

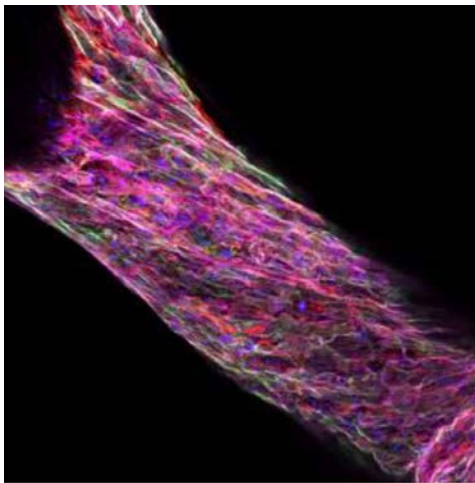
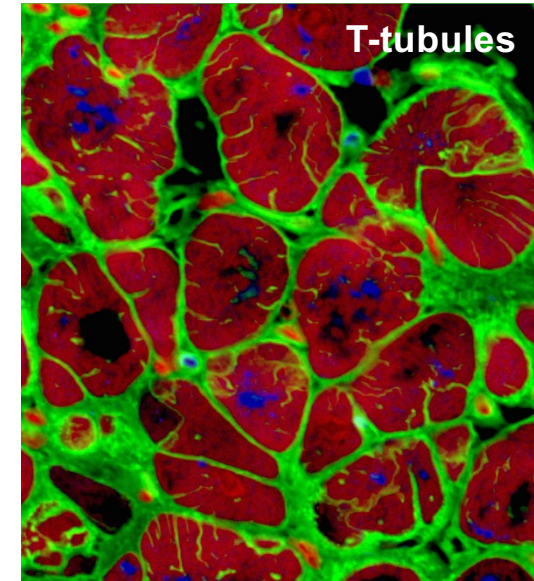
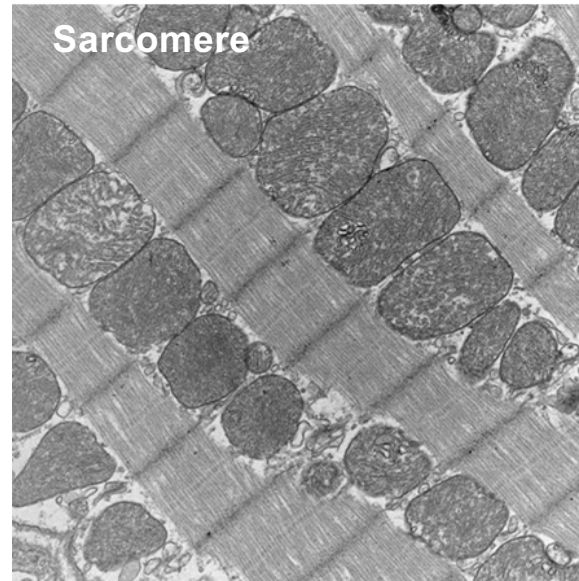
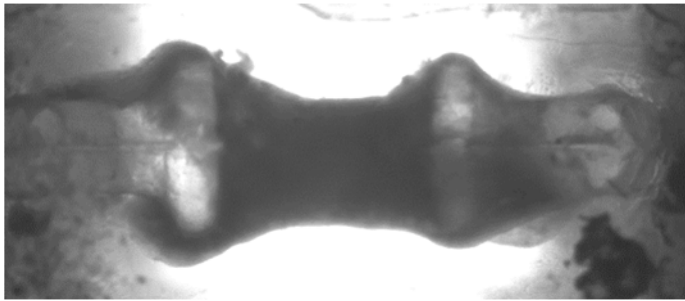
Bioengineering studies of exosomes In the context of heart injury



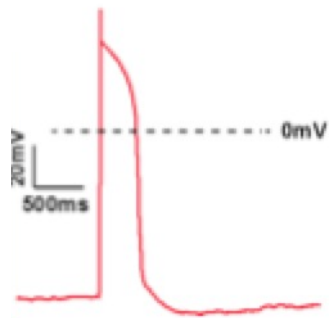
Gordana Vunjak-Novakovic
Columbia University

Workshop on Extracellular Vesicles, Exosomes, and Cell-Cell Signaling
in Response to Environmental Stress, NCATS and NIEHS
September 30, 2021

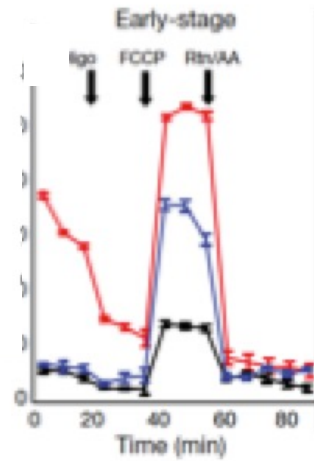
Engineered heart muscle:



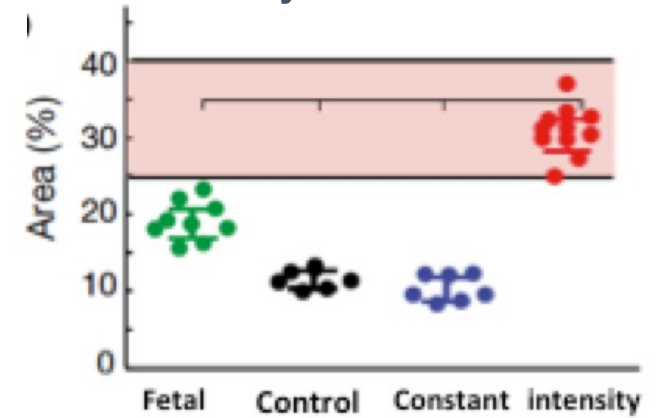
Action potential



Oxidative metabolism



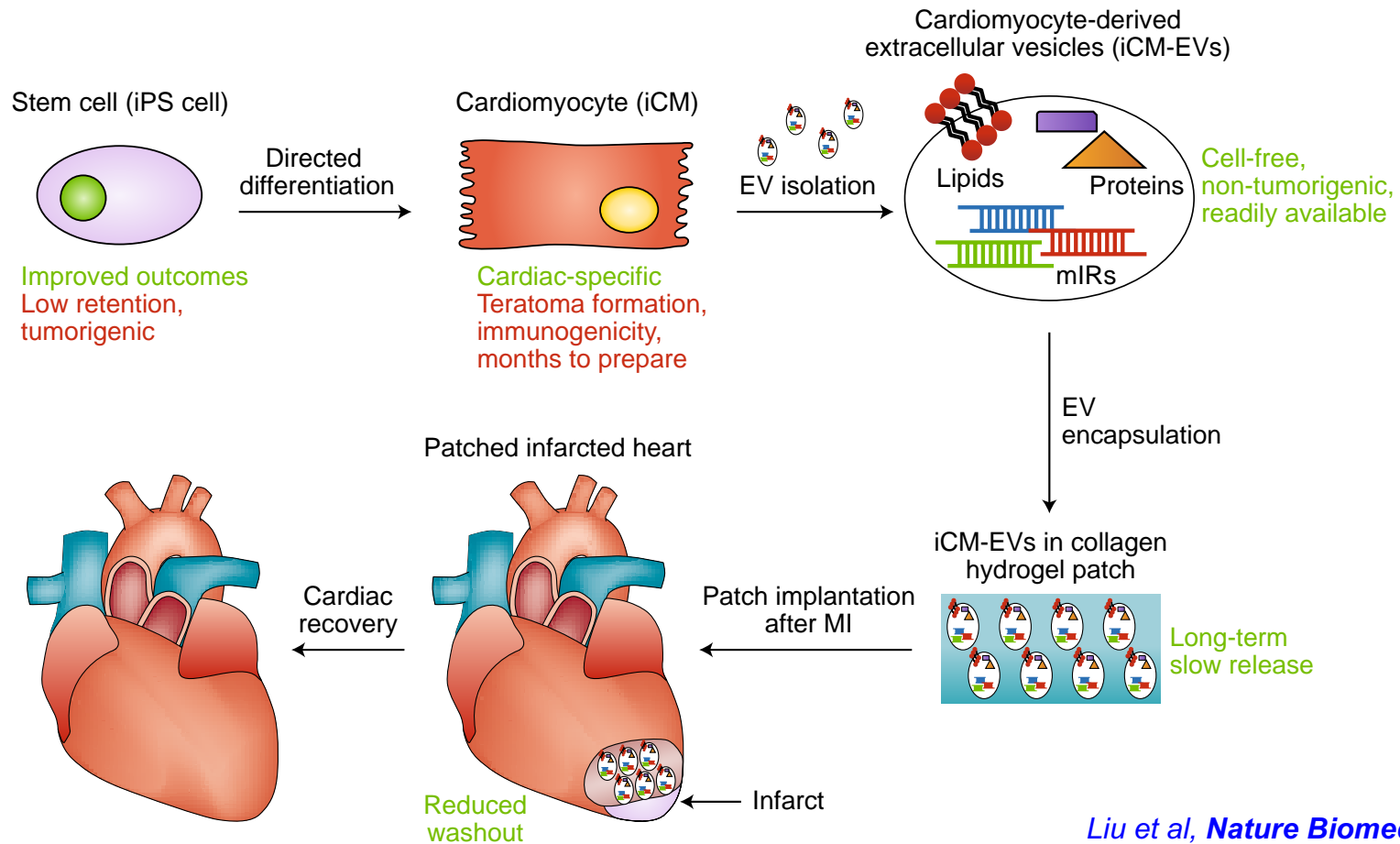
Density of mitochondria



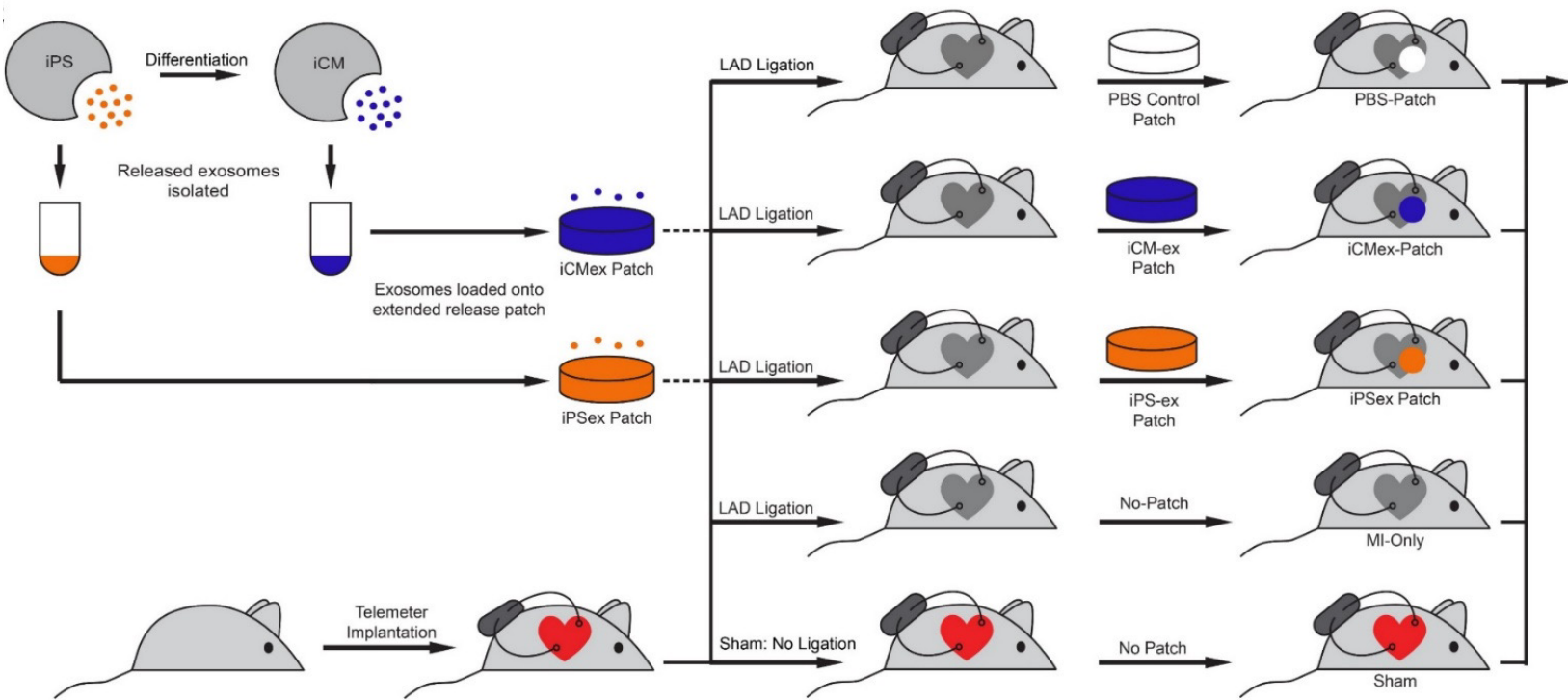
Tamargo, Fleischer et al *ACS Biomaterials* (2021)

Ronaldson-Bouchard et al, *Nature*, 2018

Heart therapy by sustained release of exosomes:

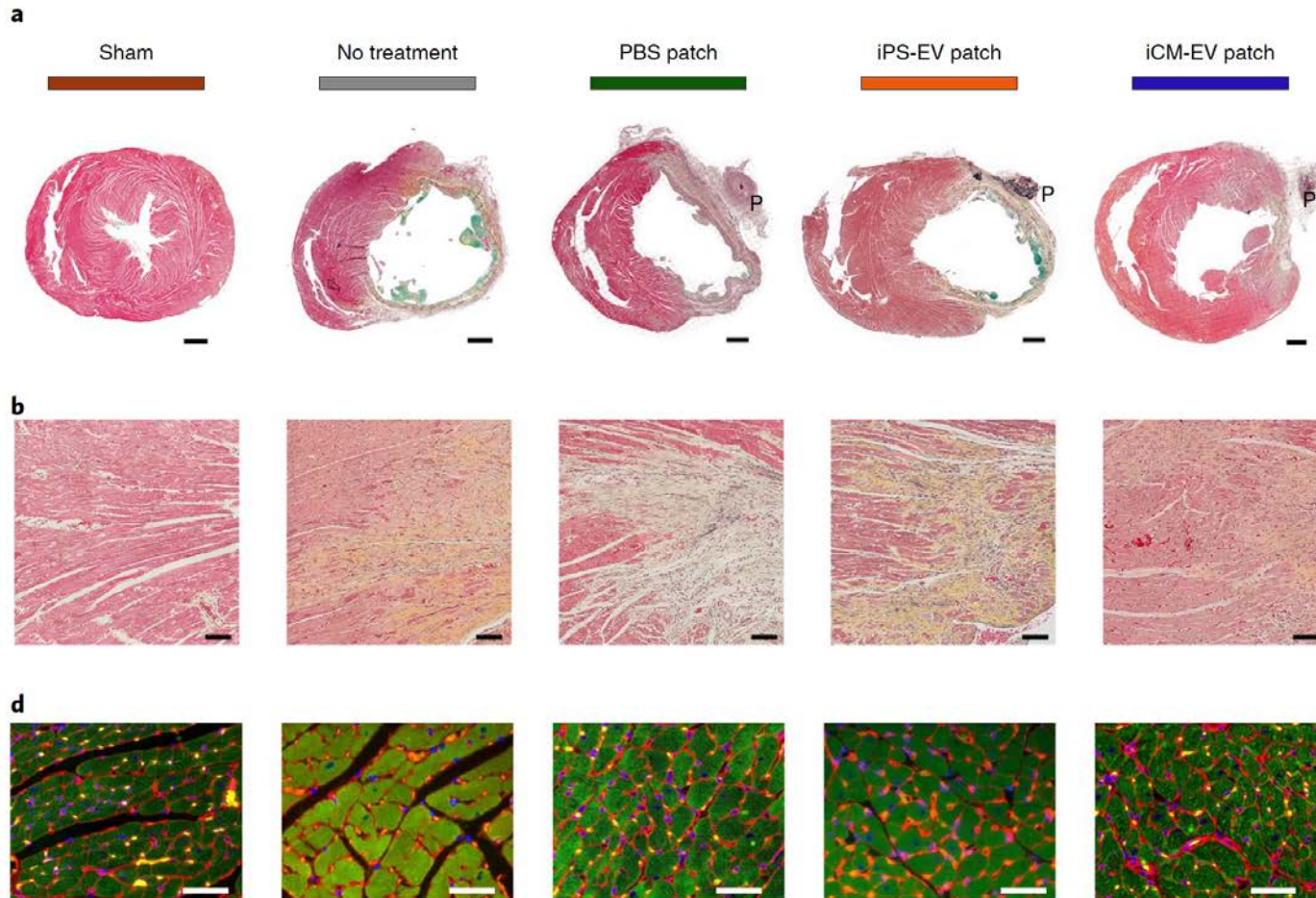


iPS-CM EVs reduce infarct size in a rat model:

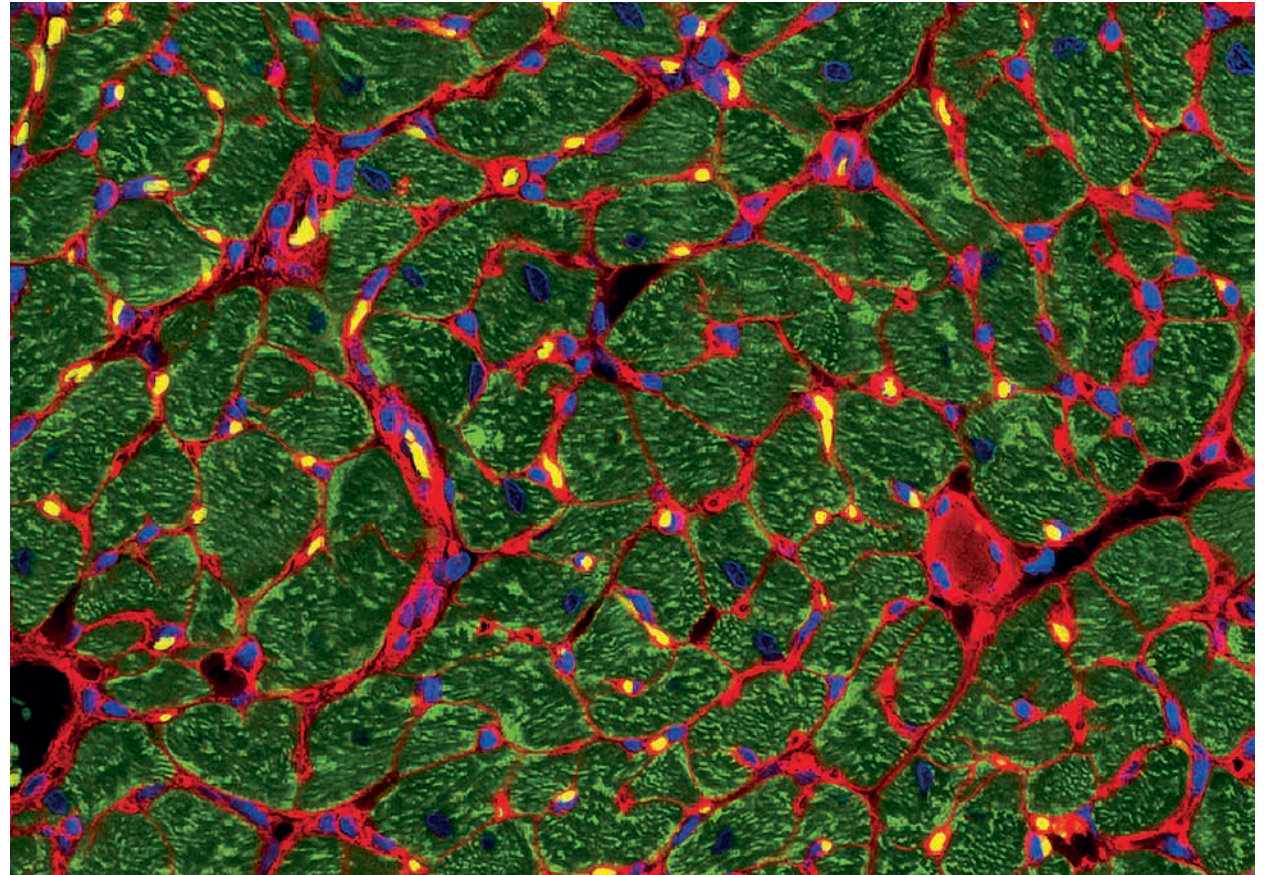
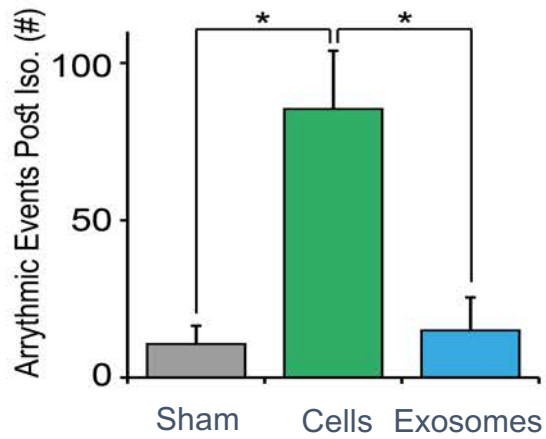
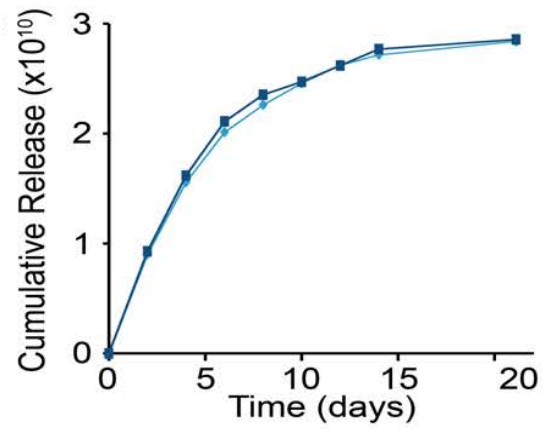


Liu et al, *Nature Biomed Eng* (2018)

Histological data (1 month post-MI):



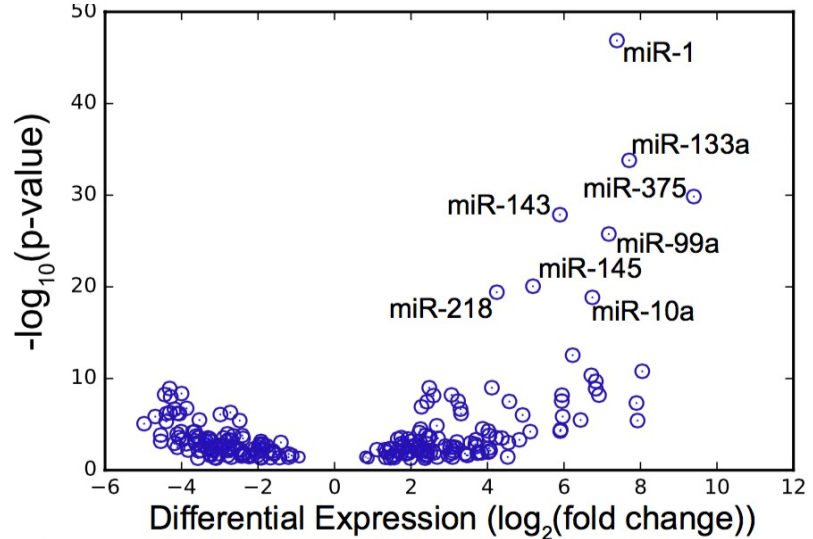
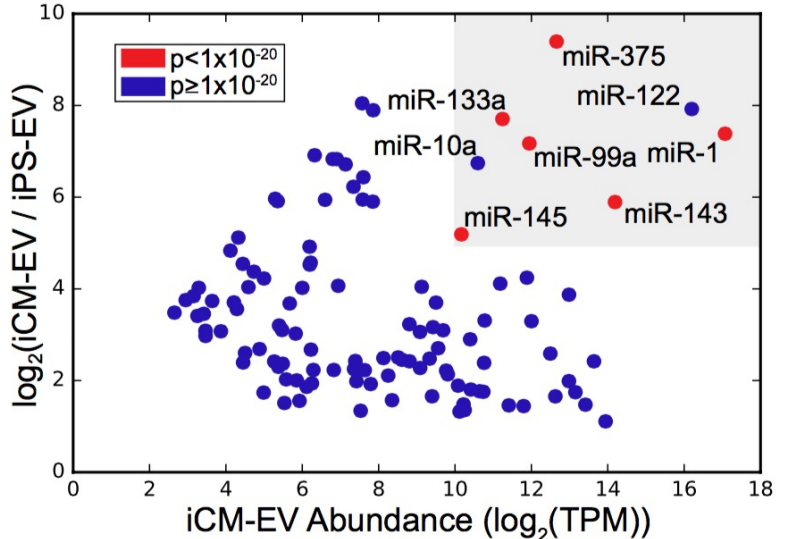
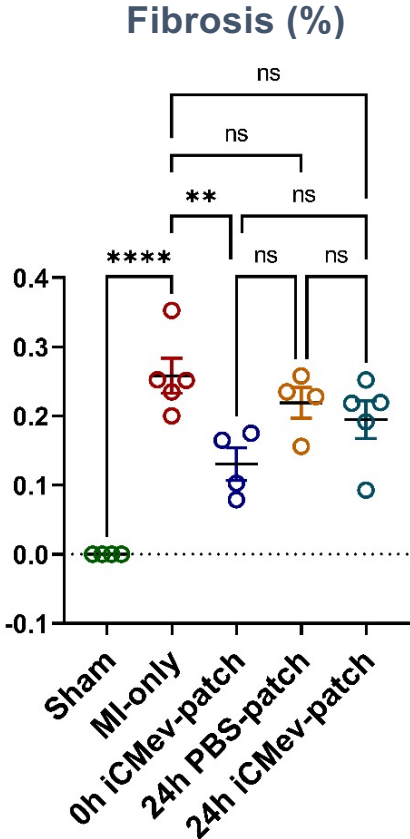
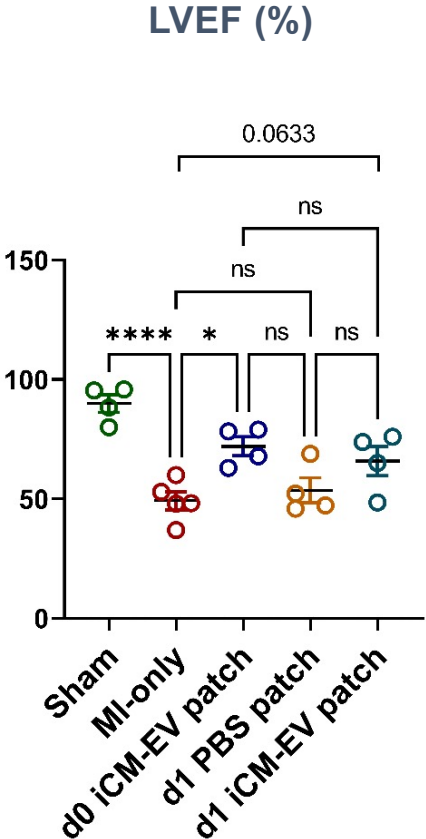
Effects of sustained delivery of exosomes:



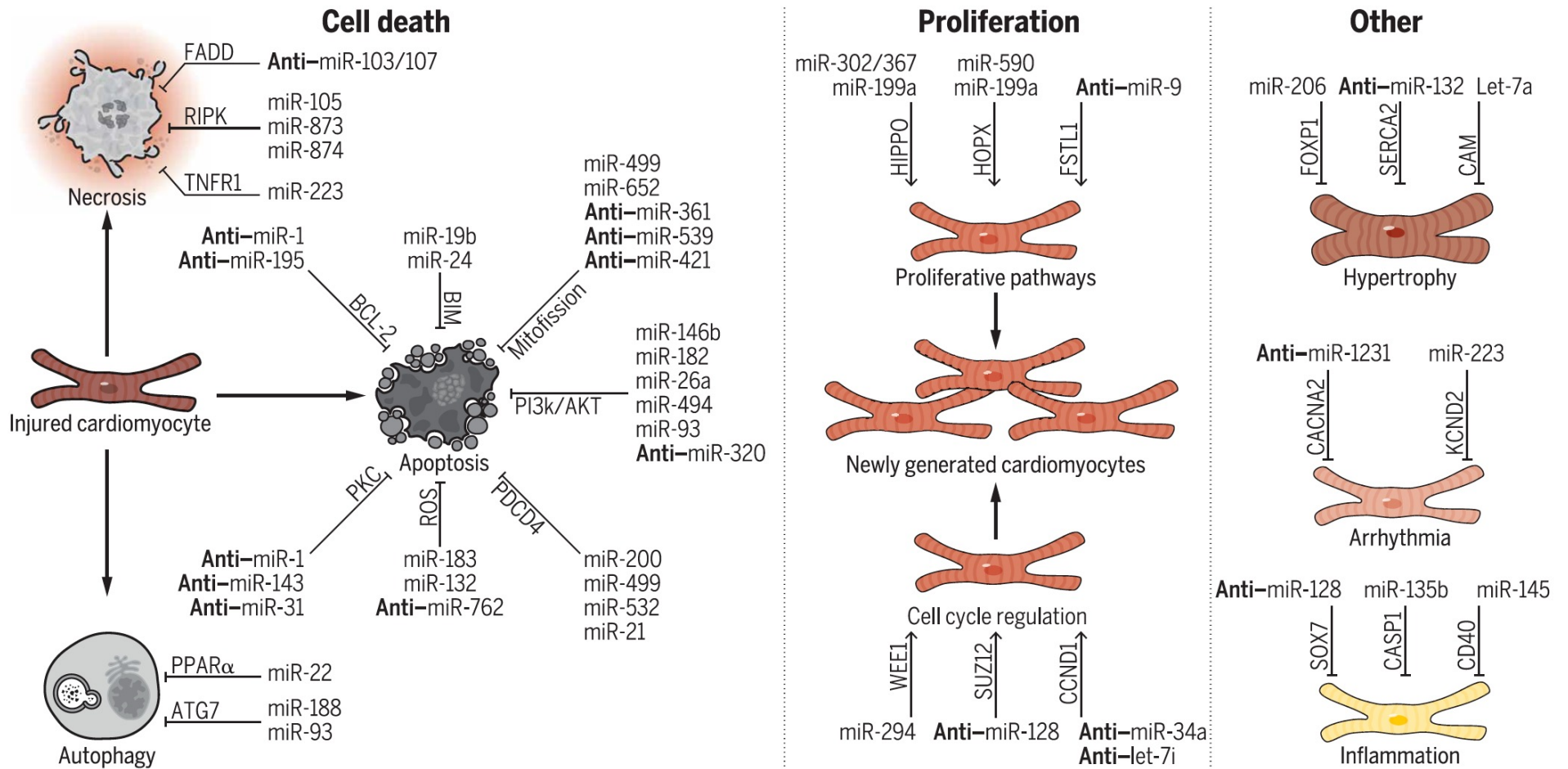
1 month post-MI

Liu et al, *Nature Biomed Eng* (2018)

miRNA cargo:

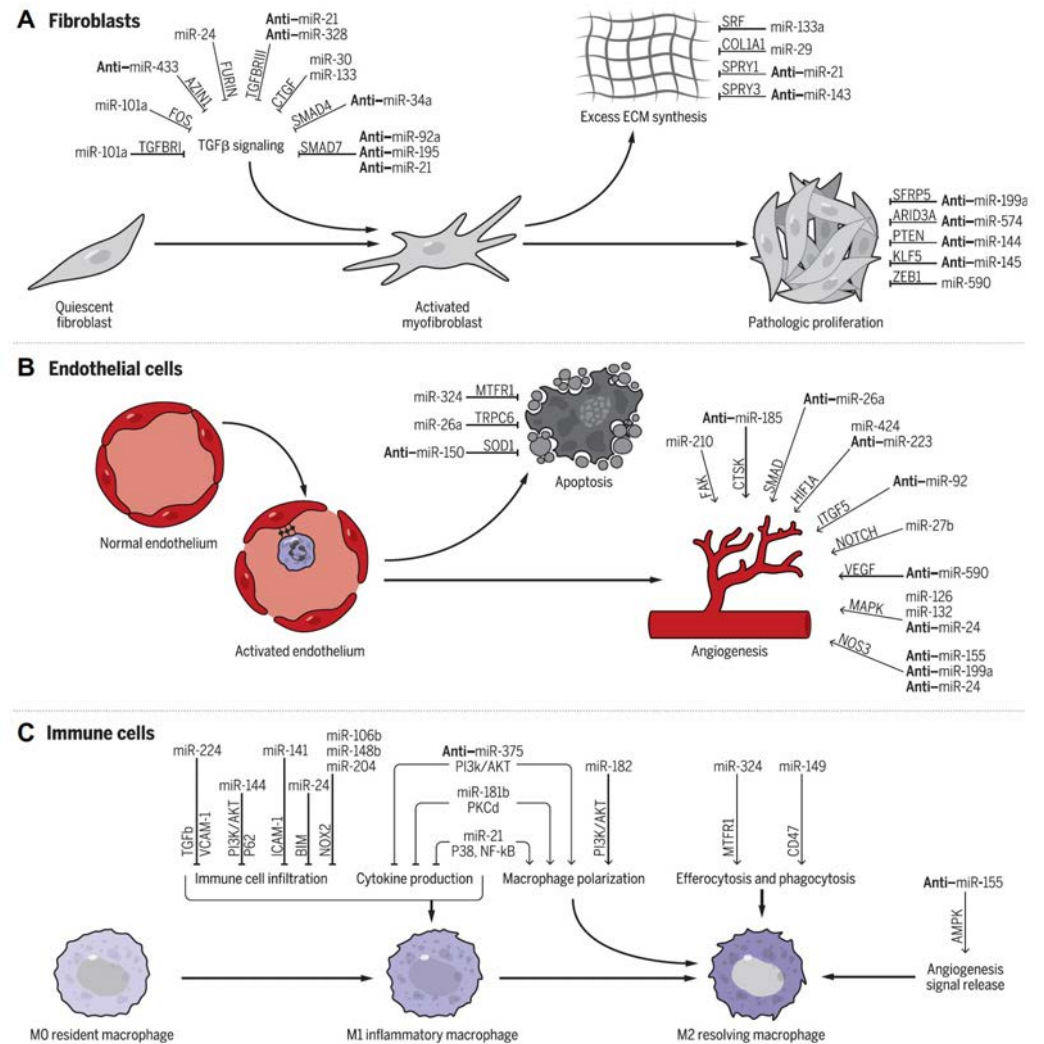


miRNAs targeting CMs post-MI:



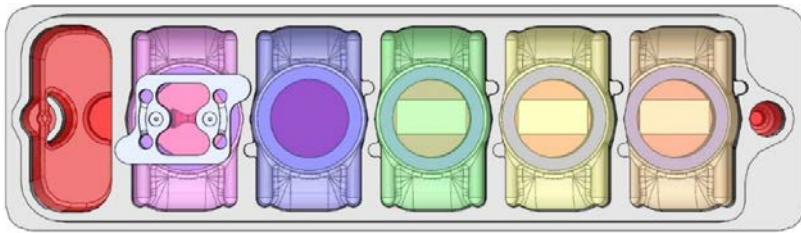
Liu et al, *Science Transl. Medicine* (2020)

miRNAs targeting cardiac fibroblasts, endothelial and immune cells post-MI:

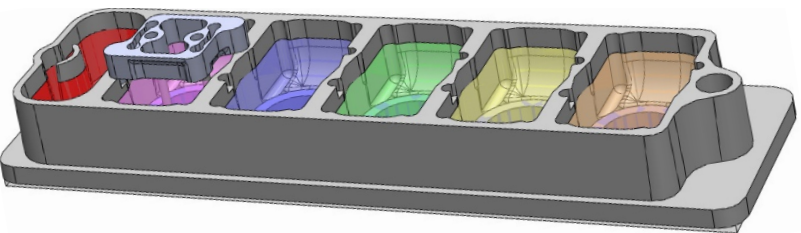


Integrated tissue platforms with vascular perfusion:

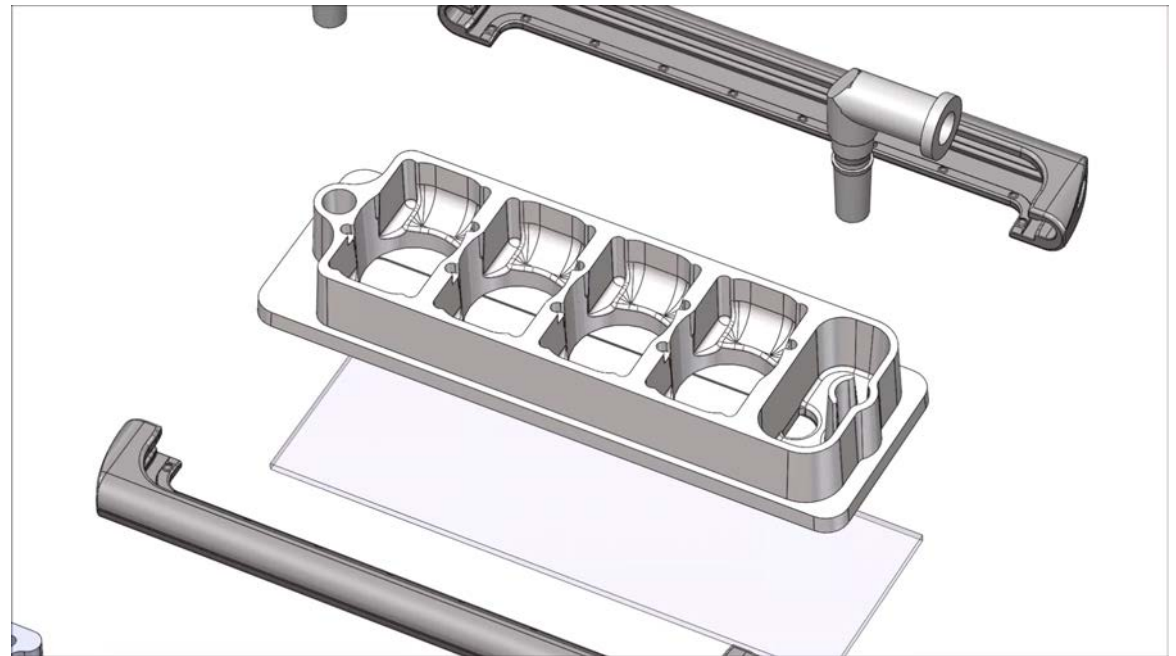
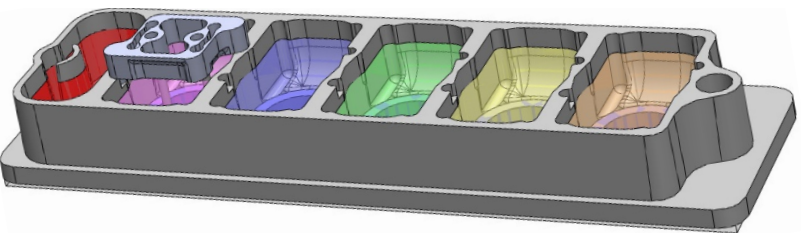
Top view



Bottom view



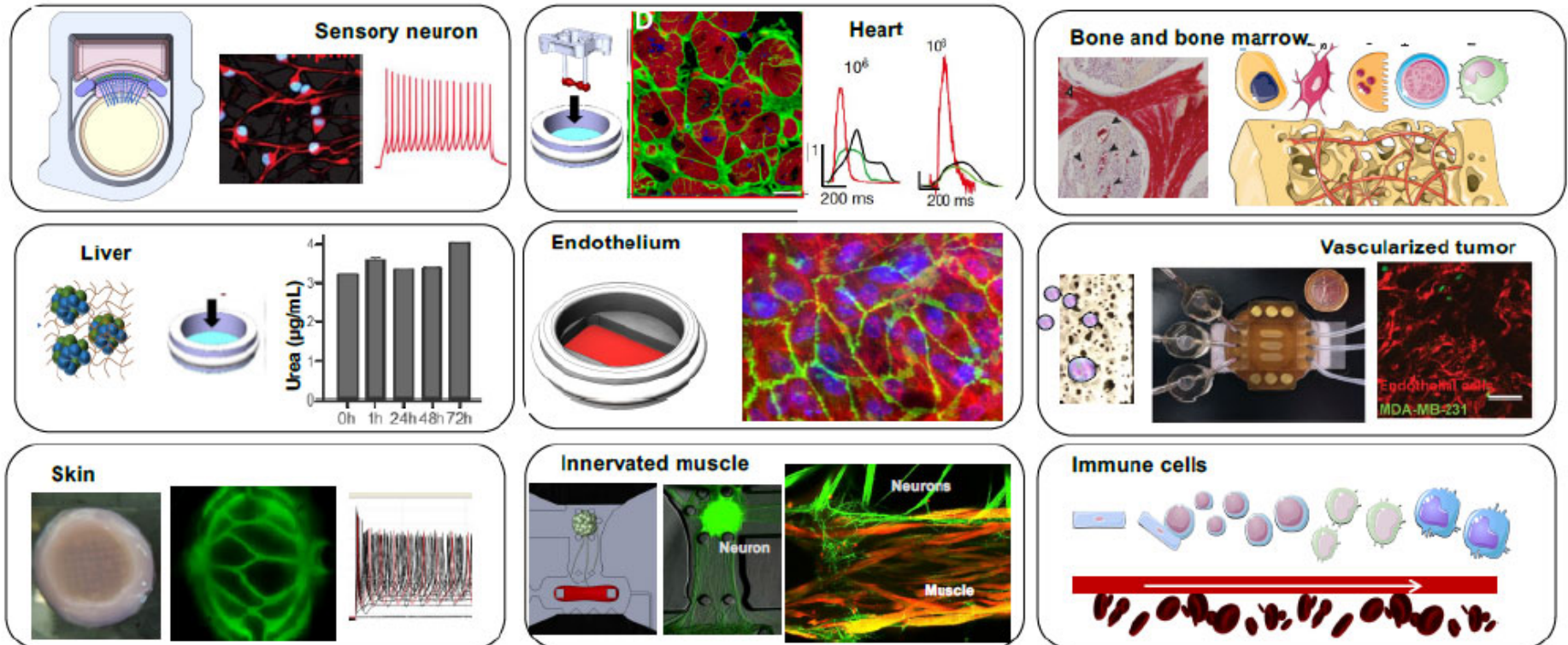
Side view



Key properties:

- **Configurability**
 - To form physiological units; vary tissue scaling and order
- **Biological specificity**
 - Individualized settings, defined genetics (iPSCs)
- **Stable tissue phenotypes**
 - Weeks to months
- **Tissue connectivity**
 - Individual control, links by vascular perfusion
- **Functional readouts in real time**
 - On-line, longitudinal studies
- **Building complexity**
 - Co-culture, vascularization, innervation, immune cells

A menu of matured human tissues:



Summary:

- **Extracellular vesicles:** Biomarkers, cell communication vehicles, therapeutics
- **Model systems:** Cell culture (CM, CF, co-cultures)
Matured engineered tissues
Multi-tissue platforms
- **miRNAs:** Powerful regulators of post-injury remodeling
Affecting different cell populations, in different ways
Divergent effects, beneficial and harmful, on different cells
- **Challenges:** Cell-secreted or bioengineered?
Specifying cargo, dosages and routes of delivery
Better understanding of the effects and mechanisms of action for different cell populations

The lab team:

@GVNlab



Funding:

NIBIB
NCATS
NCI
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NASA
BARDA
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Blavatnik Foundation
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