



Consiglio Nazionale delle Ricerche

Istituto di Biologia Cellulare e Neurobiologia

Institute of Cell Biology and Neurobiology

CNR-IBCN

AVVISO DI SEMINARIO

SEMINAR ANNOUNCEMENT

Cardiac regeneration using small RNA drugs

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Padriciano –Trieste

01 December 2017, 11:00 – 12:30

Monterotondo CNR Seminar Room, Building 21

Highlights: There is an impelling need to develop innovative therapies that promote cardiac repair in patients with myocardial infarction and heart failure. In contrast to other species that can regenerate the heart throughout their entire life, post-natal damage to the myocardium in mammals is repaired through formation of a scar. Copious evidence nonetheless indicates that the capacity for myocardial renewal, albeit limited, also exists in adult mammals. During the last years, my laboratory has become interested in developing methods to search for factors able to foster this cardiac regenerative capacity. We follow two parallel strategies, both based on unbiased, functional screenings. In one strategy, we have generated two libraries in AAV, one corresponding to the secretome (all secreted factors encoded by the genome, approximately 1200 cDNAs) and the second one to the miRNAome (800 pri-miRNA genes). We developed a procedure (named FunSel) for the functional selection of therapeutic factors after in vivo administration of pools from this AAV library to the heart after myocardial infarction. With the other strategy, we searched for small RNAs inducing cardiac regeneration by the ex vivo, high throughput screening of miRNAs and miRNA-inhibitors able to promote cardiomyocyte proliferation using whole genome libraries. We identified at least 8 microRNAs that increase cardiomyocyte proliferation in mice, rats and pigs, as well as in human cardiomyocytes from fetal hearts, or derived from hES cells. Delivery of two of these miRNAs in vivo, either using AAV9 vectors or as synthetic mimics after myocardial infarction markedly reduced infarct areas and improved cardiac function in both mice and pigs. These microRNA directly activate the proliferative potential of differentiated cardiomyocytes thus bypassing stem cell involvement. These results indicate that finding novel biotherapeutics for myocardial infarction and heart failure is an attainable goal, including proteins or small RNAs capable to induce cardiac regeneration.

Host: Prof. Fabio Mammano