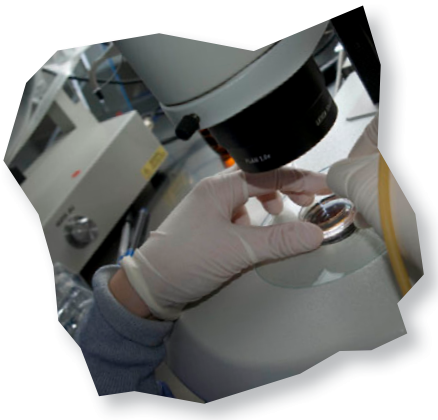
- Genome wide analysis of transcription, DNA polymorphisms, and chromatin immunoprecipitation (ChIP-chip). These analyses are performed using microarrays produced by Affymetrix. For all of these analytical methods, the Functional Genomics Core Facility provides a complete service including initial consultation 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 dimensions 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, 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** aims to provide scientific-technical support to the IRB Barcelona community for the identification and characterisation of a broad range of biological species, from small molecules to large biomolecules (eg, intact proteins), as well as to contribute to the study of the conformation, structural biology and non-covalent interactions of these biomolecules and 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

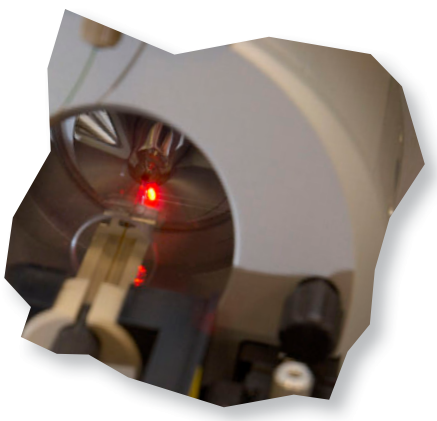


this technology. This may entail obtaining pre-generated mice, modified embryonic stem (ES) cells or gene targeting vectors from various public resources or the generation of de *novo* models, for use by the IRB Barcelona research community. The Facility aims to provide a full 'concept to mouse' service 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 problems 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) 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 Protein Expression Core Facility 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 (for example, mammalian cells, insect cells or yeasts) will be implemented shortly. In the future 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.



Facts and Figures

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Board of Trustees

The Board of Trustees, the governing body of IRB Barcelona, consists of 11 members and is chaired by the Minister of Innovation, Universities and Business of the Government of Catalonia. The Board is responsible for approving the Institute's annual budget and overseeing the strategic plan.

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Minister of the Department of Innovation, Universities and Business, Government of Catalonia

First Vicepresident

Marina Geli Fàbrega
Minister of the Department of Health, Government of Catalonia

Second Vicepresident

Màrius Rubiralta Alcáñiz
Vice-Chancellor of the University of Barcelona

Members

Ramon Moreno Amich
Director General for Research of the Department of Innovation, Universities and Business, Government of Catalonia (April 2007—present)

Francesc Xavier Hernández Cardona
Director General for Research of the Department of Innovation, Universities and Business, Government of Catalonia (October 2005—July 2006; December 2006—April 2007)

Joan Roca Acín
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Josep Samitier Martí

Pro-Vice-Chancellor for Innovation and International Research Programmes, University of Barcelona (January 2007—present)

Isidre Ferrer Abidanza

Pro-Vice-Chancellor of Science Policy, University of Barcelona (October 2005—January 2007)

Fernando Albericio Palomera

General Director, Barcelona Science Park

Roser Artal Rocafort

Manager, Barcelona Science Park (June 2007—present)

Maria Montserrat Vendrell Rius

Assistant Director, Barcelona Science Park (October 2005—March 2007)

Board of Trustees members at the last biannual meeting held at IRB Barcelona

Executive Board

The Executive Board of IRB Barcelona is responsible for executing and implementing the functions delegated by the Board of Trustees. The Board also conducts the day-to-day follow up of the Institute's administrative and management tasks.

President

José Jerónimo Navas Palacios

Director of the Research Centres Programme, Department of Health, Government of Catalonia

Members

Ramon Moreno Amich

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

Josep Samitier Martí

Pro-Vice-Chancellor for Innovation and International Research Programmes, University of Barcelona

Isidre Ferrer Abidanza

Pro-Vice-Chancellor of Science Policy, University of Barcelona (October 2005—January 2007)

Other Participants

Fernando Albericio Palomera

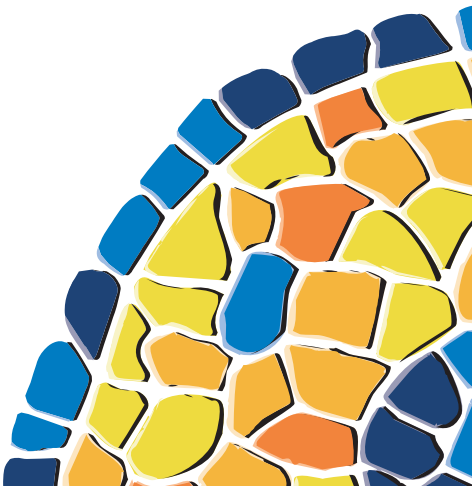
General Director, Barcelona Science Park

Joan J Guinovart Cirera

Director, IRB Barcelona

Margarida Corominas Bosch

Managing Director, IRB Barcelona



External Advisory Board

The External Advisory Board is comprised of a panel of 15 leading international scientists in the field of biomedicine. The Board provides advice and guidance on the Institute's research programmes and activities, and plays a key role in shaping future strategic directions.

Members

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The Netherlands Institute of Developmental Biology, The Netherlands

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Program in Molecular Medicine, University of Massachusetts Medical School, USA

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Department of Chemistry and Physics, University of Cambridge, United Kingdom

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Consejo Superior de Investigaciones Científicas (CSIC), Spain

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Tim Hunt
Cancer Research UK, United Kingdom

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Imperial College London, United Kingdom

Bernd Meyer
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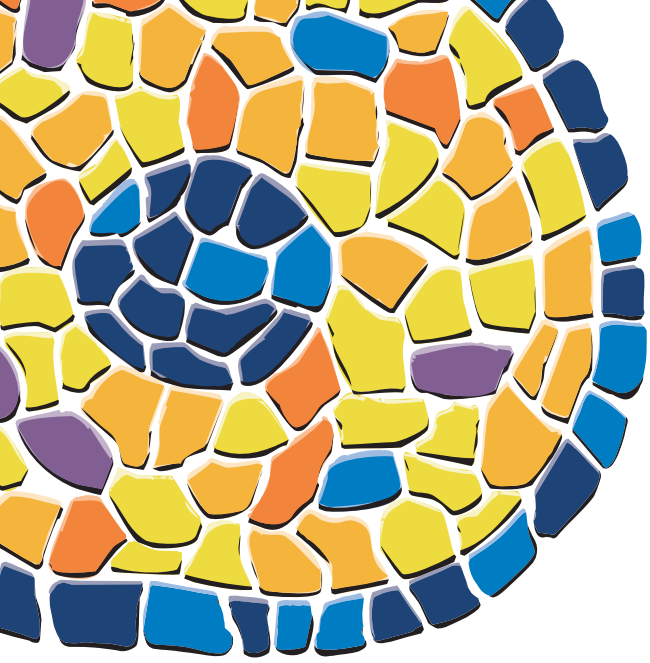

Bruce Spiegelman
Department of Cell Biology, Harvard Medical School, USA

Karen Vousden
Beatson Institute for Cancer Research, United Kingdom

Funding Sources

During 2007, IRB Barcelona received the majority of core funding for its research activities from the Government of Catalonia through the Ministry of Innovation, Universities and Business and the Ministry of Health. Additional core funding was secured from the Spanish Ministry of Education and Science (through the programme 'Ayudas a Parques Científicos y Tecnológicos'), the Spanish Ministry of Health and Consumer Affairs (to support the MetLab and the Oncology Programme) and the European Union, through FEDER Funds.

IRB Barcelona researchers also received funding through competitive grants obtained from public and private agencies.

The University of Barcelona, the Catalan Institution for Research and Advanced Studies (ICREA), the Spanish National Research Council (CSIC) and several CIBER networks (CIBERDEM, CIBERNED, CIBERER and CIBERBBN) also contributed by funding scientists who are contracted by these entities and work at IRB Barcelona.

Core Funding

Generalitat de Catalunya

Other Funding Sources

GOBIERNO DE ESPAÑA | MINISTERIO DE EDUCACIÓN Y CIENCIA | MINISTERIO DE SANIDAD Y CONSUMO | Instituto de Salud Carlos III

EUROPEAN REGIONAL DEVELOPMENT FUND

Scientific Output Summary

Scientific Publications

During 2007, IRB Barcelona researchers published a total of 177 scientific articles in peer-reviewed biomedical journals, 70 of which were international collaborations with partners from academia and industry.

The selected publications listed below appeared in journals with an Impact Factor above 7.0 (ISI 2006).

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Astigarraga S, Grossman R, Díaz-Delfín J, Caelles C, Paroush Z and Jiménez G. A MAPK docking site is critical for downregulation of Capicua by Torso and EGFR RTK signalling. *EMBO J*, **26**(3), 668-77 (2007)

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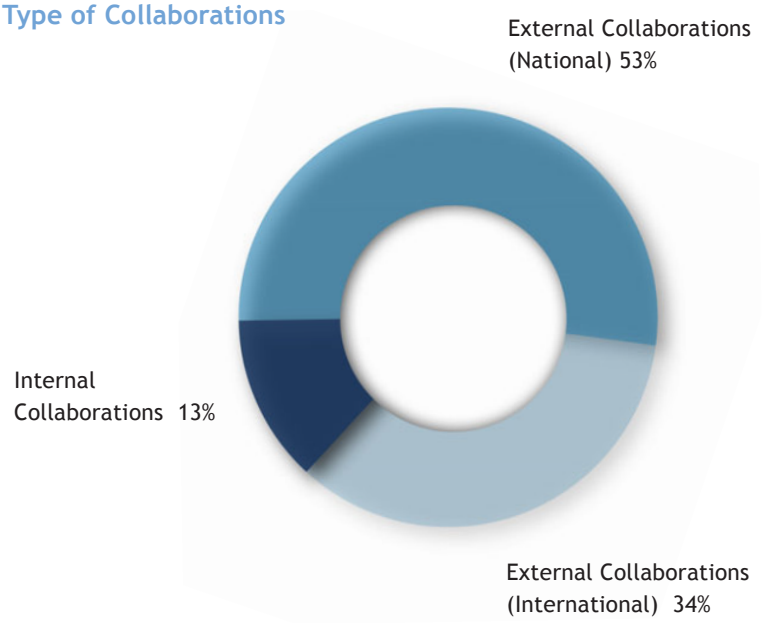
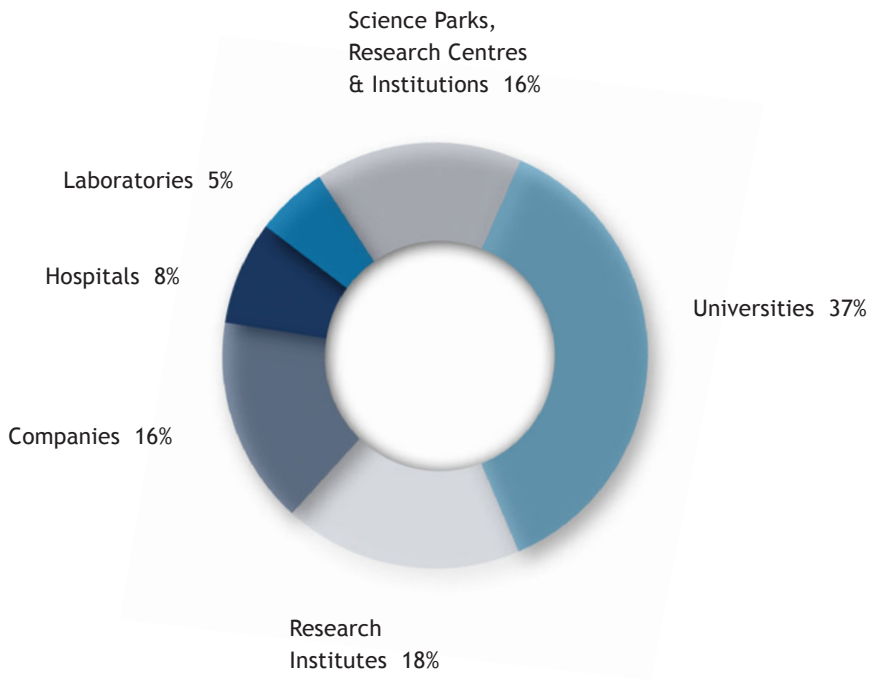
Research Collaborations

In 2007, IRB Barcelona researchers participated in a total of 128 collaborations with national and international leading research centres and institutions, universities, laboratories, hospitals and biomedical companies. A further 19 collaborations were internal partnerships among IRB Barcelona research groups.

Type of Collaborations



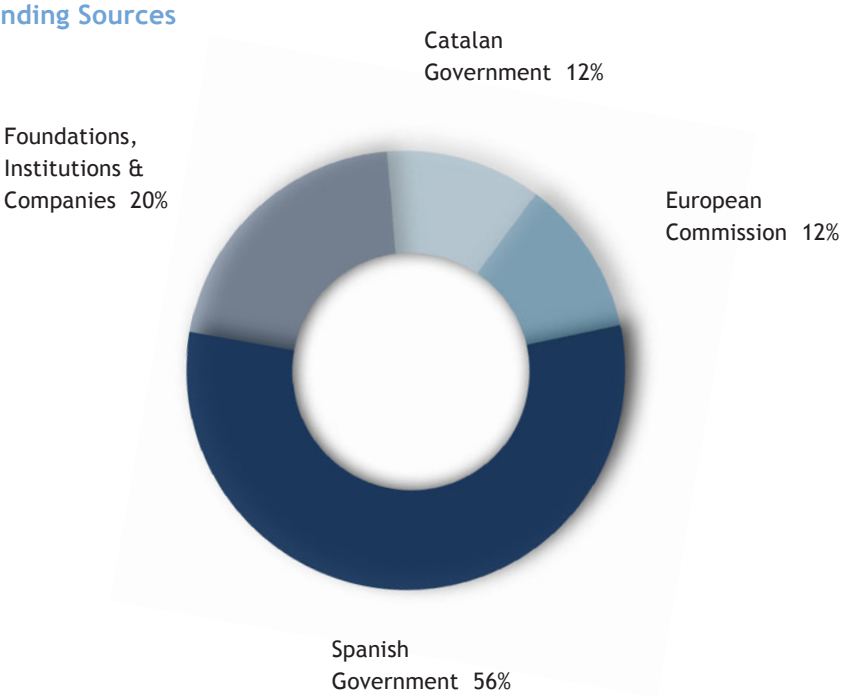
External Collaborations by Sector



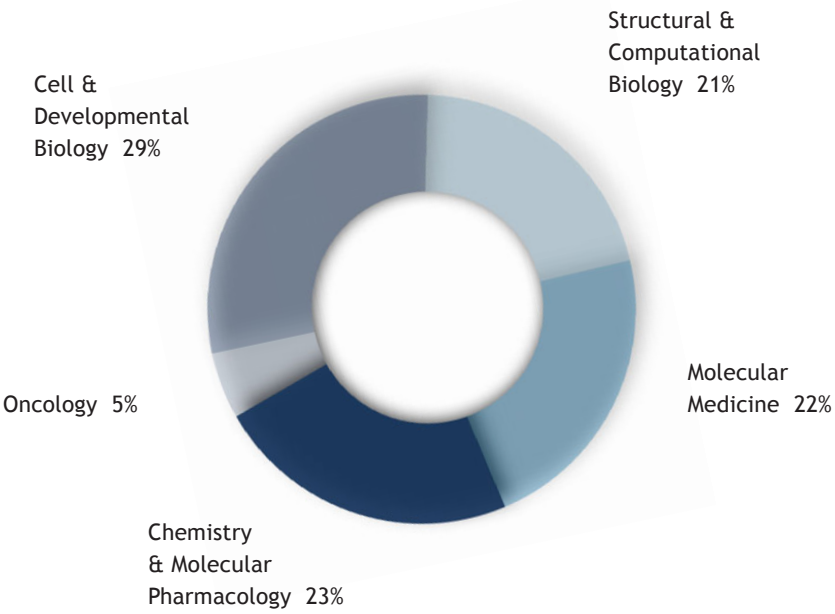
Research Grants and Networks

In 2007, IRB Barcelona researchers participated in a total of 137 research grants and networks with national and international partners. The activities were funded by the Government of Catalonia, the Spanish Ministry of Education and Science, the Spanish Ministry of Health and Consumer Affairs, the European Commission and public and private foundations, institutions and companies.

Funding Sources



Research Areas



The following list comprises funding obtained by IRB Barcelona researchers through research grants in 2007.

Research Grants in 2007	Total amount (euros)
Ministerio de Educación y Ciencia	4,364,439
European Commission	1,087,378
Instituto de Salud Carlos III	436,195
Fundación Banco Bilbao Vizcaya Argentaria	300,000
Fundació La Marató de TV3	295,623
Fundación Marcelino Botín	275,000
Agència de Gestió d'Ajuts Universitaris i de Recerca	192,391
Fundació "La Caixa"	187,959
Fundación Caja Navarra	111,678
European Science Foundation	47,914
Esteve	35,838
Agencia Española de Cooperación Internacional	35,500
Oncostem Pharma	31,866
Novo Nordisk Pharma	27,600
Fundación para la Investigación y la Prevención del Sida en España	23,453
Mutua Madrileña	20,500
Almirall	19,262
Ferrer	19,262
European Molecular Biology Organization	18,750
Sylentis, Pharmamar	9,430
Total	**7,540,038**

IRB Barcelona also received funding through personnel grants, including PhD students (with Agaur, MEC and ISCIII grants) and researchers at the Postdoc or Associate Researcher level (with programmes such as Juan de la Cierva, Ramon y Cajal, I3 and Beatriu de Pinós).

PhD Theses

IRB Barcelona hosts an established community of more than 150 PhD students from across the world currently doing their practical training in one of the Institute's research laboratories. During their doctoral stay, PhD students are given guidance and close mentoring as well as access to a wide range of scientific activities and services to ensure a solid start to their careers.

Throughout 2007, 21 PhD theses were successfully defended by students upon completion of their research project in an IRB Barcelona group.

Anàlisi del complex bitòrax de Drosophila melanogaster i contribució de les proteïnes dSAP18 i GAGA a la seva regulació

Silvia Pérez Lluch
University of Barcelona (2007)
Supervisor: Lluïsa Espinas

Aplicación de poliaminoácidos en la administración de péptidos y proteínas de interés terapéutico

Oscar Peña
University of Barcelona (2007)
Supervisor: Ernest Giralt

Caracterización del transportador SteT: primer modelo procariota de la familia LAT

César del Rio Merino
University of Barcelona (2007)
Supervisor: Manuel Palacín

Cid, la variant centromèrica de la histona H3 de Drosophila: mecanismes de deposició i anàlisis funcional

Olga Moreno Moreno
Autonomous University of Barcelona (2007)
Supervisor: Ferran Azorín

Disseny, síntesi i avaluació d'inhibidors de dimerització de la proteasa del VIH-1

Eulàlia Pinyol i Ollé
University of Barcelona (2007)
Supervisor: Anna Diez

DNA-gyrase A model peptides as potential probes to evaluate the antibacterial activity of quinolones: design, synthesis and interaction studies

Mireia G Piqueras
University of Barcelona (2007)
Supervisor: Ernest Giralt

Estudio de dos vías de modulación del receptor TRPV1 implicadas en dolor inflamatorio

Martina Quintanar
University of Barcelona (2007)
Supervisors: Fernando Albericio, Antonio Ferrer Montiel

Funcionalització de N- i O-heterocicles. Interacció d'isonitrils amb azines, sals d'azines, dihidroazines i èters d'enol cíclics

Carme Masdeu
University of Barcelona (2007)
Supervisor: Rodolfo Lavilla

Functional study of the DOR gene

Jordi Duran i Castells
University of Barcelona (2007)
Supervisor: Antonio Zorzano

Implicación de JNK en el mecanismo de acción antidiabética de las TZDs/PPAR□

Julieta Díaz Delfín
University of Barcelona (2007)
Supervisor: Carme Caelles

Ligandos duales, una nueva estrategia para el desarrollo de agentes terapéuticos que interaccionen con GPCRs

Marc Vendrell
University of Barcelona (2007)
Supervisor: Fernando Albericio; co-supervisor: Miriam Royo

NMR as a tool to elucidate the rules that govern WW domain binding specificity and stability

Ximena Ramirez-Espain
Universidad Autónoma de Madrid (2007)
Supervisor: Maria Macias

Noves aproximacions sintètiques per a la química paral.lelitzable

Aina Colombo
University of Barcelona (2007)
Supervisors: Fernando Albericio, Pilar Forns

Papel de la antiadhesina renal podocalixina en el desarrollo del sistema nervioso

Nathalia Vitureira Serpa
University of Barcelona (2007)
Supervisor: Eduardo Soriano

Papel de la MKP-1/Dusp-1 en la acción antiinflamatoria de los glucocorticoides en ratón

Salvador Ferré Benedicto
University of Barcelona (2007)
Supervisor: Carme Caelles

Physiology and pharmacology of the soluble form and the membrane of the SSAO/VAP-1 membrane

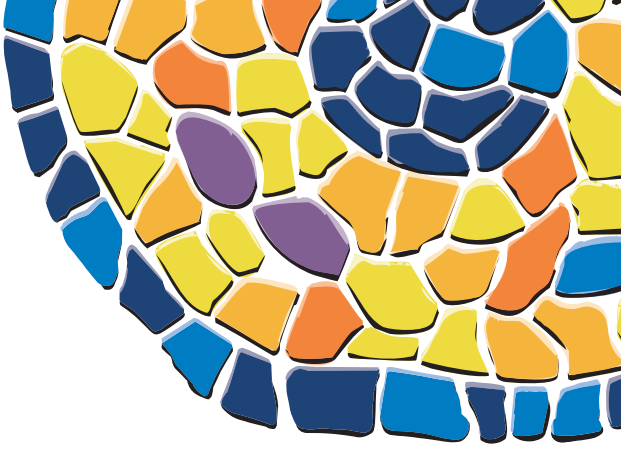
Silvia García Vicente
University of Barcelona (2007)
Supervisor: Antonio Zorzano

Preparació de derivats de polisacàrids i la seva aplicabilitat com a selectors quirals en la separació d'enantiòmers per cromatografia de repartiment centrífug (CPC)

Eva Pérez Palomar
University of Barcelona (2007)
Supervisor: Cristina Minguillón

Regulación de la proliferación de los progenitores neurales en el telencéfalo adulto: efecto de las aferencias neuronales sobre la proliferación en el hipocampo y funciones de la proteína priónica celular

Xavier Fontana García
University of Barcelona (2007)
Supervisor: José A del Río



Regulation of the IA-β and MKP-1genes by the AP1 complex

Cristina Casals Casas
University of Barcelona (2007)
Supervisor: Antonio Celada

Síntesi de nous catalitzadors per a reaccions d'organocatàlisi

Noemí García-Delgado
University of Barcelona (2007)
Supervisor: Xavier Verdaguer

Síntesi de substrats i inhibidors de la SSAO/VAP-1

Francesc Yraola
University of Barcelona (2007)
Supervisor: Fernando Albericio; co-supervisor: Miriam Royo

Technology Transfer Activities

In 2007, IRB Barcelona researchers were actively engaged in a series of technology transfer activities with industry partners. Below is a list of scientific work that resulted in granted patents and patent applications to secure exclusive rights to discoveries and inventions. In addition, the start-up company Omnia Molecular, which was founded in 2005 by IRB Barcelona researcher Lluís Ribas de Pouplana, was also granted two patents and closed its first round of investment with the incorporation of the venture capital firm 'Caixa Capital Risk'.

Anti tumoural compounds

Tulla-Puche J, Marcucci E, Bayó-Puxan N and Albericio F
Provisional patent application by PharmaMar and identified as Attorney Docket No. 07380361

Arylalkylamine vanadium (v) salts for the treatment and/or prevention of diabetes mellitus

Royo Exposito M, Marti Clauzel L, Abella Martin A, Garcia Vicente S, Testar Yinbert X, Zorzano Olarte A, Palacin Prieto M, Albericio Palomera F, Yraola Font F and Mian A
Publication info: US 2007066682 A1 20070322 CAN 146:309354 AN 2007:333004

Compounds that act as a vehicle for delivery through the blood-brain barrier and charge delivery vehicle constructions

Giralt E and Teixidó M
Publication info: PCT/ES2007/0401, WO2008025867

Indole derivatives as antitumoural compounds

Reyes Benitez JF, Francesch Solloso A, Cuevas Marchante C, Altuna Urquijo M, Pla Queral D, Alvarez Domingo M and Albericio Palomera F
Publication info: WO2007054748 A120070518 CAN146:528181 AN2007:538679

Inhibition of alpha-synuclein aggregation

Zurdo J, Fowler S, Stallwood Y, Giralt E, Teixidó M and Carulla N
Publication info: PCT/GB2007/002469, WO2008003943

Método de identificación de compuestos para terapia de enfermedades relacionadas con la acumulación de glucógeno y uso de compuestos para preparar medicamentos contra dichas enfermedades

Rodriguez de Cordoba S and Guinovart J
Solicited

New polymers and their use as fluorescent labels

Aymamí J, Albericio F, Aviñó A, Farrera J, Royo M, Navarro I and Eritja R
Publication info: 07112386.3-2101

Pharmaceutical compositions comprising a tungsten salt (VI) for the treatment of neurodegenerative disorders, particularly Alzheimer's disease and schizophrenia

Gomez A, Corominola H, Zafra D, Gomis de Barbara R, Avila de Grado J, Dominguez J and Guinovart J
Publication info: WO2007014970, CA2616960

Proton acceptor immonium-type coupling reagents

Albericio F, El-Faham A, Luxembourg Y and Ewenson A
Provisional patent application to be filed in the USA, and identified as Attorney Docket No. 39712

Barcelona BioMed Seminars

During 2007, IRB Barcelona held a series of weekly seminars devoted to keep researchers abreast of the latest scientific developments in the biomedical sciences. Barcelona BioMed Seminars brought together dozens of leading international scientists from relevant areas of expertise to present their current work and latest results to the IRB Barcelona community. Organised by researchers at the Institute, the seminars were also open to the local scientific community.

17 January 2007

Transcription regulation: from parts list to genomic network

Nicholas Luscombe, European Bioinformatics Institute, Wellcome Trust Genome Campus, Cambridge, UK

26 January 2007

Development of new adenovirus vectors with specific tropism for the intestinal epithelium

Miguel Chillón, Gene Therapy Laboratory, Centre de Biotecnologia Animal i Teràpia Genètica, Universitat Autònoma de Barcelona, Barcelona, Spain

2 February 2007

Mitochondrial membrane dynamics in human cells: actors, mechanisms and (dys)functions

Manuel Rojo, Inserm, Institut de Myologie, Paris, France

6 February 2007

Transcriptional mechanisms underlying mammalian differential gene expression

Bart Deplancke, University of Massachussets Medical School, Massachussets, USA

9 February 2007

Nuclear PTEN: a tale of many tails

Rafael Pulido, Centro de Investigación Príncipe Felipe, Valencia, Spain

16 February 2007

Sharp boundaries of Dpp signalling trigger local cell death required for Drosophila leg morphogenesis

Magali Suzanne, Centre de Biochimie, Université Nice Sophia Antipolis, Nice, France

19 February 2007

Phenotypic driven mammalian functional genomics: Applications to cancer and stem cell biology

Frank Buchholz, Max Planck Institute for Molecular Cell Biology and Genetics, Munich, Germany

20 February 2007

The ubiquitin-proteasome system: novel levels of regulation and biomedical applications

Bernat Crosas, Institute of Molecular Biology of Barcelona, CSIC, Barcelona, Spain

21 February 2007

Regulation of Rho signalling in tumour cell movement

Emmanuel Vial, Institute of Signalling Developmental Biology and Cancer, Nice, France

23 February 2007

Regulatory networks determining T cell versus macrophage/dendritic cell commitment

Thomas Graf, Center for Genomic Regulation, Barcelona, Spain

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02 March 2007

Xenopus oocytes, MAP kinases and cancer

Angel Nebreda, Spanish National Cancer Research Centre (CNIO), Madrid, Spain

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09 March 2007

A supramolecular approach to the molecular recognition of protein surfaces

Javier de Mendoza, Institute of Chemical Research of Catalonia (ICIQ), Tarragona, Spain

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16 March 2007

Hedgehog-Gli signalling in stem cells, cancer and cancer stem cells

Ariel Ruiz Altaba, University of Geneva Medical School, Geneva, Switzerland

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23 March 2007

Finding new roles for p38MAPKs

Ana Cuenda, Centro Nacional de Biotecnología, Madrid, Spain

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30 March 2007

Glyoxylyl peptide chemistry and novel methods for the preparation of peptide microarrays

Oleg Melnyk, Institut de Biologie de Lille, Lille, France

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13 April 2007

Genetic analysis of cell cycle kinases using mouse models

Marcos Malumbres, Spanish National Cancer Research Centre (CNIO), Madrid, Spain

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04 May 2007

Effects of hyperglycemia on gene expression in human muscle and adipose tissue: potential implications in glucose toxicity

Hubert Vidal, Institut National de la Santé et de la Recherche Médicale (Inserm), Lyon, France

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18 May 2007

Insulin signalling in Drosophila melanogaster

Aurelio Teleman, European Molecular Biology Laboratory, Heidelberg, Germany

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24 May 2007

Functional genomics in biomedical research

Herbert Auer, IRB Barcelona, Barcelona, Spain

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25 May 2007

Anopheles and plasmodium: immunogenomics of vector/pathogen interactions

Fotis Kafatos, Imperial College London, London, UK

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29 May 2007

Cyclic cystine knot motif as a basis for design of stable molecular scaffolds

Masa Cemazar, Institute for Molecular Biosciences, University of Queensland, Brisbane, Australia

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30 May 2007

Cryo-EM studies on the regulation of ribosomal translocation

Sean Connel, Institut für Medizinische Physik und Biophysik, Berlin, Germany

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31 May 2007

A quest for the physico-chemical principles that govern protein folding, misfolding and aggregation

Xavier Salvatella, University of Cambridge, Cambridge, UK

1 June 2007

Molecular control of cell polarity and assymetric cell division in Drosophila

Andreas Wodarz, University of Göttingen, Göttingen, Germany

8 June 2007

Winners and losers during growth of the Drosophila wing

Laura A Johnston, College of Physicians and Surgeons, Columbia University, New York, USA

15 June 2007

Genomics and systems biology approaches to the study of virulence in human malaria

Hernando del Portillo, Centre for International Health Research (CRESIB), Barcelona, Spain

22 June 2007

Keeping mitochondria and endoplasmic reticulum together: can mitofusin-2 be helpful?

Luca Scorrano, Venetian Institute of Molecular Medicine, Padova, Italy

29 June 2007

Functional genetic approaches identify cancerous miRNAs

Reuven Agami, The Netherlands Cancer Institute, Amsterdam, The Netherlands

6 July 2007

Identification of novel Hypoxia Inducible Factor (HIF)-target genes

Luis del Peso, Instituto de Investigaciones Biomédicas, Madrid, Spain

13 July 2007

Silencing of the genome through histone demethylation

Ramin Shiekhatar, Centre for Genomic Regulation, Barcelona, Spain

27 July 2007

Regulation of Groucho-dependent repression by RTK signalling

Ze'ev Paroush, The Hebrew University, Jerusalem, Israel

14 September 2007

The ENCODE Project: Uncovering the transcriptional complexity of the human genome

Roderic Guigó, Centre for Genomic Regulation, Barcelona, Spain

21 September 2007

Non-transcriptional control of DNA replication by c-Myc

David Domínguez, Institute for Cancer Genetics, Columbia University Medical Center, New York, USA

26 September 2007

p38a, master regulator of myoblast proliferation and differentiation

Eusebio Perdiguero, Centre for Genomic Regulation, Barcelona, Spain

28 September 2007

Towards structure-based protein functional annotation and rational engineering

Mayte Pisabarro, Biotechnologisches Zentrum, Dresden, Germany

28 September 2007

Enhanced mucosal IgA response and solid protection against viral challenge induced by a novel dendrimeric peptide

David Andreu, Proteomics & Protein Chemistry, DCEXS-UPF-PRBB, Barcelona, Spain

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5 October 2007

The Protein Expression Core Facility: Implementing high through-put cloning and expression technologies at IRB Barcelona

Nick Berrow, Protein Expression Core Facility, IRB Barcelona, Barcelona, Spain

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19 October 2007

Targeting ubiquitin signalling networks

Ivan Dikic, Johann Wolfgang Goethe University, Institute of Biochemistry, Frankfurt, Germany

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26 October 2007

Decoding the Notch signal: transcriptional events elicited by Notch signalling

Sarah Bray, Cambridge University, Cambridge, UK

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2 November 2007

Genetic analysis of chromosome break metabolism in eukaryotic cells

John Petrini, Memorial Sloan-Kettering Cancer Center, New York, USA

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9 November 2007

Molecular chaperones and the dynamic remodelling of nuclear receptor action

Andrew Cato, Institute of Toxicology and Genetics, Karlsruhe, Germany

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16 November 2007

Choline binding repeats as recognition elements in pneumococcal choline-binding proteins (CBPs)

Margarita Menéndez, Instituto de Química-Física Rocasolano (CSIC), Madrid, Spain

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23 November 2007

Studying structure and function of protein complexes by solid-state NMR spectroscopy

Marc Baldus, Max Planck Institute for Biophysical Chemistry, Göttingen, Germany

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14 December 2007

Molecular regulation of epithelial polarity and morphogenesis

Fernando Martín-Belmonte, Centro de Biologia Molecular Severo Ochoa, Madrid, Spain

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19 December 2007

The role of the Mre11 complex in apoptosis and tumour suppression

Travis Stracker, Memorial Sloan-Kettering Cancer Center, New York, USA

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21 December 2007

Multifaceted roles of p38¤ signalling in inflammation and gene regulation

Jin Mo Park, Massachussets General Hospital, Massachussets, USA

Barcelona BioMed Conferences

IRB Barcelona researchers organised during 2007 a series of Barcelona BioMed Conferences in collaboration with scientists from prestigious institutes around the world. Twenty speakers chosen from among the top international researchers in their field were 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.

The conference series is made possible in part thanks to the BBVA Foundation's commitment to promoting basic and applied biomedical research. Events are generously hosted by the Institut d'Estudis Catalans in downtown Barcelona.

26—28 March 2007

Barcelona BioMed Conference

THE REGULATION OF CHROMATIN FUNCTIONS

Organisers: Ferran Azorín (IRB Barcelona/CSIC) and Tony Kouzarides (Wellcome Trust/Cancer Center, Gurdon Institute, London, UK)

25—27 June 2007

Barcelona BioMed Conference

INFLAMMATION AND CHRONIC DISEASE

Organisers: Carme Caelles (IRB Barcelona) and Michael Karin (University of California at San Diego, La Jolla, USA)

1—3 October 2007

Barcelona BioMed Conference

STEM CELLS AND CANCER

Organisers: Eduard Batlle (IRB Barcelona) and Hans Clevers (Hubrecht Laboratory, Utrecht, Netherlands)

Other Conferences

26—27 April 2007

Fundación Ramon Areces/IRB Barcelona Joint Conference

MOLECULAR MECHANISMS OF MACROPHAGE ACTIVATION: CLASSICAL AND ALTERNATIVE

Organisers: Antonio Celada (IRB Barcelona) and Francisco Lozano (University of Barcelona, Spain)

24—25 May 2007

BSC-IRB Barcelona Conference on Computational Biology

BIOMOLECULAR SIMULATIONS, BIOINFORMATICS AND SUPERCOMPUTING

Organiser: Modesto Orozco (IRB Barcelona, Barcelona Supercomputing Center)

Outreach Activities

IRB Barcelona principal investigators, research associates, postdoctoral fellows and PhD students were involved throughout 2007 in several outreach activities organised by the Barcelona Science Park and open to the general public. The goal was to bring science to a wider audience and spread awareness of the research carried out at IRB Barcelona.

3 & 10 March 2007 | 3, 10, 16, 17 & 31 May 2007 | 17 November 2007 | 1 December 2007

RESEARCH!

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

Participants: Elisabeth Castellanos[1], Consol Farrera[2], Ana Janic[1], Leire Mendizabal[1] and Maria Serra[2]
IRB Barcelona groups on cell division[1] and macrophage biology

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

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24—25 March 2007

FESTA DE LA CIÈNCIA 2007

A research festival at the Ciutadella Park with live experiments and demonstrations

Participants: Elisabeth Aguilar and Ana Janic
IRB Barcelona cell division laboratory

Topic: DNA extraction from saliva

March—December 2007

RESEARCH IN PRIMARY SCHOOLS

A bimonthly activity to bring science closer to primary school students through active participation in research experiments

Participants: Carme Cortina and Elisa Espinet
IRB Barcelona colorectal cancer laboratories I and II

Activities: Hands-on research workshop for primary school students and guided tour of the Barcelona Science Park

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

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12—13 April 2007

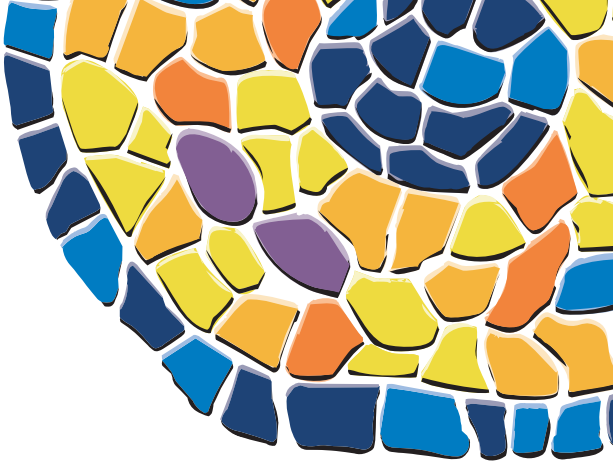
LIVE RESEARCH FAIR

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

Participants: Paola Bartoccioni, Hans Burghardt, Carles Cantó and Meritxell Orpinell
IRB Barcelona group on molecular pathology and therapy in heterogenic and polygenic diseases

Topic: Beyond our genes. Why do we get sick?

Primary school students visit the IRB Barcelona fly room during one of the guided tours of the Barcelona Science Park



1 July—30 September 2007

SPEND THE SUMMER AT THE PARK!

A student programme directed at undergraduates in the final years of their degrees who wish to familiarise themselves with the world of research

Participants: Patrick Aloy[1], Carme Caelles[2], Antonio Celada[3], Anna Diez[4], Ernest Giralt[5], Joan Guinovart[6], Maria Macias[7], Miquel Pons[8], Antoni Riera[9], Neus Serrat[3], Teresa Tarragó[5], Meritxell Teixidó[5], Anabel F Valledor[3] and Xavier Verdaguer[9]
IRB Barcelona groups on structural bioinformatics[1]; cell signalling[2]; macrophage biology[3], bioactive peptidomimetic and heterocycles[4]; design, synthesis and structure of peptides and proteins[5]; metabolic engineering and diabetes therapy[6]; biomolecular NMR spectroscopy[7], biomolecular NMR: structure and dynamics of proteins and protein complexes[8]; and research unit on asymmetric synthesis[9]

Activities: Hands-on collaboration in projects performed by research groups, research centres and companies located in the Barcelona Science Park

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July 2007—March 2008

TUTORING FOR SECONDARY SCHOOL STUDENTS

An academic activity to assist secondary school students in their research projects

Participants: Elisabeth Aguilar[1], Carlos Alegret[2], Roman Bonet[3], Danuel Cifuentes[4], Carme Cortina[5], Ana Janic[1], Marc Liesa[6], Carles Martínez[4], Laura Nocito[4], Neus Rafel[7], Lidia Ruiz[3] and Dèlia Zafra[4]
IRB Barcelona groups on cell division[1]; asymmetric synthesis[2]; biomolecular NMR spectroscopy[3]; metabolic engineering and diabetes therapy[4]; colorectal cancer[5]; molecular pathology and therapy in heterogenic and polygenic diseases[6]; and development and growth control laboratory[7]

Activities: Tutoring and assistance to 16-year-old students for their research project and hands-on experience in laboratories at the Barcelona Science Park

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13—15 November 2007

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

A hands-on experience in laboratories for secondary school students

Participants: Carme Cortina and Elisa Espinet
IRB Barcelona colorectal cancer laboratories I and II

Activities: Hands-on experiments in the IRB Barcelona colorectal cancer laboratory, assisted by researchers

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

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Organisation Chart

Board of Trustees

External Advisory Board

Executive Board

Director
Joan J Guinovart

Adjunct Director
Joan Massagué

Internal Scientific Commitee

Marco Milán
(as of December 2007)
Cayetano González
(until December 2007)
Miquel Coll
Antonio Zorzano
Ernest Giralt
Eduard Batlle

Managing Director
Margarida Corominas

Research Programmes

Cell and Developmental Biology
Ferran Azorín
Jordi Casanova
Cayetano González
Marco Milán
Lluis Ribas
Eduardo Soriano

Structural and Computational Biology
Patrick Aloy
Miquel Coll
Ignasi Fita
Maria Macias
Modesto Orozco
Miquel Pons

Molecular Medicine
Carme Caelles
Antonio Celada
Joan J Guinovart
Manuel Palacín
Antonio Zorzano

Chemistry and Molecular Pharmacology
Fernando Albericio
Ramon Eritja
Ernest Giralt
Antoni Riera
Màrius Rubiralta

Oncology
Eduard Batlle
Elena Sancho
MetLab

Core Facilities and Services

Advanced Microscopy

Bioinformatics/Biostatistics

Functional Genomics
Herbert Auer

Mass Spectrometry
Marta Vilaseca

Mouse Mutant

Protein Expression
Nick Berrow

Administration

Finance and Purchasing
Carles Coarasa

Human Resources
Sylvia Martínez

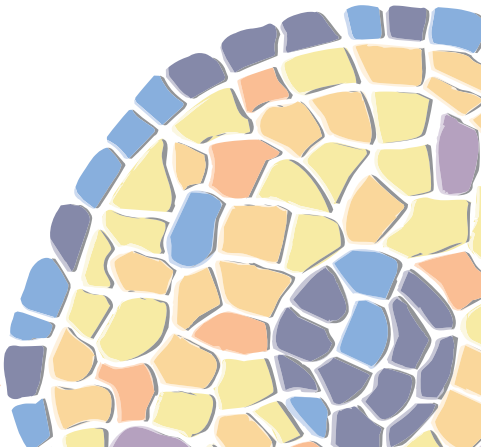
Communications and External Relations
Sarah Sherwood

Information Technology Services
Francisco Lozano

Research and Academic Administration
Margarita Navia

Scientific structure

Administrative structure, supporting scientific activities



Directorate and Administration Staff

Directorate

Director
Joan Guinovart

Managing Director
Margarida Corominas

Adjunct Director
Joan Massagué

Directorate Secretary
Maria Estévez

Research Programmes

Cell and Developmental Biology Programme

Programme Coordinator
Marco Milán
(as of December 2007)

Programme Secretary
Isabel Santori

Programme Coordinator
Cayetano González
(until December 2007)

Structural and Computational Biology Programme

Programme Coordinator
Miquel Coll

Programme Secretary
Vanessa Llobet

Molecular Medicine Programme

Programme Coordinator
Antonio Zorzano

Programme Secretary
Dulce Tienda
(until September 2007)

Programme Secretary
Natàlia Molner
(as of October 2007)

Chemistry and Molecular Pharmacology Programme

Programme Coordinator
Ernest Giralt

Programme Secretary
Eva Poca

Oncology Programme

Programme Coordinator
Eduard Batlle

Programme Secretary
Sara Martorell

Research and Academic Administration

Head of Research and Academic Administration
Margarita Navia

Academic Officer
Clara Caminal

Communications and External Relations

Head of Communications and External Relations
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Conference Secretary
Meritxell Gavaldà

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Head of Human Resources
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HR Technician
Silvia Aguadé

Information Technology Services

Head of Information Technology Services
Francisco Lozano

Systems Administrator
David Villanueva

Systems Architect
Roberto Bartolomé

Systems Administrator
Jesús Sánchez

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Head of Finance and Purchasing
Carles Coarasa

Purchasing
Anna Oñatevia (until November 2007)

Accounting Officer
Silvia Ramírez

Purchasing
Sara López

Projects and Inventory
Stel·la Serra

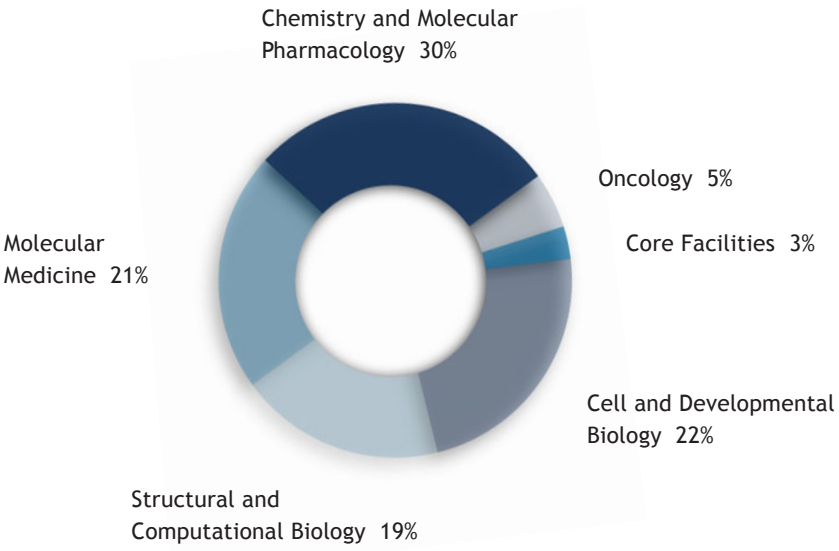
Purchasing
Mª Jesús López

Human Resources Statistics

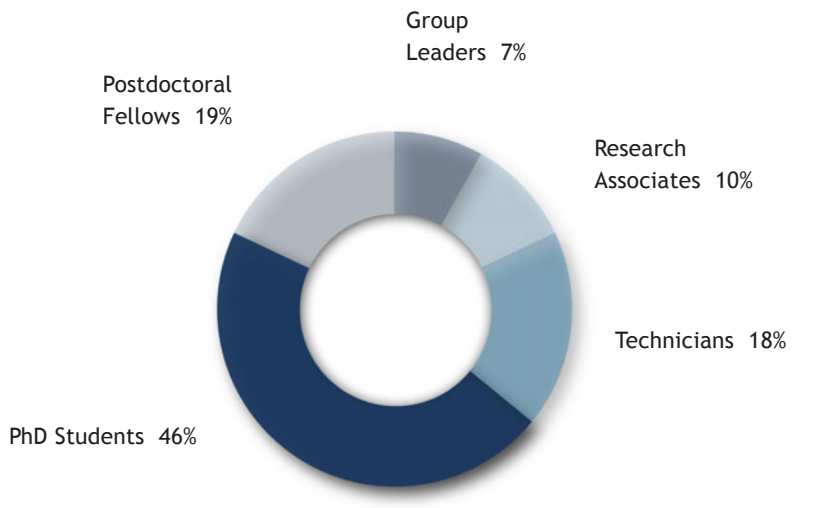
Total IRB Barcelona members	
Administration	28
Researchers	354
Total	**382**

Total IRB Barcelona employees vs total members	
IRB Barcelona Employees	114
Others	268
Total	**382**

Scientific staff by research programme



Scientific staff by professional category



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Barcelona Science Park

The PCB will increase the area from 32,000 m^2 to 90,000 m^2 by 2011

The Barcelona Science Park (PCB, Parc Científic de Barcelona) is a cluster of research of excellence that hosts institutes and companies with the aim to promote innovation, mainly in life sciences. Established by the University of Barcelona in 1997, the Barcelona Science Park was the first science park in Spain and today is an international reference to foster interactions between universities and companies.

Today, the Park hosts more than 2,200 professionals, four research institutes, more than 45 companies, a biotech enterprise bioincubator, more than 70 research groups, and a wide range of technological support services for research activities.

The Barcelona Science Park will almost quadruple in size, growing from its 32,000 m^2 to a total of 90,000 m^2, as part of its development plans for the period up to 2011. The development, which was foreseen when the Park was first created, will see an increase in the number of biotech and pharmaceutical firms, research centres and institutes, technology platforms, and scientific and innovation support services that are housed within the Park. The expansion plans also foresee an increase in the number of professionals working in R&D from 2,200 to 4,000 in 2011.

This growth will entail the creation and adaptation of new premises, as well as the renovation of existing facilities. The Modular Building (which until now has housed most of the PCB's research laboratories and technology services) will be extended, the tower blocks on the site bordered by the streets Josep Samitier, Baldiri Reixac and Dr Marañón will be redesigned and the Administrative Building will be renovated. In this context, the Park built a new laboratory building, named Helix Building, in 2007.

This new building offers more than 6,500 m^2 of laboratory space and provides a home for over thirty research groups and centres from both the public and business sectors (IRB Barcelona, IBMB-CSIC, IBEC, Oryzon genomics, Ordesa, Combino Pharm, etc.). The building also houses the new PCB-Santander Bioincubator, which comprises over ten technology-based spin-off companies.

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