AAV Targets Cardiac Myofibroblasts Post-Myocardial Infarction

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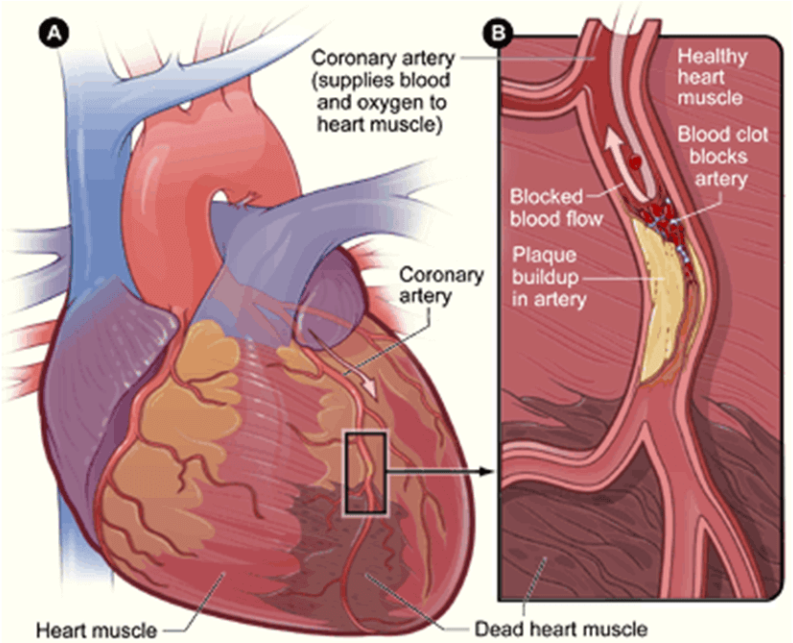
Myocardial infarction (MI)

- The single most common cause of heart failure is myocardial infarction (MI) which results in the irreversible loss of cardiac muscle
- Annually, ~790,000 Americans have a heart attack

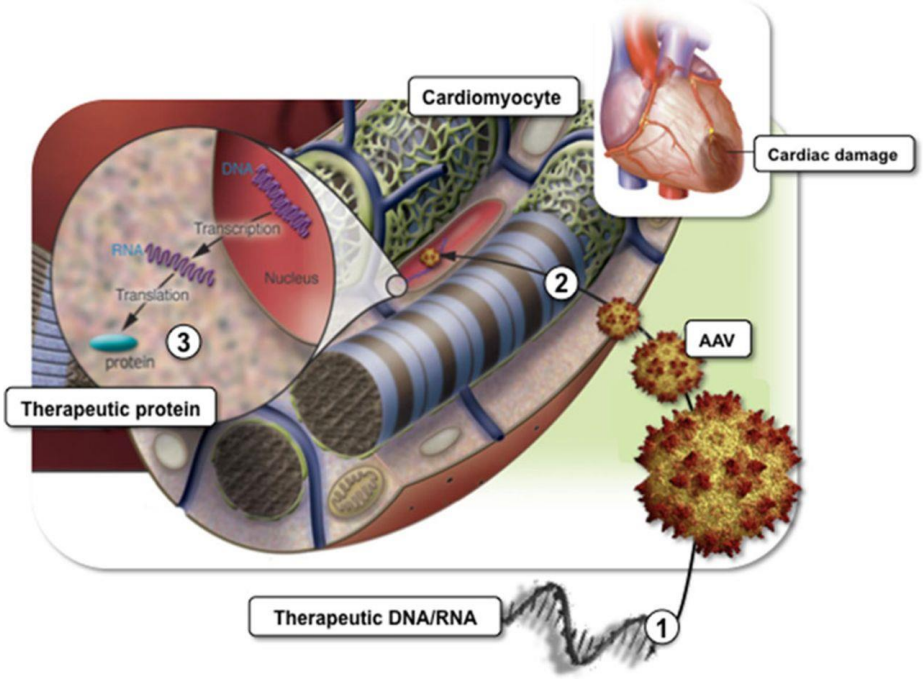
- <u>Clinical Problem</u>:
  - Current therapies can only slow or reverse isolated aspects of heart failure
  - No reliable methods for regeneration or replacement of cardiomyocytes lost to heart attack



AAV9 for Cardiac Regeneration

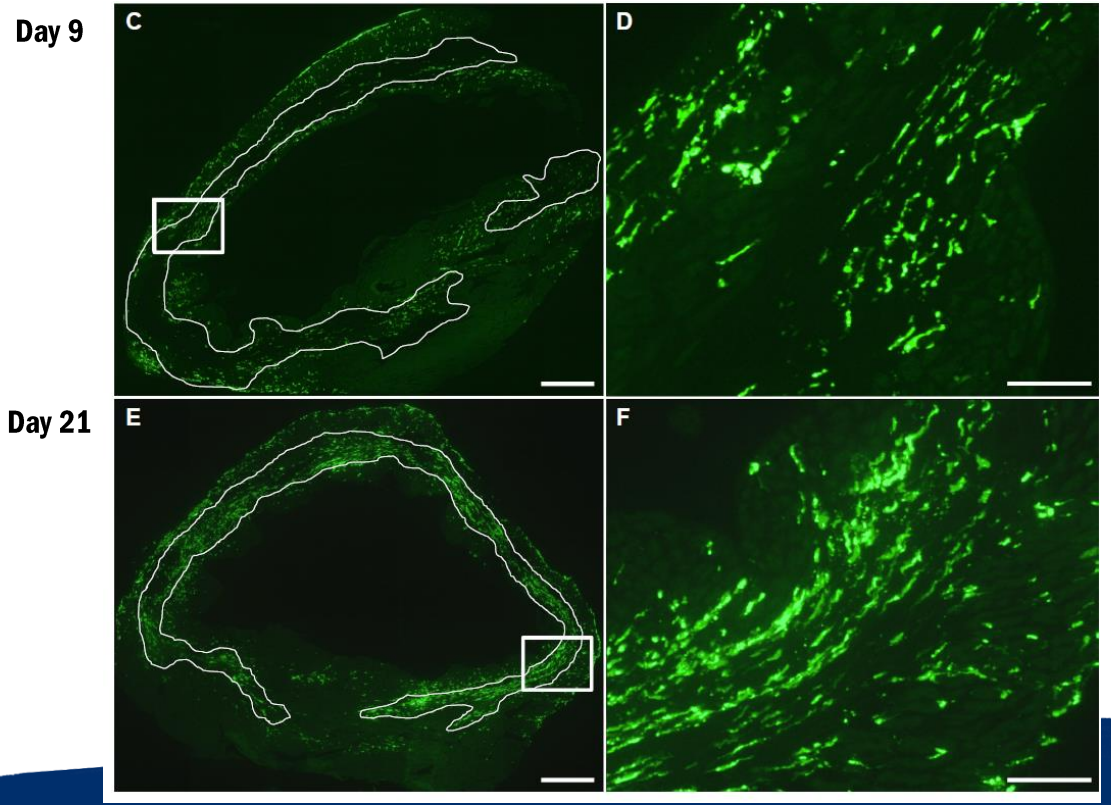
Solution: Researchers at the University of Virginia have developed an AAV9-based gene therapy for cardiac regeneration

- Can be administered via I.V. to curtail left ventricle remodeling, improve cardiac function, and prevent heart failure
- Demonstrate that cardiomyocytes in the post-infarct heart can be genetically-reprogrammed to divide in the infarct border zone at rates adequate to support the regeneration of lost muscle tissue



Effective Delivery of AAV9 and Long Term Gene Expression

Delivery of AAV9 into Flox-GFP expressing mice. Imaged on Day 9 and Day 21 post-MI to demonstrate effective delivery and long term gene expression.



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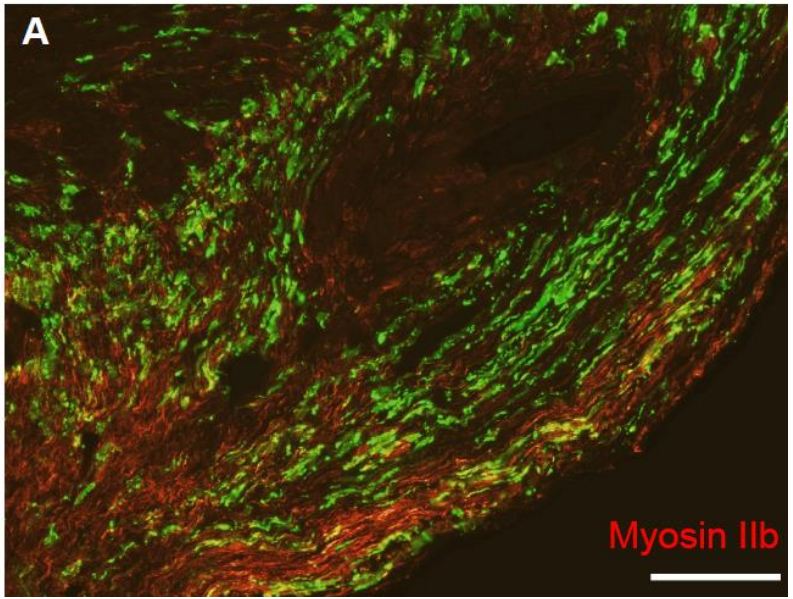
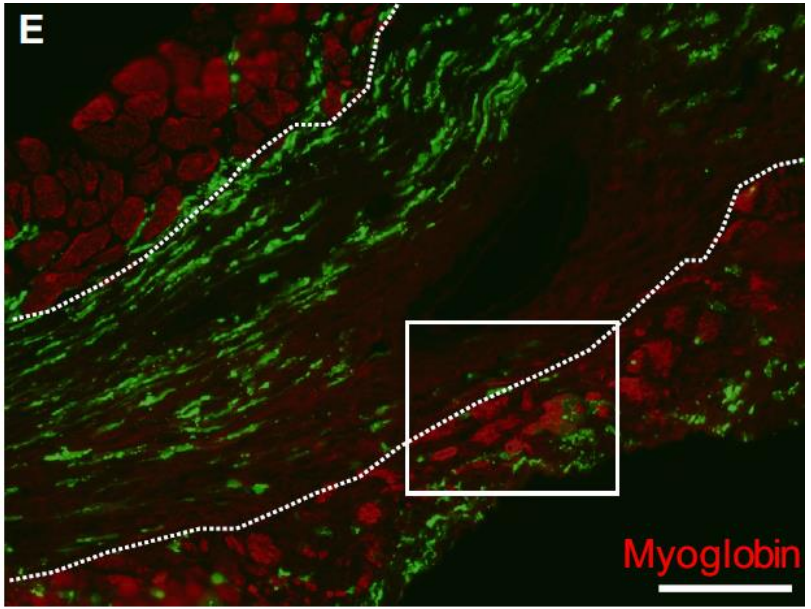
GFP+ Cells in the Infarct/Border Zones Express Myofibroblast Markers





The infarct/border zones of Flox-GFP mice treated with AAV9 analyzed via immunofluorescence show expression of myofibroblast markers, myosin IIb and myoglobin (day 21 post-MI).

Relevant Publications

- Gene Therapy. 2016 Feb 23, 469-178. **French BA**, et al.
- PLoS One. 2013 Sep 24;8(9):e75894. **French BA**, et. al.
- Circ Cardiovasc Imaging. 2013 May 1;6(3):478-86. **French BA**, et. al.
- J Gene Med. 2012 Sep-Oct; 14(9-10):609-20. **French BA**, et. al.

Intellectual Property

- UVA Tech ID: FRENCH-TRANS
  - Title: Compositions and methods for adeno-associated virus mediated gene expression in myofibroblast-like cells
  - PCT Application PCT/US2017/020113 filed March 1, 2017