Final Report

Project acronym:*INCIPIT*

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M-ERA.NET Call 20*16*

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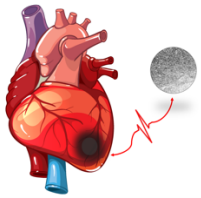
Publishable project summary



The aim of INCIPIT was the development of an innovative technological product for the treatment and improvement of the quality of life of patients suffering from cardiovascular diseases and in particular myocardial infarct, leading cause of mortality in the world. Current therapies do not restore the functionality of damaged myocardial tissue. The only effective therapeutic intervention is an approach able to stimulate the autonomous regeneration of myocardium. The INCIPIT product is an acellularized patch for the engineering of in vivo cardiac tissue, designed to attract endogenous stem cells and favour their cardiac differentiation and to contrast ventricular remodelling in situ. The in vivo approach is the scientific option that poses the most ambitious challenges, but it is also the most attractive option for the market of smart therapies in cardiovascular field. Microstructured, bioartificial, electroconductive patches were produced and tested using a large set of physico-chemical, morphological, mechanical, and functional characterizations by CNR-IPCF and UMINHO groups. Integrated and nano-functionalized patches showed good mechanical properties, improved conductivity, a controlled biodegradability, molecular recognition capability and a controlled release of drug. In vitro cytocompatibility and cardioinductivity of patches were assessed by UNITO and UMINHO groups, before and after nano-functionalization, by using cell lines like H9C2 and C2C12, primary cells like hMSCs and NMCs as well as IPSC-CMs produced by Pluricell Biotech. In vitro migration tests using hMSCs and NMCs showed chemoattractive capacity of the patches. In addition, a cell-sheet technology was validated to recreate a “tissue like” structure. In vitro conductive assays using IPSC-CMs on functionalized patches were performed by UNITO showing improved cell-cell interactions and cell beating synchronicity. The selected products were implanted in an experimental rat animal model of ischemic heart failure at the Center for Experimental Biomedicine of CNR. Histological, immunofluorescence and biomarkers analysis indicate how the implantation of the patch does not seem to cause damage to the myocardium, the functionalized patch seems to recruit undifferentiated (stem) cells into the damaged myocardium and to trigger their differentiation towards the cardiac lineage. In view of a possible commercialization of the patch, regulatory aspects, classification of the therapeutic product, requirements for safety and performance, swot analysis and risks associated to cardiac patch manufacturing were considered by Pluricell Biotech and CNR-IPCF. The technology transfer phase was undertaken and further evidence for efficacy in more translational models will be discussed with potential commercialization partners and investors.