

INNOVATION – Investigating lncRNA regulated pathways driving cardiac regeneration

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One of the main causes underlying the high death toll of cardiovascular disease is the lack of significant cardiac regeneration of the adult heart. In marked contrast, for a short period of time after birth, newborn mice and possibly humans can fully regenerate the heart after a heart attack. INNOVATION is an interdisciplinary 3-years program financed at around 1.1M€, which brings together 5 European countries and aims to decipher the molecular circuitries underlying the striking difference between newborn heart regeneration and fibrotic infarct healing of the adult heart. At University of Aveiro we are particularly focused on the “dark matter” of the genome which is comprised of tens of thousands of long non-coding RNAs (lncRNAs) and on metabolic circuitries that are required for the establishment and maintenance of normal gene

expression networks, thus controlling developmental and disease processes. Here, we will translate molecular circuitries that distinguish the regenerating from the non-regenerating heart with the ultimate goal to liberate cardiomyocytes regeneration in the adult, and in particular, in the diseased heart. To do so, INNOVATION deviates from conventional studies which predominantly focus on protein coding genes. Instead, we will gain insight into the role of lncRNAs which are emerging as functionally conserved regulators of cardiac regeneration in mouse and humans. Identifying molecular pathways underlying the inability of adult cardiomyocytes to divide is of paramount importance for the development of novel, innovative treatment options aiming at regenerating the diseased heart through stimulation of cardiomyocytes proliferation.

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Aims:

- I. Sex and cell type specific lncRNA atlas of the regenerating heart
- II. Functional in vitro & in vivo investigation of lncRNAs in major cardiac cell types
- III. lncRNA-based therapeutic approaches to enhance cardiac regeneration