

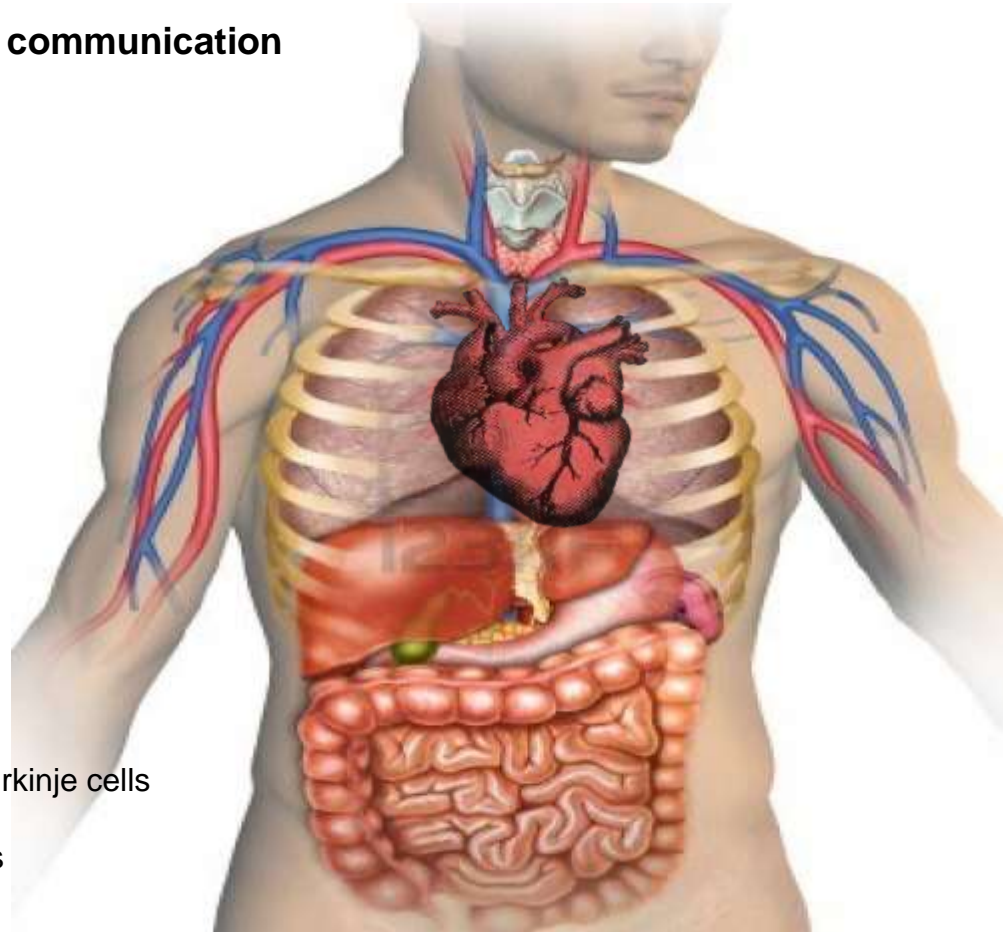
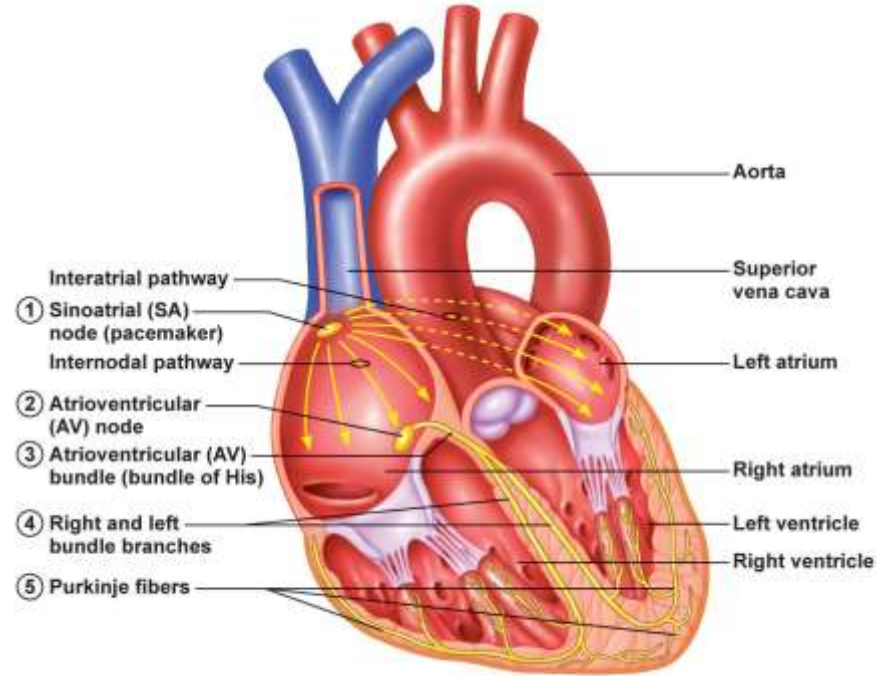
A Importância da Comunicação para Manutenção de um Coração Ativo e Saudável



group of ubiquitin-dependent proteolysis
and intercellular communication

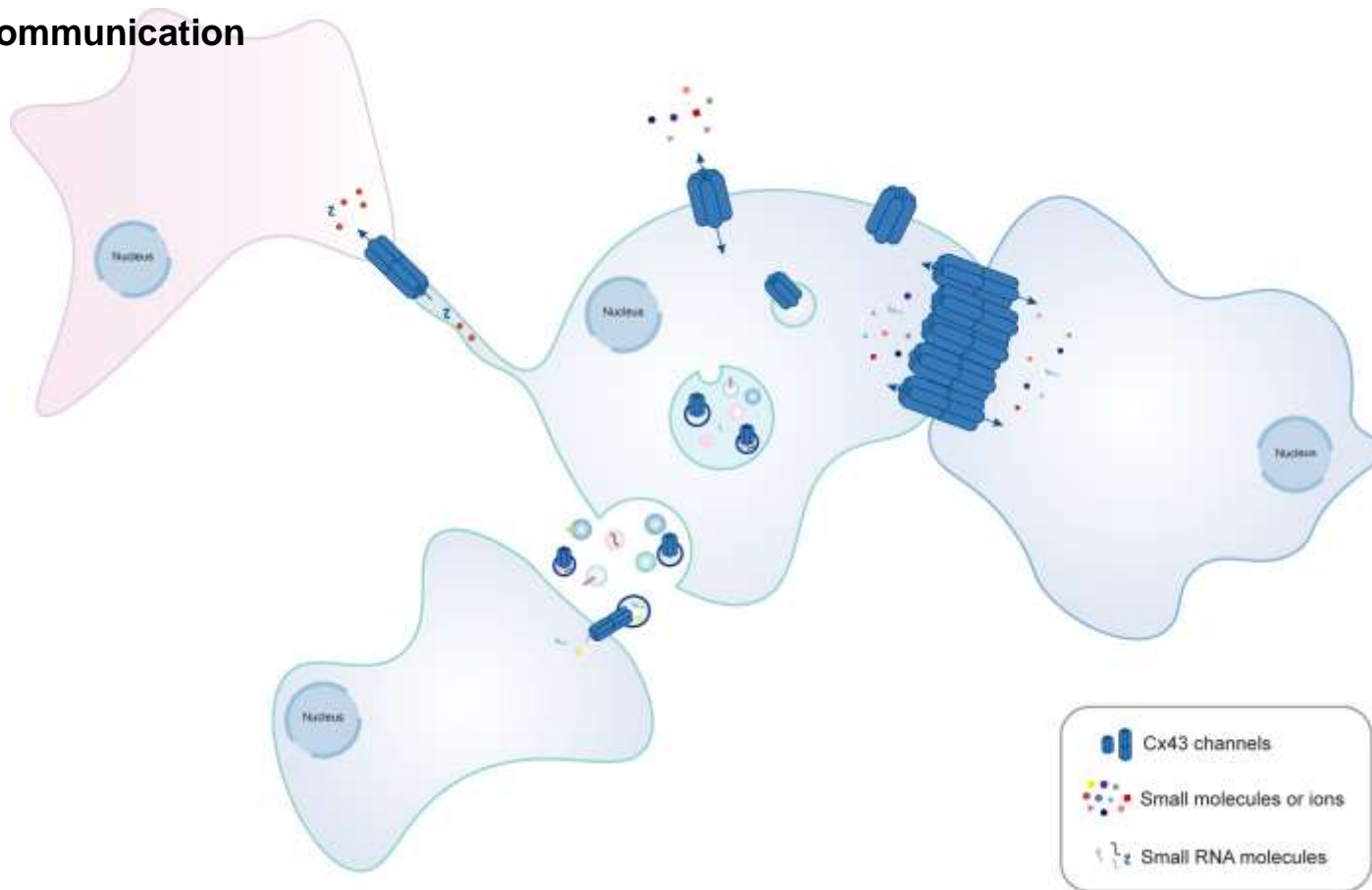
HENRIQUE GIRÃO
Faculty of Medicine University of Coimbra

The pumping heart: the importance of intercellular communication



- **Excitable:** **CARDIOMYOCYTES**, pacemaker cells, Purkinje cells and smooth muscle cells
- **Non-excitable:** fibroblasts, endothelial cells, and adipocytes

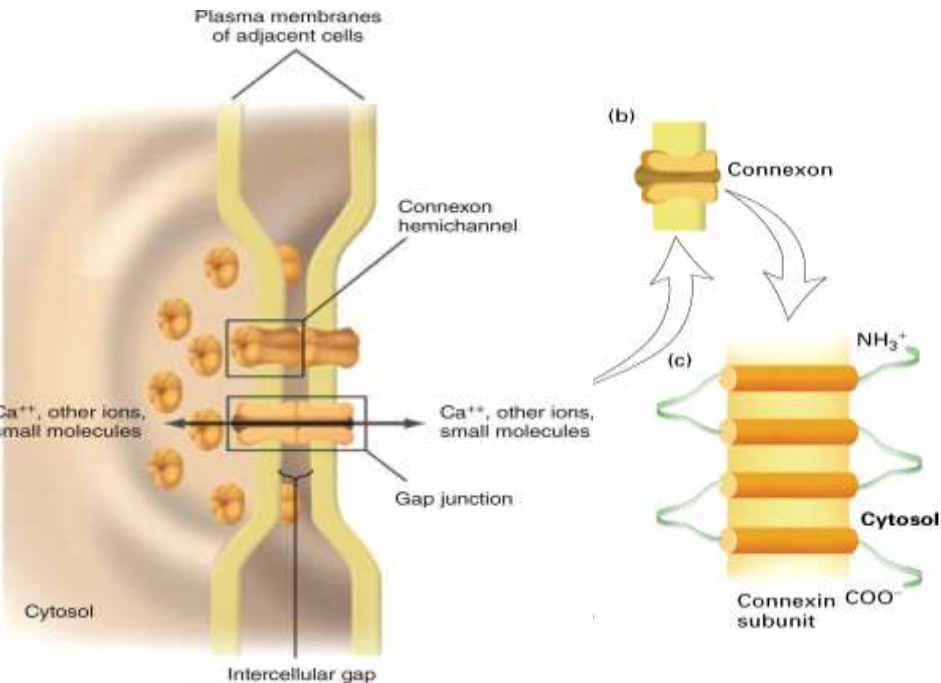
Intercellular communication



Intercellular communication strategies

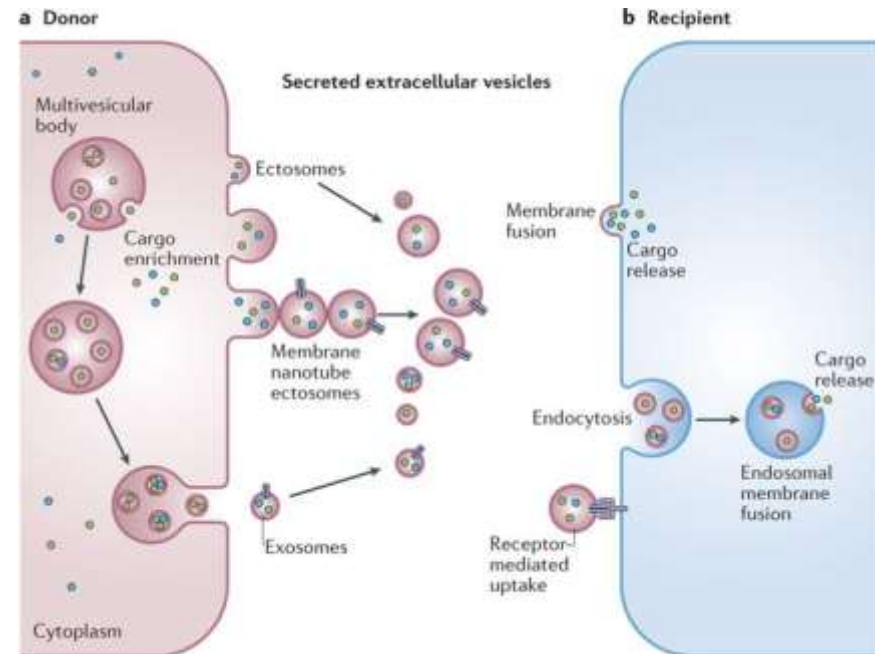
Gap junctions

Coupling between connected cells



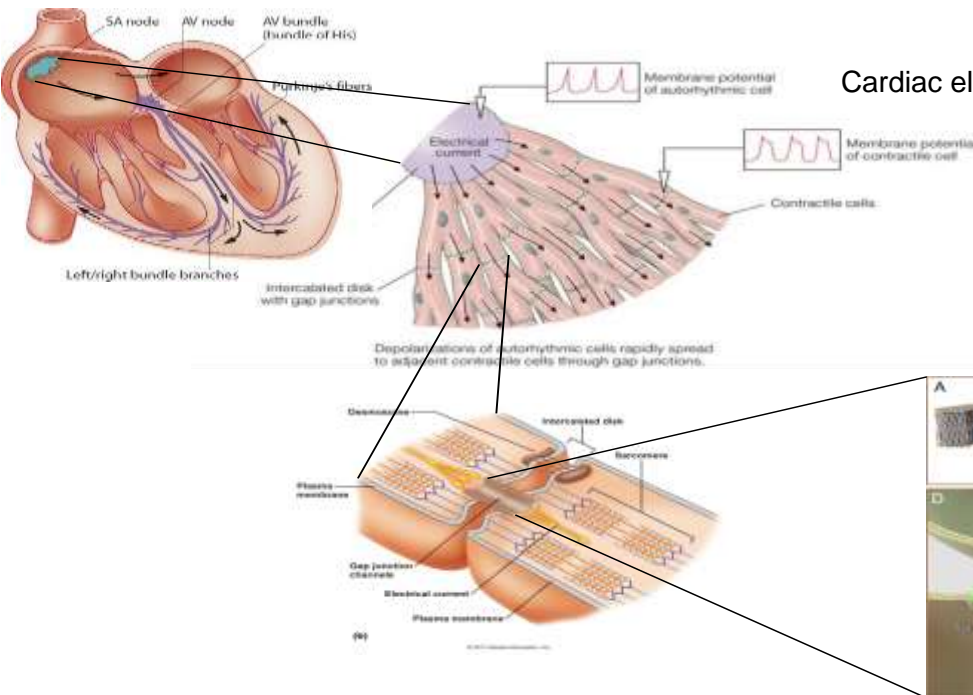
Extracellular Vesicles

Long distance communication



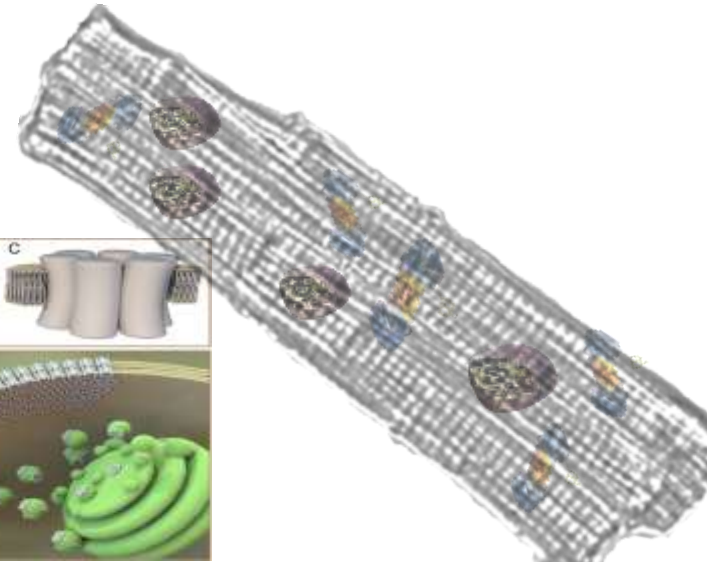
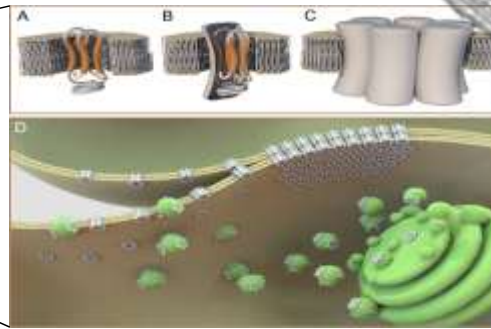
Gap Junction-mediated intercellular communication in the heart

Highly synchronized heart beating and contraction depends on Gap Junctions Intercellular Communication

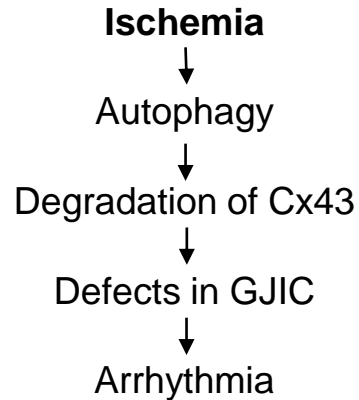
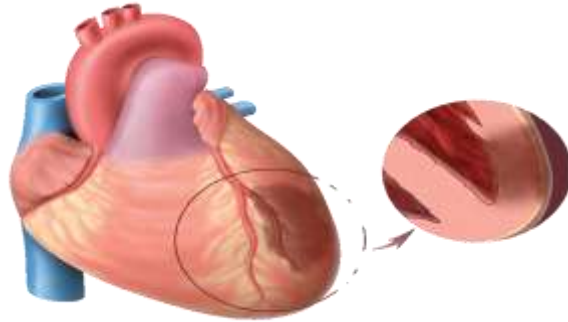


Cardiac electrical impulse travels through Gap Junctions

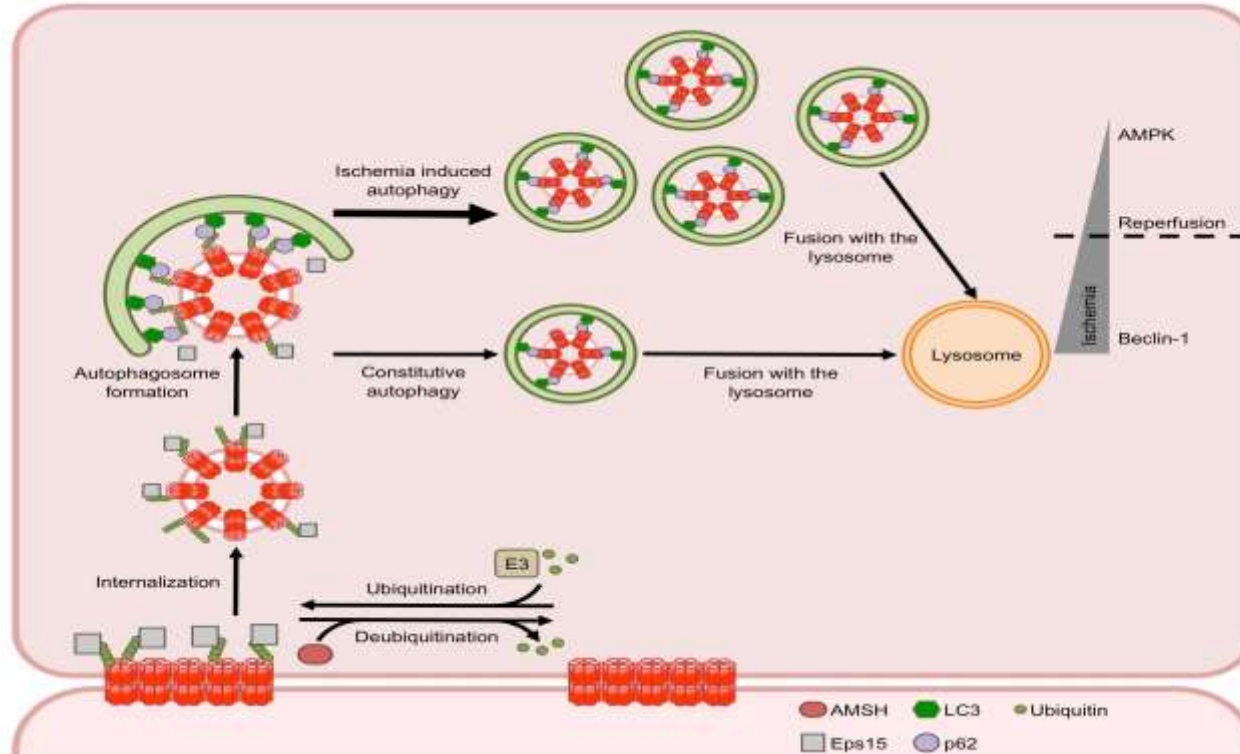
Defects in GJIC are associated with heart diseases



Ischemia impairs communication between cardiomyocytes



Autophagy-mediated degradation of Cx43 in ischemic cardiomyocytes

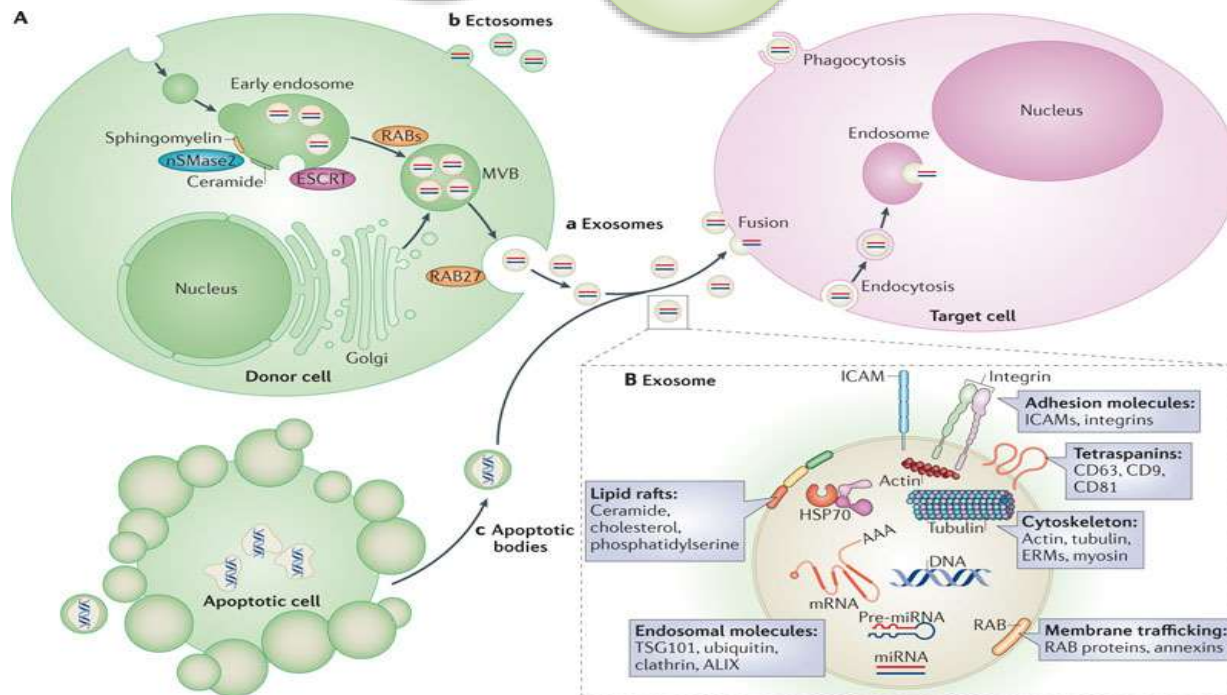


Diagnosis

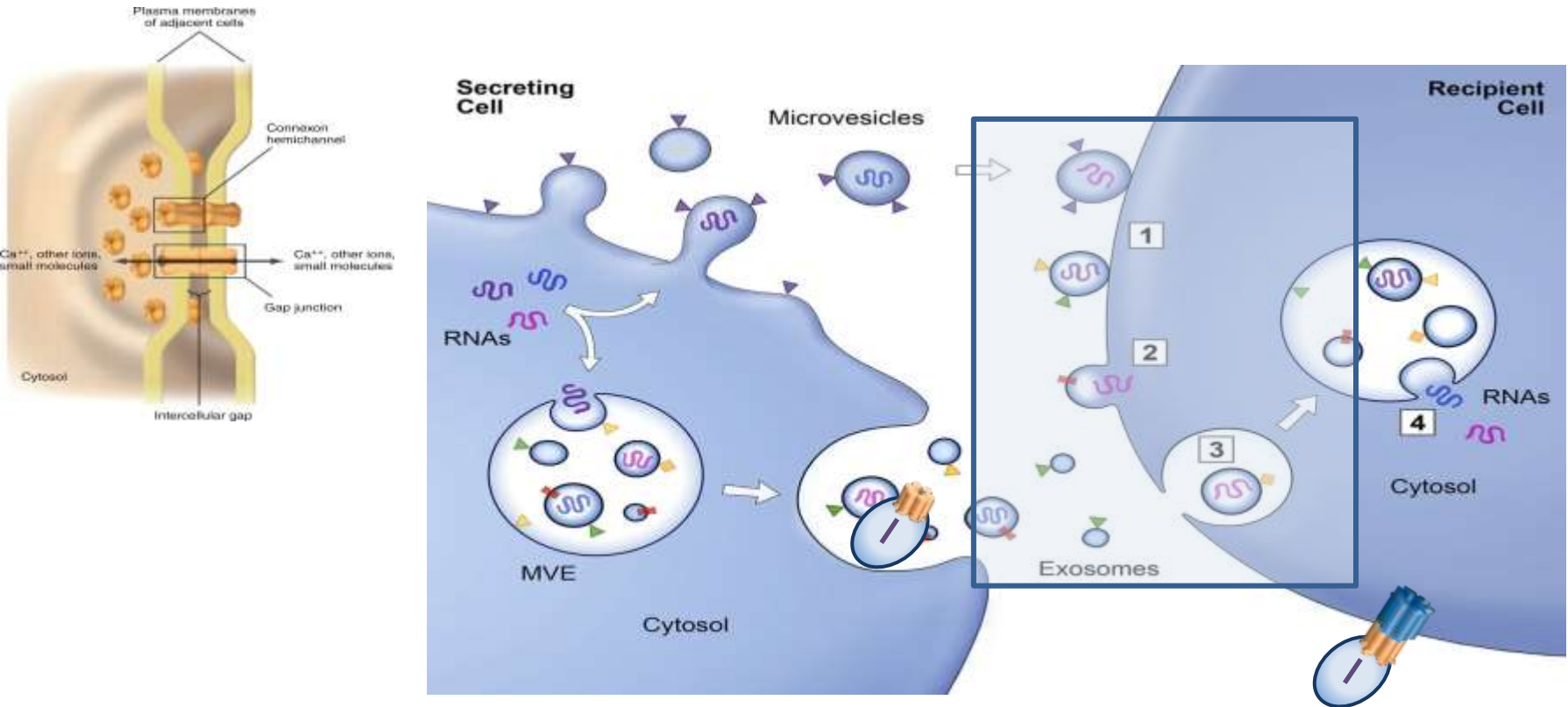
Therapies

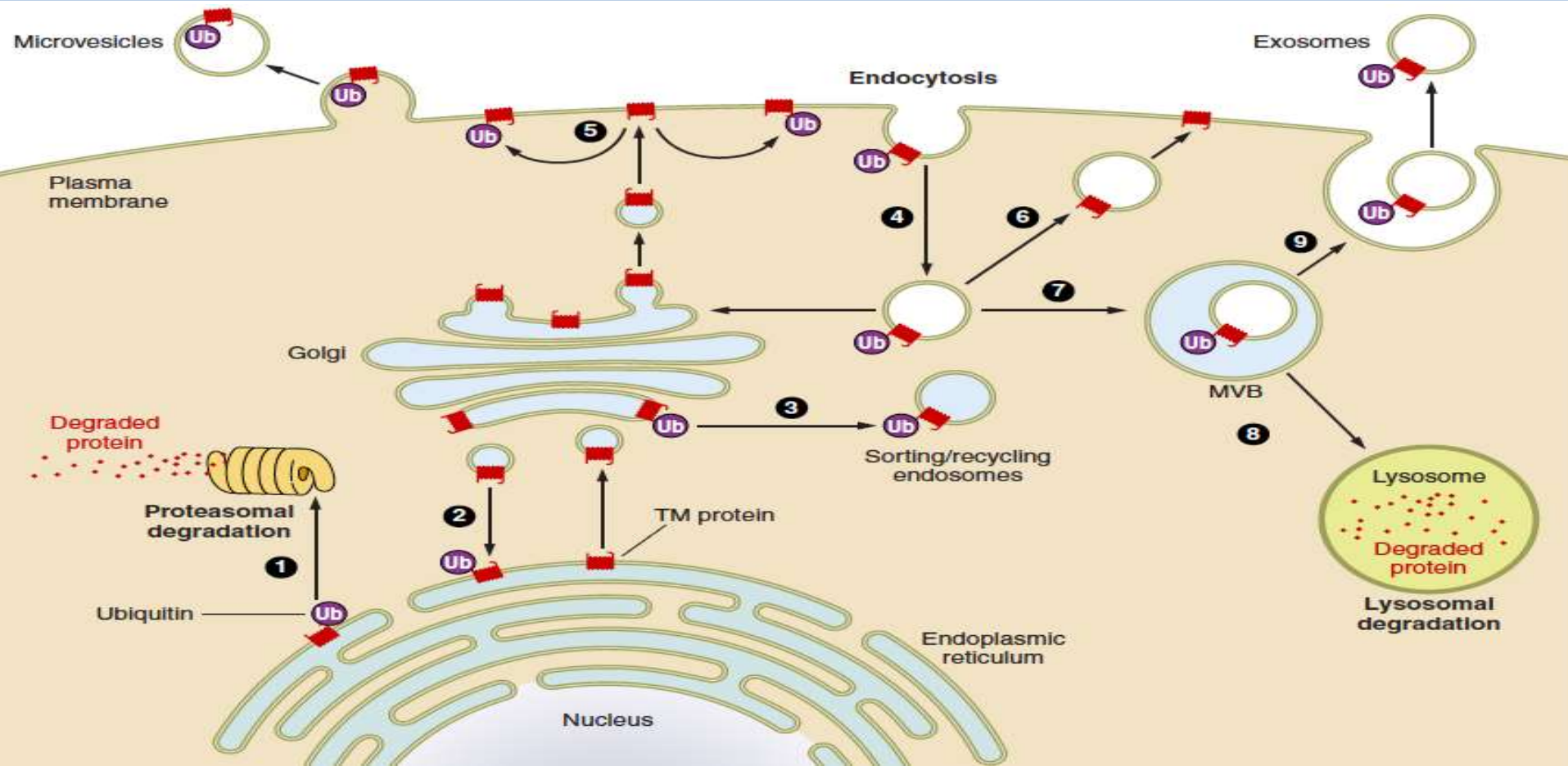
Biomarker

Extracellular vesicles-mediated intercellular communication

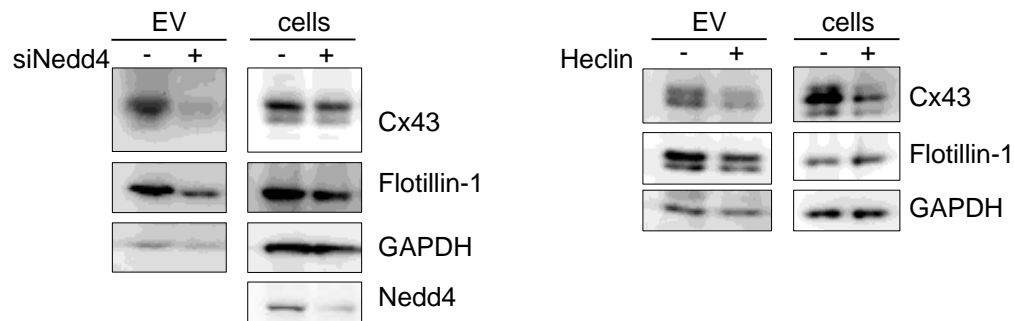


ConECT : Connexin43-mediated Exosome-Cell Transfer

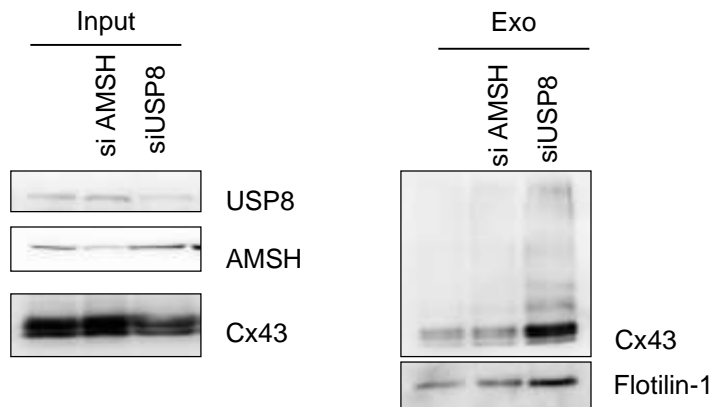




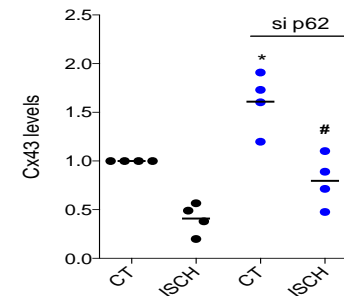
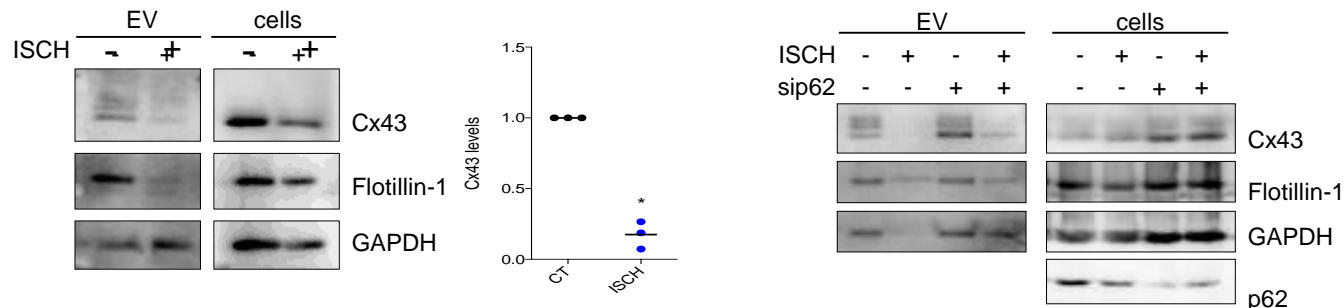
Inhibition of Nedd4-mediated ubiquitination decreases secretion of Cx43 in EVs



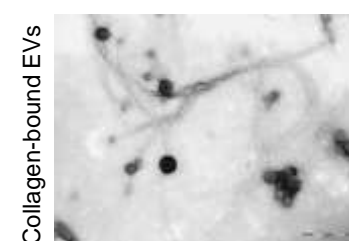
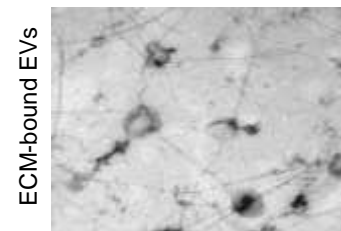
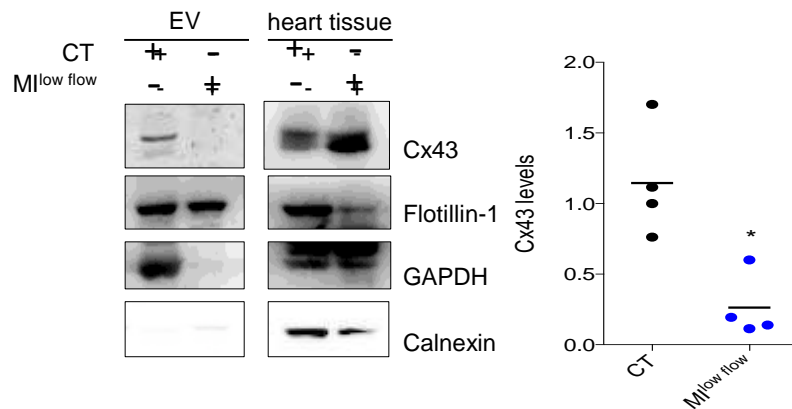
Downregulation of USP8-mediated deubiquitination of Cx43 promotes its secretion in EVs



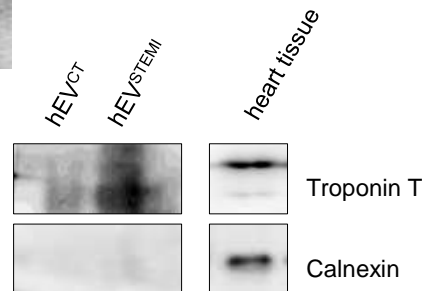
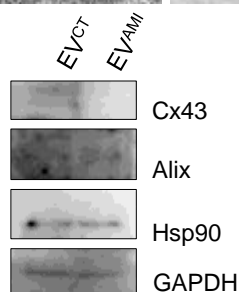
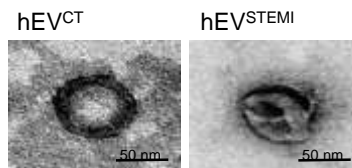
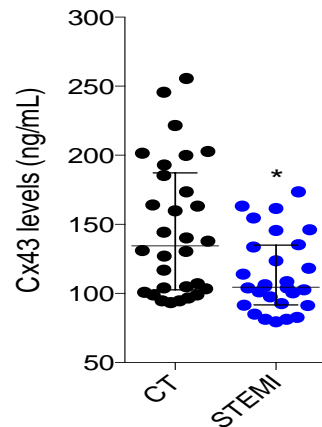
Ischemia leads to a decrease in Cx43 EVs released by cardiomyocytes



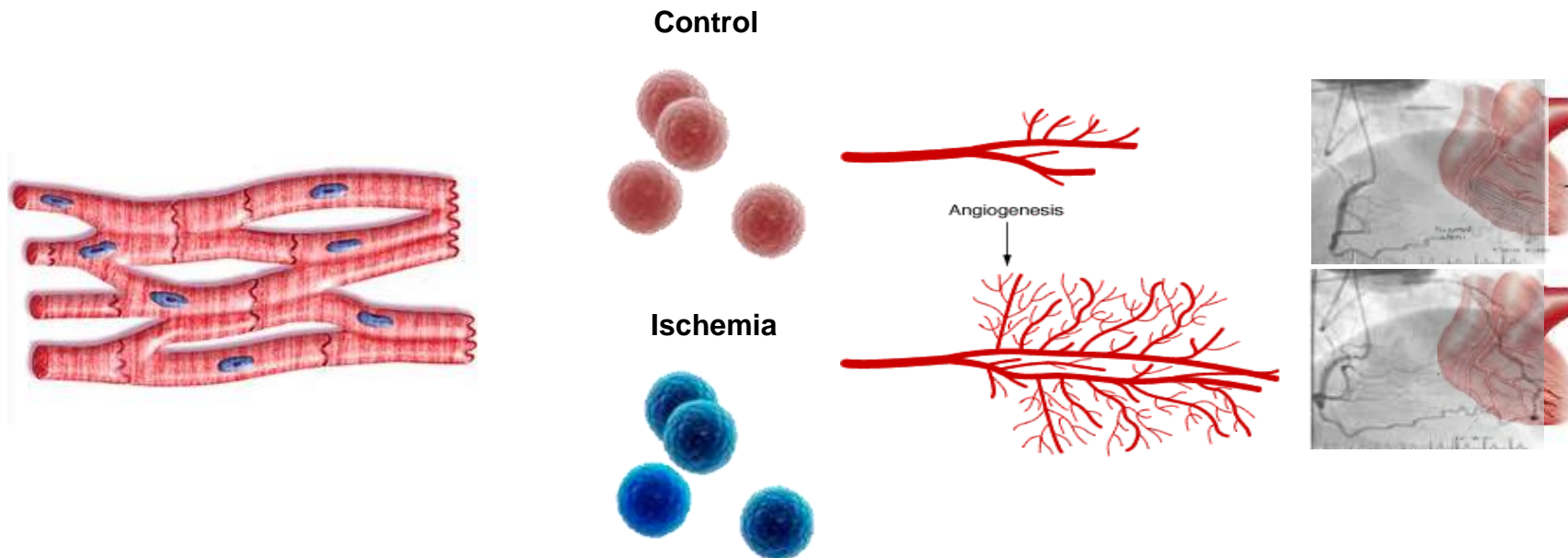
The amount of Cx43 decreases in EVs entrapped in ECM in ischemia



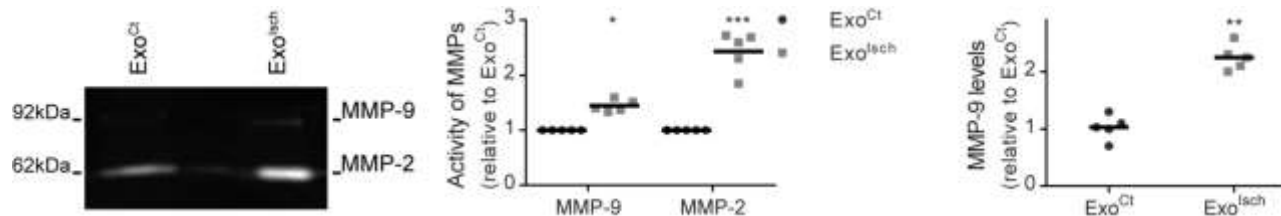
The levels of Cx43 in circulating exosomes decrease in myocardial infarction



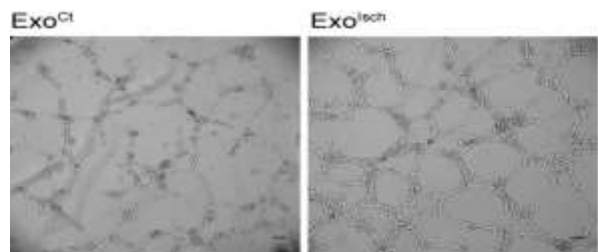
How extracellular vesicles released by cardiomyocytes under ischemia affect angiogenesis?



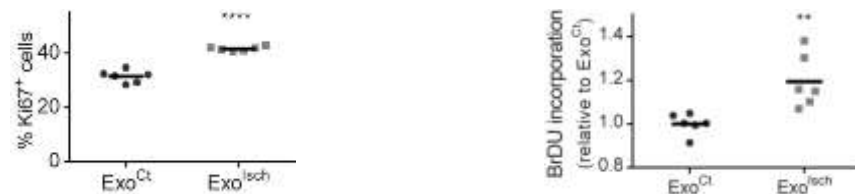
EVs released by cardiomyocytes in ischemia promote ECM degradation



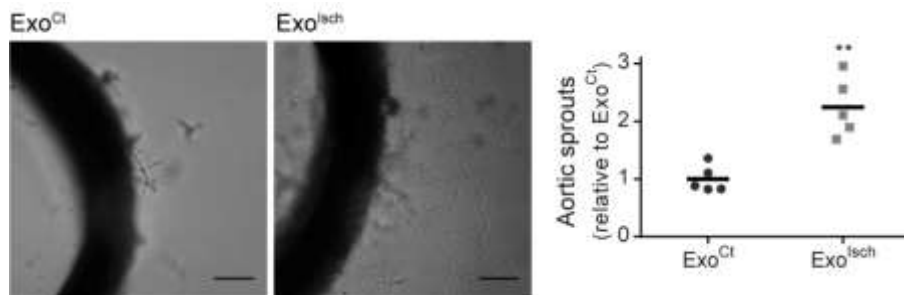
EVs from ischemic CM promote tubulation



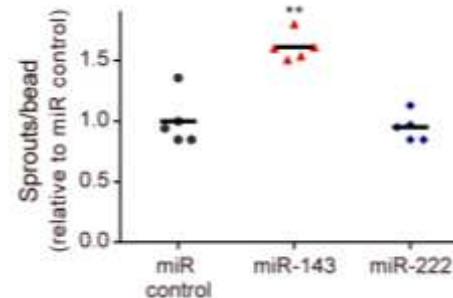
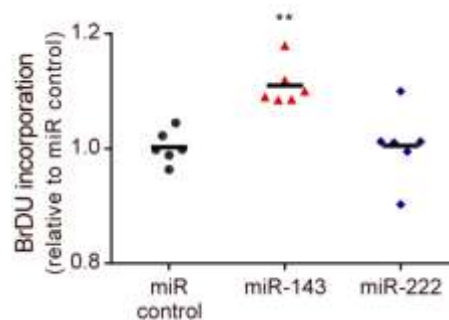
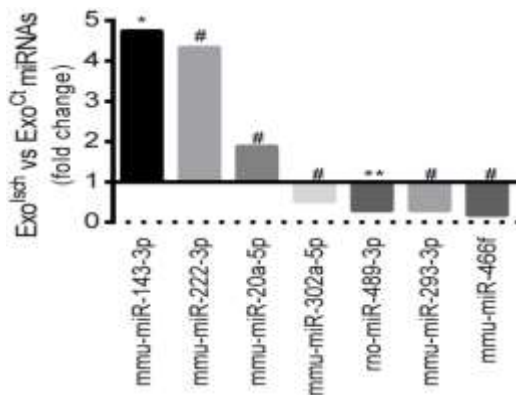
Ischemic exosomes promote ECs proliferation and survival upon stress



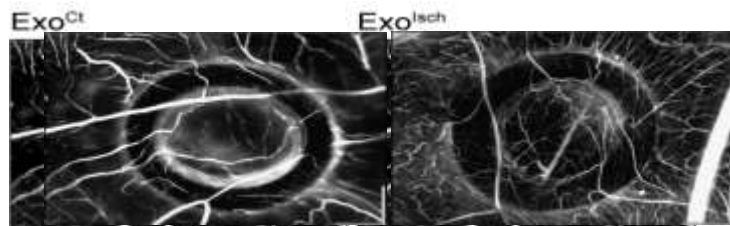
EVs from ischemic CM promote sprouting



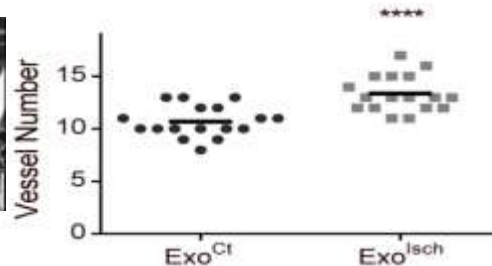
EVs from ischemic CM are enriched in miR-143 and miR-222



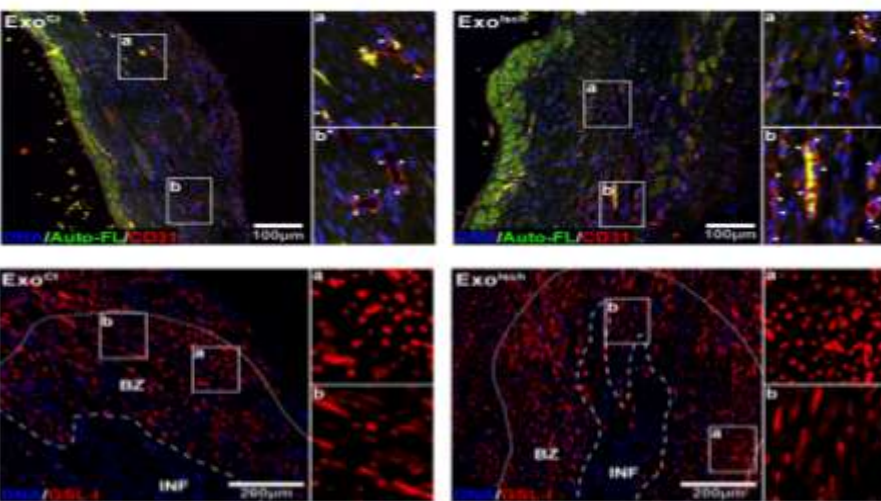
Ischemic EVs promote angiogenesis in vivo



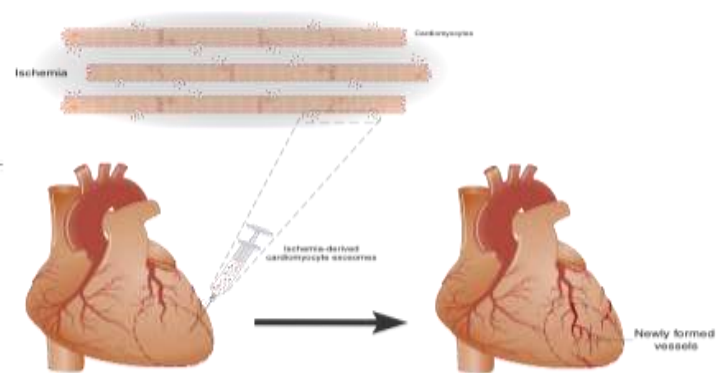
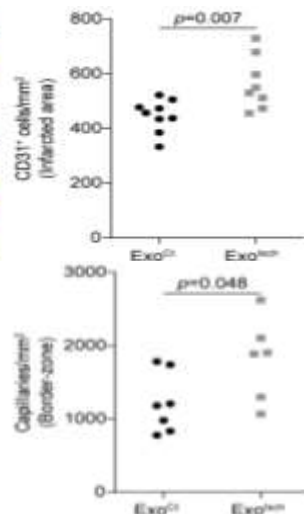
CAM assay



Ischemic exosomes promote angiogenesis following MI



- higher numbers of CD31⁺ ECs in the infarcted region
- lectin-perfused vessels in the infarction border zone



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THANK YOU!



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