MSC-released extracellular NAD+ reprograms ischemic senescence in cardiac fibroblasts

Brent M. Bijonowski PhD[1,2,3] and Nicholas A. Kurniawan PhD[1,2]

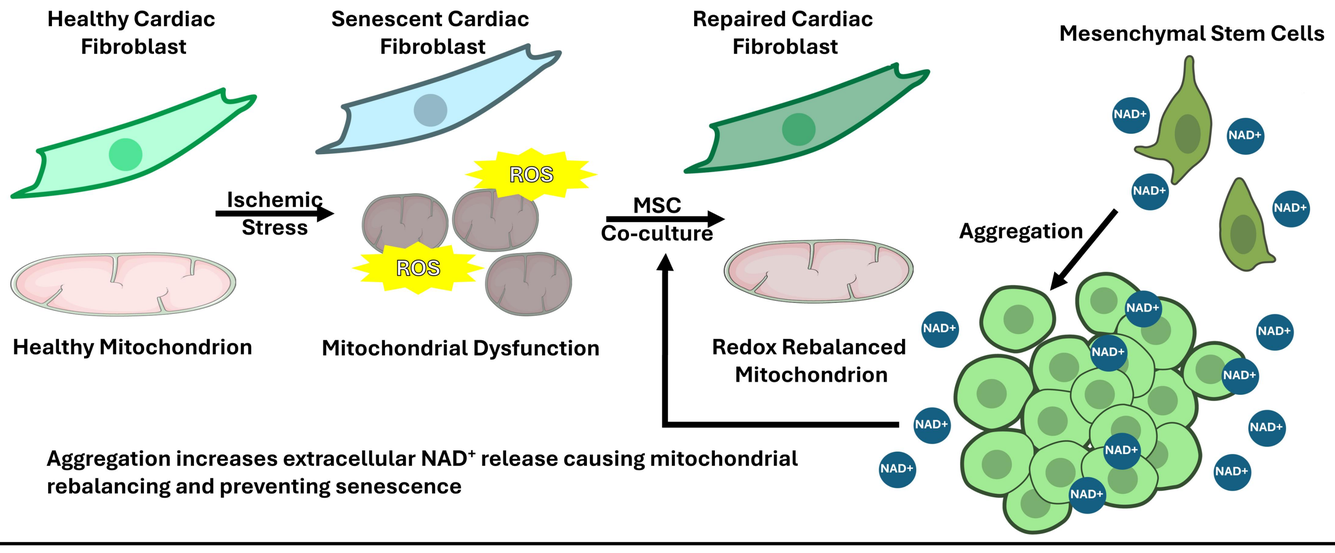
[1] Department of Biomedical Engineering Eindhoven University of Technology, 5612AZ Eindhoven, the Netherlands
[2] Institute for Complex Molecular Systems, Eindhoven University of Technology, 5612AZ Eindhoven, the Netherlands
[3] Biofabrication and Molecular Recognition, International Iberian Nanotechnology Laboratory, 4715-330 Braga, Portugal

Introduction:

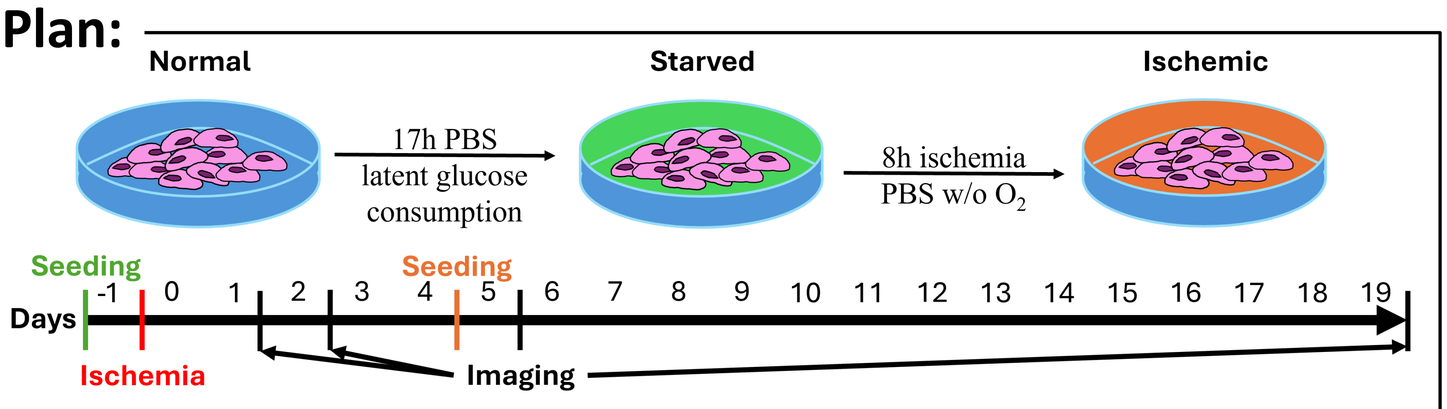
Post myocardial infarction, the heart wall undergoes a reduction in cellular content and an increase in fibrotic matrix deposition as the wall becomes thinner yet stiffer. In conjunction with this, the tissue surrounding the infarct undergoes an induction to senescence.[1]

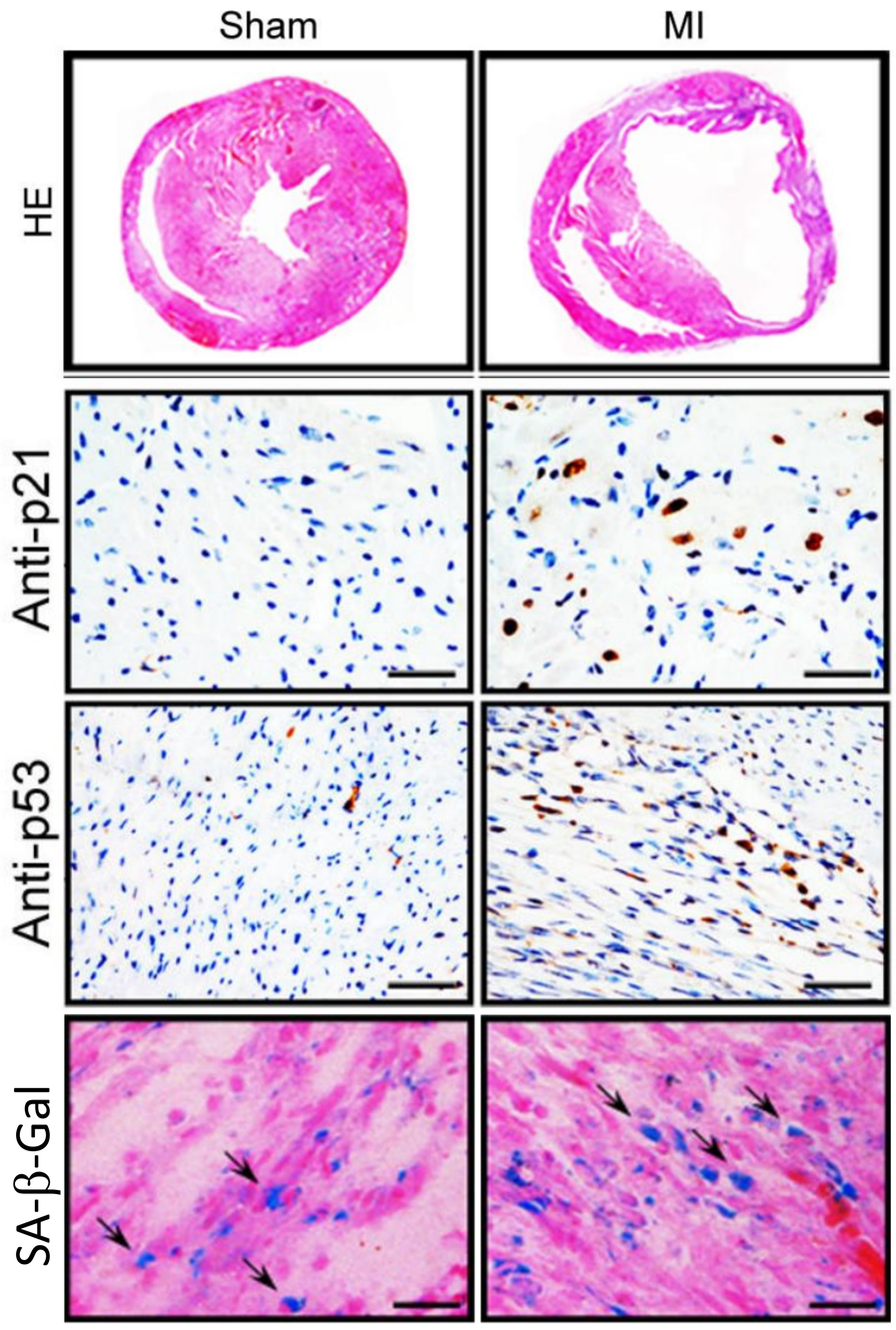
Hypothesis:

MSC-released NAD^+ can be increased by mechanical loading during aggregation and can re-establish redox potential in cardiac fibroblasts following ischemia.



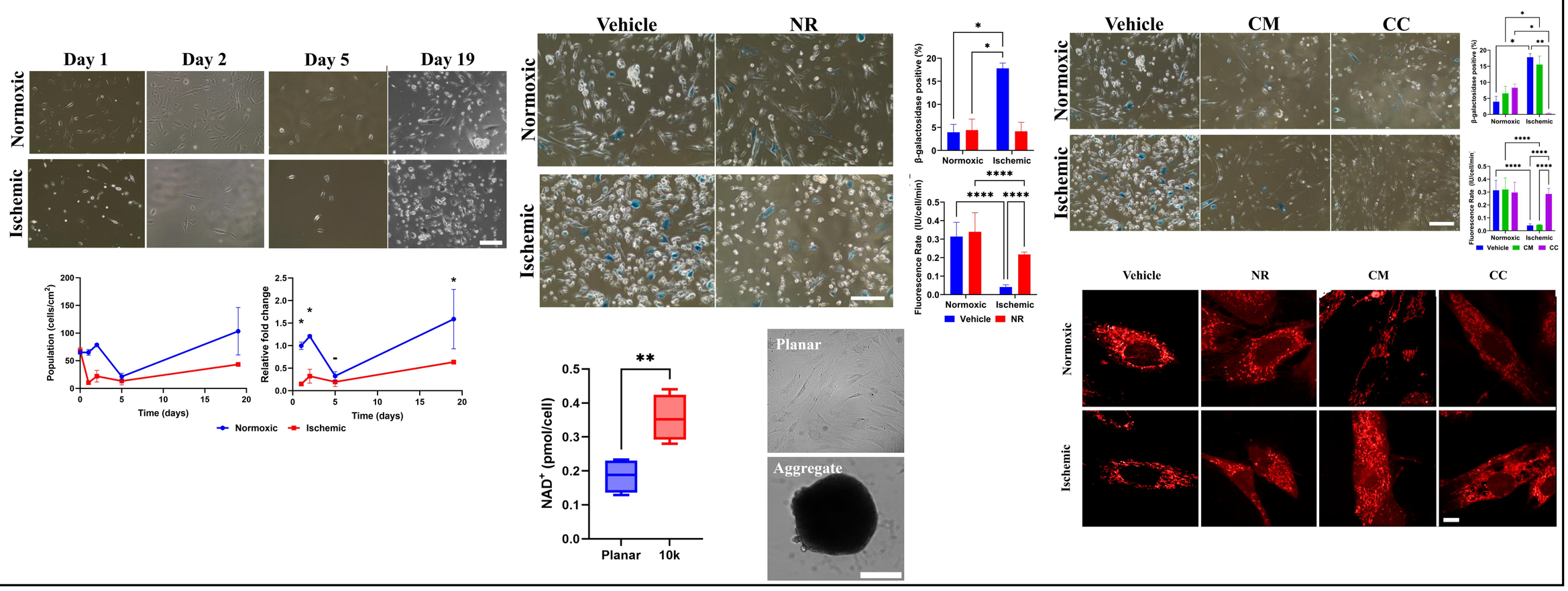
Plan:





[1] Zhu, Fuli, et al. "Senescent cardiac fibroblast is critical for cardiac fibrosis after myocardial infarction." *PloS one* 8.9 (2013): e74535.

Results:



Conclusions:

Ischemia induces senescence, as characterized by reduced proliferation, induced β-gal staining to a similar level as that in the infarct border region[1] and reduced mitochondrial redox potential, along with smaller and rounder mitochondria. These effects can be countered by the addition of either MSC aggregates, due to extracellular NAD^+, or nicotinamide riboside, an NAD^+ precursor.