



Research Project Proposal
Academic year 2016-2017

Project Nº 48 ASIGNADO
Title: Therapeutic potential of induced cardiovascular progenitors in models of myocardial infarction
Department/ Laboratory Department of Cell Therapy, Laboratory 2.06, Center for Applied Medical research, Center for Applied Medical research, CIMA
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Summary <p>Heart disease remains one of the leading causes of mortality. The ischemia eventually leads to irreversible damage and death of the tissue which is substituted by a non-functional scar. The success of cardiac cell therapy will be determined by the development of methods to improve engraftment and generation of cells capable to regenerate the damaged tissue. The reprogramming towards induced pluripotent stem cells (iPSC) enable the generation of a variety of cells. However, the tumorigenic potential of iPSC limits their clinical use. We hypothesize that induced cardiovascular progenitors (iCVP) are the right population of cells for cardiac therapy since: iCVP are able to proliferate and produce all lineages of the heart; patient-specific iCVP could be obtained using a direct and short (weeks) process; and iCVP derivatives would be likely to couple electromechanically. The methodology able to convert human fibroblasts into iCVP has not been established yet, and despite significant research efforts, human CVP cannot be expanded robustly without genetic manipulation.</p> <p>In our laboratory we pursue the following specific aims: 1) to decipher the cell signalling pathways controlling human CVP self-renewal versus differentiation fate decisions; 2) to demonstrate the potential of iCVP to contribute to cardiac regeneration in models of MI through increased engraftment and tissue coupling; and 3) to reprogram resident cardiac fibroblasts into iCVP in vivo using Adeno-associated virus (AAV). To accomplish this, we will use diverse CVP tracking tools developed in our laboratory and small animal models of myocardial infarction.</p>



References References could be added (no more than three)

1. Lalit, P.A., et al. Lineage Reprogramming of Fibroblasts into Proliferative Induced Cardiac Progenitor Cells by Defined Factors. *Cell Stem Cell* **18**, 354-367 (2016).
2. Zhang, Y., et al. Expandable Cardiovascular Progenitor Cells Reprogrammed from Fibroblasts. *Cell Stem Cell* **18**, 368-381 (2016).
3. <http://dx.doi.org/10.1016/j.scr.2016.03.006>

POSSIBILITY OF PhD

YES *

* (PhD grant required)