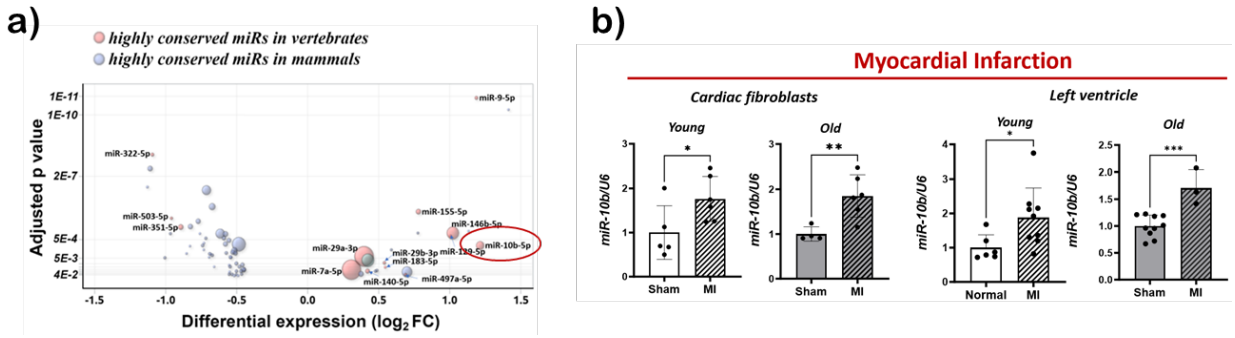
Scientific report in 2023

Fundamental mechanisms of post-infarction remodeling in old heart at fibroblast population level

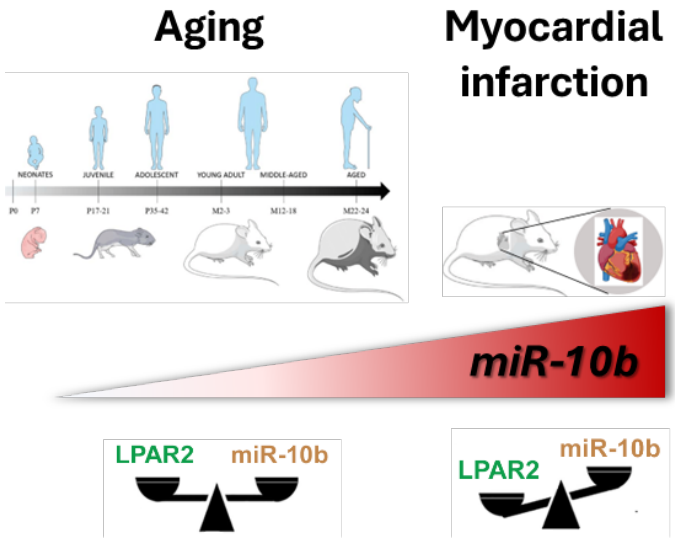
Cardiac fibrosis remains an important health concern, but its study has been hindered by the existence of multiple cell populations contributing to fibrosis. The understanding of the crosstalk between cardiac cells after myocardial infarction is important not only for accelerating the understanding of the molecular mechanisms underlying this pathology, but also for identifying new therapeutic targets.

The main results obtained this year care summarized below:

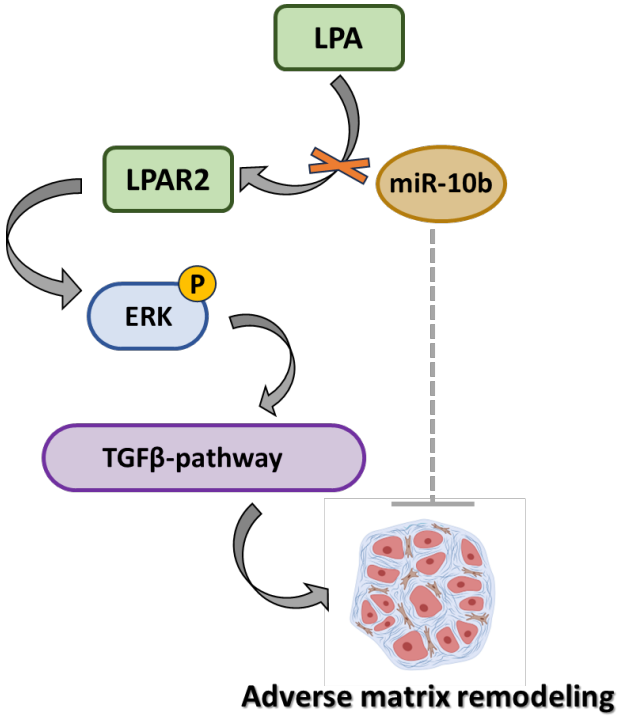
1. miR-10b is increased in the aged heart, as well as in myocardial infarction, as a result of its upregulated expression in the cardiac fibroblasts.



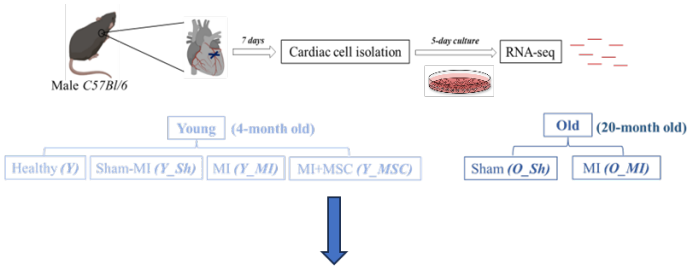
2. Target prediction analysis, validated by in vitro and in vivo studies of gene expression modulation, indicated LPAR2 (a protein involved in TGF-β dependent signaling) as a potential miR-10b target.



3. Mechanistically, miR-10b overexpression in cardiac fibroblasts resulted in LPAR2 downregulation, with direct impact on TGF-β production through ERK and Akt-signaling pathways, thus limiting ECM remodeling in aging and MI-induced fibrosis. Our data suggests an adaptive response of the heart for limiting myocardial infarction-induced adverse remodeling and aging-associated tissue fibrosis.



4. RNA seq data analysis revealed that epithelial-mesenchymal transition (EMT) pathway is significantly up-regulated in infarcted heart-derived cardiac fibroblasts (in both young and old animals) and reversed by MSC therapy.



Gene set enrichment analysis (GSEA)

Gene set	MI young *(vs Y-sham)*	MI young + MSC *(vs MI-young)*	MI old *(vs. MI young)*
TNFA_SIGNALING_VIA_NFKB	UP	UP	UP
EPITHELIAL_MESENCHYMAL_TRANSITION	UP	*DN*	UP
HYPOXIA	UP	*n.s*	UP
APOPTOSIS	UP	*n.s*	*n.s*
G2M_CHECKPOINT	*DN*	UP	*DN*
E2F_TARGETS	*DN*	UP	*DN*