



**Proyecto PDC2021-120817-I00 financiado por MCIN/ AEI/10.13039/501100011033 y por la Unión Europea Next GenerationEU/PRTR**

#### **Identificación del proyecto:**

Generación de células madre y progenitores hematopoyéticos derivados de células embrionarias pluripotentes (hum-HT)

#### **Descripción del proyecto:**

Generation of hematopoietic stem cells (HSCs) remains a big challenge in the hematopoietic field. Despite many efforts addressing how HSC cells are specified and generated in a robust and safe way, no breakthroughs in the field have yet come that lead to clinical applications. Latest research in endothelial cell reprogramming and ES cell induction to form HSCs has not been generally reproduced and although the merit of the proof of concept remains, the question is how to make a synthetic system reproducible. One of the main reasons for preventing the advance in this field is the lack of knowledge about the HSC generation process that occurs during embryonic development. My group has widely investigated the HSC generation process in the mouse embryo and mouse ES cells, and has identified several key regulators. However, to have a real translation of this research into clinical applications, we must translate this knowledge to the human ES cells. For this reason, we propose now to use the human Pluripotent stem cell systems and set up blood differentiation protocols in classical EBs and new 3D-gastruloid system to push the process of hematopoietic development to obtain Hematopoietic Stem and Progenitor cells (HSPC) and other blood cell progenitor and mature types. We will take advantage of an inducible CRISPR activation system develop in the course of a previous project to demonstrate the importance of specific factors in the induction of the hematopoietic lineage. In addition, we will take advantage of our knowledge on the Notch signals to manipulate the balance between cell fate decisions. We will push cells to either maintain the HSC phenotype or to push to T-cell differentiation depending on the amount of Notch activity.

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**133.400,00€**

**Este proyecto está cofinanciado por la Unión Europea NextGenerationEU/ PRTR**