Barcelona Institute of Science and Technology

PRESS RELEASE

Five new projects to receive a "Seed Grant"

The BIST Ignite programme: pushing multidisciplinary research to the limit

- **The objectives of the selected projects are: to develop new therapies for diseases for which no treatment is currently available, such as Huntington's chorea and triple-negative breast cancer; to eliminate senescent cells that cause age-related pathologies; to test drugs for muscular dystrophies in a personalised and non-invasive way; and to modulate the properties of matter by means of light.**
- **Ten research teams from various BIST centres (CRG, IBEC, ICFO, ICIQ, ICN2, and IRB Barcelona) will combine their capabilities in genetics, chemistry, molecular biology, bioengineering, photonics, biosensors, and new materials to provide new scientific answers to major open challenges in health and fundamental physics.**

Barcelona, 28 June 2021. The **Barcelona Institute of Science and Technology** (BIST) announced the five winners of the first phase of this year's **BIST Ignite Programme** today. This is the fifth edition of the programme, which promotes multidisciplinary collaborations at the frontiers of knowledge to solve **scientific and societal challenges that have yet to be solved by cutting-edge research**.

Once again this year, most of the grant-winning projects focus on health and more specifically on the search for new therapeutic alternatives for diseases that have no cure. These include neurodegenerative diseases such as Huntington's chorea, triple negative breast cancer, muscular dystrophies such as Duchenne disease, and the pathological accumulation of senescent cells. The independent panel of experts who selected the projects also valued the scientific advancement that the TeraFox project, which will explore the interaction between light and matter in the field of new materials, has proposed.

PolySTOP: understanding and controlling the genetic alteration of the polyglutamines that cause Huntington's chorea

The expansion of certain amino acid chains (polyglutamines, PolyQ) in various proteins found in neuronal cells is responsible for neurodegenerative diseases such as Huntington's chorea, which currently has cure and no treatment to slow down its development.

Benedetta Bolognesi, leader of the Protein Phase Transitions in Health and Disease Group at the Institute for Bioengineering of Catalonia (IBEC), and **Xavier Salvatella**, leader of the Laboratory of Molecular Biophysics at the Institute for Research in Biomedicine (IRB Barcelona), lead PolySTOP. The project will combine the methodology developed by Bolognesi's lab to measure these amino acid expansions in vivo —which will apply to the more than 300 mutations of the Htt-Nt protein responsible for Huntington's disease— with the experience of Salvatella's team in the structural study of these expansions and the design of peptides.

"Our methodology allows us to analyse the propensity of thousands of PolyQ sequences to produce amyloid plaques. It is a systematic way to measure how these chains and their 'adjacent regions' impact

aggregation. With this we can obtain 'mutational landscapes' that will allow us to understand what exactly these areas do in the aggregation process. Xavier's team will then be able to study their structure and design peptides that can bind to glutamines and control their aggregation," explains Dr Bolognesi, *"This may offer therapeutic alternatives not only for Huntington's, but also for other neurodegenerative diseases that are currently untreatable."*

EXPLODE-TNBC: using cellular mechanisms of protein degradation to cure currently incurable cancers

Inhibiting the IMPDH2 enzyme stops the proliferation of cancer cells, but the enzyme is needed by all cells in the body, so inhibiting it is toxic. Recent research has revealed that IMPDH2 is also found in the chromatin (cell nucleus) of triple-negative breast tumours - which do not respond to any treatment - but is less present in the cell nuclei of tumours that respond well to therapy. "*This gives us a new scientific objective*," explains **Sara Sdelci**, leader of the Cancer Epigenetics and Metabolism Group at the Centre for Genomic Regulation (CRG), "*which is not to inhibit, but to degrade the enzyme in the cell nucleus. The challenge is therefore twofold: to degrade the enzyme we are interested in and to do so only in the cell nucleus*".

To do so, **Antoni Riera**, leader of the Cancer Science Unit at the Institute for Research in Biomedicine (IRB Barcelona), and his team are designing a bifunctional molecule, "*one part of which will adhere to the enzyme being degraded and another part that will mark it so that the proteosome - the natural mechanism cells have for degrading proteins - degrades IMPDH2*". A protein that is only found in the cell nucleus will be used as a marker, allowing for degradation of the protein only where it matters. The advantage of this therapeutic approach is that the bifunctional molecule remains active after it has "tagged" a protein molecule in a particular cell and can continue to do so in other cells.

SENESGOLD: eliminating senescent cells by synthesising senolytic drugs within the cells themselves

Senescent cells are damaged cells that have stopped their replication mechanism and are supposed to be eliminated by our immune system. However, this does not always happen, leading to a pathological accumulation of senescent cells. This is linked to age-related diseases, as well as to the side effects of very aggressive treatments like chemotherapy. Eliminating these senescent cells is a therapeutic objective to treat these diseases, and is the goal of the SENESGOLD project, co-led by **Marc Montesinos** and **José Alberto López**, Postdoctoral Researchers at the Institute of Chemical Research of Catalonia (ICIQ) and IRB Barcelona, respectively.

"*The project combines two very novel research areas: research in the biology of senescent cells, and the catalysis of drugs within the cells themselves. The challenge of this project is to carry out this catalysis inside the specific cells we want*," explains José Alberto López. To do this, the project uses the beta-galactosidase enzyme, which is most active in senescent cells, as a marker. This enzyme will activate small molecules containing gold atoms inside the cells, "*which in several recent studies has been shown to activate bonds with organic compounds that other metallic compounds cannot*", says Marc Montesinos, with the aim of developing a catalytic drug production system (prodrug) that has the capacity to eliminate senescent cells "in vivo".

ASITOC: muscles-on-a-chip and biomagnetism sensors to accelerate the design of new muscular dystrophy treatments

There are more than 30 hereditary diseases that cause muscular dystrophy. Some are very severe and rapidly developing, such as Duchenne disease, which affects mostly boys. "*Muscles with dystrophy move, but differently from healthy muscles. For example, they have weakness and longer relaxation times. What we're trying to do is reproduce the characteristic movements of diseased muscles in a microfluidic device (organ-on-a-chip) and integrate magnetic sensor technology to measure the contraction dynamics*," explains **Juan Manuel Fernández-Costa**, IBEC postdoctoral researcher and project co-leader together with **Michael Tayler**, postdoctoral researcher and "la Caixa" Junior Leader at the Institute of Photonic Sciences (ICFO).

Both technologies are very novel and present the added challenge of reproducing the muscle movement affected by a pathology, and measuring this movement's extremely weak biomagnetic disturbances. "*The measurement of magnetic fields from biological sources is already being applied to the brain (magneto-encephalography) and the heart. But the magnetic fields produced by these organs are three times the order of magnitude of those generated by a muscle-on-a-chip*," stresses Michael Tayler. "*The project is absolutely pioneering in this field*".

The ultimate goal is to have a device capable of measuring the changes that occur in the muscle when certain compounds are applied to it, which would allow us to use it for testing new drugs and treatments. The system could have applications not only for the most severe cases of dystrophy, but also for the more than 700 known muscle diseases and even in other pathologies where there is a change in biomagnetic potential that could be measured by this technology.

TeraFox: modulating properties of matter with light

TMOs (*Transition Metal Oxides*) are metal oxide compounds of great interest in science, but also in industry, due to their unique properties. These include ferroelectricity (which allows their electrical polarisation to be changed when an external voltage is applied, something that can be employed in numerous electronic devices, such as memory or electro-mechanical actuators), and superconductivity (which allows an electric current to be conducted without dissipation of energy, something of great interest in electric motors or magnetic sensors). Traditionally, attempts to manipulate these properties have been carried out by altering the chemical composition or acting on the structure of the compound. The TeraFox project, co-led by **Ekaterina Khestanova**, a postdoctoral researcher at ICFO, and **David Pesquera**, a postdoctoral researcher at the Catalan Institute of Nanoscience and Nanotechnology (ICN2), proposes a completely new approach, using light.

"Instead of applying mechanical stress or an electric field, we want to act on the properties of the TMOs by placing them inside a terahertz cavity, where we 'trap' the light between two mirrors. This is not visible light, but rather electromagnetic waves of a precise length, with the exact energy to allow us to interact with these materials ", explains Ekaterina Khestanova.

The challenge of this project lies as much in the design and production of the cavity as in its coupling with the TMOs. To succeed would mean having a new, more efficient method to control the functionality and optimise the properties of materials with a wide range of applications, from energy saving and storage to the development of much more precise sensors or the manufacturing of more efficient medical devices and computers.

Each of the five projects will receive a grant of 20,000 euros to carry out the first ten-month phase, after which, depending on the results obtained, a panel of experts will select two of the projects to receive additional funding of 50,000 euros. The aim of the programme is to help projects with a **highly innovative approach and strong potential**, which may subsequently apply for competitive funding calls, to get off the ground. Since the launch of the first call in December 2016, there have been **five editions of the BIST Ignite Programme**, with a total of **23 projects** receiving funding, for a total amount of €810,000, and with the participation of more than 170 researchers from the seven BIST centres.

About BIST

The Barcelona Institute of Science and Technology (BIST) is a leading institution of multidisciplinary research encompassing seven Catalan research centres of excellence. By fostering collaboration among members of its diverse scientific community, BIST aims to play a leading role in pushing the frontiers of science while becoming a global reference for training outstanding research talent.

The centres of the BIST are the Centre for Genomic Regulation (CRG), the Institute for Bioengineering of Catalonia (IBEC), the Institute of Photonic Sciences (ICFO), the Institute of Chemical Research of Catalonia (ICIQ), the Catalan Institute of Nanoscience and Nanotechnology (ICN2), the Institute for High Energy Physics (IFAE), and the Institute for Research in Biomedicine (IRB Barcelona).

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