

LAUNCH OF NOSTRUM BIODISCOVERY, A SPIN-OFF THAT APPLIES SUPERCOMPUTING TO SPEED UP DRUG DISCOVERY.



The company will use cutting-edge technologies, and one of its business lines will involve supporting the development of drugs for precision medicine.

The efforts of scientists and various research institutions have led to the creation of Nostrum BioDiscovery, a spin-off aimed at the development of drugs and molecules of biotechnological interest by means of supercomputational modelling.

Nostrum BioDiscovery boasts leading bioinformatic technologies developed by researchers Modesto Orozco and Victor Guallar and their respective teams at the Institute for Research in Biomedicine (IRB) in Barcelona and the Barcelona Supercomputing Center - National Supercomputing Center (BSC -CNS), with support from the Bosch i Gimpera Foundation at the University of Barcelona and the Catalan Institute for Research and Advanced Studies (ICREA).

The quality of the research performed by Drs. Orozco and Guallar has been recognised through the award of an ERC Advanced Grant each—the most prestigious research distinction in the European Union. Furthermore, in 2007 and 2012 they received support from the Technology Transfer Programme run by the Botín Foundation, which provides funding and HR support to allow companies to get their early-stage products and biotech services into the market.

DESCRIPTION OF NOSTRUM BIODISCOVERY

Nostrum BioDiscovery seeks to support companies devoted to the discovery of drugs and molecules of biotechnological interest with the commercialisation of new products. With this aim, Nostrum BioDiscovery applies cutting-edge supercomputational technologies related to protein modelling, the study of protein interactions with therapeutic agents, and enzyme engineering for the development of biotech products.

When combined, the technologies provided by Nostrum BioDiscovery significantly speed up and increase the accuracy of studies prior to the commercialisation of pharmaceuticals and biotechnological products.

In the most favourable cases, it is estimated that the approach used by Nostrum BioDiscovery can reduce the early-stage drug development by up to two years (the discovery phase prior to pre-clinical trials) and cut costs by 15-20% in this first phase, implying an estimated saving on average of 40 million euros.

These technologies have also proven optimal for drug discovery in the context of precision medicine, since they allow the study of the most appropriate drug for each therapeutic target on the basis of the genetic characteristics of the latter.

CUTTING-EDGE TECHNOLOGIES

Nostrum BioDiscovery provides the following:

PELE Simulation Software for predicting the dynamic interactions between proteins and ligands and with uses, for example, in drug design, in the drug response to receptor mutations and in the optimisation of enzymes for industrial processes. The efficacy of PELE (Protein Energy Landscape Exploration) in predicting protein-ligand interactions was considered exceptional in the last Community Structure-Activity Resource (CSAR) competition (www.csardock.org), which was funded by the National Institute of Medical Science of the US and organised by the University of Michigan (see article CSAR 2014: A Benchmark Exercise Using Unpublished Data from Pharma, published in May 2016). ([See article CSAR 2014: A Benchmark Exercise Using Unpublished Data from Pharma, publicat el maig de 2016](#)).

ED/MD simulation: Method to explore the flexibility of macromolecular targets and their use in rational drug design. This method can be used to improve the calculation of protein-ligand bonds, thereby allowing the identification of alternative configurations of the active site in a computationally efficient manner.

MDWeb suite: A set of programmes that facilitates rapid work flows to automate molecular dynamics calculations, from the configuration processes to the analysis of trajectories.

MoDEL database: A database that holds simulations of more than 1700 proteins on the basis of their properties, dynamics and trajectories. This is the second-largest database of this nature worldwide.

WHO CAN BENEFIT FROM ITS SERVICES

Nostrum BioDiscovery's potential customers are companies operating in the pharmaceutical and biotech industry, at a time when the innovation policies and development of these companies are experiencing rapid change of business model. The key to this change lies in moving towards "in-house" drug discovery—a model that involves the partial outsourcing of R&D policies. This change allows companies not only to lower costs but also to implement a risk-sharing strategy, as subcontractors usually have expertise in their own technologies.

It is in this context that Nostrum Biodiscovery aims to help its clients speed up the first stage of drug development, namely that corresponding to the study and discovery of the most appropriate molecules, prior to pre-clinical trials. The relation between the company and potential clients can be established through the contracting of a service or through a specific contractual relationship for each project.

The product model and business model of Nostrum BioDiscovery have been designed based on the results of an exhaustive market study that included direct feedback from senior executives and participants in decision-making processes of leading companies in the pharmaceutical, biotech and venture capital fund sectors in the US, Europe and Asia. The yearly turnover of the pharmaceutical industry amounts to about \$ 1 billion. A report by PricewaterhouseCoopers entitled "Pharma 2020: From vision to decision" predicts that by 2020 this figure will reach \$ 1.6 billion, taking into consideration population growth, aging, and lifestyle.

COMPETITIVE ADVANTAGES

The services provided by Nostrum BioDiscovery are at the cutting-edge of technologies for the development of drugs and biotech products *in silico*. The contribution of this company to the development of new molecular entities against therapeutic targets of interest is highly valuable for companies working in the pharmaceutical and biotech sectors.

The main assets of Nostrum BioDiscovery are its technology, computing power, and experience and excellence of its team, which has a long track record of constant, meticulous, highly specialised work at the forefront of science. These three pillars allow Nostrum BioDiscovery to offer a service that few academic groups can provide.

SYSTEM OF CONTINUOUS INNOVATION

Nostrum BioDiscovery arose from the joint IRB-BSC Computational Research Programme, which was launched in 2007 and now includes the Centre for Genomic Regulation, which joined in 2014. The technologies and experience offered by the company have been developed in this framework of cooperation, the continuity of which is ensured through Nostrum BioDiscovery as a new component of this system. Researchers at the centres and Nostrum BioDiscovery share experiences, research lines and complementary bioinformatics tools developed under the joint programme. These efforts are highly effective when there is scarce information about a given therapeutic target.

The company is a limited company and its shareholders include the Botín Foundation as a partner from the private sector, the Barcelona Supercomputing Center - National Supercomputing Center, the Institute for Research in Biomedicine (IRB Barcelona), the University of Barcelona, the Catalan Institute for Research and Advanced Studies, and the entrepreneurial team itself. Nostrum BioDiscovery will be based at the offices of the Barcelona Supercomputing Center - National Supercomputing Center.

THE TEAM

Modesto Orozco, PhD (President of Nostrum BioDiscovery and scientific advisor).

Principal investigator of the Molecular Modelling and Bioinformatics Laboratory at the Institute for Research in Biomedicine (IRB Barcelona), full professor of Biochemistry and Molecular Biology at the Faculty of Chemistry, University of Barcelona (UB), and ICREA Academia professor. He holds a degree in Chemistry (1985) and a PhD in Biochemistry (1990) from the Universitat Autònoma de Barcelona and has received many awards, among them a European Research Council Advanced Grant (2012-2017). He is the director of the Structural Bioinformatics Node of the Spanish Institute of Bioinformatics (INB).

His research activity focuses on the theoretical study of biological systems, with an emphasis on the use of physical models to explain the behaviour of nucleic acids and proteins. He has published about 400 articles in general and specialised leading international journals, such as Nature, Nature Genetics, Nature Biotech, Nature Methods, Nature Communications, Proc. Natl.Acad.Sci.USA, and Angew. Chem.Int.Ed. His articles have more than 20000 citations (GS) and a Hirsch index (H) of 75. He has the second highest H index among Spanish chemists working in "ISI-Multidisciplinary Chemistry Area" and the fifth highest in "ISI-Biochemistry and Molecular Biology Area", according to <http://indice-h.webcindario.com/>.

THE TEAM

Victor Guallar, PhD. (Director of the Scientific Advisory Board).

Currently an ICREA Professor, Dr. Guallar performed his PhD between the University Autonomous of Barcelona and UC Berkeley (Berkeley, USA). After three years as a postdoctoral researcher at Columbia University (New York, USA), in 2003 he was appointed assistant professor at Washington University School of Medicine (St Louis, USA), before moving his group to the Barcelona Supercomputing Center (BSC) in 2006. In the last 10 years, his laboratory (EAPM) has grown considerably, keeping a productive international character, and developing important contributions in computational biophysics, such as the protein-ligand modeling software PELE, and biochemistry, including computational algorithms to study long-range electron transfer processes and enzyme engineering. As a BSC researcher, Prof. Guallar has secured ~2.5 million euros in external funding in the last 6 years, including the award of a prestigious advanced ERC grant (the youngest researcher to receive it in Spain).

Robert Soliva, PhD. (Scientific Director).

Robert Soliva took his BSc in Molecular Biology and Biochemistry at the University of Barcelona (UB). Later, he took his PhD thanks to a CIRIT grant from the Generalitat de Catalunya in the group of Dr. Modesto Orozco (UB). He worked in the Drug Discovery unit of Laboratorios Uriach for more than 12 years during which he actively contributed to the development of several clinical candidates that were licensed to first-tier pharma companies. During the last 5 years he has been working for the firm ZBM Patents&Trademarks and has still been linked to academic discovery projects via the joint BSC-IRB program.

Oriol Pla (Chief Operating Officer (COO)).

Oriol Pla will be in charge of the financial and legal issues of NBD as interim manager. He is the Financial and Legal Director of Orim Management. He holds a Degree in Law and a Master degree in International Business Law and a Master in Corporate Finance & Law from ESADE Business School. The last 7 years he has worked in Leitat Technological Center as Legal Director. Oriol Pla has also experience in local consulting companies specialized in legal advice, advice, protection and management of intellectual property rights and corporate operations (KimBcn). In Orim Management his activities are mainly focused on the execution of tech technology transfer procedures; managing the protection and commercialization of IP Rights, legal and financial assessment, start-up setting up, implementation of funding rounds and economic valuations of assets/projects/companies.

THE TEAM

Jazmin Vasco (Marketing director).

Degree in Audiovisual Communication in Ramon Llull University (URL) and Master in Design Management in Polytechnic University of Catalonia (UPC). She has developed his professional career managing communication plans and design applied to international companies. As Manager of innovation projects for more than 8 years in the field of digital transformation, she is specialized in Branding and User Experience Design (UI / UX) She is graduate degree in this discipline by the Open University of Catalonia (UOC) in 2015.

Josep Oriol Nicolàs, PhD (CEO).

Dr. Nicolas brings to NBD his managing experience related to the drug discovery sector since we was the CEO of Readycell (2011-2015), a biotech company dedicated to provide innovative in vitro tools for DMPK and cosmetics assays. His main role in ReadyCell was focused in designing and coordinating the commercial expansion of the company worldwide. In addition, he managed international alliances, private & public fundraising and in-out licensing agreements with CROs and pharmaceutical companies.

He started his career in Laboratorios Almirall prior to obtaining his PhD based on the study of Neuronal cell pathways in Creutzfeldt-Jakob Syndrome and a Master's degree in Administration of Pharmaceutical Industry. He also has experience in international technology transfer management (US department of Defense) and technology brokerage in a strategic consultancy firm (KimBcn).

SCIENTIFIC ENDORSEMENT OF THE TECHNOLOGIES DEVELOPED BY NOSTRUM BD

The outstanding scientific and technical quality of the tools developed by Nostrum BioDiscovery has been demonstrated in several scientific articles, of which special mention is given to the following:

[CSAR 2014: A Benchmark Exercise Using Unpublished Data from Pharma](#). Carlson HA et al. Journal of chemical information and modeling (2016 May 17).

[Binding Mode and Induced Fit Predictions for Prospective Computational Drug Design](#). Grebner C. et al. Journal of chemical information and modeling. (2016 Apr 25)

[Computational Prediction of HIV-1 Resistance to Protease Inhibitors](#). A Hosseini, et al. Journal of chemical information and modeling 56 (5), 915-923 (2016)

[Rational Enzyme Engineering Through Biophysical and Biochemical Modeling](#). S Acebes et al. ACS Catalysis 6 (3), 1624-1629 (2016)

[Ligand Binding Mechanism in Steroid Receptors: From Conserved Plasticity to Differential Evolutionary Constraints](#). K Edman et al. Structure 23 (12), 2280-2290 (2015)

[New Monte Carlo Based Technique To Study DNA–Ligand Interactions](#). I Cabeza de Vaca et al. Journal of chemical theory and computation 11 (12), 5598-5605 (2015)

[Monte Carlo free ligand diffusion with Markov state model analysis and absolute binding free energy calculations](#). R Takahashi et al. Journal of chemical theory and computation 10 (1), 282-288 (2013)

[MDWeb and MDMoby: an integrated web-based platform for molecular dynamics simulations](#). Hospital A et al. Bioinformatics. (2012 May)

[Application of Drug-Perturbed Essential Dynamics/Molecular Dynamics \(ED/MD\) to Virtual Screening and Rational Drug Design](#). Chaudhuri R et al. Journal of Chemical Theory and Computation. (2012 Jul 10)

[MoDEL \(Molecular Dynamics Extended Library\): a database of atomistic molecular dynamics trajectories](#). Meyer T et al. Structure. (2010 Nov)

SUPPORTING INSTITUTIONS

Barcelona Supercomputing Center (BSC).

Barcelona Supercomputing Center (BSC) is the national supercomputing centre in Spain. BSC specialises in high performance computing (HPC) and its mission is two-fold: to provide infrastructure and supercomputing services to European scientists, and to generate knowledge and technology to transfer to business and society.

BSC is a Severo Ochoa Center of Excellence and a first level hosting member of the European research infrastructure PRACE (Partnership for Advanced Computing in Europe). BSC also manages the Spanish Supercomputing Network (RES).

BSC is a consortium that includes Spanish Government (40%), Catalan Government (30%) and Technical University of Catalonia Barcelona-Tech (10%) www.bsc.es

Institut de Recerca Biomèdica (IRB Barcelona).

Founded in 2005 by the Government of Catalonia, IRB Barcelona has been recognised as a Severo Ochoa Centre of Excellence since 2011, a distinction that was renewed in 2015. Its 22 laboratories and seven technological platforms are devoted to basic and applied research addressing biomedical problems with a high socioeconomic impact, especially cancer and metastasis. It is an international centre that hosts more than 400 employees covering 36 nationalities. It boasts 13 ICREA researchers and has received 8 ERC Grants.

IRB Barcelona's mission is to translate its results to clinical practice, and with the launch of Nostrium BioDiscovery it has given rise to four biotech spin-offs. Located in the Barcelona Science Park, IRB Barcelona is part of the Barcelona Institute of Science and Technology (BIST). . www.irbbarcelona.org

Universitat de Barcelona/Fundació Bosch i Gimpera. The University of Barcelona, founded in 1450, is the first public university in Catalonia both by number of students, about 66,000, and by educational offer. It ranks first in scientific production in the state and is among the top hundred European universities in innovation, being the first Spanish institution in this category according to Reuters Top 100: Europe's Most Innovative Universities.

The Bosch i Gimpera is the technology and innovation transfer office of the University of Barcelona. The Bosch i Gimpera is responsible for transferring to society the results of research through the creation of spin-offs, patent licensing, and signing contracts with companies and institutions, thus contributing to business competitiveness and improving social welfare. The University of Barcelona becomes a shareholder of its own spin-offs through Innovative and Scientific Culture (CIC-UB), the company of the UB Group devoted to the management of shares in the spin-offs of the UB. The aim of CIC-UB is to facilitate the creation of technology-based companies, obtaining economic and social return for the UB Group and society, and creating highly-skilled jobs www.fbg.ub.edu

SUPPORTING INSTITUTIONS

Institució Catalana de Recerca i Estudis Avançats (ICREA).

ICREA, Catalan Institution for Research and Advanced Studies, is a foundation supported by the Catalan Government and guided by a Board of Trustees. ICREA was created in response to the need to seek new hiring formulas that would make it possible to compete with other research systems on a similar if not an equal footing. Its aim is to recruit top scientists for the Catalan R&D system, scientists capable of leading new research groups, strengthening existing groups, and setting up new lines of research. ICREA is an institution without walls.

To achieve its objectives it works closely with Catalan universities and research centres based in Catalonia by means of long-term agreements that allow ICREA researchers to integrate in research groups within these universities and centers. It also plans to keep offering new research positions each year and to continue helping increase research in Catalonia. Cooperation, international openness and excellence are ICREA's hallmark www.icrea.cat

Fundación Botín. The Marcelino Botín Foundation was set up in 1964 by Marcelino Botín Sanz de Sautuola and his wife, Carmen Yllera, to promote social development in Cantabria. Today, 50 years on, the Foundation contributes to the development of society as a whole by exploring new approaches to identify creative talent and to support such talent in order to generate cultural, social and economic wealth. This organisation serves the fields of art and culture, education, science, and rural development, and supports welfare organisations in Cantabria in order to help those most in need. The Botín Foundation is active throughout Spain, particularly in Cantabria, but also in Ibero-America.

Technology Transfer Programme of the Botín Foundation. From 2007 to 2012, Dr. Modesto Orozco's group participated in the Technology Transfer Programme run by the Botín Foundation. This programme provides funding and the support of a professional entrepreneurial team devoted to identifying the results with greatest potential, as well as their later evaluation and valorisation, and to searching for the partners necessary to ensure that the results reach the market and thus fuel socioeconomic development. Nostrum BioDiscovery came about directly from this programme www.fundacionbotin.org

SUPPORTING INSTITUTIONS

The Mind the Gap of the Botín Foundation.

The Nostrum BioDiscovery project is a beneficiary of the Mind the Gap Programme, an initiative launched in 2010 that seeks to support early-stage entrepreneurial biotech projects. Through this programme, the Foundation assigns financial and human resources to set up companies devoted to technology-based products and services.

The resources provided take the form of participation via shares, a system that makes Mind the Gap an innovative 'impact investment' model. The Mind the Gap Programme is currently involved in six active projects, of which five are companies that have already been set up. In 2015, these companies had a turnover of more than 600,000 euros, and since the start of the programme they have secured 8.8 million euros of private funding.

Through the Mind the Gap Programme, the Botín Foundation grants each project up to a maximum of 500,000 euros over two years on the condition that they fulfil a series of objectives with respect to the development of the technology or service. Furthermore, the programme provides managerial support in the form of supervision, assessment, and orientation.

