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2020 ESC First Contact Initiative Grant report

Dear ESC Council on Basic Cardiovascular Science,

Firstly, I would like to sincerely thank the ESC Council on Basic Cardiovascular Science for awarding me the 2020 First Contact Initiative Grant. This gave me the opportunity to join the laboratory of Professor Klaus Ley, MD at La Jolla Institute for Immunology (La Jolla, California, USA), from September to December 2020.

My PhD thesis project is focused on the understanding of the immune reactions behind heart disorders in order to find cell-specific targets for diagnosis and therapy. We are now aiming to explore novel strategies for the discovery of immune-signature-derived candidates for precision medicine in a high-dimensional untargeted manner. This grant has been of great help to this endeavor.

During this short-term stay, I have been able to learn how to work with advanced techniques of single-cell characterization of peripheral blood leukocyte populations from patients with cardiovascular disease. The host lab has special interest in validating and improving the application of CITE-seq (Cellular Indexing of Transcriptomes and Epitopes by Sequencing) technologies such as those developed by BD (Rhapsody) or 10x Genomics. The main advantage of these technologies is the fact that it allows the extensive characterization of the repertoire of membrane markers plus the transcriptome on a single cell level in the same sample. Antibodies recognizing different surface markers are barcoded with unique oligonucleotides, which permits their identification and quantification by scRNAseq.

During these months, I have particularly contributed to the analysis of surface and transcriptomic markers of cardiovascular disease in patients living with HIV in peripheral blood leukocytes.

During the first weeks, I have learnt how to process human blood samples so that to be run through the advanced CITE-seq analyzers. Afterwards, I joined the lab's experts in bioinformatics, who helped me to acquire fundamental skills required to analyze and understand the data generated after using these complex techniques. Some of the pipelines and software used were Seurat, CIBERSORTx, SeqGeq (FlowJo). At the end of my stay and after combining different single-cell CITE-seq and RNAseq experiments datasets generated in the lab, we were able to identify specific subpopulations of classical monocytes, whose proportions and transcriptome vary in peripheral blood with cardiovascular disease and after cholesterol treatment. The data generated open venues to find evidence-based cell-type specific targets for diagnosis and precision use of existing and novel drugs.

Finally, I would like to express my sincere gratitude to all the members of the host lab, who constantly shared advice and feedback. I specially thank Dr. Klaus Ley for being supportive and sharing his vast knowledge with me. Thanks to this grant, I have been able to live this unforgettable experience that greatly contributed to strengthen my PhD thesis and boost my scientific career.

Yours sincerely,

Rafael Blanco Domínguez