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Foreword

Building an institute and a new culture as Barcelona becomes a city of science

Catalonia is known for its outstanding artists, architects and musicians, and although we have produced excellent scientists, few of our research institutes have achieved international recognition.

That is changing quickly, thanks to a dedicated effort by the Catalan Government who is transforming Catalonia into an internationally recognised focal point for science. IRB Barcelona, founded by Ministry of Innovation, Universities and Business and the Ministry of Health of the Catalan Government, the University of Barcelona and the Barcelona Science Park, is a central figure in this process. Our goal is to ensure that we make a vital contribution to the dramatic scientific revolution that is now sweeping the globe – one which promises to significantly improve the quality of our lives, to eradicate diseases that cause immense suffering throughout the world, and to bring economic benefits to those who contribute.

Numbers give a hint at how serious our contribution is: IRB Barcelona was founded a mere two years ago, but we already comprise more than 350 research, technical and administrative staff. We will continue to grow over the next two or three years, adding new groups, platforms, and expertise that will widen our focus and bring in new disciplines. Yet even at the current size we are getting things done. This can be seen from the publications of our scientists, listed in the Scientific Reports that accompany this volume, which have been achieved in the short time since the groups moved in.

Our goal is that we make a vital contribution to the dramatic scientific revolution that is now sweeping the globe

The shift which is occurring in science has to do with a new understanding of diseases that have been virtually unassailable through current medical practices. In the 19th century, researchers like Pasteur and Koch launched a new era in medicine by discovering that microorganisms cause infectious diseases. That insight was the key to developing vaccines, which take advantage of the highly-evolved animal immune system. Viruses, bacteria, and parasites are still a huge problem the world over; novel infectious diseases continue to arise, and old enemies mutate to emerge as new threats. Even so, in the developed world these are no longer the major killers. They have been supplanted by conditions that arise from flaws in our own cells. These mostly strike in old age, and we have not evolved defenses against them. To find cures, we will have to emulate our predecessors of the 19th century and first develop a deep understanding of the causes. This means discovering how mutations or other problems with molecules become so disruptive that they end in suffering and death.

We have an entirely new arsenal of tools to investigate these questions. The microscopes and dyes of a century ago have been enhanced by methods from genetics, chemistry, physics, and computation. These types of science arose in separate institutes and university departments, and for a long time they focused on different problems. Even the life sciences have arisen from many sub-disciplines – such as structural biology, biochemistry, cell biology, genetics and developmental biology – which have been too isolated in the past.

Only with the arrival of the genome age have all of these types of science truly started to come together, yet they still need a push to take the last steps toward integration. Over the last half-century, the focus of most biological research was to zoom in on single molecules and then to study their local interactions – how they mesh with each other. The next half-century will be devoted to zooming out and studying how the levels are nested within each other. Disciplines are coming together to assemble an integrated picture of life: how single molecules combine into machine-like structures; how these machines change the behaviour of cells; and how those cells work with their neighbours, under the influence of the environment, to produce a healthy or damaged organism. Insights into these processes have led to the vision of a new type of medicine in which our understanding of how molecules work will allow us to repair them, without disrupting the delicate balance of all the higher systems in which they function.

In the past, a scientist's work was usually quite focused; very few gained a broad view of the many levels of life and its true complexity. Yet this is the type of scientist we will need to create a new type of medicine, and we will also require a new kind of laboratory. This realisation led to our formulation of a vision, several years ago, of an institute that would bring together different disciplines and a spectrum of expertise under one roof. From different directions, our groups would aspire to a common aim: to make new discoveries in basic research that can be translated into medical applications.

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That goal explains the components that have been assembled in 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:

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.

Chemistry and Molecular Pharmacology specialises 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.

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.

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.

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. This research line is directed by Joan Massagué and is operated in coordination with the Cancer Biology and Genetics programme that he chairs at the Memorial Sloan-Kettering Center, in New York.

We are committed to doing our work at an extremely high level and have put into place a series of structures to help us achieve this. Our scientific work will be regularly assessed by an External Advisory Board which comprises 15 leading international researchers in biomedicine. Its main task is to provide guidance in shaping our research and related activities.

Research is most likely to achieve excellence with superb technical support and a fertile environment. We are in the process of setting up new service units to provide our researchers with state-of-the-art facilities. These will widen an already considerable palette of service units and technology platforms established and operated by the Barcelona Science Park and by the Scientific and Technical Services of the University of Barcelona.

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.

The level of research and the collection of activities and platforms at IRB Barcelona provides 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 the Barcelona BioMed Seminar Series. These events are organised several times a week and ensure that PhD students keep abreast of the latest advances in biomedicine. IRB Barcelona's location within and strong ties to the University of Barcelona provide a lively and stimulating setting in which students may complete their training.

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 meetings called the Barcelona BioMed Conferences. They are organised in collaboration with the BBVA Foundation and provide a new, creative platform where leading researchers can meet and discuss the most recent breakthroughs in several fields of the biomedical sciences. 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 further 40 highly experienced participants for three days of intensive discussions on the latest research in their fields.

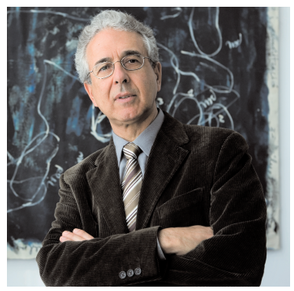
We are building an institute for the future, and we are doing so at a very special time in science

A constant flow of international visitors provides another crucial link to the world, both for the expertise they bring and the rich cultural experiences that arise from their stay. IRB Barcelona hosts visitors at all stages of their scientific careers.

We believe that institutes which have the potential to change society need to discuss their research with the public and help prepare people for those changes. IRB Barcelona actively explains the work done at the institute through the mass media at a level that people can understand, through education activities, and through the Barcelona BioMed Forums. These events are aimed at increasing public awareness and encouraging a better understanding of progress in the biomedical sciences.

As a major stakeholder in biomedical research, IRB Barcelona is firmly committed to the Catalan Government's intent to develop the area into a dynamic hub for biomedicine. This will require working together toward a common vision. We are establishing strong ties to other Catalan research institutes and hospitals in the development of the Bioregion of Catalonia. IRB Barcelona will profit greatly from the presence of other new, major infrastructures that can complement each other in wonderful ways. Synchrotron radiation, which will be practiced at the future Alba facility, began as a tool for physicists but has evolved into the most commonly-used technique to investigate molecular structures. We will profit immensely from our close proximity to this institute, as well as to the Barcelona Supercomputing Center which hosts the MareNostrum Supercomputer. The daily conduct of life involves such complex patterns that describing them – and simulating them – will be the hardest tasks ever asked of computers.

In summary, our aims are ambitious, and success will depend on both internal and external factors. We are building an institute for the future, and we are doing so at a very special time in science. Researchers have suddenly gained access to a vast, virtually uncatalogued library of genomic information; they have new tools to study and intervene very precisely in living systems; and for the first time, the normal researcher has access to high-throughput techniques that provide a snapshot of life in all of its complexity. Adapting to this changing environment will continue to require creativity and administrative flexibility. Under the guidance of our Board of Trustees, IRB Barcelona is quickly becoming a research institute of excellence, recognised at the international level. I am deeply appreciative of the efforts of our highly motivated team which have made the launch of IRB Barcelona a great success.



Joan J Guinovart
Director, IRB Barcelona

Scientific Summaries

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

Cell and Developmental Biology Programme

On a scale stretching from the size of single molecules up to the human body, 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 huge 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 understand 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 studied in quite separate disciplines, but in the meantime they have been growing together rapidly. Cell biologists are getting a handle on the processes that enable cells to create larger structures, and developmental biologists have become interested in the cellular mechanisms that underlie the growth of embryos.

Bringing these themes together requires multi-disciplinary 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 themes including how signals are passed within and between cells, what controls cell migration, and how boundaries form between tissues during development. Other topics include cell division in development and disease, epigenetic regulation and chromatin function, and how controlling the output of genes can be used for biomedical purposes. The research groups in the Programme pursue these questions in several model organisms including *C. elegans*, *Drosophila*, 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 is that the DNA in the nucleus is wrapped around proteins and other molecules in a form called *chromatin*. These molecules have an important role to play because they help pack an immense amount of DNA into the small space of the nucleus; another function is to make genes accessible (or inaccessible) to the machines that transform them into other types of molecules. **Ferràn Azorín's lab** studies the molecular processes that structure chromatin and thus control its biological effects. The main question they are working on involves how large blocks of DNA are rendered inactive, also known as "silencing", and how the cell keeps them that way. Some regions of DNA are almost permanently silenced; others are switched on and off to achieve particular developmental effects. Azorín and his colleagues are studying both types.

Making proteins in pathogens

To survive, cells have to transform information in their genome into RNAs and then proteins. Carrying out this latter step, called translation, requires a complicated network of molecules that scientists are beggining to understand in detail. The group of **Lluís Ribas de Pouplana** is exploring this network in single-celled protozoa that infect human beings. Another of the group's interests is the study of the evolution of the gene translation machinery. It underwent significant changes with the emergence of *eukaryotic* cells such as yeast, plants, and animals. Pouplana and his colleagues hope to get a better grasp of how these types of cells evolved by studying molecules related to translation.

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: it works differently in the cells of the early embryo, or as stem cells specialise into blood, neurons and hundreds of other types, or within a rapidly-growing tumour. **Cayetano González's** lab is taking a multidisciplinary approach to study cell division, combining genetics, molecular biology, and advanced *in vivo* microscopy. 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 the development of cancer in the fruit fly.

Signals that organise cells into body structures

Building a complex organism requires that cells specialise by changing the way they divide, their shapes, and behaviours such as when and where they migrate. These morphogenetic changes are coordinated by cues from the environment, for example, molecules secreted by other cells. Those have to be interpreted properly inside the cell, which means passing information along a pathway of signalling molecules. The same signal may have different 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** group is taking this approach using as models the development of the trachea and the Torso receptor signalling pathway in flies.

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** group is taking advantage of nearly a century of genetic studies of the fruit fly to study 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 sub-territories and clear boundaries between tissues. Cells at the boundary lines secrete signalling molecules such as *Wg/Wnt* and *Dpp/TGFβ,* that guide the pattern development and growth of the entire limb. Milán and his colleagues aim to understand how these molecules control such complex processes as the generation of adult limbs with a size, shape and pattern specific to a species.

Building and rebuilding the brain

The development of the brain requires 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. Then they have to respond properly to stimulation to permit memory and learning. Accomplishing these steps require that cells activate specific genes at the right time, properly interpret signalling molecules on the surfaces of other cells (or secreted by them), and respond in the right way. **Eduardo Soriano's** lab is identifying new genes that contribute to these processes. Another theme of the group's work is to study the difference between brain cells in the embryo and early childhood, which can develop and make repairs, 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, whose behaviour 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 will require linking the behaviour of these components to their structures. This perspective is also crucial in the investigation of genetic diseases, which are often caused by small structural changes in molecules. And it is needed to improve drugs and create 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 usually impossible to know exactly how they work.

The **Structural and Computational Biology Programme** gathers a wide range of expertise to investigate 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" built of many molecules. In many cases it is possible to deduce structural information about new proteins and their interactions by comparing their sequences to other known molecules. This requires the use of innovative computational tools which still need to be developed and improved – another strength of IRB Barcelona's programme. The potential of such tools has grown enormously now that scientists can draw on the wealth of information that has been produced in genome projects.

Molecules that bind to DNA

Miquel Coll's group relies on several techniques to study how DNA behaves when it is linked to proteins and other molecules. Their primary method 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 focus 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 themes include the study of unique DNA structures and novel drugs that dock onto DNA, rather than proteins.

NMR and protein purification

Another 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 which correlate to the distances between atoms, thereby providing a representative family of structures. **Maria J Macias'** laboratory has specialised in the use of this technique to study the structures and proteins and their complexes as well as how they fold. Her group has also set up an efficient collaboration process that helps other labs to determine protein structures by providing supervision and the protocols necessary to produce pure proteins at the milligram scale.

How interactions change structures

NMR is particularly useful in watching very quick changes that happen when proteins interact with each other or with small molecules such as drugs. **Miquel Pons'** group is using the technique to study what happens during these interactions. Changes may occur deep within a molecule – the way that tightening a single screw can change the shape of a huge bookshelf. The structure of a protein may change when it binds to a single partner; the addition or removal of molecules in a complex can also cause rearrangements. Binding to small molecules, like the active components of drugs, may have similar effects. Pons and his colleagues are developing new computational and NMR screening tools to look for small molecules that can restructure complexes in a therapeutically promising way.

Molecular machines

Proteins play key roles in most biological processes, but they seldom act alone. Often a molecule binds to dozens of other proteins, RNAs, or other molecules to perform a particular job. Advances in mass spectrometry and other techniques have allowed scientists to create detailed parts lists of molecular complexes, but it has been difficult to observe details of their inner structures and in some cases even to discover where they work in the cell. To address these questions, **Ignasi Fita's** lab is combining X-ray crystallography, mass spectrometry, and cryo-electron microscopy, which has a high enough resolution to show some of the complexes. The group has developed new methods using these techniques and is particularly interested in complexes that play a role in disease processes. They have obtained detailed structural pictures of signalling molecules and viruses bound to receptor proteins that allow them to enter cells. Current work focuses on enzymes that become active when the cell becomes overloaded with highly-reactive oxygen atoms, and membrane proteins that participate in diseases.

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 is designing 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.

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 directly observed. They have to be understood through models which incorporate information from many sources. **Modesto Orozco's** group is combining 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.

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 attacked with vaccines, antibiotics, or existing drugs. Scientists have a wide range of new tools to understand the origins of disease and many new ways to intervene in processes within cells. Those tools have already revolutionised medical diagnostics, and the vision for the next decades is to learn to use them to directly manipulate the molecules responsible for diseases. The aim of the **Molecular Medicine Programme** is to further our knowledge in these areas and to find new ways of putting discoveries to use.

A broad palette of expertise is present in the programme: 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' laboratory studies the principles that govern cross-talk between some of the cell's most important signalling pathways in the context of anti-inflammation. Pro-inflammatory signals initiate the inflammatory response, 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 famly involved in the regulation of the cell division cycle.

Biology of macrophages and the immune system

Antonio Celada's group studies macrophages, cells which play a key role in inflammation. At an early stage, they eliminate microorganisms (bacteria, parasites, yeast, *etc*) present at the site of inflammation. Later, they repair lesions formed during inflammation that can cause scarring. Macrophages also play a key role in chronic inflammatory processes, such as rheumtoid arthritis, and they induce the formation of blood vessels, promoting growth of cancer cells. For these reasons, it is important to understand how these cells work and how to help them when they are beneficial and to stop them when they cause harm. Celada and his colleagues study the signals induced by molecules that activate macrophages and how the genes that activate their different functions are regulated. Their goal is to find new therapeutic targets to design drugs that alter the activity of these cells so that they can reproduce, differentiate, become activated or die and disappear.

Metabolic engineering and diabetes therapy

Glucose excess 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 altered in pathologies like diabetes mellitus. IRB Barcelona Director **Joan J Guinvoart's** group aims to understand how these processes are altered and to correct them using compounds with anti-diabetic properties. One task of the group is to identify novel proteins involved in glycogen metabolism and to describe their role in various tissues. The group has discovered some significant differences in the way glycogen is processed in the liver and muscle. For example, key enzymes migrate to different locations in the cell depending on glycogen synthesis and breakdown status. This probably contributes to glycogen metabolism regulation and may represent one of the steps impaired in diabetes mellitus. The group has also discovered a compound with anti-diabetic and anti-obesity properties. Phase 1 clinical trials of the compound have been completed, and Phase 2 trials are about to begin.

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, and affects over 40% of people over 60 years. Recent studies suggest that some of these problems may stem from common genetic and cellular mechanisms. **Antonio Zorzano's** laboratory is trying to identify genes responsible for the development of insulin resistance associated with obesity or type 2 diabetes. They are focusing 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 identifying 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.

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 have to 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** laboratory is studying 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. Different 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* that are responsible for the transport of some amino acids and are disrupted during PIA diseases. Currently the scientists are analyzing the structures of HATs to gain a better understanding of how they carry out their transporter functions.

Chemistry and Molecular Pharmacology Programme

Making new 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, 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 the design of drugs. The goal is to identify targets, understand their functions and the nature of their interactions to other molecules, and to build or modify molecules that can influence that behaviour. Groups in the programme synthesise a large variety of bioactive compounds, with special focus on nucleic acids, peptides, proteins, peptidomimetics - molecules that resemble or imitate natural peptides - and other chemical compounds. The groups use innovative methods such as enantioselective synthesis, solid-phase synthesis of libraries of bioactive compounds and multi-component reactions.

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

Inventing new compounds

Fernando Albericio's group aims to discover and synthesise new compounds that might be useful as therapies against central nervous system disorders and cancer. The team is taking an integrated approach based on peptides and small molecules which are being investigated in joint collaborations with researchers from industry.

Building artificial DNAs and RNAs

The successful development of the vast majority of scientific projects depends on the ability to create small, artificial DNA or RNA molecules. **Ramon Eritja's** group synthesises these molecules out of their subunits, called nucleotides. The group's projects 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 be able to study the surface of any part of any protein and design a very 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 trying to understand the principles that govern the way molecules recognise and bind to each other. The laboratory is focusing on several issues that have been difficult to resolve: getting cells to take up foreign substances (drugs); finding ways to break up clumps of proteins that form in Alzheimer's disease and several other neurodegenerative diseases; and getting drugs across the blood-brain barrier. The group has been working to improve the methods needed to address these questions: obtaining structural information from NMR, improvements in solid-phase peptide synthesis (a way of artificially designing proteins that don't require cells to produce the molecules) and improving computer algorithms to assist in drug discovery.

Improving methods in compound development

Antoni Riera's lab is developing new biologically active compounds that are needed at various stages of drug development, and improving the methods of creating them. The group has a special focus on asymmetric synthesis. This is crucial because many of the processes that create small molecules produce *enantiomers* ("left- and right-handed" versions – in other words, molecules that have the same properties but are mirror images of each other). Biological molecules may react very differently to the two types, so it is crucial to produce and purify only the desired version. Other efforts are devoted to finding ways to create higher quantities and a better quality of compounds which are of great therapeutic interest. Finally, the group is helping to prepare chemical libraries that can be used for biological screening.

Looking for new bioactive molecules

Màrius Rubiralta's group is working in the development of technologies addressed to obtain key bioactive compounds in pure form. Thus, synthetic procedures are developed to reach new peptide-like molecules or heterocyclic containing compounds, structures frequently found in drugs, and also to separate the enantiomers of the obtained molecules.

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 Oncology 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** laboratory 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 is focusing on what happens to cell signalling pathways at different stages in the development of colorectal cancers. The development of a full-blown malignant tumour happens 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. Close collaborations with clinical researchers have given the lab access to specimens of colorectal cancer at different stages of the malignancy, permitting an analysis of the molecular alterations most frequently associated with each step of the disease.

The Tumoural Metastasis Laboratory (MetLab)

Intricate signaling networks within cells control their division, differentiation, movement, organisation and death. Cancer cells disobey these signals during tumor 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 tumor cells make of them instruments for metastasis. Such functions are responsible for allowing metastatic cells escape the primary tumor site to the circulation, the invasion of distant organs by theses cells and finally, the formation of 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 tumor samples from patients. By understanding how combinations of biological changes facilitate vital organ invasion by metastatic cells, they will be able to efficiently tackle the disease by using drug combinations against the putative therapeutic targets

Facts and Figures

Board of Trustees

IRB Barcelona was founded in October 2005 by the Government of Catalonia (through the Ministry of Innovation, Universities and Business and the Ministry of Health), the University of Barcelona and the Barcelona Science Park. The governing body of the institute is the Board of Trustees, formed by 11 members and chaired by the Minister of Innovation, Universities and Business of the Government of Catalonia.

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Minister of the Department of Innovation, Universities and Business, Government of Catalonia (November 2006–present)

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Minister of the Department of Education and Universities, Government of Catalonia (May 2006–November 2006)

Manel Balcells i Diaz
Minister of the Department of Universities, Research and Information Society, Government of Catalonia (April 2006–May 2006)

Carles Solà i Ferrando
Minister of the Department of Universities, Research and Information Society, Government of Catalonia (October 2005–April 2006)

FIRST VICEPRESIDENT
Marina Geli i Fàbrega
Minister of the Department of Health, Government of Catalonia (October 2005–present)

SECOND VICEPRESIDENT
Màrius Rubiralta i Alcáñiz
Vice-Chancellor of the University of Barcelona (October 2005–present)

MEMBERS
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Director General for Research of the Department of Innovation, Universities and Business, Government of Catalonia (October 2005–July 2006; December 2006-April 2007)

Xavier Testar i Ymbert
Director General for Research of the Department of Universities, Research and Information Society, Government of Catalonia (July 2006–December 2006)

Joan Roca Acín
Director of Interdepartmental Ministry of Research and Technology Innovation (CIRIT), Department of Innovation, Universities and Business, Government of Catalonia (December 2006–present)

Ramon Agustí i Comes
Director of Interdepartmental Ministry of Research and Technology Innovation (CIRIT), Department of Education and Universities, Government of Catalonia (July 2006-December 2006)

Marta Aymerich i Martínez
Director of Interdepartmental Ministry of Research and Technology Innovation (CIRIT), Department of Universities, Research and Information Society, Government of Catalonia (October 2005-July 2006)

José Jerónimo Navas i Palacios
Director of the Research Centres Programme, Department of Health, Government of Catalonia (October 2005-present)

Marta Segura i Bonet
General Secretary of Health, Department of Health, Government of Catalonia (July 2006-present)

Manel Balcells i Diaz
Director of Coordination and Strategy, Department of Health, Government of Catalonia (October 2005-May 2006)

Maria Carme Verdaguer i Montanyà
Director of the Innovation Centre, Fundació Bosch i Gimpera, University of Barcelona (October 2005–present)

Josep Samitier i Martí
Pro-Vice-Chancellor for Innovation and International Research Programmes, University of Barcelona (January 2007-present)

Isidre Ferrer i Abidanza
Pro-Vice-Chancellor of Science Policy, University of Barcelona (October 2005–January 2007)

Fernando Albericio i Palomera
Director General, Barcelona Science Park (October 2005–present)

Maria Montserrat Vendrell i Rius
Assistant Director, Barcelona Science Park (October 2005–March 2007)

Executive Board

The Executive Board is the governing body responsible for periodic follow-up on administrative and management tasks of IRB Barcelona, and also completes all functions delegated by the Board of Trustees. The members of the Executive Board also sit on the Board of Trustees.

PRESIDENT
José Jerónimo Navas i Palacios
Director of the Research Centres Programme, Department of Health, Government of Catalonia (October 2005-present)

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

Xavier Testar i Ymbert
Director General for Research of the Department of Universities, Research and Information Society, Government of Catalonia (July 2006–December 2006)

Josep Samitier i Martí
Pro-Vice-Chancellor for Innovation and International Research Programmes, University of Barcelona (January 2007-present)

Isidre Ferrer i Abidanza
Pro-Vice-Chancellor of Science Policy, University of Barcelona (October 2005–January 2007)

OTHER PARTICIPANTS
Fernando Albericio i Palomera
Director General, Barcelona Science Park (October 2005–present)

Joan J Guinovart i Cirera
Director, IRB Barcelona (October 2005-present)

Margarida Corominas i Bosch
Manager, IRB Barcelona (September 2006-present)

External Advisory Board

The scientific work of IRB Barcelona is regularly assessed by an External Advisory Board which comprises 15 leading international researchers in biomedicine. Its main task is to provide guidance in shaping our research and related activities.

Hans Clevers
The Netherlands Institute of Developmental Biology, The Netherlands

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

Christopher M Dobson
Department of Chemistry and Physics, Cambridge University, UK

José Elguero
Consejo Superior de Investigaciones Científicas (CSIC), Spain

Samuel H Gellman
Faculty of Chemistry, University of Winsconsin, USA

David M Glover
Department of Genetics, University of Cambridge, UK

Jan-Åke Gustafsson
Center for Biotechnology, Karolinska Institute, Sweden

Andrew Hamilton
Department of Chemistry, Yale University, USA

Robert Huber
Max-Planck-Institute für Biochemie, Germany

Tim Hunt
Imperial Cancer Research Fund, UK

Fotis C Kafatos
Imperial College London, UK

Bernd Meyer
Institute for Organic Chemistry, University of Hamburg, Germany

Charles J Sherr
Department of Genetics and Tumor Cell Biology, St Jude Children's Research Hospital, USA

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

Karen Vousden
Beatson Institute, UK

Scientific Output Summary

SCIENTIFIC PUBLICATIONS
During 2006, IRB Barcelona researchers published a total of 138 of scientific articles in peer-reviewed journals, 14 of which were internal collaborative papers, co-authored by IRB Barcelona researchers from at least two different groups.

The following is a list of selected publications, appearing in journals with an Impact Factor above 7.0 (ISI list 2005). For a full list of publications, see the individual group reports in the Scientific Report volume that accompanies this summary.

Alcantara S, Pozas E, Ibañez CI and Soriano E (2006) BDNF-modulated spatial organisation of Cajal-Retzius and GABAergic neurons in the marginal zone plays a role in the development of cortical organisation. Cereb Cortex, 16: 487-499

Aloy P and Russell RB (2006) Structural systems biology: modeling protein interaction networks. Nature Rev Mol Cell Biol, 7:188-197

Badia D, Camacho A, Pérez-Lago L, Escandón C, Salas M and Coll M (2006) The structure of phage f29 transcription regulator p4-DNA complex reveals an N-hook motif for DNA binding. Mol Cell, 22:73-81

Botella-López A, Burgaya F, Gavín R, García Ayllón MS, Gómez-Tortosa MS, Peña-Casanova J, Ureña J, del Río JA, Blesa R, Soriano E and Sáez-Valero J (2006) Reelin expression and glycosylation patterns are altered in Alzheimer's disease. Proc Natl Acad Sci USA, 103:5573-5578

Bravo J and Aloy P (2006) Target selection for complex structural genomics. Curr Opin Struct Biol, 16:385-392

Brodu V and Casanova J (2006) The RhoGAP crossveinless-c links trachealess and EGFR signalling to cell shape remodelling in *Drosophila* tracheal invagination. Genes Dev, 20:1817-1828

Casacuberta E and Pardue M-L (2006) RNA interference has a role in regulating *Drosophila* telomeres. Genome Biol, 7:220

Clevers H and Batlle E (2006) EphB/EphrinB receptors and Wnt signalling in colorectal cancer. Cancer Res, 66:2-5

Dames SA, Aregger R, Vajpai N, Bernado P, Blackledge M and Grzesiek S (2006) Residual dipolar couplings in short peptides reveal systematic conformational preferences of individual amino acids. J Am Chem Soc, 128:13508-13514

Dopazo J and Aloy P (2006) Discovery and hypothesis generation through bioinformatics. Genome Biol, 7:307

Feliz M, García J, Aragón E and Pons M (2006) Fast 2D-NMR ligand screening using Hadamard spectroscopy. J Am Chem Soc, 128:7146-7147

Franch-Marro X, Martín N, Averof M and Casanova J (2006) Association of tracheal placodes with leg primordia in *Drosophila* and implications for the origin of insect tracheal systems. Development, 133:785-790

Galisteo ML, Yang Y, Ureña J and Schlessinger J (2006) Activation of the nonreceptor protein tyrosine kinase Ack by multiple extracellular stimuli. Proc Natl Acad Sci USA, 103:9796-9801

Gavin AC, Aloy P, Grandi P, Krause R, Boesche M, Marzioch M, Rau C, Jensen LJ, Bastuck S, Dumpelfeld B, Edelmann A, Heurtier MA, Hoffman V, Hoefert C, Klein K, Hudak M, Michon AM, Schelder M, Schirle M, Remor M, Rudi T, Hooper S, Bauer A, Bouwmeester T, Casari G, Drewes G, Neubauer G, Rick JM, Kuster B, Bork P, Russell RB and Superti-Furga G (2006) Proteome survey reveals modularity of the yeast cell machinery. Nature, 440:64.47131-636

Gomis RR, Alarcon C, He W, Wang Q, Seoane J, Lash A and Massagué J (2006) A FoxO-Smad synexpression group in human keratinocytes. Proc Natl Acad Sci USA, 103:12747-12752

Gomis RR, Alarcon C, Nadal C, Van Poznak C and Massagué J (2006) C/EBPβ at the core of the TGFβ cytostatic response and its evasion in metastatic breast cancer cells. Cancer Cell, 10:203-214

Gomis-Rüth FX and Coll M (2006) Cut and move: DNA processing in bacterial conjugation. Curr Opin Struct Biol, 16:744-752

Herranz H, Morata G and Milán M (2006) Calderón encodes an organic cation transporter of the major facilitator superfamily required for cell growth and proliferation of *Drosophila* tissues. Development, 133:2617-2625

Herranz H, Stamataki E, Feiguin F and Milán M (2006) Self-refinement of Notch activity through the transmembrane protein Crumbs: modulation of γ-secretase activity. EMBO Rep, 7:297-302

Jaumot J, Eritja R, Tauler R and Gargallo R (2006) Resolution of a structural competition involving dimeric G-quadruplex and its C-rich complementary strand. Nucleic Acids Res, 34:206-216

Kogan M, Bastus NG, Amigo R, Grillo D, Araya E, Turiel A, Labarta A, Giralt E and Puntes V (2006) Nanoparticle-mediated local and remote manipulation of protein aggregation. Nano Letters, 6:110-115

Mingorance A, Sole M, Muneton V, Martinez A, Nieto-Sampedro M, Soriano E and Del Rio JA (2006) Regeneration of lesioned entorhino-hippocampal axons *in vitro* by combined degradation of inhibitory proteoglycans and blockade of Nogo-66/NgR signalling. FASEB J, 20:491-493

Montagna G, Teijido O, Eymard-Pierre E, Muraki K, Cohen B, Loizzo A, Grosso P, Tedeschi G, Palacín M, Boespflug-Tanguy O, Bertini E, Santorelli FM and Estevez R (2006) Vacuolating megalencephalic leukoencephalopathy with subcortical cysts: functional studies of novel variants in MLC1. Hum Mutat, 27:292

Moreno-Moreno O, Torras-Llort M and Azorín F (2006) Proteolysis restricts localisation of CID, the centromere specific histone H3 variant of *Drosophila*, to centromeres. Nucleic Acids Res, 34:6247-6255

Muncan V, Sansom OJ, Tertoolen L, Phesse TJ, Begthel H, Sancho E, Cole AM, Gregorieff A, de Alboran IM, Clevers H and Clarke AR (2006) Rapid loss of intestinal crypts upon conditional deletion of the Wnt/Tcf-4 target gene c-Myc. Mol Cell Biol, 26:8218-8426

Oleksi A, Blanco AG, Boer R, Usón I, Aymamí J, Rodger A, Hannon MJ and Coll M (2006) Molecular recognition of a three-way DNA junction by a metallosupramolecular helicate. Angewandte Chemie Int Ed 45:1227-1231

Pujals S, Fernandez-Carneado J, Kogan M, Martinez J, Cavelier F and Giralt E (2006) Replacement of a proline with silaproline causes a 20-fold increase in the cellular uptake of a pro-rich peptide. J Am Chem Soc, 128:8479-8483

Rueda M, Luque FJ and Orozco M (2006) G-DNA can maintain its structure in the gas phase. J Am Chem Soc, 128:3608-3619

Soriano FX, Liesa M, Bach D, Chan DC, Palacín M and Zorzano A (2006) Evidence for a mitochondrial regulatory pathway defined by peroxisome proliferator-activated receptor-γ coactivator-1α, estrogen-related receptor-α, and mitofusin 2. Diabetes, 55:1783-1791

Soteras I, Lozano O, Gómez-Esqué A, Escolano C, Orozco M, Amat M, Bosch J and Luque FJ (2006) On the origin of stereoselectivity in the alkylation of oxazolopiperidone enolates. J Am Chem Soc,128:6581-6588

Spengler J, Bottcher C, Albericio F and Burger K (2006) Hexafluoroacetone as protecting and activating reagent: New routes to amino, hydroxy and mercapto acids and their application for peptide, glyco- and depsipeptide modification. Chem Rev, 106:4728-4746

Vaquero A, Scher M, Lee DH, Sutton A, Cheng HL, Alt F, Serrano L, Sternglanz R and Reinberg D (2006) SirT2 is a histone deacetylase with preference for histone H4 Lys 16 during mitosis. Genes Dev, 20:1256-1261

Wodarz A and González C (2006) Connecting cancer to the asymmetric division of stem cells. Cell, 124:1121-1123

Zuliani C, Kleber S, Klussmann S, Wenger T, Kenzelmann M, Schreglmann N, Martínez A, Del Río JA, Soriano E, Vodrazka P, Kuner R, Groene HJ, Herr I, Krammer PH and Martin-Villalba A (2006) Control of neuronal branching by the death receptor CD95 (Fas/Apo-1). Cell Death Differ, 13:31-40

RESEARCH NETWORKS AND GRANTS

During 2005-2006, IRB Barcelona researchers received a total of 147 grants. 24 of these were awarded by the EC, a further 15 of which had an IRB Barcelona member as the main recipient or coordinator. 72 grants were awarded by the Spanish Government, 66 of which had an IRB Barcelona member as the main recipient or coordinator; 25 grants were awarded by the Catalan Government, 19 of which had an IRB Barcelona member as main recipient or coordinator. 26 grants were received from foundations (23) or industry (3).

COLLABORATIONS

IRB Barcelona researchers participated in a total of 179 collaborations during 2005-2006. 25 of these were internal or included researchers from at least two different IRB Barcelona groups. 23 collaborations involved industrial partners. Excluding industry and internal collaborations, 45 collaborations were purely international, 73 were purely national and 7 were a combination of national and international partners. A total of 9 collaborations took place among IRB Barcelona research groups and units from the Barcelona Science Park.

For a full list of publications, research networks and grants and collaborations, see the individual group reports in the Scientific Report volume that accompanies this summary.

Funding Sources

During 2005-2006, IRB Barcelona received the majority of funding for its research activities and infrastructure from the Government of Catalonia, through the Ministry of Innovation, Universities and Business, and the Ministry of Health. Additional core funding was provided by the Spanish Ministry of Health and the European Union, through FEDER funds. Other sources included competitive grants from public and private agencies at both the national and the European levels, as well as private sponsors. The University of Barcelona, the Catalan Institution for Research and Advanced Studies (ICREA) and the Spanish National Research Council (CSIC) also contribute by funding scientists who are contracted by these entities and work at IRB Barcelona.

CORE FUNDING

Generalitat de Catalunya
Departament d'Innovació, Universitats i Empresa

Generalitat de Catalunya
Departament de Salut

OTHER FUNDING SOURCES

MINISTERIO DE EDUCACIÓN Y CIENCIA

EUROPEAN REGIONAL DEVELOPMENT FUND

PRIVATE DONORS

Rosa Soler Mòdena, in memory of her sister, Esperança

PhD Theses

IRB Barcelona PhD activities aim provide life sciences students from across the world with the opportunity to do training and research toward their degree in a unique international and multidisciplinary scientific environment. IRB Barcelona is commited to high quality training for its students, offering close mentoring and access to a wide variety of scientific activities, services and networks. Our goal is to give our students everything they need for a solid start to a successful career in biomedical science.

Students spend up to four years at IRB Barcelona working on a research project chosen in mutual agreement with their group leader. They also participate in all day-to-day activities of the laboratory to learn a variety of skills and techniques. In addition to their laboratory work, students can participate in a wide variety of related activities, including internal programme seminars, the Barcelona BioMed series of seminars and conferences, journal clubs and outreach and education activities.

The following is a list of PhD theses defended by students belonging to IRB Barcelona research groups during 2005-2006.

Aminoàcids conformacionalment restringits i d'interès farmacològic. Síntesi d'anàlegs de fenilalanina i beta-hidroxi-alfa-aminoàcids
Mónica Alonso
University of Barcelona (2006)
Supervisor: Antoni Riera

Productes naturals com a font de nous fàrmacs: Síntesi en fase sòlida de depsipèptids cíclics i aïllament d'agents antitumorals d'esponges marines
Nuria Bayó
University of Barcelona (2006)
Supervisor: Fernando Albericio

Dinámica de sistemas de interés biológico. Estudios de flexibilidad y estabilidad en sistemas de puente de hidrógeno
José Ramón Blas Pastor
University of Barcelona (2006)
Supervisor: Modesto Orozco

Structure of the exonuclease Trex-1
Marina Bruces Vinyals
University of Barcelona (2006)
Supervisor: Antonio Celada

On the search of type 2 diabetes susceptibility genes: DOR and AIB3
Hans Burghardt
University of Barcelona (2005)
Supervisor: Antonio Zorzano

Procesos no-biomiméticos con dihidropiridinas y sales de piridinio: reducción, oxidación y reacciones multicomponente
Inés Carranco
University of Barcelona (2006)
Supervisor: Màrius Rubiralta

Asymmetric stem cell division and cancer in *Drosophila*
Emmanuel Caussinus
Toulouse University (2005)
Supervisor: Cayetano González

Evolution of glycogen metabolism mechanisms of control
Daniel Cifuentes Buira
University of Barcelona (2006)
Supervisor: Joan J Guinovart

NMR in drug discovery. From screening to structure-based design of antitumoral agents
Luis Javier Cruz
Universitat de Barcelona (2006)
Supervisors: Fernando Albericio and Ernest Giralt

Aplicaciones del método MST a sistemas bioquímicos
Carles Curutchet Barat
University of Barcelona (2005)
Supervisor: Modesto Orozco

Análisis bioinformática de les mutacions puntuals patológiques
Carles Ferrer i Costa
University of Barcelona (2005)
Supervisor: Modesto Orozco

Molecular bases of cystinuria type I and non-I. Development of a murine knockout of LAT2
Mariona Font-Llitjos
University of Barcelona (2005)
Supervisor: Manuel Palacín

Netrin1 and secreted Semaphorins: role in axonal guidance in the hippocampus and cerebellum
Patricia Guijarro Larraz
University of Barcelona (2006)
Supervisors: Eduardo Soriano and José A del Río

Structure-function relationship of heteromeric amino acid transporters: subunit stoichiometry and relevant cysteine residues
Maite Jiménez-Vidal
University of Barcelona (2005)
Supervisor: Manuel Palacín

Aplicacions sintètiques dels adductes de pauson-Khand del norbornadiè. Aproximació a la síntesi de prostaglandines i fitoprostans
Agustí Lledó
University of Barcelona (2006)
Supervisor: Antoni Riera

Transport of arginine in macrophages. Response to activation, proliferation and GM-CSF
Lorena Martín
University of Barcelona (2006)
Supervisor: Manuel Palacín

Roles of Nogo/MAG in regeneration of hippocampal connections
Ana Mingorance Jiménez de la Espada
University of Barcelona (2006)
Supervisor: José A del Río

Síntesi enantioselectiva de aminoalcoholes biológicamente activos mediante apertura de epòxidos insaturados
Caterina Murruzzu
University Barcelona (2005)
Supervisor: Antoni Riera

Role of Reelin and mDab1 in neural migration and axonal growth
Lluis Pujadas Puigdomènech
University of Barcelona (2006)
Supervisor: Eduard Soriano

Péptidos con aplicaciones biomédicas: SIDA y cáncer
Ricard-Aleix Rodríguez Mías
Universitat de Barcelona (2006)
Supervisors: Fernando Albericio and Ernest Giralt

Estudio teórico sobre la influencia del solvente en la estructura y dinámica del ADN
Manuel Rueda Borrego
University of Barcelona (2006)
Supervisor: Modesto Orozco

Early steps regulating proliferation and activation in macrophages
Ester Sánchez Tilló
University of Barcelona (2006)
Supervisor: Antonio Celada

Disseny, síntesi i aplicacions de dendrímers basats en cadenes de poliprolina
Glòria Sanclimens
University of Barcelona (2005)
Supervisors: Fernando Albericio and Ernest Giralt

Role of Reelin signalling in Central Nervous System migration
Sergi Simó Olivar
University of Barcelona (2006)
Supervisor: Eduardo Soriano

Lligands hemilàbils en la reacció de Pauson-Khand intermolecular i asimètrica
Jordi Solà
University of Barcelona (2006)
Supervisor: Antoni Riera

Nous mètodes per al disseny, síntesi i avaluació de pèptids amb capacitat per travessar la barrera hematoencefàlica
Meritxell Teixidó
University of Barcelona (2005)
Supervisors: Fernando Albericio and Ernest Giralt

Eines computacionals basades en LINGO per al disseny molecular i la predicció de propietats
David Vidal Montull
University of Barcelona (2006)
Supervisor: Miquel Pons

Regulation of the transport and metabolism of arginina in macrophage
Andrée Yeramian
University of Barcelona (2006)
Supervisor: Antonio Celada

Molecular mechanism of action of the antidiabetic agent sodium tungstate
Delia Zafra López
University of Barcelona (2006)
Supervisor: Joan J Guinovart

Molecular mechanisms of DOR action
Meritxell Orpinell
University of Barcelona (2006)
Supervisor: Antonio Zorzano

MASTERS THESIS
Development of an automated target selection strategy for complex structural genomics
Roland Pache
Eberhard Karls Universität Tübingen, Germany (2006)
Supervisor: Patrick Aloy

Technology Transfer Activities

Research at IRB Barcelona is rapidly becoming a key source of innovation and new technologies. This is thanks to an atmosphere which encourages innovation and makes technology transfer easy for our scientists. Our location within the Barcelona Science Park and the resources available have allowed our researchers to undertake several technology transfer activities for work conducted in their groups.

Examples of exclusive IRB Barcelona technology transfer activities during 2005-2006 include the following:

In 2005, the start-up company, **Omnia Molecular Ltd,** was formed, based on research originating in Lluís Ribas de Pouplana's group. The company's goal is to bring drug-screening technology to an industrial setting.

In 2006, Omnia Molecular Ltd filed the following patent applications:

A screening method for identifying new drugs
Ribas de Pouplana L and Bori-Sanz T
European Patent Office application number:
EP06116233

A screening method for identifying new aminoacyl-tRNA synthetase inhibitors
Ribas de Pouplana L, Castro de Moura M, Geslain R and Bori-Sanz T
European Patent Office application number:
EP06120049

Barcelona BioMed Seminars

Leading international scientists from different areas of the biomedical sciences are invited to present and discuss their results and ideas in a series of weekly seminars. These seminars allow IRB Barcelona researchers and the local scientific community to learn about the latest developments in the life sciences, and provides an oppotunity for direct contact with each seminar speaker. Barcelona BioMed Seminars are open to the local scientific community.

17 October 2005
New light on the co-c bond activation in B12-dependent enzymes from density functional theory
Pawel Kozlowski, Department of Chemistry University of Louisville, Kentucky, USA

20 October 2005
Aplicacions de la biocalorimetria
Rafel Prohens, Unitat de Química Fina, Serveis Científico-tècnics, Parc Científic de Barcelona, Spain

21 October 2005
Splicing and meiotic regulation in Schizosaccharo-*myces pombe*
A José Ayté del Olmo, Cell Signalling Unit, Universitat Pompeu Fabra, Barcelona, Spain

26 October 2005
Single molecule experiments in biological physics: exploring the thermal behaviour of small systems
Felix Ritort, Departament de Fisica Fonamental Facultat de Fisica Universitat de Barcelona, Spain

3 November 2005
Identification of a gene that causes sudden death in young Bedoin children in the North of Israel
Elon Pras, Director of Institute of Human Genetics, Sheba Medical Center, Israel

10 November 2005
Nano-domains in the immune system control cell adhesion and pathogen uptake
María García Parajo, IBEC, Parc Científic de Barcelona, Spain

11 November 2005
Mechanisms of centrosome duplication in C. elegans *and beyond*
Pierre Gonczy, Swiss Institute for Experimental Cancer Research (ISREC), Lausanne, Switzerland

14 November 2005
Carbon to replace silicon as the top engineering material?
Marc Madou, Department of Mechanical and Aerospace Engineering, University of California, Irvine, CA, USA

17 November 2005
Structural insights into natively unfolded proteins using NMR and Small Angle X-ray Scattering
Pau Bernadó, EMBL, Hamburg, Germany

17 November 2005
Maximum likelihood in 3D-electron microscopy with parallels to X-ray crystallography
Sjors Scheres, Biocomputing Unit, National Center for Biotechnology, Madrid, Spain

2 December 2005
Human herpesvirus-8/ KSHV transforms angiogenic hematopoietic cells: A cell and animal model of virally induced Kaposi's sarcoma
Agata Mutlu, Laboratory of Viral Oncogenesis, Weill Medical College-Cornell University, NY, USA

16 December 2005
Ojoplano and the morphogenesis of the vertebrate eye
Juan Martínez, EMBL Heidelberg, Germany

16 December 2005
Mechanism of collagenase cleavage of triple helical collagens: Helical stability and enzyme action
Hideaki Nagase, Kennedy Institute of Rheumatology, Imperial College London, London, UK

16 December 2005
The role of TIMPs in pericellular proteolysis; the specificity is in the detail
Gillian Murphy, Department of Oncology, Cambridge Institute for Medical Research, Cambridge, UK

21 December 2005
The dynamics of translation as inferred by cryo-electron microscopy of ribosomal complexes
Joachim Frank, Howard Hughes Medical Institute, New York, USA

22 December 2005
APC/CCdc20 controls the ubiquitin-mediated degradation of p21 during early mitosis
Virginia Amador, Department of Pathology, New York University School of Medicine, USA

13 January 2006
Molecular mimicry, biotechnological applications, and opportunities in Barcelona
Brian FC Clark, Department of Molecular Biology, University of Aarhus, Denmark

13 January 2006
Tumour suppression by p53, p16 and Arf
Manuel Serrano, CNIO, Madrid, Spain

16 January 2006
Neoangiogenesis as a target in cancer therapy. Examples of natural and derived marine compounds inhibiting angiogenesis
Chantal Barthomeuf, UMR Inserm-484-Lab de Pharmacognosie et Biotechnologies, Faculté de Pharmacie, Clermont-Ferrand, France

17 January 2006
Tumour suppression by the TSC1/TSC2 complex
James Brugarolas, Dana-Farber Cancer Institute, Harvard Medical School, Boston, USA

19 January 2006
Mechanisms of alternative splicing regulation
Juan Valcárcel, Centre de Regulació Genomica, Barcelona, Spain

20 January 2006
The amino acid kinase family: enzymes, controllers, gene regulators and multiprotein complexes
Vicente Rubio, Instituto de Biomedicina de Valencia-CSIC, Spain

6 February 2006
Structure and activity of MICAL, an axon guidance protein
Mario Amzel, Department of Biophysics and Biophysical Chemistry, Johns Hopkins Medical School, USA

10 February 2006
A structural approach to understanding neurodegeneration
Analisa Pastore, National Institute for Medical Research, London, UK

16 February 2006
Marine natural products from sea slugs: chemistry and ecology
Conxita Ávila, Centre d'Estudis Avançats de Blanes (CEAB-CSIC), Spain

24 February 2006
DNA damage signalling through the Mre11 complex
Mònica Morales, Memorial Sloan Kettering Cancer Center, New York, USA

2 March 2006
How to get your research published in the media
Sabine Louet, News Editor, Nature Biotechnology, UK

9 March 2006
The flexibility of RNA
Nicola J Stonehouse, Institute of Molecular and Cellular Biology and Astbury Centre for Structural Molecular Biology, University of Leeds, UK

10 March 2006
Why we do science, a personal history
Peter Lawrence, Laboratory of Molecular Biology, Medical Research Council, Cambridge,UK

10 March 2006
Molecular engineering: From cooperativity in weak interactions to the assembly of complex systems
Salvador Tomas, Krebbs Institute for Chemical Biology, University of Sheffield, UK

17 March 2006
Papel del factor de transcripción RUNX3 en células mieloides
Angel Corbi, Centro de Investigaciones Biológicas, CSIC, Madrid, Spain

17 March 2006
Design and synthesis of new structures related to indole. Alkaloids and other natural products
David Black, School of Chemistry, The University of New South Wales, Sydney, Australia

24 March 2006
VX-680, an Aurora kinase inhibitor from chemogenomics and structure based design
Juan Miguel Jiménez, Director de Investigación Química, Vertex Pharmaceuticals, Oxford, UK

30 March 2006
Application of nanotechnologies in gastrointestinal cancer research and diagnostics
Jürgen Schnekenburger, Department of Medicine, University of Münster, Germany

31 March 2006
Mapping the structure of the human genome using the chemistry of the hydroxyl radical
Tom Tullius, Department of Chemistry, Boston University, USA

7 April 2006
Active site structure and reaction mechanisms of human peroxidases
Christian Obinger, Department of Chemistry, BOKU-University of Natural Resources and Applied Life, Vienna, Austria

20 April 2006
Conflictes de valors en la biologia moderna. L'experiencia del Grup Europeu d'Ètica de les Ciències i les Noves Tecnologies
Pere Puigdomenech, Laboratori de Genetica Molecular Vegetal, CSIC-IRTA, Barcelona, Spain

20 April 2006
Dissecting Notch functions during hematopoietic ontogeny in the mouse embryo
Anna Bigas, Centre Oncologia Molecular, IDIBELL-Institut de Recerca Oncologica, Barcelona, Spain

27 April 2006
Aurora A: from gene to drug
Jim Bischoff, Director del Programa de Terapias Experimentales del CNIO, Madrid, Spain

28 April 2006
DNA replication checkpoint: ATR/ATM-independent pathways
Neus Agell, Department de Biologia Cellular, Fac. Medicina, Universitat de Barcelona, Spain

4 May 2006
The Curie Institute, an integrated comprehensive cancer center: from the bench to the bedside
Daniel Louvard, Director del Centre de Investigació del Institut Curie, Paris, France

5 May 2006
The evolution of alternative splicing
Eduardo Eyras, ICREA, Research Unit of Biomedical Informatics, Universitat Pompeu Fabra, Barcelona, Spain

12 May 2006
Centrosomal and acentrosomal microtubule assembly pathways during spindle assembly
Isabelle Vernos, Centre de Regulació Genómica, Barcelona, Spain

18 May 2006
Genetic and environmental factors contributing to developmental learning and memory disorders
Mara Dierssen, Centre de Regulació Genómica, Barcelona, Spain

19 May 2006
New functional interactions of G protein-coupled receptor kinases (GRKs)
Federico Mayor, Departamento de Biología Molecular. Centro de Biología Molecular "Severo Ochoa," CSIC, Universidad Autónoma de Madrid, Madrid, Spain

26 May 2006
New functions of the antagonists of death receptors in the nervous system
Joan X Comella, Department of Basical Medical Sciences, Facultat de Medicina, Universitat de Lleida, Lleida, Spain

2 June 2006
Structural insight into chromatin targeting and remodeling
Christoph W Müller, EMBL Grenoble, France

6 June 2006
Genomic plasticity in the developing immune system: risks, benefits, safeguards
Stephen V Desiderio. John Hopkins University, School of Medicine, Baltimore, USA

8 June 2006
Total chemical synthesis of model proteins: Reagents, structures, nanobioscience
Knud Jensen, Department of Chemistry, Denmark Technical University, Lyngby, Denmark

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Structural and functional analysis of NFAT/Calcinerum interactions
Juan Miquel Redondo, Centro de Biologia Molecular Severo Ochoa (CBM-CSIC), Universidad Autonoma de Madrid and Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain

19 June 2006
Structural and Computational Programme Seminar Principios y aplicaciones de la ultracentrifugación analitica en biologia estructural
German Rivas, Centro de Investigaciones Biológicas (CSIC), Madrid, Spain

23 June 2006
Differences in ROS production provide a molecular explanation for the phenotypes associated to common mouse mitochondrial DNA variants
Jose Antonio Enriquez, Universidad de Zaragoza, Zaragoza, Spain

30 June 2006
Functional characterisation of the vav3 proto-oncogene product using structural and animal model techniques
Xose Bustelo, Centro de Investigacion del Cancer and Instituto de Biologia Molecular y Celular del Cancer, CSIC-University of Salamanca, Salamanca, Spain

7 July 2006
Organising microtubules in space and time
Damian Brunner, Cell Biology and Biophysics Unit, EMBL Heidelberg, Germany

10 July 2006
The role of H-NS in regulation of DNA packaging and transcription in bacteria
John Ladbury, Department of Biochemistry and Molecular Biology and ISMB, University College London, London, UK

17 July 2006
Roles of disabled adaptor proteins in development and cell biology
Jonathan A Cooper, Fred Hutchinson Cancer Research Center, University of Washington, Department of Biochemistry, School of Medicine, Washington, USA

21 July 2006
Anti-inflammatory and antidiabetic-roles of PPAR in macrophages
Mercedes Ricote, Fundación del Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Madrid, Spain

26 July 2006
Picture stories - Electron microscopy of complex biological structures
Bettina Böttcher, Structural and Computational Biology Unit, EMBL Heidelberg, Germany

1 September 2006
Dynamic coupling of self-assembly processes: the surfing of kinetochore rings on the microtubule depolymerisation wave
Eva Nogales, Howard Hughes Medical Institute at UC Berkeley and Scientist at Lawrence Berkeley National Laboratory, Berkeley, USA

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Cell differentiation in microbial eukaryotes: a response to oxidative stress?
Wilhelm Hansberg, Instituto de Fisiología Celular, Universidad Nacional Autónoma de Mexico Mexico City, Mexico

14 September 2006
Identification of peptides derived from tumour antigens for future immunotherapy against cancer
Stephanie E McArdle, School of Biomedical and Natural Sciences, Nottingham Trent University, Nottingham, UK

15 September 2006
Inflammation as a pathogenic cause of cardiovascular disease
Lisardo Boscá, Centro Nacional de Invetigaciones Cardiovasculares, Madrid, Spain

6 October 2006
Molecular bioimaging of eukaryotic gene transcription
Patrick Cramer, Department of Chemistry and Biochemistry, Gene Center, University of Munich Munich, Germany

13 October 2006
DNA repair helicases: ironic observations from the archaea
Malcolm White, St Andrews University, Centre for Biomolecular Sciences, St Andrews, Scotland

27 October 2006
Some remaining challenges for modern NMR: some thoughts on the occasion of the Catalan-Sabatier Prize
Geoffrey Bodenhausen, Ecole Normale Superior Paris Paris, France and Ecole Polytechnique Fédérale, Lausanne, Switzerland

30 October 2006
Kinetic capillary electrophoresis – An analytical Swiss Army knife
Sergey N Krylov, Department of Chemistry, York University, Toronto, Ontario, Canada

8 November 2006
Continuous analysis of gene expression with single cell resolution in C. elegans
Robert Waterston, Department of Genome Sciences, University of Washington, Seattle, USA

3 November 2006
Ensuring mitotic fidelity beyond the spindle assembly checkpoint
Helder Maiato, Institute for Molecular and Cell Biology, University of Porto, Portugal

9 November 2006
Life in boiling water: How archaea (archaebacteria) synthesise ATP
Volker Müller, Molecular Microbiology and Bioenergetics, Institute of Molecular Biosciences, Johann Wolfgang Goethe University, Frankfurt, Germany

10 November 2006
Structural studies of biological macromolecules in solution by small-angle x-ray and neutron scattering
Dmitri Svergun, European Molecular Biology Laboratory, Hamburg, Germany and Institute of Crystallography, Russian Academy of Sciences, Moscow, Russia

24 November 2006
Interplay between Notch and epigenetic factors in cancer
María Domínguez, Instituto de Neurociencias de Alicante, Spain

1 December 2006
Evolution of the mammalian blastocyst and embryonic pluripotency
Miguel Manzanares, Instituto de Investigaciones Biomédicas CSIC-UAM, Madrid, Spain

1 December 2006
Recent advances in degradomic identification and quantitation of proteases and their substrates in complex proteomes
Christopher Overall, Centre for Blood Research, University of British Columbia, Vancouver, Canada

4 December 2006
Peptides mediating interaction networks
Rob Russell, Structural Bioinformatics, EMBL Heidelberg, Germany

19 December 2006
Towards a systems biology-based approach to the interpretation of genome scale experiments
Joaquín Dopazo, Bioinformatics Department, Centro de Investigaciones Príncipe Felipe Valencia, Spain

Barcelona BioMed Conferences

Barcelona BioMed Conferences provide a new platform where leading researchers can meet to present and discuss breakthroughs in several fields of the biomedical sciences. The conferences are organised according to a unique formula, which aims to provide a highly-focused think-tank atmosphere for a select group of participants. About twenty speakers, chosen from among the top international researchers in their field, are joined by a further 40 participants, selected on the basis of their scientific experience, for an intensive three-day hands-on discussion of latest research in their field.

Barcelona BioMed Conferences are organised by IRB Barcelona researchers in collaboration with colleagues from prestigious institutes around the world. This approach affords us a unique opportunity to bring the world of life sciences research to Barcelona, but also to bring the life sciences research done here in Barcelona to the world.

The conference series is made possible in part thanks to the BBVA Foundation, reflecting their ongoing commitment to promoting basic and applied biomedical research.

19-21 October 2006
Barcelona BioMed Conference
NMR IN DRUG DISCOVERY
A BBVA Foundation and IRB Barcelona conference focusing on the rapidly growing field of NMR structure-based drug discovery
Organisers: Ernest Giralt (IRB Barcelona/University of Barcelona), Miquel Pons (IRB Barcelona/University of Barcelona) and Maurizio Pellecchia (The Burnham Institute, La Jolla, CA, USA)

11-13 December 2006
Barcelona BioMed Conference
RNAi: BASIC BIOLOGY TO CLINICAL IMPACT
A BBVA Foundation and IRB Barcelona conference focusing on the rapidly growing field of RNAi and non-coding RNAs
Organisers: Ramón Eritja (IRB Barcelona/CSIC) and Greg Hannon (Cold Spring Harbor Laboratory, NY, USA)

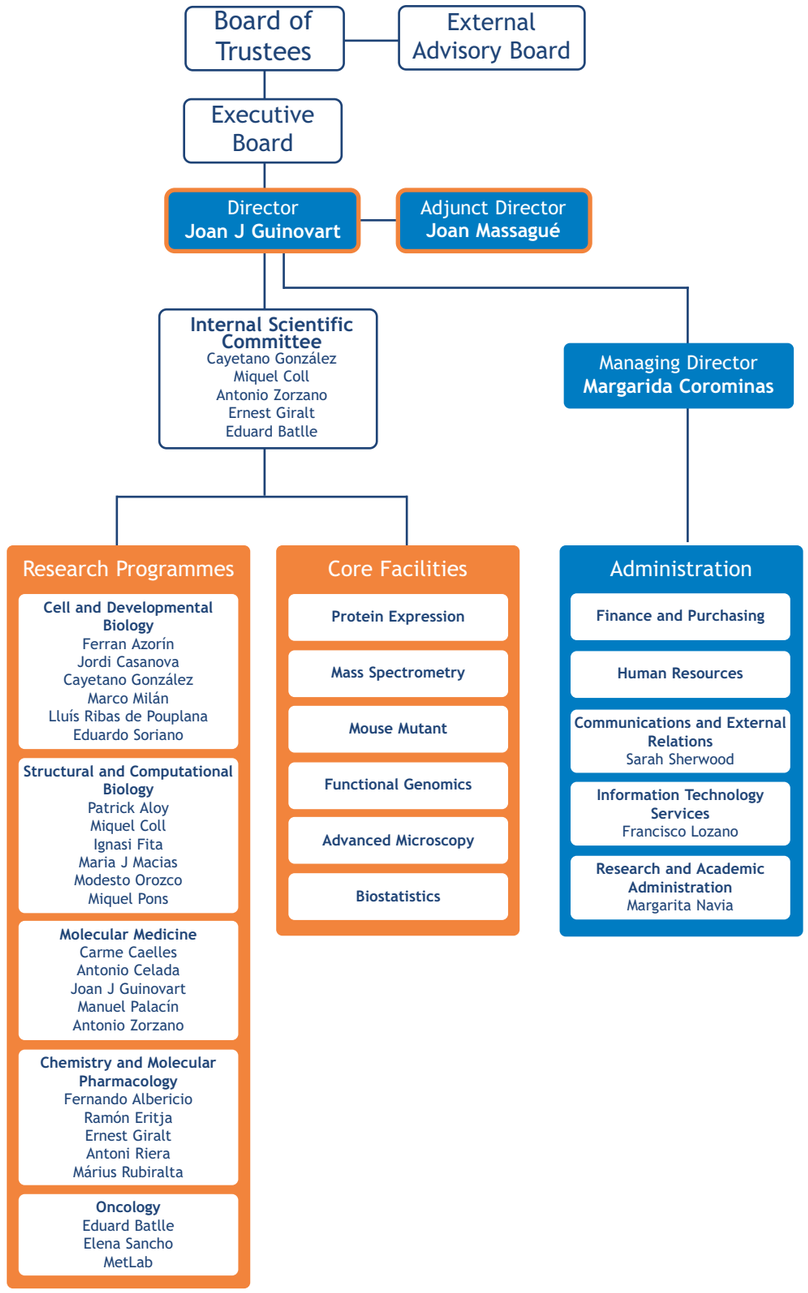
Fundación **BBVA**

OTHER CONFERENCES

5-7 October 2006
ICREA-IRB Barcelona joint conference
DROSOPHILA AS A MODEL FOR HUMAN DISEASES
An ICREA-IRB Barcelona joint conference on state-of-the-art research that exploits Drosophila as a model system to study human disease and define therapeutic strategies
Organisers: Cayetano González and Marco Milán (ICREA-IRB Barcelona)

IRB Barcelona Organigram

Scientific structure
Administrative structure, supporting scientific activities



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Human Resources Statistics

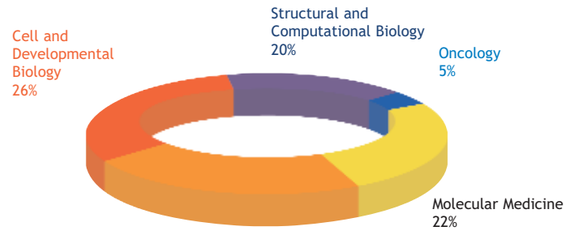
Total IRB Barcelona members

Administration	16
Research groups	335
	351

IRB Barcelona employees vs total members

IRB Barcelona employees	67
Others	284
	351

SCIENTIFIC STAFF. Distributed by research programme



Total	335

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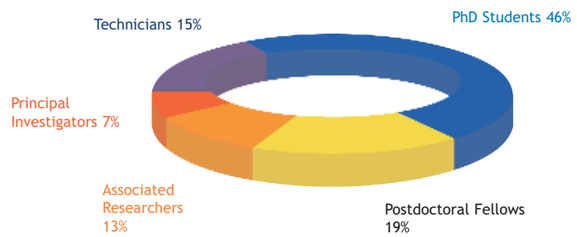

Total	335

Data from December 2006

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Alejandro Vaquero (junior)
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Barcelona Science Park

THE BARCELONA SCIENCE PARK NEW OPPORTUNITIES IN THE KNOWLEDGE ECONOMY

The Parc Científic de Barcelona (PCB, Barcelona Science Park) is a cornerstone of the innovation system developed by the Universitat de Barcelona (UB, University of Barcelona), with the support of the Fundació Bosch i Gimpera (FBG, Bosch and Gimpera Foundation) and the Caixa Catalunya. The Park hosts research groups from both the public and private sectors and offers a wide range of technological facilities.

The convergence of public research centres and private enterprise makes the PCB a pioneering reference in the promotion of knowledge and technology transfer, and also facilitates the setting up of new technology-based companies.

Situated on the Diagonal Campus, the PCB hosts companies, three research centres, and the CIDEM-PCB Bioincubator, all of which work in emerging research areas of chemistry, pharmacy, biotechnology and nanobioengineering. These research activities are located in a 20,000 m² laboratory building, which is also home modern platforms that support R+D+I activities.

The PCB also brings together numerous research centres from a wide range of fields in the experimental, human and social sciences.

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