The REACTIVA project, led by CNIC scientist Dr. Miguel Torres, receives ERC Advanced Grant funding

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The CNIC project will use innovative approaches to investigate cardiac regeneration

The **REACTIVA** project, directed by Dr. Miguel Torres at the Centro Nacional de Investigaciones Cardiovasculares (CNIC), has been awarded an ERC Advanced Grant to fund innovative approaches to the investigation of cardiac regeneration. The award provides €2,500,000 in funding over a period of 60 months

The hearts of newborn mammals have abundant diploid cardiomyocytes, allowing them to efficiently regenerate damaged tissue. However, this ability is lost son after birth, and the hearts of adult mammals are unable to regenerate because the fully differentiated cardiomyocytes they contain have a limited capacity to proliferate.

“Heart failure is a global epidemic. Its impact in terms of avoidable deaths, ill health, and health care costs is immense. Because the adult human heart lacks the ability to regenerate, the loss of myocardial tissue that occurs in many heart conditions is irreversible and often leads to fatal heart failure,” said Dr. Torres.

The goal of the REACTIVA project is to establish a new strategy for cardiac regeneration based on the reactivation of the heart’s dormant endogenous mechanism. This will represent a major advance in cardiac regenerative biology. Research in mice has shown that the regenerative capacity of the adult heart is related to the proportion of diploid cardiomyocytes; however, so far it has been difficult to characterize the molecular profile of these cells, and this has held back understanding of their role in cardiac regeneration.

Thanks to a new method for sequencing RNA in individual cardiomyocytes, the Genetic Control of Organ Development and Regeneration laboratory at the CNIC, which Dr. Torres leads, has identified a molecular signature of diploid adult cardiomyocytes that is related to the fetal program and is controlled by a transcriptional repressor. Inhibition of this repressor in the hearts of newborn mice increases both the numbers of diploid cardiomyocytes in adulthood and their proliferative activity.

The team propose that diploid adult cardiomyocytes are the vestige of an endogenous regenerative mechanism, and that stimulating these cells could promote cardiac regeneration in the adult mammalian heart. REACTIVA will build on these findings to provide a complete characterization of the regulatory network in diploid adult cardiomyocytes, identify and track these cells in the adult heart, and use this knowledge to induce their activation and promote cardiac regeneration in adulthood.

Together with Dr. Hesham Sadek, Dr. Torres coordinates the CNIC Cardiovascular Regeneration Program, whose goal is to identify endogenous mechanisms that stimulate the regenerative capacity of the heart and the vascular system and to use the knowledge gained to design therapies for patients.

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