Description of Funded Research Projects

1st Call for H.F.R.I. Research Projects to support Post-Doctoral Researchers

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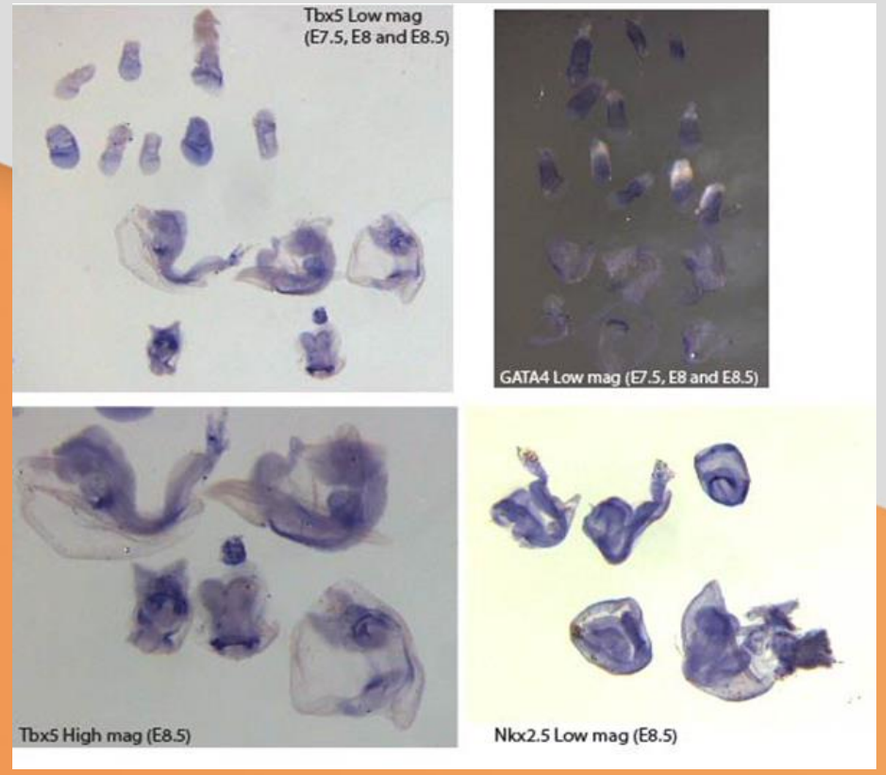
Research Project Title:

Investigation of the plasticity of cardiac progenitors

Principal Investigator:
Ioannis Kokkinopoulos



Popular Title:
Characterisation of heart progenitors for cardiac repair

Scientific Field:
Developmental Biology

Host Institution:
Biomedical Research Foundation, Academy of Athens

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During development, the cardiomyocyte lineage is highly specialised, comprising of cardiac progenitor cells allocated in a discrete and temporal order. At embryonic day 7.5 in mice, the heart tube is the prime structure that will eventually give rise to the heart proper. It is populated by two distinct sets of cardiac progenitors cell subsets, derived from two anatomical regions; the first heart field (also known as the cardiac crescent) which will give rise to the left ventricle and parts of the atria, and the second heart field that contributes towards the right ventricle, outflow tract and the remaining parts of the atria, including the septum. These fields are genetically distinguishable, at embryonic day 7.5, by expression of specific transcription factors. Congenital heart defects are often linked to transcriptional networks that orchestrate heart development. Tbx5, the T-box transcription factor is haploinsufficient in Holt-Oram syndrome, and is one of the cardinal TFs essential for cardiac development. Its expression is also of paramount importance for obtaining CMs from embryonic stem cells, human induced pluripotent stem cells, or via direct reprogramming of any cell type. Recent experiments performed in the adult zebrafish, reported re-expression of tbx5 (among other cardinal transcription factors) upon ventricular ablation leading to complete heart regeneration. Thus, the Tbx5 transcriptional network is important not only for initiating early cardiac specification, but also to prime the regenerative mechanism in adult lower vertebrates. The importance of this TF in mammalian heart regeneration has not been examined in detail, primarily because of the lack of specific molecular markers able to distinguish between cardiac progenitor cell progenies.

Project Impact on Society

Congenital heart defects are usually apparent at birth, characterised by structural abnormalities, such as atrial or ventricular septation defects, electrical conduction abnormalities or cardiomyopathies. One of the primary causes of cardiomyopathies is the loss and/or damage of cardiomyocytes. In order to replenish the lost/damaged cells, an appropriate source is needed as a cell-replacement therapeutic approach. An attractive candidate is cardiac progenitor cells, which could be driven to give rise to cardiomyocytes. However, our understanding of cardiac progenitor cells and how to obtain a pure and effective cardiomyocyte population for the clinical setting remains limited.

Devising methods to distinguish between distinct early cardiac progenitor cell populations and following their subsequent differentiation we will better understand the pathophysiology of congenital heart defects.

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To me, H.F.R.I. funding would mean...

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This funding will allow me to continue my work that started in the UK, allowing me to form my own lab in developmental and stem cell biology, at the BRFAA. It also provides the first step towards independence that is important for my career development.
Developmental and Stem Cell basic research in Greece is vastly expanding over the last five years and I feel that my research will contribute greatly to securing further E.U. and national funding and establish us in the field.

The Principal Investigator,
Ioannis Kokkinopoulos

Funding

Amount: **180,000 €**

Duration: **36 months**

Foundation: **H.F.R.I.**

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