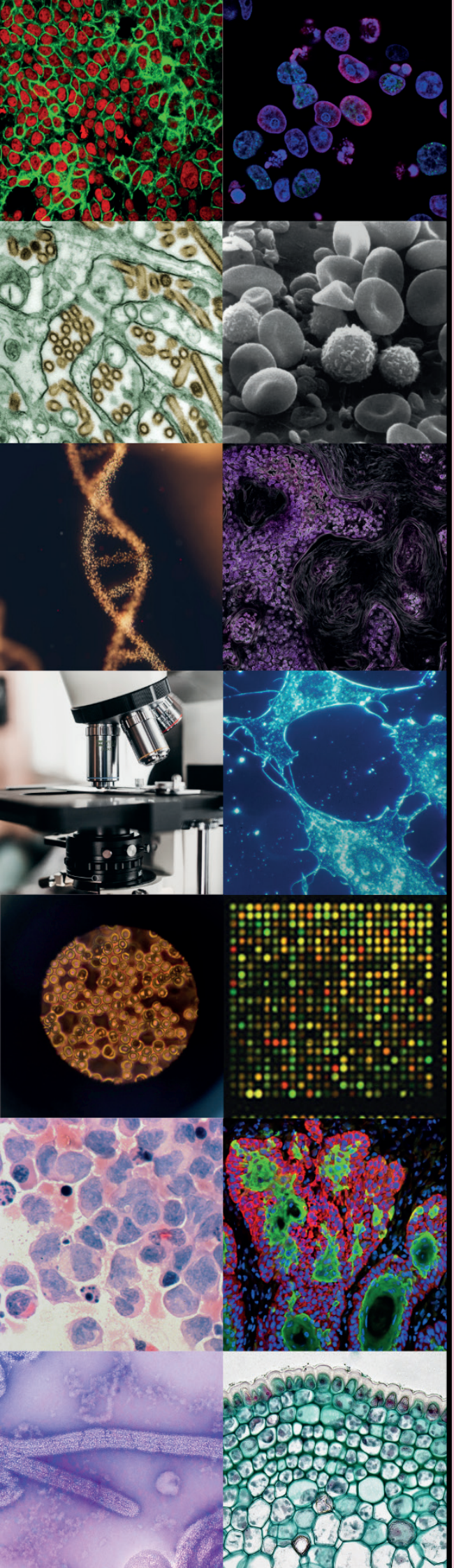


ANNUAL REPORT 2022

Institut de Biomedicina
UNIVERSITAT DE BARCELONA

CONTENTS

01. INTRODUCTION

The IBUB is a research institute that brings together more than 150 researchers with shared research interests, generating unique opportunities for complementarity and synergy. The participation of researchers with a solid background in medicinal chemistry, pharmacology, human molecular genetics, metabolism, and cellular plasticity, favor lines of research aimed at drug discovery together with several omics laboratories, focused on biological systems approaches, as a strongly distinctive characteristic of the IBUB.

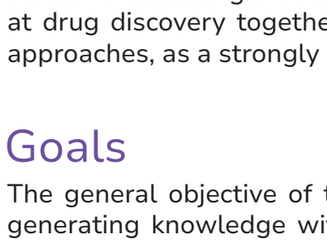
Goals

The general objective of the IBUB is to study biological processes as integrated systems, generating knowledge with a comprehensive view of biological systems. This insight into vital processes will allow the identification of new therapeutic targets and help design new bioactive compounds with possible health benefits. In fact, the intramural potential of IBUB's medicinal chemistry makes it a unique research organization structure within the panorama of biomedical institutes in Spain. Ultimately, IBUB's main goal is to promote better health at all stages of life through science and the development of smart medicines.

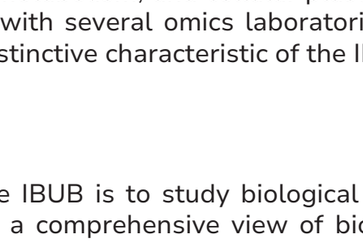
The IBUB aims to contribute scientific advances that improve people's health and quality of life and to do so in a framework of sustainability, with the highest ethical standards and with a strong international projection. Not least, the IBUB is a highly transdisciplinary academic base unit that also aims to provide excellent training to researchers, both at undergraduate and postgraduate levels.

Faculty of Biology of the University of Barcelona

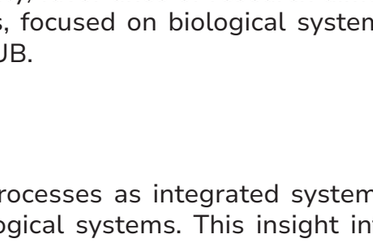
Faculty of Food and Nutrition Torribera Campus of the University of Barcelona



Parc Científic de Barcelona



Faculty of Pharmacy and Food sciences of the University of Barcelona



Faculty of Chemistry of the University of Barcelona

Encourage and promote research within and between the different programs of the Institute.

Promote and encourage collaboration between research groups from different academic disciplines, to obtain biomedical research results of added value thanks to complementarities and synergies.

Identify strategic areas in emerging biomedical research, to integrate research teams that can increase the added value of the Institute.

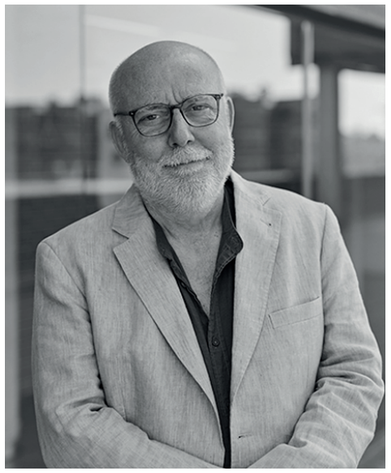
Optimizing the highly qualified infrastructure and resources already available on the BKC campus for scientific and technological innovation, thus contributing to cutting-edge interdisciplinary research between programs.

Promote academic activities related to the scope of the Institute.

Fulfill the advisory functions of public bodies

Encourage and promote the transfer of knowledge and technology, as well as the generation of spin-off companies in the biomedical and pharmaceutical fields.

Institut de Biomedicina
UNIVERSITAT DE BARCELONA



Marçal Pastor-Anglada, Director

Santiago Vázquez, Secretary

Permanent commission

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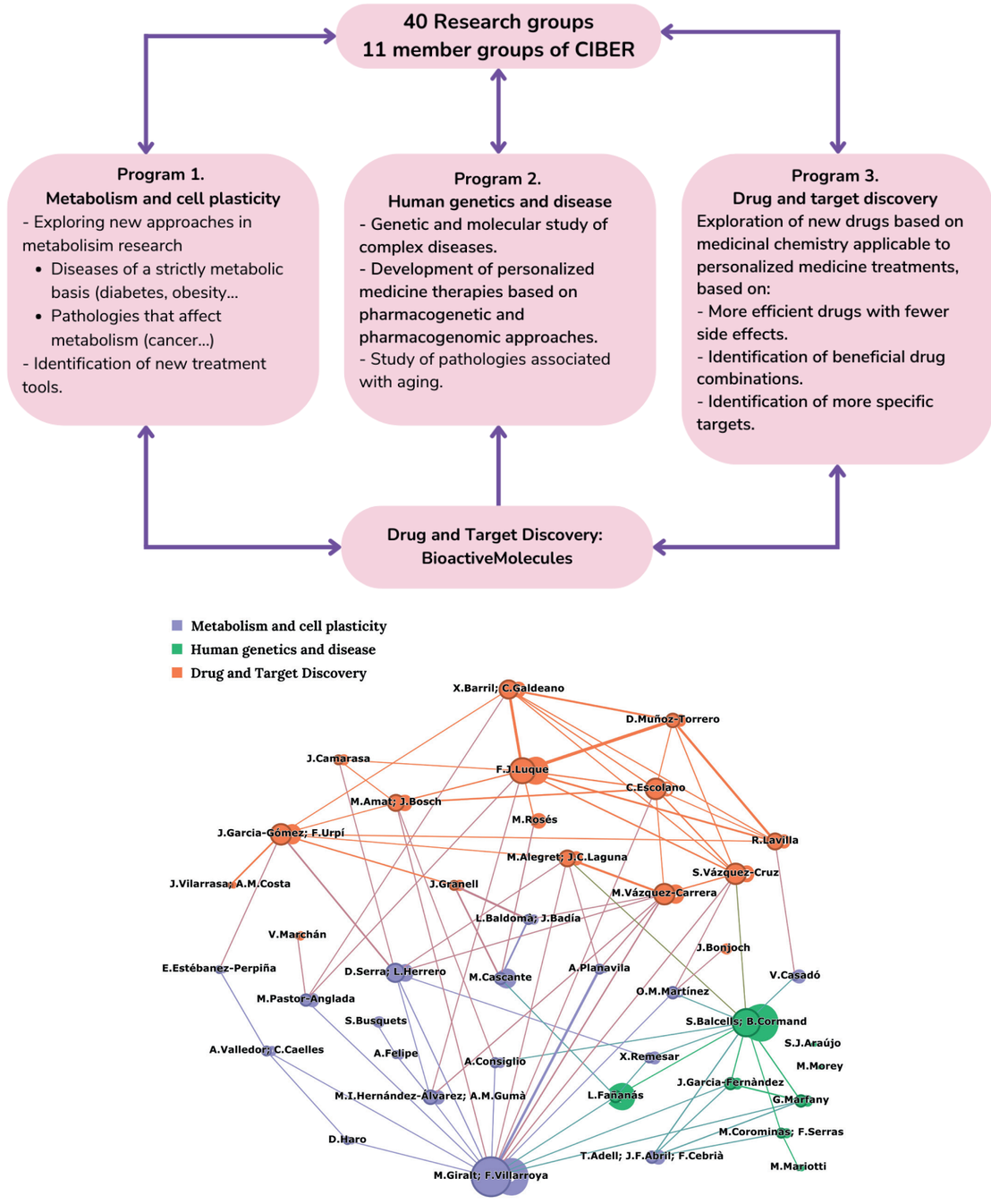
02. RESEARCH



Program 1. Metabolism and cell plasticity

Formed by working groups aimed at exploring new approaches in metabolism research based on prevalent diseases, ranging from those strictly based on metabolism, such as diabetes, obesity or cardiovascular pathologies, as well as others metabolic diseases, such as cancer, or other emerging forms such as regenerative medicine.
Apart from the development of detection and prevention strategies, they also aim to identify new treatment tools.

Biochemistry and Molecular Biology of Cancer	Argilés, J.M.; Busquets, S.
Gut microbiota-host interaction	Baldomà, L.
Molecular Neurobiology	Casadó, V.
Integrative Systems Biology, Metabolomics and Cancer	Cascante, M.
Neural Commitment and Differentiation	Consiglio, A.
Structural Biology of Human Nuclear Receptors	Estébanez-Perpiñà, E.
Molecular physiology	Felipe, A.
Molecular basis of metabolic pathologies and associated to membrane transporters	Gumà, A.; Hernández-Álvarez, M.I.
Nutritional Cell Signaling	Haro, D.; Marrero, P.
WT1 in cell plasticity	Martínez, O. M
Molecular Pharmacology and Experimental Therapeutics (MPET)	Pastor-Anglada, M.
Molecular Cardiology	Planavila, A.
Nitrogen-Obesity	Remesar, X.
Development and Regeneration Biology	Saló, E.; Adell, T.
Lipid metabolism in obesity, diabetes and cancer	Serra, D.; Herrero, L.
Nuclear Receptors in metabolism, immune responses and cancer	Valledor, A.; Caelles, C.
Molecular metabolism and disease	Villarroya, F.; Giralt, M.

Program 2. Human genetics and disease

This program aims to apply sequencing technology and genetic exploitation tools to understand the molecular basis of both rare diseases and highly prevalent multigenic / multifactorial diseases.
These studies open up the possibility of developing real personalized medicine, taking advantage of pharmacogenetic and pharmacogenomic approaches, while allowing the application of their lines of research in the field of complex diseases associated with aging.

Genetics of Cell Behavior in Development	Aráujo, S. J.
Human Molecular Genetics	Balcells, S.; Cormand, B.
Developmental Biology and Genomics Group	Corominas, M.; Serras, F
Environmental Risk factors related to mental disorders and the GxExD interaction Model	Fañanás, L.
Evolution and Development (Evo-Devo)	Garcia-Fernández, J.
Molecular genetics of retinal inherited dystrophies	Marfany G.

Program 3. Drug and target discovery

This program includes a medicinal chemistry approach that complements and adds value to the findings of the other two programs, especially aimed at the discovery of new drugs intended for personalized medicine treatments and characterized by:
- More efficient drugs with fewer harmful side effects.
- The need to identify drug combinations that benefit patients, anticipating unwanted drug interactions, ideally at a preclinical level.
- The need to identify alternative and better doseable targets.

Research and Development Center of Organic Synthesis for Chemical and Pharmaceutical Companies (SINTEFARMA)	Amat, M.
Computational Chemistry and Drug Discovery	Barril, X.; Galdeano, C.
Synthetic Methodology and Natural Product Synthesis	Bonjoch, J.
Neurotoxicity and Neuropharmacology of amphetamine derivatives	Camarasa, J.
Stereoselective Synthesis of Antitumoral and Antiviral Compounds	Costa, A.M.
Group of Medicinal Chemistry for Unmet Medical Needs	Escolano, C.
Synthetic Methodology Applied to Bioactive Products	García, J.
Bioimaging, bioconjugation, structural studies and therapeutic applications involving small molecules, peptides and oligonucleotides	Marchán, V.
Synthesis and Applications of Cyclometallated Composites	Granell, J.
Nuclear receptor and pharmacology of metabolism	Laguna, J.C.; Alegret, M.
New Chemical Methodologies for Facilitated Biology-Oriented Synthesis	Lavilla, R.
Computational Biology, Chemistry and Gastronomy	Luque, F.J.
Multitarget anti-Alzheimer and chemotherapeutic compounds	Muñoz-Torrero, D.
Physico-chemical characterization and estimation of the biological activity of bioactive compounds	Rosés, M.
Polycyclic Compounds with Biological Activity	Vázquez, S.
Pharmacological targets in inflammation and metabolic diseases	Vázquez Carrera, M.

03. PUBLICATIONS

ChREBP-driven DNL and PNPLA3 Expression Induced by Liquid Fructose are Essential in the Production of Fatty Liver and Hypertriglyceridemia in a High-Fat Diet-Fed Rat Model

DRUG AND TARGET DISCOVERY

Molecular Nutrition & Food Research

Velázquez, A. L., Bentanachs, R., Sala-Vila, A., Lázaro, I., Rodríguez-Morató, J., Sánchez, R. M. G., Pallàs, M., Roglans, N., & Laguna, J. C. (2022). Molecular Nutrition & Food Research, 66(7), 2101115.

The aim of this study is to delineate the contribution of dietary saturated fatty acids (FA) versus liquid fructose to fatty liver and hypertriglyceridemia. Three groups of female rats are maintained for 3 months in standard chow (CT); High-fat diet (46.9% of fat-derived calories, rich in palmitic and stearic FA, HFD); and HFD with 10% w/v fructose in drinking water (HFHFr). Zoometric parameters, plasma biochemistry, and liver Oil-Red O (ORO) staining, lipidomics, and expression of proteins involved in FA metabolism are analyzed. Both diets increase ingested calories without modifying body weight. Only the HFHFr diet increases liver triglycerides (x11.0), with hypertriglyceridemia (x1.7) and reduces FA β-oxidation (x0.7), and increases liver FA markers of DNL (de novo lipogenesis). Whereas HFD livers show a high content of ceramides, HFHFr samples show unchanged ceramides, and an increase in diacylglycerols. Only the HFHFr diet leads to a marked increase in the expression of enzymes involved in DNL and triglyceride metabolism, such as carbohydrate response element binding protein β (ChREBPβ, x3.2), a transcription factor that regulates DNL, and patatin-like phospholipase domain-containing 3 (PNPLA3, x2.6), a lipase that mobilizes stored triglycerides for VLDL secretion.

Knocking on GDF15's door for the treatment of type 2 diabetes mellitus

DRUG AND TARGET DISCOVERY

Trends in Endocrinology & Metabolism

Aguilar-Recarte, D., Barroso, E., Palomer, X., Wahli, W., & Vázquez-Carrera, M. (2022). Trends in Endocrinology and Metabolism, 33(11), 741-754.

Despite the high number of drugs currently available for the management of type 2 diabetes mellitus (T2DM), many patients do not achieve adequate disease control, emphasizing the need for new drugs.
Targeting growth differentiation factor 15 (GDF15), a cytokine induced by the integrated stress response (ISR), has emerged as a therapeutic option for obesity and T2DM.
GDF15 reduces food intake and body weight through its central receptor glial cell line-derived neurotrophic factor (GDNF)-like alpha-1 (GFRAL), but its peripheral effects through an unknown receptor also contribute to ameliorating insulin resistance.
Encouraging findings in animal models indicate that GDF15-based therapies are promising for the treatment of obesity and T2DM, but clinical studies in humans are needed to confirm this.

The Glycolytic Gatekeeper PDK1 defines different metabolic states between genetically distinct subtypes of human acute myeloid leukemia

METABOLISM AND CELL PASTICITY

nature communications

Erdem, A., Marin, S., Pereira-Martins, D. A., Cortés, R., Cunningham, A., Pruis, M., De Boer, B., Van Den Heuvel, F. A., Geugien, M., Wierenga, A. T. J., Brouwers-Vos, A. Z., Rego, E. M., Huls, G., Cascante, M., & Schuringa, J. J. (2022). Nature Communications 13(1).

Acute myeloid leukemia remains difficult to treat due to strong genetic heterogeneity between and within individual patients. Here, we show that Pyruvate dehydrogenase kinase 1 (PDK1) acts as a targetable determinant of different metabolic states in acute myeloid leukemia (AML). PDK1^{low} AMLs are OXPHOS-driven, are enriched for leukemic granulocyte-monocyte progenitor (L-GMP) signatures, and are associated with FLT3-ITD and NPM1cyt mutations. PDK1^{high} AMLs however are OXPHOS^{low}, wild type for FLT3 and NPM1, and are enriched for stemness signatures. Metabolic states can even differ between genetically distinct subclones within individual patients. Loss of PDK1 activity releases glycolytic cells into an OXPHOS state associated with increased ROS levels resulting in enhanced apoptosis in leukemic but not in healthy stem/progenitor cells. This coincides with an enhanced dependency on glutamine uptake and reduced proliferation in vitro and in vivo in humanized xenograft mouse models. We show that human leukemias display distinct metabolic states and adaptation mechanisms that can serve as targets for treatment.

A non-dividing cell population with high pyruvate dehydrogenase kinase activity regulates metabolic heterogeneity and tumorigenesis in the intestine

METABOLISM AND CELL PLASTICITY

nature communications

Article Highlight

Sebastian, C., Ferrer, C. M., Serra, M. P., Choi, J. H., Ducano, N., Mira, A., Shah, M. S., Stopka, S. A., Perciaccante, A. J., Isella, C., Moya-Rull, D., Vara-Messler, M., Giordano, S., Maldi, E., Desai, N., Capen, D. E., Medico, E., Cetinbas, M., Sadreyev, R. I., Brown, D., Rivera, M. N., Sapino, A., Breault, D.T., Agar, N. Y. R. & Mostoslavsky, R. (2022). Nature Communications, 13(1).

Although reprogramming of cellular metabolism is a hallmark of cancer, little is known about how metabolic reprogramming contributes to early stages of transformation. Here, we show that the histone deacetylase SIRT6 regulates tumor initiation during intestinal cancer by controlling glucose metabolism. Loss of SIRT6 results in an increase in the number of intestinal stem cells (ISCs), which translates into enhanced tumor initiating potential in APC^{min} mice. By tracking down the connection between glucose metabolism and tumor initiation, we find a metabolic compartmentalization within the intestinal epithelium and adenomas, where a rare population of cells exhibit features of Warburg-like metabolism characterized by high pyruvate dehydrogenase kinase (PDK) activity. Our results show that these cells are quiescent cells expressing +4 ISCs and enteroendocrine markers. Active glycolysis in these cells suppresses ROS accumulation and enhances their stem cell and tumorigenic potential. Our studies reveal that aerobic glycolysis represents a heterogeneous feature of cancer, and indicate that this metabolic adaptation can occur in non-dividing cells, suggesting a role for the Warburg effect beyond biomass production in tumors.

Coordination of mitochondrial and lysosomal homeostasis mitigates inflammation and muscle atrophy during aging

METABOLISM AND CELL PLASTICITY

Irazoki, A., Martinez-Vicente, M., Aparicio, P., Aris, C., Alibakhshi, E., Rubio-Valera, M., Castellanos, J., Lores, L., Palacín, M., Gumà, A., Zorzano, A., & Sebastián, D. (2022). Aging Cell, 21(4).

Sarcopenia is one of the main factors contributing to the disability of aged people. Among the possible molecular determinants of sarcopenia, increasing evidences suggest that chronic inflammation contributes to its development. However, a key unresolved question is the nature of the factors that drive inflammation during aging and that participate in the development of sarcopenia. In this regard, mitochondrial dysfunction and alterations in mitophagy induce inflammatory responses in a wide range of cells and tissues. However, whether accumulation of damaged mitochondria (MIT) in muscle could trigger inflammation in the context of aging is still unknown. Here, we demonstrate that BCL2 interacting protein 3 (BNIP3) plays a key role in the control of mitochondrial and lysosomal homeostasis, and mitigates muscle inflammation and atrophy during aging. We show that muscle BNIP3 expression increases during aging in mice and in some humans. BNIP3 deficiency alters mitochondrial function, decreases mitophagic flux and, surprisingly, induces lysosomal dysfunction, leading to an upregulation of Toll-like receptor 9 (TLR9)-dependent inflammation and activation of the NLRP3 (nucleotide-binding oligomerization domain (NOD)-, leucine-rich repeat (LRR)-, and pyrin domain-containing protein 3) inflammasome in muscle cells and mouse muscle. Importantly, downregulation of muscle BNIP3 in aged mice exacerbates inflammation and muscle atrophy, and high BNIP3 expression in aged human subjects associates with a low inflammatory profile, suggesting a protective role for BNIP3 against age-induced muscle inflammation in mice and humans. Taken together, our data allow us to propose a new adaptive mechanism involving the mitophagy protein BNIP3, which links mitochondrial and lysosomal homeostasis with inflammation and is key to maintaining muscle health during aging.

Brown fat resolves hepatic inflammation in obesity

METABOLISM AND CELL PLASTICITY

Villarroya, F., & Gavaldà-Navarro, A. (2022). Nature metabolism 4(6), 649-650.

Hepatic infammation is a major co-morbidity in obesity. New work shows that activated brown adipose tissue releases maresin-2, a lipid molecule derived from docosahexaenoic acid, which targets the liver and actively protects against obesity-induced hepatic infammation.

Oleic acid is an endogenous ligand of TLX/NR2E1 that triggers hippocampal neurogenesis

METABOLISM AND CELL PLASTICITY

Kandel, P., Semerci, F., Mishra, R., Choi, W. W., Bajić, A., Baluya, D. L., Ma, L., Chen, K. J., Cao, A. C., Phongmekhin, T., Matinyan, N., Jiménez-Panizo, A., Chamakuri, S., Raji, I. O., Chang, L., Fuentes-Prior, P., MacKenzie, K. R., Benn, C. L., Estébanez-Perpiñá, E., Venken, K., Moore, D. D., Young, D. W. & Maletic-Savatic, M. (2022). Proceedings of the National Academy of Sciences, 119(13).

Neural stem cells, the source of newborn neurons in the adult hippocampus, are intimately involved in learning and memory, mood, and stress response. Despite considerable progress in understanding the biology of neural stem cells and neurogenesis, regulating the neural stem cell population precisely has remained elusive because we have lacked the specific targets to stimulate their proliferation and neurogenesis. The orphan nuclear receptor TLX/NR2E1 governs neural stem and progenitor cell self-renewal and proliferation, but the precise mechanism by which it accomplishes this is not well understood because its endogenous ligand is not known. Here, we identify oleic acid (18:1ω9 monounsaturated fatty acid) as such a ligand. We first show that oleic acid is critical for neural stem cell survival. Next, we demonstrate that it binds to TLX to convert it from a transcriptional repressor to a transcriptional activator of cell-cycle and neurogenesis genes, which in turn increases neural stem cell mitotic activity and drives hippocampal neurogenesis in mice. Interestingly, oleic acid-activated TLX strongly up-regulates cell cycle genes while only modestly up-regulating neurogenic genes. We propose a model in which sufficient quantities of this endogenous ligand must bind to TLX to trigger the switch to proliferation and drive the progeny toward neuronal lineage. Oleic acid thus serves as a metabolic regulator of TLX activity that can be used to selectively target neural stem cells, paving the way for future therapeutic manipulations to counteract pathogenic impairments of neurogenesis.

Non-G Base Tetrads

DRUG AND TARGET DISCOVERY

Escaja, N., Mir, B., Garavís, M., & González, C. (2022). Molecules, 27(16), 5287.

Tetrads (or quartets) are arrangements of four nucleobases commonly involved in the stability of four-stranded nucleic acids structures. Four-stranded or quadruplex structures have attracted enormous attention in the last few years, being the most extensively studied guanine quadruplex (G-quadruplex). Consequently, the G-tetrad is the most common and well-known tetrad. However, this is not the only possible arrangement of four nucleobases. A number of tetrads formed by the different nucleobases have been observed in experimental structures. In most cases, these tetrads occur in the context of G-quadruplex structures, either inserted between G-quartets, or as capping elements at the sides of the G-quadruplex core. In other cases, however, non-G tetrads are found in more unusual four stranded structures, such as i-motifs, or different types of peculiar fold-back structures. In this report, we review the diversity of these non-canonical tetrads, and the structural context in which they have been found.

miRNA signatures associated with vulnerability to food addiction in mice and humans

HUMAN GENETICS AND DISEASE

JCI The Journal of Clinical Investigation

García-Blanco, A., Domingo-Rodriguez, L., Cabana-Domínguez, J., Fernàndez-Castillo, N., Pineda-Cirera, L., Swann, J. R., Burokas, A., Espinosa-Carrasco, J., Arboleya, S., Latorre, J., Stanton, C., Cormand, B., Fernández-Real, J. M., Martín-García, E., & Maldonado, R. (2022). Journal of Clinical Investigation, 132(10).

Food addiction is characterized by a loss of behavioral control over food intake and is associated with obesity and other eating disorders. The mechanisms underlying this behavioral disorder are largely unknown. We aimed to investigate the changes in miRNA expression promoted by food addiction in animals and humans and their involvement in the mechanisms underlying the behavioral hallmarks of this disorder. We found sharp similitudes between miRNA signatures in the medial prefrontal cortex (mPFC) of our animal cohort and circulating miRNA levels in our human cohort, which allowed us to identify several miRNAs of potential interest in the development of this disorder. Tough decoy (TuD) inhibition of miRNA-29c-3p in the mouse mPFC promoted persistence of the response and enhanced vulnerability to developing food addiction, whereas miRNA-665-3p inhibition promoted compulsion-like behavior and also enhanced food addiction vulnerability. In contrast, we found that miRNA-137-3p inhibition in the mPFC did not lead to the development of food addiction. Therefore, miRNA-29c-3p and miRNA-665-3p could be acting as protective factors with regard to food addiction. We believe the elucidation of these epigenetic mechanisms will lead to advances toward identifying innovative biomarkers and possible future interventions for food addiction and related disorders based on the strategies now available to modify miRNA activity and expression.

Deficiency of the ywhaz gene, involved in neuro developmental disorders, alters brain activity and behaviour in zebrafish

HUMAN GENETICS AND DISEASE

Molecular Psychiatry

Antón-Galindo, E., Vecchia, E. D., Orlandi, J. G., De Castro, G. R., Gualda, E. J., Young, A. J., Guasch-Piqueras, M., Arenas, C., Herrera-Úbeda, C., Garcia-Fernàndez, J., Aguado, F., Loza-Alvarez, P., Cormand, B., Norton, W. T., & Fernàndez-Castillo, N. (2022). Molecular Psychiatry, 27(9), 3739-3748.

Genetic variants in YWHAZ contribute to psychiatric disorders such as autism spectrum disorder and schizophrenia, and have been related to an impaired neurodevelopment in humans and mice. Here, we have used zebrafish to investigate the mechanisms by which YWHAZ contributes to neurodevelopmental disorders. We observed that ywhaz expression was pan-neuronal during developmental stages and restricted to Purkinje cells in the adult cerebellum, cells that are described to be reduced in number and size in autistic patients. We then performed whole-brain imaging in wild-type and ywhaz CRISPR/Cas9 knockout (KO) larvae and found altered neuronal activity and connectivity in the hindbrain. Adult ywhaz KO fish display decreased levels of monoamines in the hindbrain and freeze when exposed to novel stimuli, a phenotype that can be reversed with drugs that target monoamine neurotransmission. These findings suggest an important role for ywhaz in establishing neuronal connectivity during development and modulating both neurotransmission and behaviour in adults.

Inhibition of the succinyl dehydrogenase complex in acute myeloid leukemia leads to a lactate-fuelled respiratory metabolic vulnerability

METABOLISM AND CELL PLASTICITY

nature communications

Erdem, A., Marin, S., Pereira-Martins, D. A., Geugien, M., Cunningham, A., Pruis, M., Weinhäuser, I., Gerding, A., Bakker, B. M., Wierenga, A. T. J., Rego, E. M., Huls, G., Cascante, M., & Schuringa, J. J. (2022). Nature Communications, 13(1).

Metabolic programs can differ substantially across genetically distinct subtypes of acute myeloid leukemia (AML). These programs are not static entities but can change swiftly as a consequence of extracellular changes or in response to pathway-inhibiting drugs. Here, we uncover that AML patients with FLT3 internal tandem duplications (FLT3-ITD$^+$) are characterized by a high expression of succinate-CoA ligases and high activity of mitochondrial electron transport chain (ETC) complex II, thereby driving high mitochondrial respiration activity linked to the Krebs cycle. While inhibition of ETC complex II enhances apoptosis in FLT3-ITD$^+$ AML, cells also quickly adapt by importing lactate from the extracellular microenvironment. $^{13}C_3$-labelled lactate metabolic flux analyses reveal that AML cells use lactate as a fuel for mitochondrial respiration. Inhibition of lactate transport by blocking Monocarboxylic Acid Transporter 1 (MCT1) strongly enhances sensitivity to ETC complex II inhibition in vitro as well as in vivo. Our study highlights a metabolic adaptability of cancer cells that can be exploited therapeutically.

Secretory immunoglobulin A (s-IgA) reactivity to acute psychosocial stress in children and adolescents: The influence of pubertal development and history of maltreatment

HUMAN GENETICS AND DISEASE

BRAIN, BEHAVIOR, and IMMUNITY

Marques-Feixa, L., Castro-Quintas, Á., Palma-Gudiel, H., Romero, S., Morer, A., Rapado-Castro, M., Martín, M., Zorrilla, I., Blasco-Fontecilla, H., Ramírez, M. A., Mayoral, M. J., Mendez, I., Martín-Gonzalez, N. S., Rodrigo-Yanguas, M., Monteserín-García, J. L., Fañanás, L., & Group, E. S. (2022). Brain Behavior and Immunity, 103, 122-129.

Mucosal secretory immunoglobulin A (s-IgA) is an antibody protein-complex that plays a crucial role in immune first defense against infection. Although different immune biomarkers have been associated with stress-related psychopathology, s-IgA remains poorly studied, especially in youth. The present study investigated how s-IgA behaves in front of acute psychosocial stress in children and adolescents, including possible variability associated with developmental stage and history of childhood maltreatment (CM). 94 children and adolescents from 7 to 17 years (54 with a current psychiatric diagnostic and 40 healthy controls) drawn from a larger Spanish study were explored (EPI-Young Stress Project). To assess biological reactivity, participants provided five saliva samples during an acute laboratory-based psychosocial stressor, the Trier Social Stress Test for Children (TSST-C). Samples were assayed for s-IgA, as well as for cortisol. Pubertal development was ascertained by Tanner stage and CM following TASSCV criteria.

Deletion of Wt1 during early gonadogenesis leads to differences of sex development in male and female adult mice

METABOLISM AND CELL PLASTICITY

PLOS GENETICS

Torres-Cano, A., Portella-Fortuny, R., Müller-Sánchez, C., Porras-Marfil, S., Ramiro-Pareta, M., Chau, Y., Reina, M., Soriano, F. X., & Martinez-Estrada, O.M. (2022). PLOS Genetics, 18(6), e1010240.

Assessing the role of the WT1 transcription factor (WT1) during early gonad differentiation and its impact on adult sex development has been difficult due to the complete gonadal agenesis and embryonic lethality exhibited by Wt1KO mouse models. Here, we generated $Wt1^{LoxP/GFP}$;Wt1Cre mice, the first Wt1KO mouse model that reaches adulthood with a dramatically reduced Wt1 expression during early gonadogenesis. $Wt1^{LoxP/GFP}$;$Wt1^{Cre}$ mice lacked mature gonads and displayed genital tracts containing both male and female genital structures and ambiguous genitalia. We found that WT1 is necessary for the activation of both male and female sex-determining pathways, as embryonic mutant gonads failed to upregulate the expression of the genes specific for each genetic programme. The gonads of $Wt1^{LoxP/GFP}$;$Wt1^{Cre}$ mice showed a lack of production of Sertoli and pre-granulosa cells and a reduced number of germ cells. NR5A1 and the steroidogenic genes expression was modulated differently in XY and XX $Wt1^{LoxP/GFP}$;$Wt1^{Cre}$ gonads, explaining the mutant phenotypes. Further studies of the XX $Wt1^{LoxP/GFP}$;$Wt1^{Cre}$ gonads revealed that deletion of WT1 at an early stage impaired the differentiation of several cell types including somatic cells and the ovarian epithelium. Through the characterisation of this Wt1KO mouse model, we show that the deletion of Wt1 during early gonadogenesis produces dramatic defects in adult sex development.

The multivalency of the glucocorticoid receptor ligand-binding domain explains its manifold physiological activities

METABOLISM AND CELL PLASTICITY

Nucleic Acids Research

Jiménez-Panizo, A., Alegre-Martí, A., Tettey, T. T., Fettweis, G., Abella, M., Antón, R., Johnson, T. A., Kim, S., Schiltz, R. L., Núñez-Barrios, I., Font-Díaz, J., Caelles, C., Valledor, A. F., Pérez, P., Rojas, A. M., Fernández-Recio, J., Presman, D. M., Hager, G. L., Fuentes-Prior, P., & Estébanez-Perpiñá, E. (2022). Nucleic Acids Research, 50(22), 13063-13082.

The glucocorticoid receptor (GR) is a ubiquitously expressed transcription factor that controls metabolic and homeostatic processes essential for life. Although numerous crystal structures of the GR ligand-binding domain (GR-LBD) have been reported, the functional oligomeric state of the full-length receptor, which is essential for its transcriptional activity, remains disputed. Here we present five new crystal structures of agonist-bound GR-LBD, along with a thorough analysis of previous structural work. We identify four distinct homodimerization interfaces on the GR-LBD surface, which can associate into 20 topologically different homodimers. Biologically relevant homodimers were identified by studying a battery of GR point mutants including crosslinking assays in solution, quantitative fluorescence microscopy in living cells, and transcriptomic analyses. Our results highlight the relevance of non-canonical dimerization modes for GR, especially of contacts made by loop L1–3 residues such as Tyr545. Our work illustrates the unique flexibility of GR's LBD and suggests different dimeric conformations within cells. In addition, we unveil pathophysiologically relevant quaternary assemblies of the receptor with important implications for glucocorticoid action and drug design.

Remission of obesity and insulin resistance is not sufficient to restore mitochondrial homeostasis in visceral adipose tissue

METABOLISM AND CELL PLASTICITY

REDOX BIOLOGY

Gonzalez-Franquesa, A., Gama-Perez, P., Kulis, M., Szczepanowska, K., Dahdah, N., Moreno-Gomez, S., Latorre-Pellicer, A., Fernandez-Ruiz, R., Aguilar-Mogas, A., Hoffman, A., Monelli, E., Samino, S., Miró-Blanch, J., Oemer, G., Duran, X., Sanchez-Rebordelo, E., Schneeberger, M., Obach, M., Montane, J., Castellano, G., Chapaprieta, V., Sun, W., Navarro, L., Prieto, I., Castaño, C., Novials, A., Gomis, R., Monsalve, M., Claret, M., Graupera, M., Soria, G., Wolfrum, C., Vendrell, J., Fernández-Veledo, S., Enríquez, S. A., Carracedo, A., Perales, J. C., Nogueiras, R., Herrero, L., Trifunovic, A., Keller, M. A., Yanes, O., Sales-Pardo, M., Guimerà, R., Blüher, M., Martín-Subero, J. I. & Garcia-Roves, P. M. (2022). Redox biology, 54, 102353.

Metabolic plasticity is the ability of a biological system to adapt its metabolic phenotype to different environmental stressors. We used a whole-body and tissue-specific phenotypic, functional, proteomic, metabolomic and transcriptomic approach to systematically assess metabolic plasticity in diet-induced obese mice after a combined nutritional and exercise intervention. Although most obesity and overnutrition-related pathological features were successfully reverted, we observed a high degree of metabolic dysfunction in visceral white adipose tissue, characterized by abnormal mitochondrial morphology and functionality. Despite two sequential therapeutic interventions and an apparent global healthy phenotype, obesity triggered a cascade of events in visceral adipose tissue progressing from mitochondrial metabolic and proteostatic alterations to widespread cellular stress, which compromises its biosynthetic and recycling capacity. In humans, weight loss after bariatric surgery showed a transcriptional signature in visceral adipose tissue similar to our mouse model of obesity reversion. Overall, our data indicate that obesity prompts a lasting metabolic fingerprint that leads to a progressive breakdown of metabolic plasticity in visceral adipose tissue.

The mineralocorticoid receptor modulates timing and location of genomic binding by glucocorticoid receptor in response to synthetic glucocorticoids in keratinocytes

METABOLISM AND CELL PLASTICITY

Carceller-Zazo, E., Sevilla, L. M., Pons-Alonso, O., Chiner-Oms, Á., Amazit, L., Vu, T. T. N., Vitellius, G., Viengchareun, S., Comas, I., Jaszczyszyn, Y., Abella, M., Alegre-Martí, A., Estébanez-Perpiñá, E., Lombès, M., & Pérez, P. (2023).The FASEB Journal 37(1).

Glucocorticoids (GCs) exert potent antiproliferative and anti-inflammatory properties, explaining their therapeutic efficacy for skin diseases. GCs act by binding to the GC receptor (GR) and the mineralocorticoid receptor (MR), co-expressed in classical and non-classical targets including keratinocytes. Using knockout mice, we previously demonstrated that GR and MR exert essential nonoverlapping functions in skin homeostasis. These closely related receptors may homo- or heterodimerize to regulate transcription, and theoretically bind identical GC-response elements (GRE). We assessed the contribution of MR to GR genomic binding and the transcriptional response to the synthetic GC dexamethasone (Dex) using control (CO) and MR knockout (MR^{EKO}) keratinocytes. GR chromatin immunoprecipitation (ChIP)-seq identified peaks common and unique to both genotypes upon Dex treatment (1 h). GREs, AP-1, TEAD, and p53 motifs were enriched in CO and MR^{EKO} peaks. However, GR genomic binding was 35% reduced in MR^{EKO}, with significantly decreased GRE enrichment, and reduced nuclear GR. Surface plasmon resonance determined steady state affinity constants, suggesting preferred dimer formation as MR-MR > GR-MR ~ GR-GR; however, kinetic studies demonstrated that GR-containing dimers had the longest lifetimes. Despite GR-binding differences, RNA-seq identified largely similar subsets of differentially expressed genes in both genotypes upon Dex treatment (3 h). However, time-course experiments showed gene-dependent differences in the magnitude of expression, which correlated with earlier and more pronounced GR binding to GRE sites unique to CO including near Nr3c1. Our data show that endogenous MR has an impact on the kinetics and differential genomic binding of GR, affecting the time-course, specificity, and magnitude of GC transcriptional responses in keratinocytes.

Advancing in Schaaf-Yang syndrome pathophysiology: from bedside to subcellular analyses of truncated MAGEL2

HUMAN GENETICS AND DISEASE

Castilla-Vallmanya, L., Centeno-Pla, M., Serrano, M., Franco-Valls, H., Martínez-Cabrera, R., Prat-Planas, A., Rojano, E., Ranea, J. A. G., Seoane, P., Oliva, C., Paredes-Fuentes, A. J., Marfany, G., Artuch, R., Grinberg, D., Rabionet, R., Webb, B. D., & Urreizti, R. (2022). Journal of Medical Genetics, 60(4), 406-415.

Schaaf-Yang syndrome (SYS) is caused by truncating mutations in MAGEL2, mapping to the Prader-Willi region (15q11-q13), with an observed phenotype partially overlapping that of Prader-Willi syndrome. MAGEL2 plays a role in retrograde transport and protein recycling regulation. Our aim is to contribute to the characterisation of SYS pathophysiology at clinical, genetic and molecular levels. We performed an extensive phenotypic and mutational revision of previously reported patients with SYS. We analysed the secretion levels of amyloid-β 1–40 peptide ($A\beta_{1\text{-}40}$) and performed targeted metabolomic and transcriptomic profiles in fibroblasts of patients with SYS (n=7) compared with controls (n=11). We also transfected cell lines with vectors encoding wild-type (WT) or mutated MAGEL2 to assess stability and subcellular localisation of the truncated protein. Functional studies show significantly decreased levels of secreted Aβ1-40 and intracellular glutamine in SYS fibroblasts compared with WT. We also identified 132 differentially expressed genes, including non-coding RNAs (ncRNAs) such as HOTAIR, and many of them related to developmental processes and mitotic mechanisms. The truncated form of MAGEL2 displayed a stability similar to the WT but it was significantly switched to the nucleus, compared with a mainly cytoplasmic distribution of the WT MAGEL2. Based on the updated knowledge, we offer guidelines for the clinical management of patients with SYS. A truncated MAGEL2 protein is stable and localises mainly in the nucleus, where it might exert a pathogenic neomorphic effect. Aβ1-40 secretion levels and HOTAIR mRNA levels might be promising biomarkers for SYS. Our findings may improve SYS understanding and clinical management.

CRISPR/Cas9-Mediated Allele-Specific Disruption of a Dominant COL6A1 Pathogenic Variant Improves Collagen VI Network in Patient Fibroblasts

HUMAN GENETICS AND DISEASE

International Journal of Molecular Sciences

López-Márquez, A., Morín, M., Fernández-Peñalver, S., Badosa, C., Hernández-Delgado, A., Benito, D. A., Ortez, C., Nascimento, A., Grinberg, D., Webb, B. D., Roldán, M., Moreno-Pelayo, M. A., & Jimenez-Mallebrera, C. (2022). International Journal of Molecular Sciences, 23(8), 4410.

Collagen VI-related disorders are the second most common congenital muscular dystrophies for which no treatments are presently available. They are mostly caused by dominant-negative pathogenic variants in the genes encoding α chains of collagen VI, a heteromeric network forming collagen; for example, the c.877G>A; p.Gly293Arg COL6A1 variant, which alters the proper association of the tetramers to form microfibrils. We tested the potential of CRISPR/Cas9-based genome editing to silence or correct (using a donor template) a mutant allele in the dermal fibroblasts of four individuals bearing the c.877G>A pathogenic variant. Evaluation of gene-edited cells by next-generation sequencing revealed that correction of the mutant allele by homologous-directed repair occurred at a frequency lower than 1%. However, the presence of frameshift variants and others that provoked the silencing of the mutant allele were found in >40% of reads, with no effects on the wild-type allele. This was confirmed by droplet digital PCR with allele-specific probes, which revealed a reduction in the expression of the mutant allele. Finally, immunofluorescence analyses revealed a recovery in the collagen VI extracellular matrix. In summary, we demonstrate that CRISPR/Cas9 gene-edition can specifically reverse the pathogenic effects of a dominant negative variant in COL6A1.

A positive feedback loop between AMPK and GDF15 promotes metformin antidiabetic effects

DRUG AND TARGET DISCOVERY

Pharmacological research

Aguilar-Recarte, D., Barroso, E., Zhang, M., Rada, P., Pizarro-Delgado, J., Peña, L., Palomer, X., Valverde, Á. M., Wahli, W., & Vázquez-Carrera, M. (2022). Pharmacological Research, 187, 106578.

Metformin, the most prescribed drug for the treatment of type 2 diabetes mellitus, has been recently reported to promote weight loss by upregulating the anorectic cytokine growth differentiation factor 15 (GDF15). Since the antidiabetic effects of metformin are mostly mediated by the activation of AMPK, a key metabolic sensor in energy homeostasis, we examined whether the activation of this kinase by metformin was dependent on GDF15. Cultured hepatocytes and myotubes, and wild-type and Gdf15-/- mice were utilized in a series of studies to investigate the involvement of GDF15 in the activation of AMPK by metformin. A low dose of metformin increased GDF15 levels without significantly reducing body weight or food intake, but it ameliorated glucose intolerance and activated AMPK in the liver and skeletal muscle of wild-type mice but not Gdf15-/- mice fed a high-fat diet. Cultured hepatocytes and myotubes treated with metformin showed AMPK-mediated increases in GDF15 levels independently of its central receptor GFRAL, while Gdf15 knockdown blunted the effect of metformin on AMPK activation, suggesting that AMPK is required for the metformin-mediated increase in GDF15, which in turn is needed to sustain the full activation of this kinase independently of the CNS. Overall, these findings uncover a novel mechanism through which GDF15 upregulation by metformin is involved in achieving and sustaining full AMPK activation by this drug independently of the CNS.

Bempedoic Acid Restores Liver H_2S Production in a Female Sprague-Dawley Rat Dietary Model of Non-Alcoholic Fatty Liver

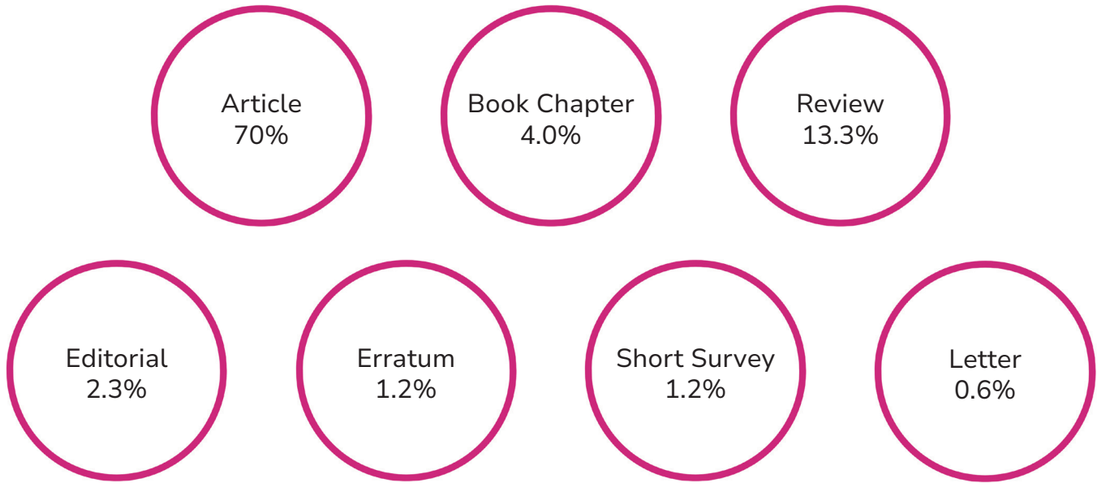
DRUG AND TARGET DISCOVERY

International Journal of Molecular Sciences

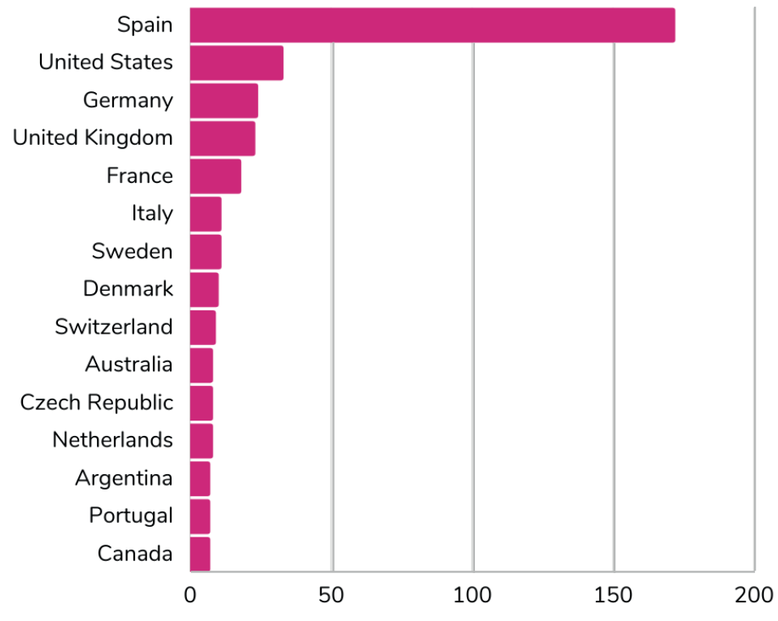
Roglans, N., Fauste, E., Bentanachs, R., Velázquez, A. L., Pérez-Armas, M., Donis, C., Panadero, M. A. T., Pallàs, M., Otero, P., Bocos, C., & Laguna, J. C. (2022). International Journal of Molecular Sciences, 24(1), 473.

We previously demonstrated that treatment with BemA (bempedoic acid), an inhibitor of ATP citrate lyase, significantly reduces fatty liver in a model of liver steatosis (HFHFr—female Sprague-Dawley rat fed a high-fat high-fructose diet). Since the hepatic production of the gasotransmitter H2S is impaired in liver disorders, we were interested in determining if the production of H2S was altered in our HFHFr model and whether the administration of BemA reversed these changes. We used stored liver samples from a previous study to determine the total and enzymatic H2S production, as well as the expression of CBS (cystathionine β-synthase), CSE (cystathionine γ-lyase), and 3MST (3-mercaptopiruvate sulfurtransferase), and the expression/activity of FXR (farnesoid X receptor), a transcription factor involved in regulating CSE expression. Our data show that the HFHFr diet reduces the total and enzymatic production of liver H2S, mainly by decreasing the expression of CBS and CSE. Furthermore, BemA treatment restored H2S production, increasing the expression of CBS and CSE, providing evidence for the involvement of FXR transcriptional activity and the mTORC1 (mammalian target of rapamycin1)/S6K1 (ribosomal protein S6 kinase beta-1)/PGC1α (peroxisome proliferator receptor gamma coactivator1α) pathway.

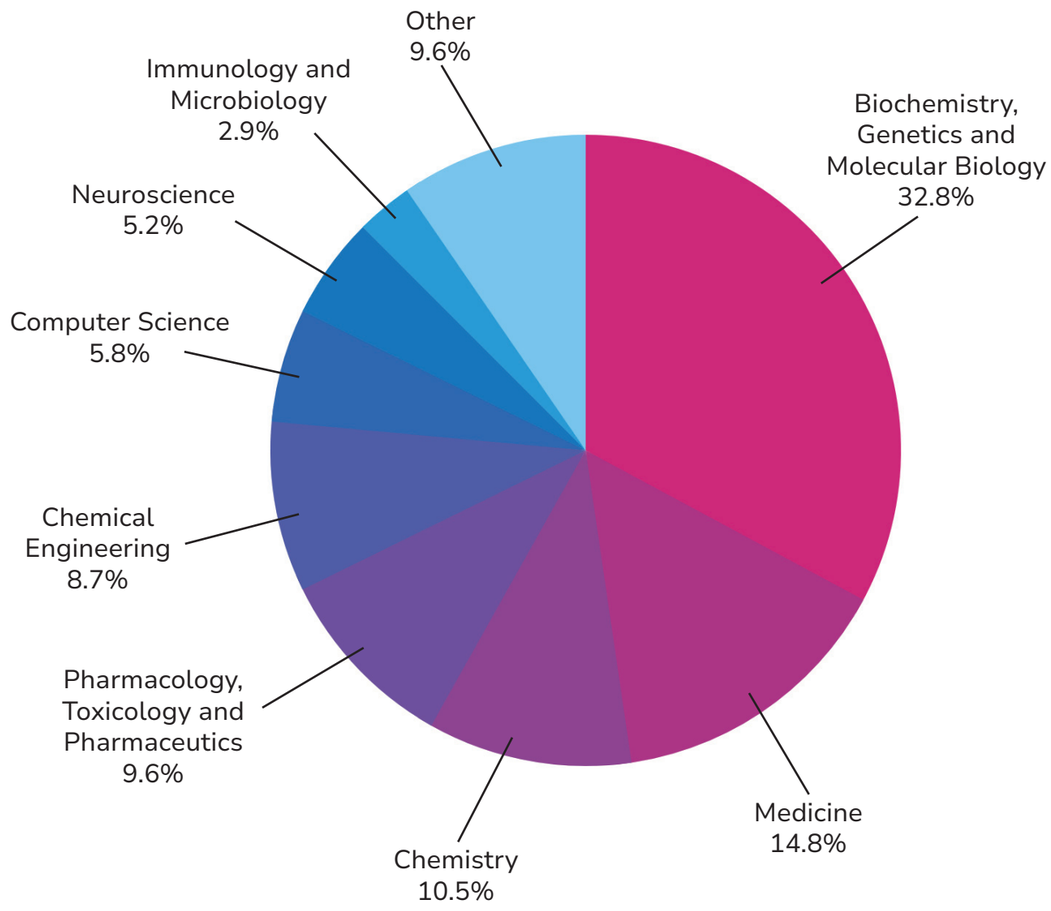
2022 Scientific publications: 173 documents

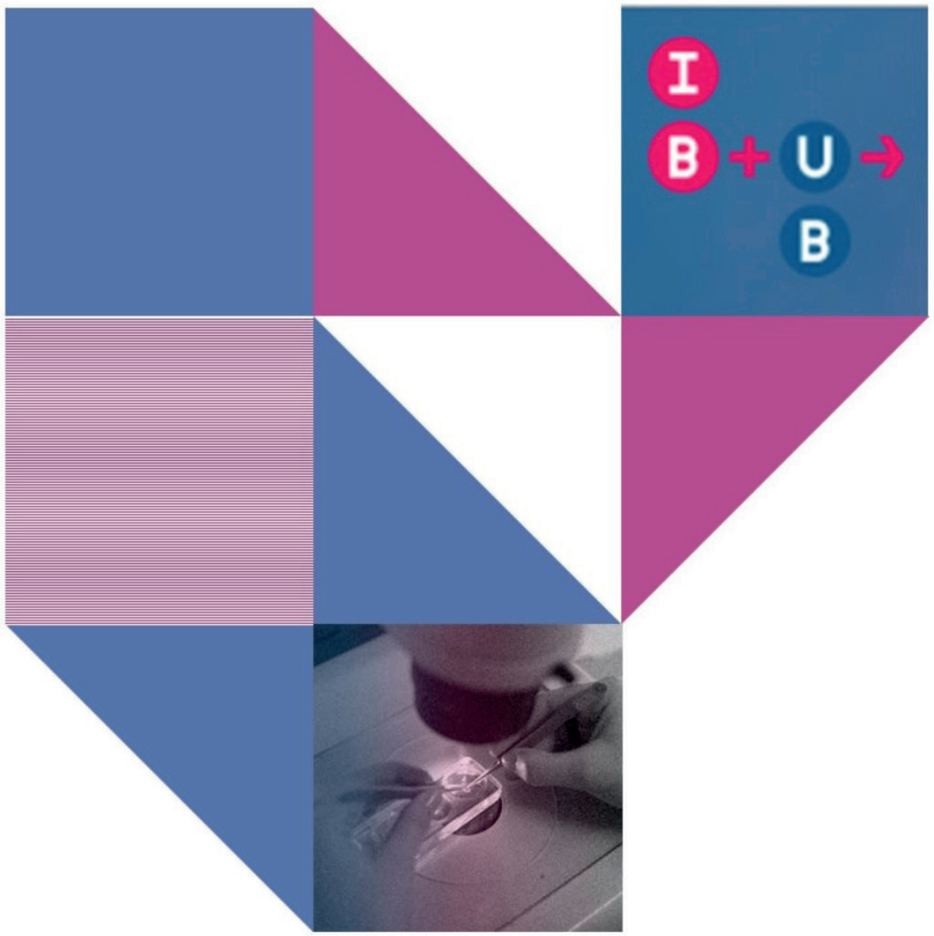


2022 documents according to the top 15 countries:



2022 documents by subject area:





IBUB SEMINARS 2022

UNIVERSITAT DE BARCELONA

The IBUB has continued and enhanced its program of free access scientific seminars, one of the most important on the Campus and among the biomedical research institutions in our area.

Computational analysis of cancer genomes
Núria Lopez-Bigas, Institute for Research in Biomedicine (IRB)

Organitzation: Carles Galdeano
January 1, 2022
A3, Facultat de Farmàcia UB

Understanding and manipulating cellular reprogramming for rejuvenation and tissue repair
Manuel Serrano, Institute for Research in Biomedicine (IRB)

Organitzation: Joan Villaroya
February 1, 2022
Aula de Graus, Facultat de Biologia UB

Present and future of Structure-Based Drug Discovery
Xavier Barril, IBUB

Organitzation: Carles Galdeano
February 7, 2022

Understanding cilia mediated autophagy in the aging brain
Olatz Pampliega, Laboratory of Glial and Neuronal Autophagy

Organization: Joan Villarroya
February 11, 2022
Aula B-101, Facultat de Farmàcia UB

Gene therapy with adipose tissue-derived stem cells to combat obesity and diabetes
Laura Herrero, IBUB

Organization: Carles Galdeano
February 21, 2022
A3, Facultat de Farmàcia UB

From gene to function in retinal hereditary diseases: paving the way to light
Gemma Marfany, IBUB

Organization: Carles Galdeano
March 7, 2022
Aula Graus, Facultat de Biologia UB

SIRT6 in DNA repair and age-related disease
Dra. Deborah Toiber, Ben Gurion University of Negev

Organization: Carles Sebastian
March 15, 2022
A-3, Facultat de Farmàcia UB

Photocontrol of neuronal activity: from singles cells to brainwaves
Dr. Pau Gorostiza, ICREA-IBEC-CIBER

Organization: Carles Galdeano
March 21, 2022
Aula Graus, Facultat de Biologia UB and online

Distinct transcriptomic of human adipose tissue immune cells in visceral vs subcutaneous depot: novel targets in obesity and metabolic disease
Dr. David Sánchez-Infantes, Universidad Rey Juan Carlos

Organization: Laura Herrero
March 28, 2022
A-4, Facultat de Farmàcia UB

Adoptive immunotherapy based on redirection of T cells with CARs
Dr. Pablo Menéndez, Josep Carreras Leukaemia Research Institute

Organization: Carles Galdeano
April 4, 2022
A-4, Facultat de Farmàcia UB

Caught in the act: Visualising the elusive mismatch repair machinery by cryoEM
Dr. Rafael Fernández-Leiro, Centro Nacional de Investigaciones Oncológicas (CNIO)

Organization: Carles Galdeano
April 25, 2022
Aula Graus, Facultat de Biologia UB

Drugging the undruggable: targeting mutant KRAS in lung càncer
Dra. Miriam Molina-Arcas, The Francis Crick Institute, London

Organization: Sandra Perez
May 2, 2022
Aula Graus, Facultat de Biologia UB

Pan-antiviral strategies and the future ahead
Dra. Nuria Izquierdo-Useros, IrsiCaixa

Organization: Carles Galdeano
May 9, 2022
A-4, Facultat de Farmàcia UB

Obesity, Diabetes and Comorbidities: A stem cell-based approach
Dra. Stefania Carobbio, Centro de Investigación Principe Felipe, Valencia

Organization: Francesc Villarroya
May 13, 2022
Aula Graus, Facultat de Biologia UB

Approaching the genetics of psychiatric disorders from different angles
Dr. Bru Cormand, IBUB

Organization: Carles Galdeano
May 25, 2022
Aula Graus, Facultat de Biologia UB

Protein structure, dynamics and function on big macromolecular assemblies from an integrative structural biology approach
Dr. Diego Gauto, ICSN-CNRS

Organization: Xavier Barril
May 27, 2022
B-101, Facultat de Farmàcia UB

Adipose tissue dysfunction, is the location all that matters?
Dra. Marijana Todorcevic, Oxford University, IBUB

Organization: Laura Herrero
May 30, 2022
Aula Graus, Facultat de Biologia UB

Targeted protein degradation: genetic determinants and drug discovery opportunities
Dra. Cristina Mayor-Ruiz, Institute for Research in Biomedicine (IRB)

Organization: Carles Galdeano
June 7, 2022
Aula Graus, Facultat de Biologia UB

Selenium recycling in obesity
Lucia Seale, University of Hawaii

Organization: Marco Mariotti
June 16, 2022
Aula Magna, Facultat de Biologia UB

Cardiokines: modulators of cardiac metamolism and disease
Dra. Anna Planavila, IBUB

Organization: Carles Galdeano
June 20, 2022
Aula Graus, Facultat de Biologia UB

Advancing epigenetic drug discovery with epi-informatics
José Luis Medina Franco, UNAM

Organization: Carles Galdeano
June 22, 2022
Aula Graus, Facultat de Biologia UB and online

Chemical space and bioactivity prediction models
Karina Martínez Mayorga, UNAM

Organization: Carles Galdeano
June 23, 2022
A4, Facultat de Farmàcia UB

A gut feeling for obesity: the gut microbiome and weight gain
Hagit Shapiro, Systems Immunology Dept., Weizmann Institute of Science

Organization: Laura Herrero
June 29, 2022
Aula Graus, Facultat de Biologia UB

Molecular hybridization within and beyond acetylcholinesterase in the pursuit of novel anti-Alzheimer drugs
Diego Muñoz-Torrero, IBUB

Organization: Carles Galdeano
July 4, 2022
A3, Facultat de Farmàcia UB

Implicación de nuevos componentes del metabolismo mineral en el daño cardiaco asociado a la insuficiencia renal
Gema Ruiz-Hurtado - Cardiorenal Translational Lab. Hspt. Univ. 12 Octubre, Madrid

Organization: Anna Planavila
October 10, 2022
Aula Graus, Facultat de Biologia UB

About overlooked types of molecular stereochemistry: mechanically chiral rotaxanes and catenanes
David Lozano, University of Southampton, United Kingdom

Organization: Santiago Vazquez
October 28, 2022
A4, Facultat de Farmàcia UB

The Role of Glucocorticoids in Metabolic Syndrome
Rodrigo Troncoso, Instituto de Nutrición y Tecnología de los Alimentos, Universidad de Chile

Organization: Maria Isabel Hernández
November 3, 2022
Aula Graus, Facultat de Biologia UB

Neuronal excitation- inhibition imbalance. A tale of membrane transporters in brain health and disease
Elena Bossi, Department of Biotechnology and Life Sciences, Università degli Studi dell'Insubria, Italy

Organization: Marçal Pastor-Anglada
November 10, 2022
Aula 15, Facultat de Biologia UB

Harnessing Thermogenic Fat to Uncouple Obesity from Comorbid Diseases
Paul Cohen - Albert Resnick, M.D., Laboratory of Molecular Metabolism, The Rockefeller University, NY, USA

Organization: Joan Villarroya
October 28, 2022
Sala Juntes, Facultat de Ciències de la Terra UB

05. ACTIVITIES

23RD METNET MEETING

FEBRURARY 4, 2022

DESCRIPTION

The 23rd MetNet meeting was organized by the Catalan Society of Biology.
In this edition there were talks from researchers from the Vall d'Hebron Institute of Oncology (VHIO), EURECAT, Centre for Genomic Regulation (CGR), Bellvitge Biomedical Research Institute (IDIBELL) and the Institute of Biomedicine at the University of Barcelona (IBUB).

ORGANIZERS

Laura Herrero, IBUB

ACKNOWLEDGEMENTS

Institut d'Estudis Catalans

Societat Catalana de BIOLOGIA

CHAIR ON RARE DISEASES

MARCH 3, 2022

DESCRIPTION

The aim of the The UB Chair on Rare Diseases is to give visibility to research and to promote the dissemination and training in these pathologies. Equally, to train students, researchers and professionals in all in genetic and clinical diagnosis, basic and translational research, as well as the knowledge transfer for citizens in order to improve the wellbeing of the patients. Among the activities of this Chair, led by the lecturer and academic vice-dean of the Faculty of Biology Albert Martínez, are the organization of courses and seminars; scientific sessions; calls for grants and awards; and several social outreach activities.

NEUROCONCIENCIA SEMINARS

APRIL 19, 2022

DESCRIPTION

Neuroscience seminars: from the clinic to research by Institut de Recerca Sant Joan de Déu (IRSJD).

TITLE

Systematic exploration of the contribution of dopamine and serotonin genes to psychiatric disorders

SPEAKER

Dr. Bru Cormand, IRSJD and IBUB

ARA ONLINE

Brain Project • Hospital Sant Joan de Déu

NEUROCONCIENCIA:

SEMINARIS DE NEUROCIÈNCIA: DE LA CLÍNICA A LA INVESTIGACIÓ

ACKNOWLEDGEMENTS

SJD Sant Joan de Déu Institut de Recerca

IRSJ-IBUB SEMINARS

APRIL 26, 2022

TITLE

Vesícules extracel·lulars de la microbiota intestinal com a moduladors de la homeòstasi intestinal i salut humana

SPEAKER

Laura Baldomà, IRSJD and IBUB

ACKNOWLEDGEMENTS

SJD Sant Joan de Déu Institut de Recerca

VIII FESTA DE LA CIÈNCIA DE LA UB

MAY 26 TO MAY 27, 2022

DESCRIPTION

The Festa de la Ciència is an event in which the University of Barcelona opens its doors to the public to make accessible, in an innovative and exciting way, the research it carries out. The value of this activity is based on the scientific rigor of the proposal, since it is the research groups themselves who propose and elaborate, in collaboration with the Scientific Culture and Innovation Unit (UCC+I) of the institution, the workshops held there.

ACKNOWLEDGEMENTS

24TH METNET MEETING

JUNE 17, 2022

DESCRIPTION

The 24th MetNet meeting was organized by the Catalan Society of Biology.
In this edition there were talks from researchers from the Biomedicine Research Institute (IRB), the Blanquerna-URL, the University of Barcelona and the Institute of Biomedicine at the University of Barcelona (IBUB).

ORGANIZERS

Laura Herrero (IBUB)

ACKNOWLEDGEMENTS

XX SEQT NATIONAL MEETING

JUNE 19 TO JUNE 22, 2022

DESCRIPTION

XX national Meeting of the spanish society of medicinal chemistry (SEQT) was held in Santiago de Compostela, Spain.
The scientific program included plenary and keynote lectures, oral communications, flash poster presentations and poster sessions, covering hot topics in drug discovery with a focus on translational medicinal chemistry.
Theme of the meeting was “from early discovery to translational medicinal chemistry”.

ACKNOWLEDGEMENTS

SEQT
Sociedad Española de Química Terapéutica

IRSJ-IBUB SEMINARS

JUNE 21, 2022

TITLE

CERKL, a retinal dystrophy gene, regulates mitochondrial function and dynamics in both mammalian neuroretina and retinal pigment epithelium

SPEAKER

Serena Mirra, IRSJD and IBUB

ACKNOWLEDGEMENTS

SJD Sant Joan de Déu Institut de Recerca

12TH SUMMER SCHOOL ON MEDICINES

JULY 1 TO JULY 7, 2022

DESCRIPTION

The 12th Summer School on Medicines (SSM12) was be held in Toulouse, France from July 1 – 7, 2022.
The curriculum of SSM12 covered the whole process of drug R&D, from target to market. Participants took part in interactive classes, case studies, a visit to a translational medicine research center and a full-day opportunity to network with experts from pharmaceutical companies in the Toulouse area.

ACKNOWLEDGEMENTS

44TH NATIONAL SEBBM CONGRESS

SEPTEMBER 6 TO SEPTEMBER 9, 2022

DESCRIPTION

The 44th Congress of the Spanish Society of Biochemistry and Molecular Biology (SEBBM) took place in Málaga. The Congress included the delivery of the IBUB Young Researcher Award to Laura Herrero.

ACKNOWLEDGEMENTS

XIX CURSO INTENSIVO CIBERSAM

SEPTEMBER 9, 2022

TITLE

El origen temprano de la salud mental. Factores ambientales de riesgo prenatal, perinatal e infantil en el trastorno mental.

ORGANIZERS

Lourdes Fañanás, CIBERSAM and IBUB
José Luis Monteserín-García, CIBERSAM and IBUB
Águeda Castro Quintas, CIBERSAM and IBUB

ACKNOWLEDGEMENTS

EUROPEAN RESEARCHERS NIGHT

SEPTEMBER 27 TO OCTOBER 2, 2022

DESCRIPTION

In Catalonia, the European Researchers Night, offers more than 200 informative activities for all audiences in various venues such as universities, museums, bars, libraries and civic centers in the five main nodes of the Catalan territory: Barcelona, Girona, Lleida, Tarragona and Vic.
Roser Urreizti Frexedas, IBUB gave a talk entitled "*Tots som Mutants*".

On the other hand, on September 30, IBUB participated in the Scientific Cafés of the UB, offering a multidisciplinary perspective on sex and gender: "*Quin paper té, ha tingut i tindrà el sexe i el gènere en l'avenç del coneixement?"*
Participants:
Mònica Serrano, BEAT.
Lídia Farré, IREA.
Meritxell Simó, IRCVM.
Maribel Hernández, IBUB.
Moderator: Gemma Marfany, Rector's delegate for Scientific Disclosure.

ACKNOWLEDGEMENTS

MARIE CURIE ACTIONS
European Commission
Horizon 2020
European Union funding for Research & Innovation

jhui

II JORNADA DELS INSTITUTS DE RECERCA PROPIS UB

OCTOBER 4, 2022

TITLE

El canvi climàtic: Potenciador de l'epidèmia global d'obesitat?

SPEAKER

Marta Giralt, IBUB

ACKNOWLEDGEMENTS

UNIVERSITAT DE BARCELONA

8TH METNET INTERNATIONAL ANNUAL MEETING

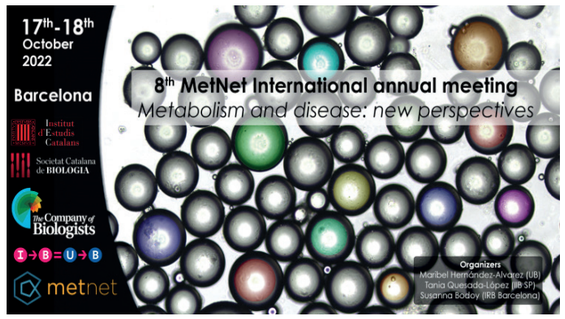
OCTOBER 17 TO OCTOBER 18, 2022

TITLE

Metabolism and disease: new perspectives

ORGANIZERS

Maribel Hernández Alvarez, IBUB
Tania Quesada-López, IIB SP
Susanna Bodoy, IRB



ACKNOWLEDGEMENTS

Institut d'Estudis Catalans
Societat Catalana de BIOLOGIA
The Company of Biologists
metnet

XIX CURSO INTENSIVO CIBERSAM

SEPTEMBER 9, 2022

TITLE

El origen temprano de la salud mental. Factores ambientales de riesgo prenatal, perinatal e infantil en el trastorno mental.

ORGANIZERS

Lourdes Fañanás, CIBERSAM and IBUB
José Luis Monteserín-García, CIBERSAM and IBUB
Águeda Castro Quintas, CIBERSAM and IBUB

ACKNOWLEDGEMENTS

UB-CIBERER MINI SYMPOSIUM ON GENETIC RARE DISEASES

NOVEMBER 7, 2022

DESCRIPTION

In a face-to-face and online format, four speakers have walked the path from the patient affected by a rare disease, who is visited by clinical experts in search of a diagnosis (Merche Serrano, Hospital Sant Joan de Déu and CIBERER), to the testing of new specific drugs for rare diseases (Pascual Sanz, IBV-CSIC and CIBERER), through genetic testing based on massive sequencing, the act of genetic counseling to patients and families (Marta Codina; IR Vall d'Hebron), and basic research on the molecular pathology underlying the mutations causing these rare diseases (Isaac Canals, Lund Stem Cell Center, Sweden). Four brilliant and didactic talks that have enlightened and inspired an audience mainly represented by young researchers in training.

jhui

ORGANIZERS

Roser Corominas, IBUB
Gemma Marfany, IBUB
Kelly Rabionet, UB
Susanna Balcells, IBUB

ACKNOWLEDGEMENTS

CELEBRATION OF MENDEL'S 200TH ANIVERSARY

SEPTEMBER 9, 2022

TITLE

Revisitant Mendel: la seqüenciació massiva i el diagnòstic genètic de malalties rares.

SPEAKER

Gemma Marfany, IBUB

ACKNOWLEDGEMENTS

THE DAY OF OBESITY BY SEEDO

DECEMBER 15, 2022

DESCRIPTION

The Spanish Society of Obesity (SEEDO) organized the "The Day of Obesity". The purpose of the event was to highlight the importance of brown fat research to combat obesity effectively.

ORGANIZERS

Ruben Cereijo, IBUB
Marta Giralt, IBUB

RISING STARS SEEDO 2022 AWARD

Laura Herrero, IBUB

ACKNOWLEDGEMENTS

06. NEWS

Fundación BBVA supports a project leaded by Carlos Sebastián.

Convocatoria
Ayudas a Proyectos de Investigación Científica
2021

Fundación BBVA

10 IBUB researchers in the "World Ranking of Top 2% Scientists" in 2021 database created by Stanford University, USA.

RANKING WEB OF UNIVERSITIES

The CSIC publishes a ranking of the 5,000 most outstanding Spanish women scientists

22 IBUB researchers in the CSIC ranking of women scientists working in Spain

GOBIERNO DE ESPAÑA · MINISTERIO DE CIENCIA E INNOVACIÓN · CSIC
Consejo Superior de Investigaciones Científicas

The "la Caixa" Foundation supports a biomedical innovation project of Santiago Vázquez's group

Fundación "la Caixa"

La Marató 2021 endorses two IBUB research projects on mental health

07. IBUB UNITS AND SERVICES

Transcriptometrics Service

The IBUB implemented a gene expression analysis service by quantitative RT-PCR based on tools obtained from the PEIR fund co-financed by the IBUB which continues to serve 8 IBUB groups with more than 1000 hours of work. It works with a computerized system of reservations and is located in the Department of Biochemistry and Molecular Biology of the Faculty of Biology and it is supported and maintained by the IBUB.

Computational biology unit

The Computational Biology Unit of the IBUB, created in 2009, has continued to develop activities within its scope. Along with the continuity work carried out by the groups of Dr. X. Barril and Dr. JF Abril, which hosted visiting researchers from the Integrative Biochemistry and Cancer Therapy group.

Electrophysiology Unit

Electrophysiology Unit (IBUB), with equipment for the determination of the membrane potential and the ionic movements generated by the cardiac action potential and the transmission of the nerve impulse, among other physiological processes.

Seahorse equipment

Since 2017, the IBUB has had a transversal “Seahorse” equipment, widely used in metabolic studies of interest to a significant number of the Institute’s research groups. This equipment is currently being used by researchers from various departments of the University of Barcelona, as well as the Research Institute of Sant Joan de Déu, the Institute of Bioengineering of Catalonia, and by private companies such as Minoryx.

H-Cube Pro equipment

The H-Cube Pro equipment for hydrogenation and continuous reactions from the manufacturer Thales Nano, acquired thanks to the 2019 call for Grants for the renewal of obsolete scientific and technological research equipment of the University of Barcelona.
This new equipment has made it possible to replace the high-pressure hydrogenation system of one liter volume, currently obsolete, with a continuous hydrogenation equipment, which does not need a supply of hydrogen gas to operate, while also allowing other catalytic reactions such as Suzuki, Sonogashira, Stille, Heck coupling reactions, etc. In addition, the new equipment can be easily adapted to allow reactions with other gases and perform other types of reaction such as carbonylation and ozonolysis.

Metabolic Cages

This is an essential equipment in research studies on metabolism in experimental animals (mouse and rat). The latest generation metabolic cage systems allow energy expenditure (O_2 consumption and CO_2 production), motor activity, temperature and intake (food and drink) to be measured. The system is able to differentiate between water loss through respiration and metabolism. This is currently an indispensable piece of equipment to be able to generate studies on metabolism of maximum impact in experimental models of pathologies such as obesity, diabetes, cardiovascular and neurodegenerative diseases, and even cancer.
Thanks to the call for grants for the renewal of obsolete scientific and technological research equipment in 2021, it was possible to acquire this equipment with 4 units of cages, half co-financed by the IBUB (50%), another part by the Dept. Biochemistry and Molecular Biomedicine from the Faculty of Biology (6.7%), and another part by the Biochemistry and Molecular Biology Section of the Dept. Biochemistry and Physiology from the Faculty of Pharmacy (1.33%).

08. TECHNOLOGY TRANSFER OPPORTUNITIES

The Institute offers a Services and Know-How guide with the aim of collecting all the transfer services, techniques and technology, which may be of interest, both to the members of the IBUB itself and to professionals and external entities.
The guide includes the set of techniques and opportunities for technology transfer and the groups that offer them, facilitating contact between those interested.

Biochemical and Biomedical Transfer Opportunities

SERVICES

Animal models

- Cancer.
- Cardiovascular diseases.
- Diabetes and Obesity.
- Drosophila and CNS diseases.
- Inflammation.
- Intrapancreatic PDAC models.
- PPARbeta/delta knock out models.

In vivo studies

- Anti-inflammatory and toxicology drug validation.
- Cardiovascular performance, ecocardiography, treadmill.
- Impact of drugs on development using Drosophila.
- Infrared thermography.
- Metabolic phenotyping of rodent models.
- Stereotaxis.

Cell-based studies

- Analysis of the mechanisms of action of anticancer drugs.
- Barrier models for drug absorption screening and drug-transporter interactions.
- Cell immortalization (fibroblasts, adipocytes...).
- In vitro assays of bacterial infection and immunosuppression.
- Mitochondrial metabolism and respiration.
- Primary cultures of specialized cell types (adipocytes, hepatocytes, neurons, intestinal barrier, macrophages, cardiomyocites...).

Structural approaches and “OMICS” services

- Biophysics assays: surface plasmon resonance/Biacore studies and competition assays.
- Computational biology and bioinformatics applied to genomes and gene/protein networks.
- Generation of high-quality leads for drug discovery.
- Metabolomics and computational analysis of metabolic fluxes.
- Protein crystallography, lead identification and validation macrophages, cardiomyocites...).

KNOW-HOW

- Gene-protein networks integration, data management and visualization.
- Infrared thermography for metabolic studies.
- Mechanisms of action of anticancer drugs.
- Mitochondrial metabolism and respiration.
- Multiomics modelling.
- Pharmacogenetics of anticancer drugs.
- Pharmacological evaluation of drugs in metabolic-related diseases.
- Protein structure- function relationship analysis and structural biology.
- Signal transduction pathways and disease.
- Targeted metabolomics.

Chemistry and Pharmacy Transfer Opportunities

SERVICES

- Biophysical characterization of ligand-protein complexes.
- Computational structure-based drug discovery: druggability, virtual screening, hit/lead optimization.
- Design and synthesis of chemical libraries and scaffolds.
- Design and synthesis of prodrugs.
- Experimental determination of physicochemical properties.
- Expert advice on new synthetic routes for organic compounds.
- Expert advice on the determination of ADMET properties.
- Expert opinion about chemical patents, infractions risks, etc.
- Expert opinion on chemical manufacturing sites.
- Fragment-based drug discovery: fragment screening, fragment evolution.
- Hit to lead optimization.
- HPLC and/or HPLC/MS of APIs, drugs and mixtures.
- Molecular modelling of biomolecules for structure-function relationships.
- Optimization and scale-up of routes of synthesis for APIs.
- Search of molecules in libraries of compounds.
- Structural elucidation and synthesis of metabolites.
- Structural elucidation, isolation and synthesis of impurities of active pharmaceutical ingredients (APIs).
- Synthesis and conjugation of Fluorophores and Small molecule Bioprobes.
- Synthesis of labelled compounds.
- Synthesis of peptides and oligonucleotides (DNA, RNA).
- Synthesis of peptides-oligonucleotides conjugates.
- Theoretical studies in structure-activity relationships.

09. 2022 IN NUMBERS

Research Groups
41

Publications
240

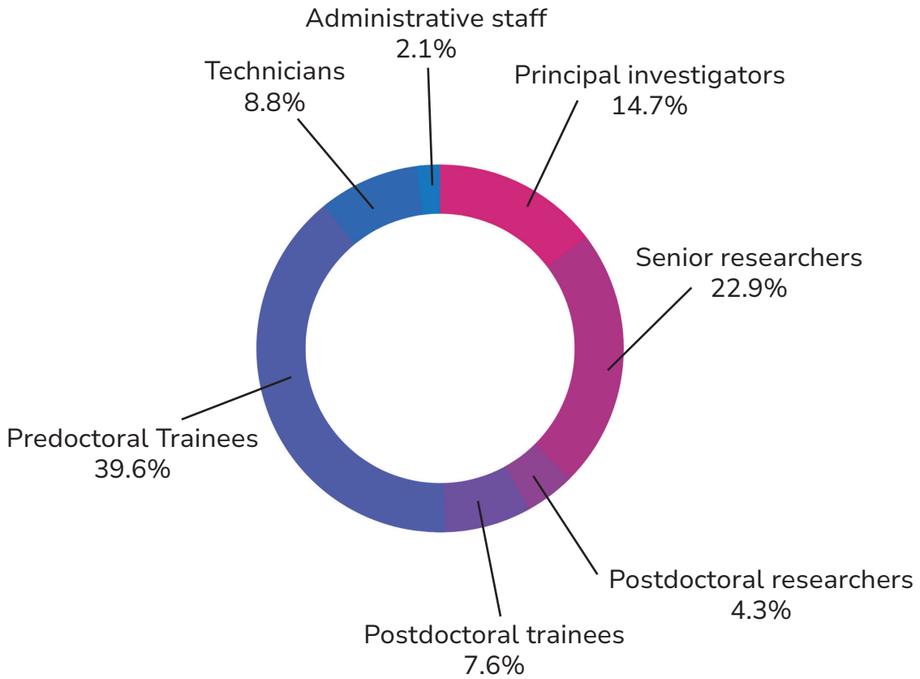
Citations
4781

Patents
5

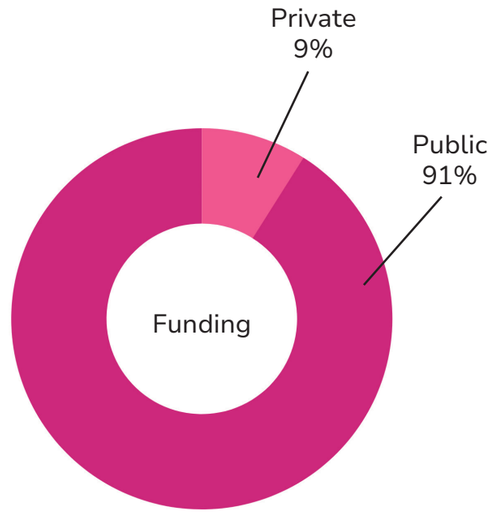
Awards
2

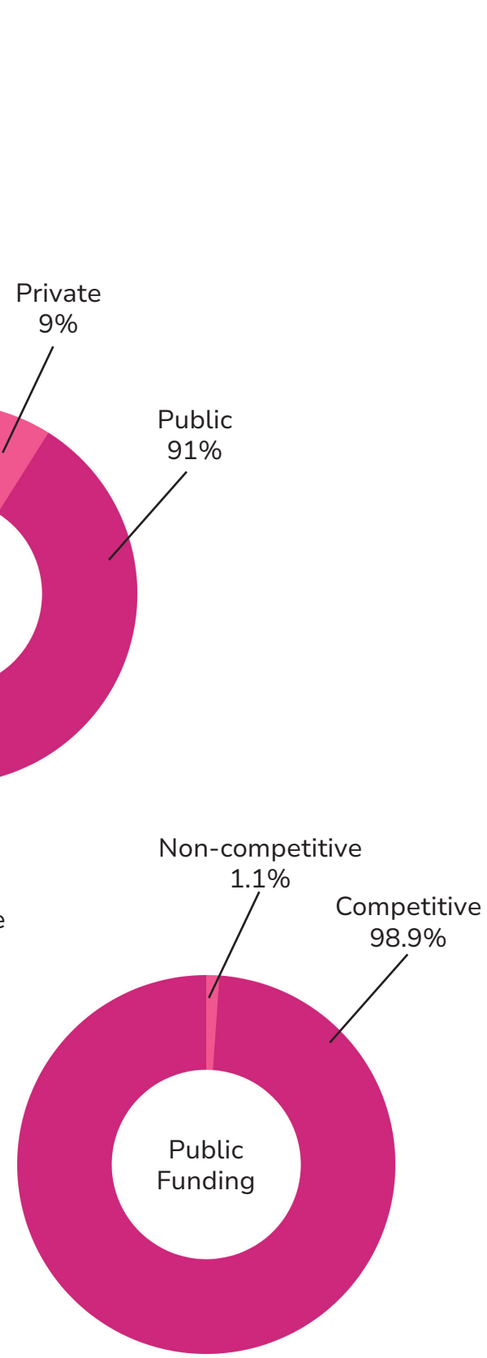
Active spin-offs
3

Human resources

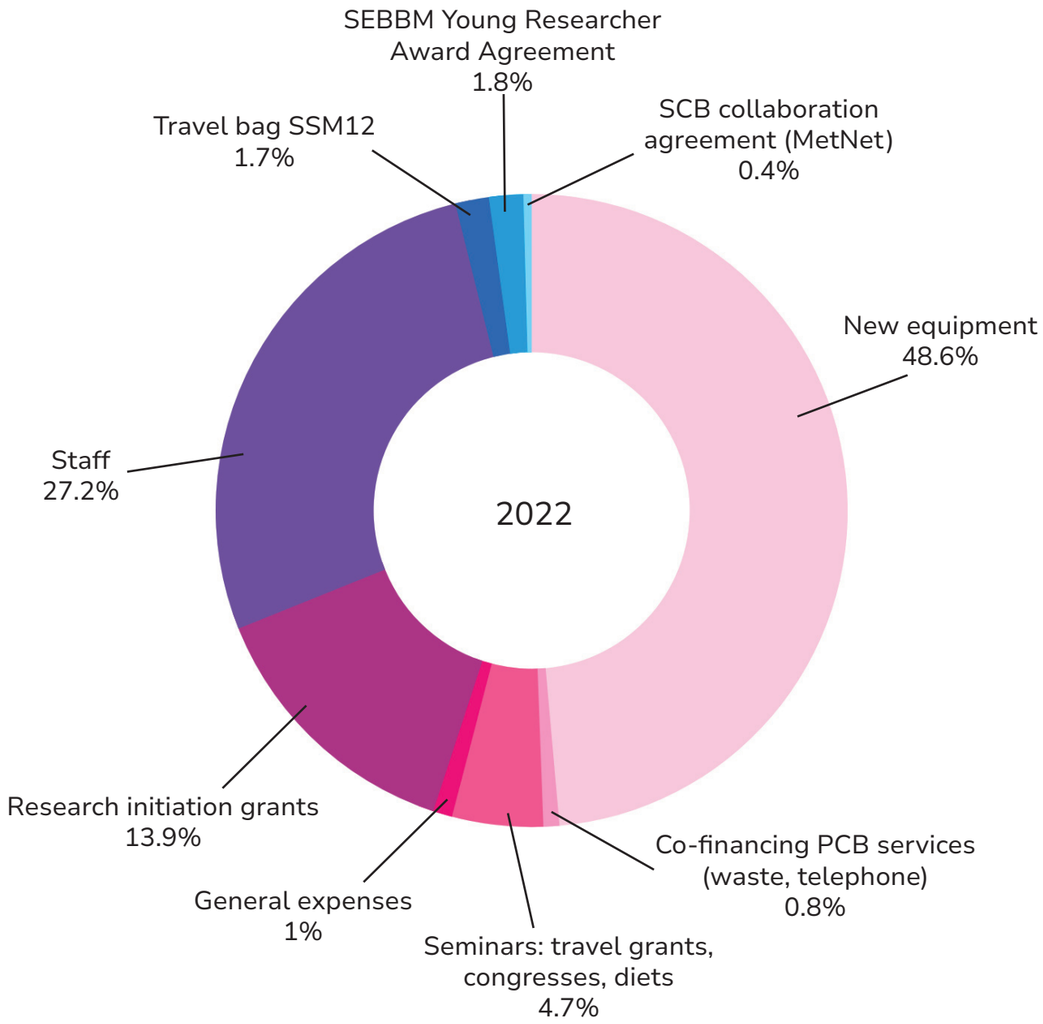


Funding





Economic Summary 2022



Research Initiation Grants 2022-2023

The aim is to facilitate access and growth in the field of research to new pre-doctoral researchers in a cooperative, interdisciplinary and excellence context within the IBUB.

La Marató TV3

In 2021, La Marató de TV3 and Catalunya Ràdio was dedicated to mental health in order to raise public awareness of disorders with many stigmas, and it raised 12.1 million euros. Now, these funds will be used to promote 36 research projects led by 81 research teams.

The ceremony took place on Thursday 3 November at the TV3 facilities. A total of 150 projects applied for this funding, and these were assessed by 111 international experts on mental health. They assessed the projects' quality, methodology and relevance. This evaluation was managed by the Catalan Agency for Health Quality and Evaluation of the Catalan Ministry of Health. Awarded projects linked to the IBUB are:

"Suicide as an extreme phenotype to understand suicidal behaviour: an approach from the interaction of the genome with the epigenome"

Antoni Benabarre, Faculty of Medicine and Health Sciences, Hospital Clínic de Barcelona and Clinic Foundation for Biomedical Research; Bárbara Arias, Faculty of Biology and Bosch i Gimpera Foundation; Thomas G. Schulze, LMU Klinikum (Germany).

"Study of vulnerability to cocaine use disorder after alcohol consumption"

Bru Cormand, Faculty of Biology, Institute of Biomedicine of the University of Barcelona (IBUB) and San Joan de Déu Research Institute (IRSJD); Rafael Maldonado, Pompeu Fabra University; Maria Francina Fonseca, Hospital del Mar Medical Research Institute Foundation (IMIM).

CaixaResearch Consolidate 2022

One of the projects chosen is from the Bosch i Gimpera Foundation, from the group of Dr. Santiago Vázquez, researcher at the Pharmaceutical Chemistry Unit of the Department of Pharmacology, Toxicology and Therapeutic Chemistry of the University of Barcelona and the Institute of Biomedicine of the UB (IBUB).

The aim of the project is to find a new treatment that can significantly reduce pain and so improve patients' lives.

IBUB-SEBBM Award 2022

The SEBBM, together with IBUB, announces the IBUB-SEBBM award in recognition of the trajectory of young researchers associated with the SEBBM in the area of Biochemistry and Molecular Biology.

Laura Herrero, from the Faculty of Pharmacy and Food Sciences of the UB and member of the IBUB, was awarded the Young Investigator Award of the Spanish Society for Biochemistry and Molecular Biology (SEBBM), the main scientific association in Spain in this field of knowledge. For the work "Transplantation of adipose tissue to fight against obesity and diabetes".

CIBER grups

Physiopathology of Obesity and Nutrition

Four groups leaded by:
- Laura Herrero/Juan Carlos Laguna
- Marta Alegret
- Diego Haro/Pedro Marrero
- Francesc Villarroya

Rare Diseases

Two groups leaded by:
- Gemma Marfany
- Susana Bacells

Hepatic and Digestive Diseases

Two groups leaded by:
- Marçal Pastor-Anglada
- Marta Cascante

Mental Health

One group leaded by:
- Lourdes Fañanas

Diabetes and Associated Metabolic Diseases

One group leaded by:
- Manuel Vázquez-Carrera

Grants to support the activities of research groups SGR 2021

2021SGR00367 *Estudi del metabolisme en l'obesitat i malalties associades (METABESITY)*
Laura Herrero Rodriguez

2021SGR00706 *Gens, ambient i Fenotips: etapes del desenvolupament en l'estudi dels trastorns mentals i altres malalties complexes en poblacions humanes (Complex_Fen_GXEXD)*
Lourdes Fañanas Saura

2021SGR00677 *Farmacologia Molecular i Teràpies Experimentals (MPET)*
Marçal Pastor Anglada

2021SGR00372 *EvoDevo-CAT*
Jordi Garcia Fernandez

2021SGR00671 *Biologia Computacional i Disseny de Fàrmacs*
Francisco Javier Luque Garriga

2021SGR00268 *Sustainable Organic Synthesis Group (SOSyn)*
Alberto Moyano Baldoire

2021SGR00293 *REGnetREG*
Montserrat Corominas Guiu

2021SGR00345 *Receptors nuclears, metabolisme energètic i teràpia de les malalties del metabolisme*
Marta Alegret Jorda

2021SGR00713 *Regulació i optimització del creixement en espècies de peixos d'interès en aqüicultura.*
Joaquin Gutierrez Fruitos

2021SGR00010 *Fisiologia Molecular*
Antonio Felipe Campo

2021SGR00227 *Metabolisme molecular i patologies associades*
Francesc Villarroya Gombau

2021SGR00350 *Grup de Bioquímica Integrativa*
Marta Cascante Serratosa

2021SGR01106 *Dianes Farmacològiques en Inflamació i Malalties Metabòliques*
Manuel Vazquez Carrera

2021SGR00248 *Caracterització de sistemes cromatogràfics i anàlisi fisicoquímica de compostos bioactius*
Marti Roses Pascual

2021SGR00329 *Metabolisme lipídic i inflamació*
Juan Carlos Domingo Pedrol

2021SGR00230 *Nanomedicina i neurofarmacologia molecular*
Vicent Casadó Burillo

2021SGR01433 *Inflamació: recerca bàsica i traslacional*
Annabel Valledor Fernandez

2021SGR00357 *Medicinal Chemistry and Pharmacology of Neurodegenerative diseases*
Maria Carmen Escolano Miron

2021SGR00090 *Neuropsicofarmacologia dels derivats amfetamínics i altres noves substàncies psicoactives*
David Pubill Sanchez

2021SGR00075 *Bioimatge, bioconjugació, estructura i teràpies amb molècules de mida petita, pèptids i oligonucleòtids*
Vicente Marchán Sancho

jhui

10. COMMUNICATION & OUTREACH

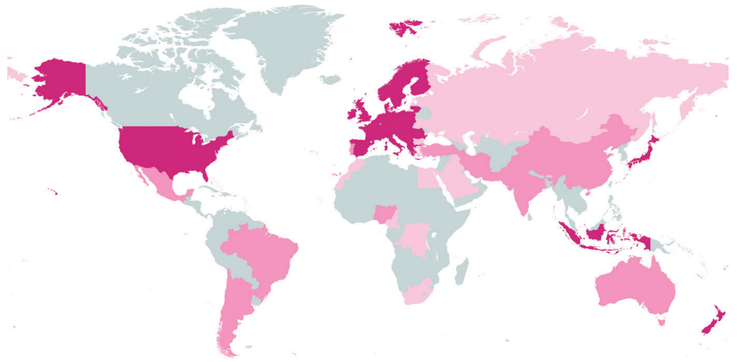
Social media and press

Press releases
96

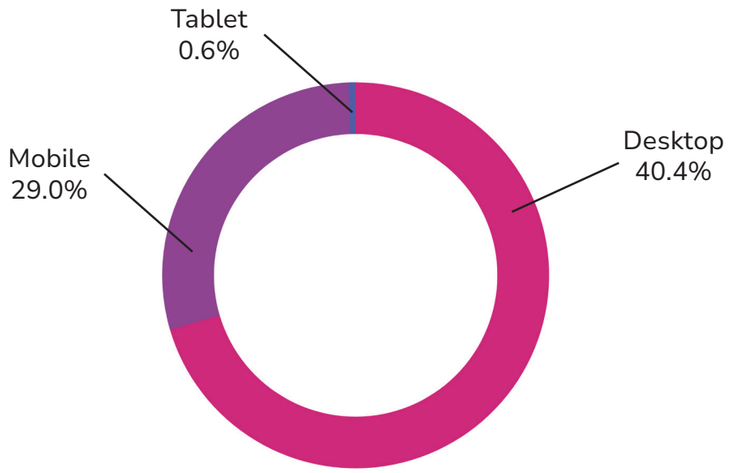
Impressions
> 50 000

350 followers

Website



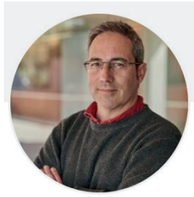
2022 visits by country



2022 users by device category

Several researchers actively participate in the dissemination of science in the general press, both written and audiovisual.

Gemma Marfany, from the Department of Genetics, Microbiology and Statistics, who participates weekly in the digital El Nacional, where she publishes articles on scientific advances with great media coverage.



THE CONVERSATION

1 abril 2022

¿Es el autismo un transtorno genético?

Marina Mitjans, *UB* y Bru Cormand, *IBUB*

¿El autista nace o se hace? ¿Pesan más los factores ambientales o los genes en estos trastornos del neurodesarrollo? Gracias a los estudios de gemelos sabemos que el secreto para entender el TEA se encuentra principalmente en el genoma.

RAC1

22 febrer 2022

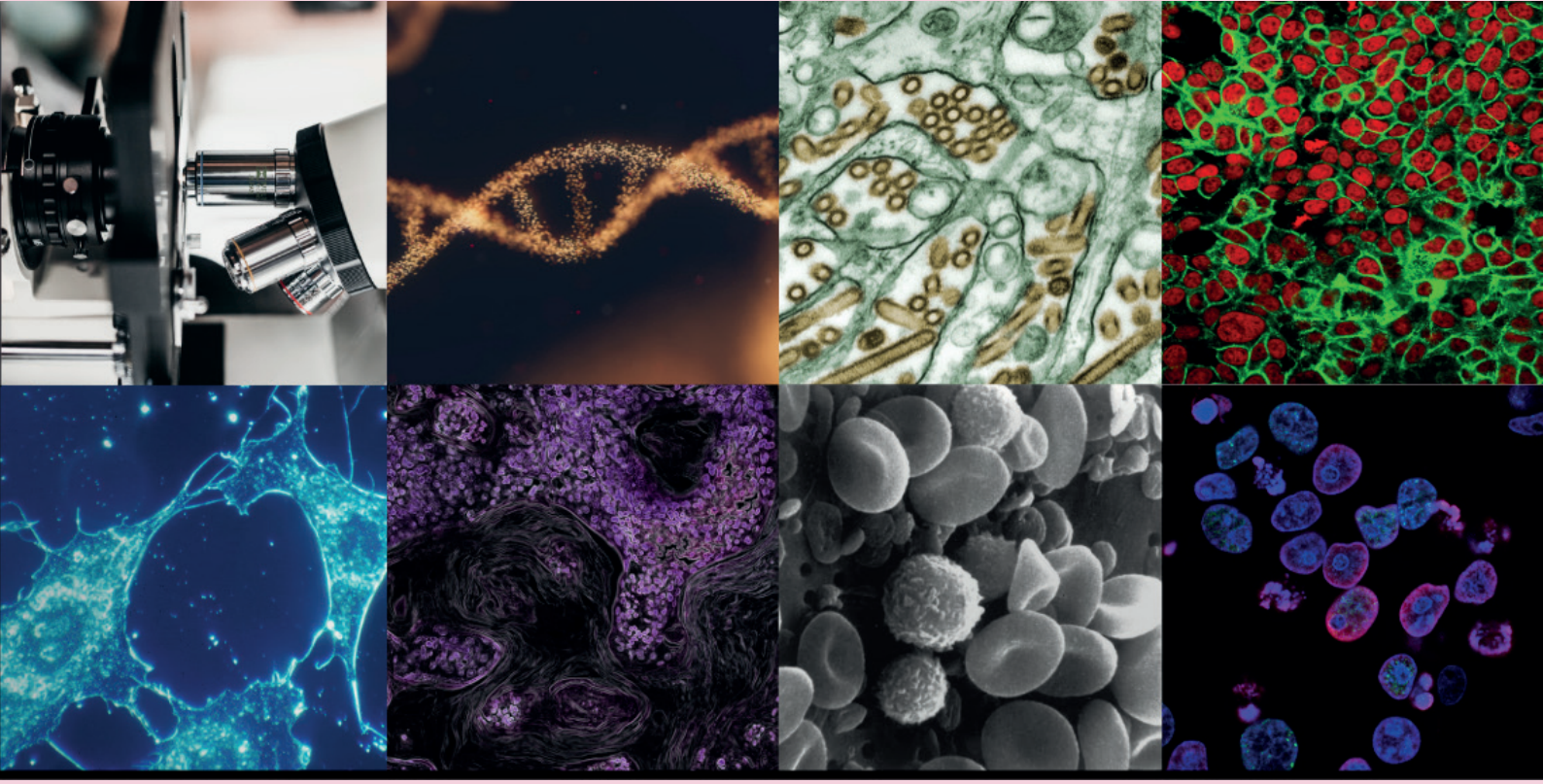
25 anys de l'ovella Dolly: èxit i fracàs de la genètica

Gemma Marfany, *IBUB*

Gemma Marfany, genetista, explica a 'El món a RAC1' de què va servir clonar el primer mamífer.

Extraordinary Master's Degree Award in Biomedicine 2019-20 Academic Year

Awarded to pre-doctoral student at TAM Lab Albert Mestres-Arenas.



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UNIVERSITAT DE BARCELONA

ANNUAL REPORT 2022

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