

CIC bioGUNE Research Interests MSCA-IF 2020

CIC bioGUNE (<http://www.cicbiogune.es/>), member of Basque Research and Technology Alliance (BRTA), is a key research center within the national and international scientific landscape and has been recognized as "*Severo Ochoa Center of Excellence*" by Spanish government, earning a place alongside the top research institutes in Spain. CIC bioGUNE is an Endorsing Institution of the "*European Charter for Researchers & Code of Conduct for Recruitment of Researchers*", guaranteeing the best framework conditions to contribute to the professional/personal development of researchers. The cutting-edge scientific activity of CIC bioGUNE explores the interface between Chemistry, Structural, Molecular and Cell Biology, with the aim of developing a more Precise Medicine for the future.

CIC bioGUNE is looking for highly-motivated experienced researcher of any nationality interested in applying for the Marie Skłodowska-Curie Actions Individual Fellowship call (H2020-MSCA-IF-2020).

The Experienced Researcher must be, at the date of the call deadline (09 September 2020), in possession of a doctoral degree or has at least four years of full-time equivalent research experience. Moreover, an international mobility is required.

- **Computational Chemistry Laboratory** - Dr. Gonzalo Jiménez Osés
- **Ubiquitin-likes and Development Laboratory** - Dr. Rosa Barrio
- **Computational Biology Laboratory** - Research Professor Antonio del Sol
- **Inflammation and Macrophage Plasticity Laboratory** - Research Professor Juan Anguita
- **Liver Disease Laboratory** - Dr. Malu Martínez Chantar
- **Cancer Heterogeneity Laboratory** - Dr. María del Mar Vivanco and Dr. Robert Kypta

Computational Chemistry Laboratory - Dr. Gonzalo Jiménez Osés

The Computational Chemistry Group (CCG) at CIC bioGUNE has developed a solid platform for the theoretical prediction of chemical and biological with strong emphasis on:

- **Enzyme Engineering and Evolution:** we use computational mutagenesis tools to predict and understand the structure-activity role of mutations in the catalytic performance of enzymes.
- **Bioorthogonal Chemistry:** we develop new concepts and methods for the site-selective modification of proteins and therapeutic antibodies.
- **Drug Discovery:** we use synthetic chemistry and in silico tools to generate small molecules and peptides with therapeutic potential.
- **Glycobiology:** we provide detailed insights on the mechanisms of chemical and biochemical glycosylation processes.

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Ubiquitin-likes and Development Laboratory - Dr. Rosa Barrio

Barrio's Lab (Researcher ID: F-8712-2011) offers a creative and collaborative atmosphere, applying state of the art techniques in the fields of molecular, cell biology, genetics and biochemistry, to answer biomedically relevant questions. One of our main interest is how posttranslational modifications by the members of the ubiquitin family shape the cellular landscape and the organism through the regulation of different cellular processes. More specifically, we are interested on how modifications alter the function of the primary cilia in relation to rare diseases, for instance Townes-Brocks Syndrome, a rare disease that causes cilia alterations by mutations of SALL1, a transcription factor modified by the Small Ubiquitin-like MOdifier, SUMO. We are developing technology to study posttranslational modifications in the cilia and other organs.

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Computational Biology Laboratory - Research Professor Antonio del Sol

A computational model of tissue homeostasis for designing liver rejuvenation strategies

Homeostasis is an emergent property of living systems that keeps key characteristics within acceptable ranges. During aging, all tissues become more susceptible to disruption of homeostasis due to the permanent growth arrest of cells, a state termed as cellular senescence, which significantly impedes their functioning. Previous studies highlighted the pronounced effect of cell-cell communication in the accumulation of senescent cells, but were unable to identify the hallmarks of cellular senescence. Especially in the context of the liver, accumulation of senescent cells is implicated in many life-threatening, age-related pathologies for which no noninvasive treatments exist. The goal of this project is to conceive a computational model that characterizes tissue homeostasis based on the communication between cells and its influence on maintaining the expression of key genes. Newly generated single-cell gene expression profiles will be leveraged to build models of liver homeostasis in young and old mice that will be used to characterize senescence-related differences and to propose an intervention strategy for liver rejuvenation. The proposed strategy will be experimentally validated by our collaborator Dr. Martínez-Chantar at CIC bioGUNE.

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Inflammation and Macrophage Plasticity Laboratory **Research Professor Juan Anguita**

1.- The microbiology of colorectal cancer

Recent studies have noted the importance of oral pathogens in colorectal cancer initiation and progression. These evidences argue for the modulation of the microbiota composition as an alternative treatment for pathobiont-related gastrointestinal pathologies. Diet has been repeatedly shown as one of the major modulators of microbiota populations including dietary phenolic metabolites. Meta-analyses of human sample data show the prevalence of putative enzymatic activities strongly associated with the prevalence of pathobionts related to CRC. Some products of these metabolic pathways could be controlling ecological dynamics within the gut affecting gut pathobiont fitness. This project will combine molecular and classical microbiology, latest generation metagenomics, structural studies, molecular modelling and mouse models to identify the microbiota transforming capacity of diet compounds as well as the enzymes involved and, as a consequence, the development of metabolites and synthetic small molecules capable of eliminating gut disorders-associated pathogens.

2.- Innate immune cell plasticity associated with pathogens and symbionts

Infectious diseases are the major cause of morbidity and mortality in the world. In spite of enormous advances in prevention, diagnosis and treatment, a large number of infections still afflict large numbers of people. Innate immune cells respond dynamically to exogenous and endogenous factors. We propose that the initiation and development of innate immune responses represent an adaptive tool, and a coevolutionary mechanism of interaction between the host and commensal microorganisms and pathogens, in particular those able to establish persistent infections. Our prediction is that the dynamic shape of the innate immune response is a general mechanism regulated by both innate immune cells and both pathogenic and symbiotic microorganisms. Through the use of *in vitro*, *in vivo* and multiomic approaches (RNAseq, proteomics, scRNAseq..), we seek to understand the plasticity of innate immune responses associated with both inflammatory insults and the time of the response.

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Liver Disease Laboratory - Dr. Malu Martínez Chantar

Liver Cancer affects one million of new patients each year and is directly connected with obesity. HCC is the fifth deadliest cancer owing to its vast heterogeneity and late detection at advanced stages. These upsetting facts prompted us to launch an exciting project, whose challenging idea was that "not everything that regulates tumor development and responses to anti-cancerous treatments is written in the genes". In this field, Liver Disease Lab leading by Malu Martinez-Chantar is looking for a motivated experienced candidate (postdoctoral fellow) that will proceed with a "forward approach," which will involve a comprehensive analysis of post-translational modifications (PTM) (NEDDylation and SUMOylation) in preneoplastic lesions to define bona-fide markers of liver cancer; analysis of biomarkers/fluids and links to metabolism/genomics.

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**Cancer Heterogeneity Laboratory - Dr. María del Mar Vivanco and Dr. Robert
Kypta**

The Cancer Heterogeneity Lab at CIC bioGUNE is looking for motivated experienced researcher to apply for the Marie Skłodowska-Curie Actions Individual Fellowship call (H2020-MSCA-IF-2019). The laboratory has several exciting projects in the area of cancer research that build on our recent publications in Oncogene (Domenici et al., A Sox2-Sox9 signaling axis maintains human breast luminal progenitor and breast cancer stem cells, 2019), Nature Communications (Murillo-Garzon et al., Frizzled-8 integrates Wnt-11 and transforming growth factor-beta signaling in prostate cancer, 2018) and others, and also has ongoing international collaborative projects on machine learning and computational analysis, as well as on biophysical analysis of breast cancer cells.

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