

2011

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Stacey House

Washington University School of Medicine in St. Louis

Carla Weinheimer

Washington University School of Medicine in St. Louis

Attila Kovacs

Washington University School of Medicine in St. Louis

David Ornitz

Washington University School of Medicine in St. Louis

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Recommended Citation

House, Stacey; Weinheimer, Carla; Kovacs, Attila; Ornitz, David, "Cardioprotection by endogenous fibroblast growth factor 2 in cardiac ischemia-reperfusion injury in vivo" (2011). Conference Abstracts and Posters. Paper 7. http://digitalcommons.wustl.edu/em_conf/7

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Cardioprotection by Endogenous Fibroblast Growth Factor 2 in Cardiac Ischemia- Reperfusion Injury *In Vivo*

**Stacey House MD PhD, Carla Weinheimer MS,
Attila Kovacs MD, and David Ornitz MD PhD**

**Washington University in St. Louis School of
Medicine**

Society for Academic Emergency Medicine
Great Plains Regional Research Forum
St. Louis, MO. September 2011
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Fibroblast Growth Factor 2

22 different FGF family members (10 in heart)

FGF2 or basic FGF – first member of the FGF family identified, expressed fairly ubiquitously

FGF2 expressed in all developmental stages of heart; found in cardiomyocytes, fibroblasts, endothelium

FGF2 known functions:

Hematopoiesis

Angiogenesis

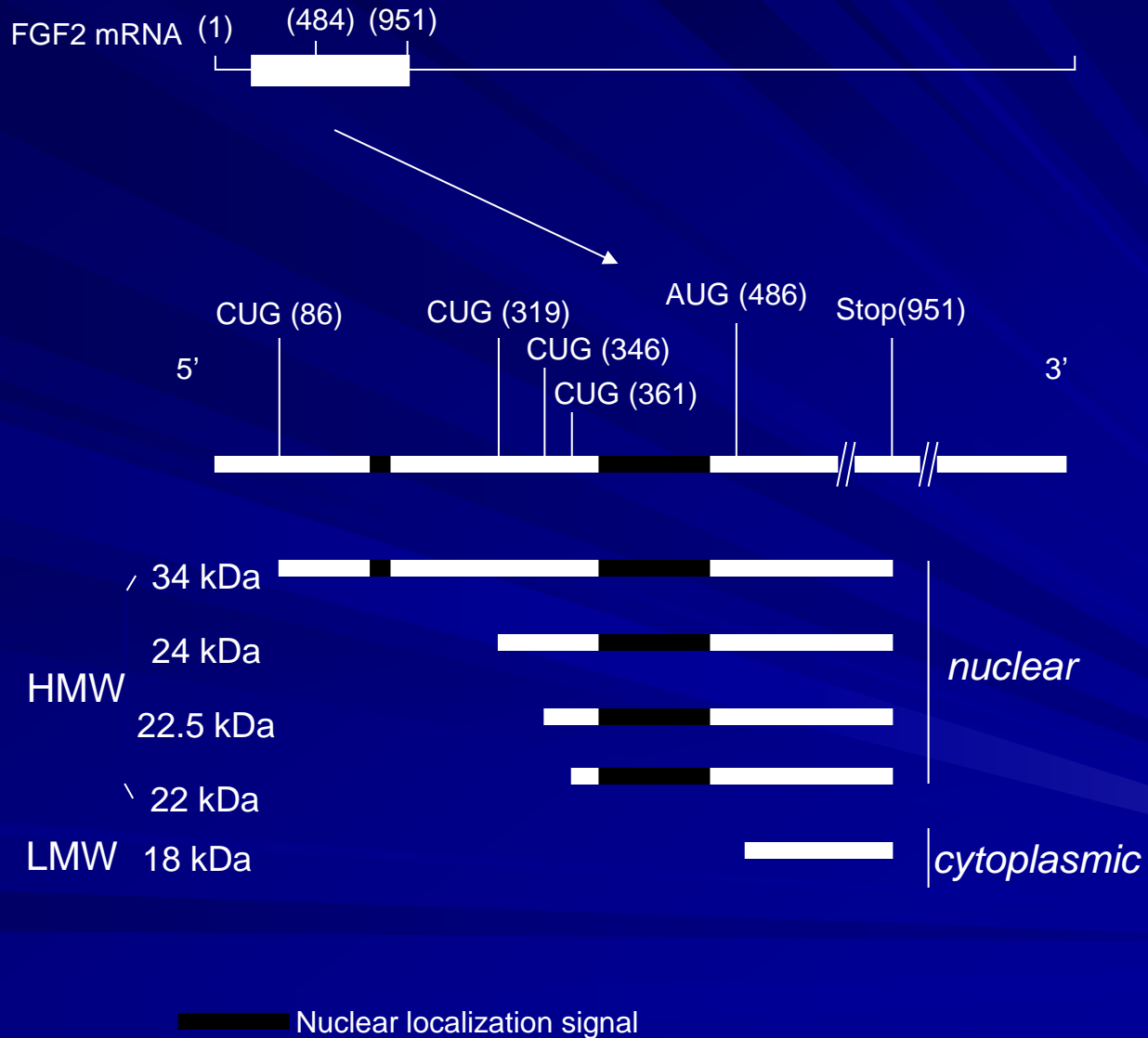
Wound Healing

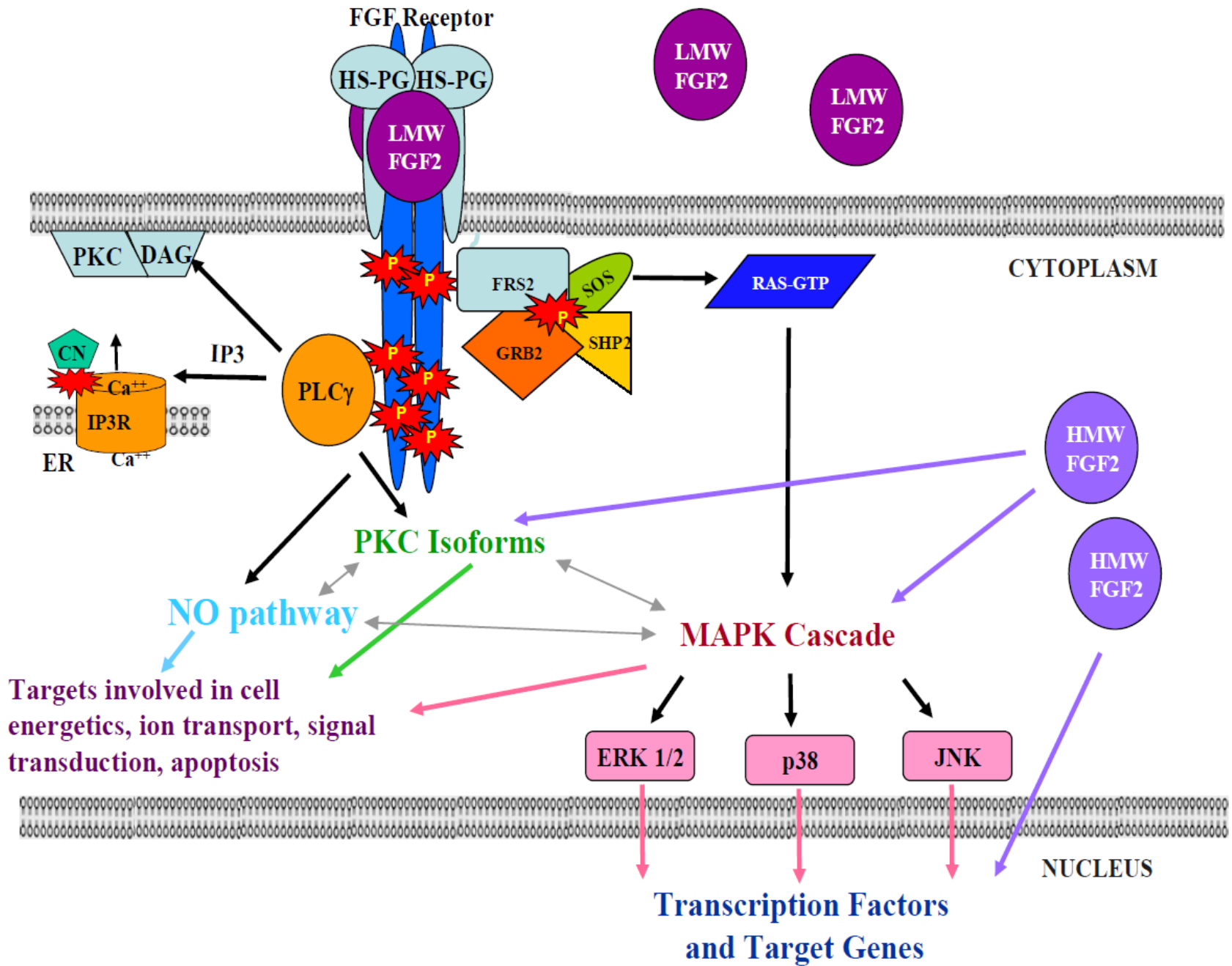
Mesoderm Induction

Cell Survival/Death

Cardiac Hypertrophy

FGF2 Isoforms





FGF2 and Cardioprotection

Isolated work-performing global low-flow IR injury-

Fgf2 KO have worsened post-ischemic function

Cardiac-specific human FGF2 Tg have

- improved post-ischemic cardiac function

- reduced infarct size

FGF2-induced cardioprotection mediated through PKC, MAPK, and NOS signaling

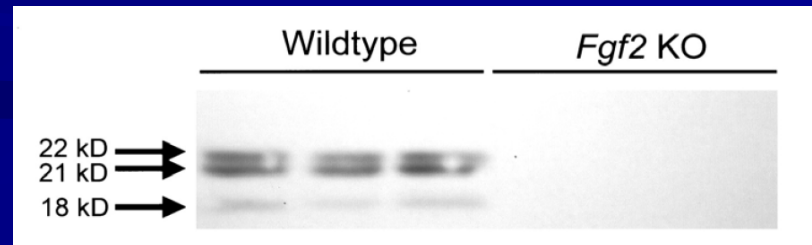
What is the *in vivo* cardioprotective efficacy of FGF2?

FGF2 Knockout

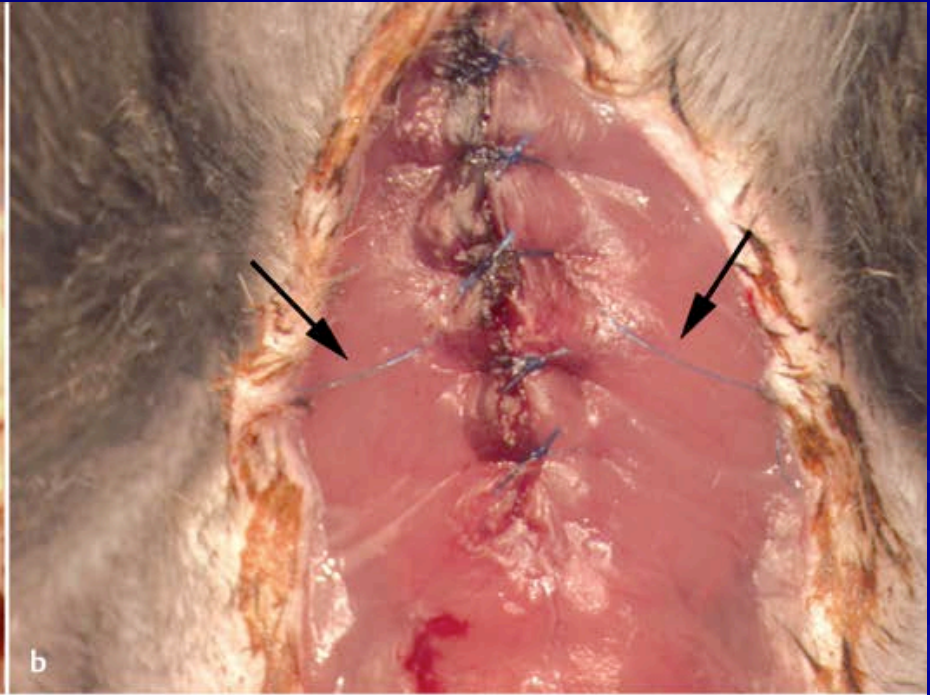
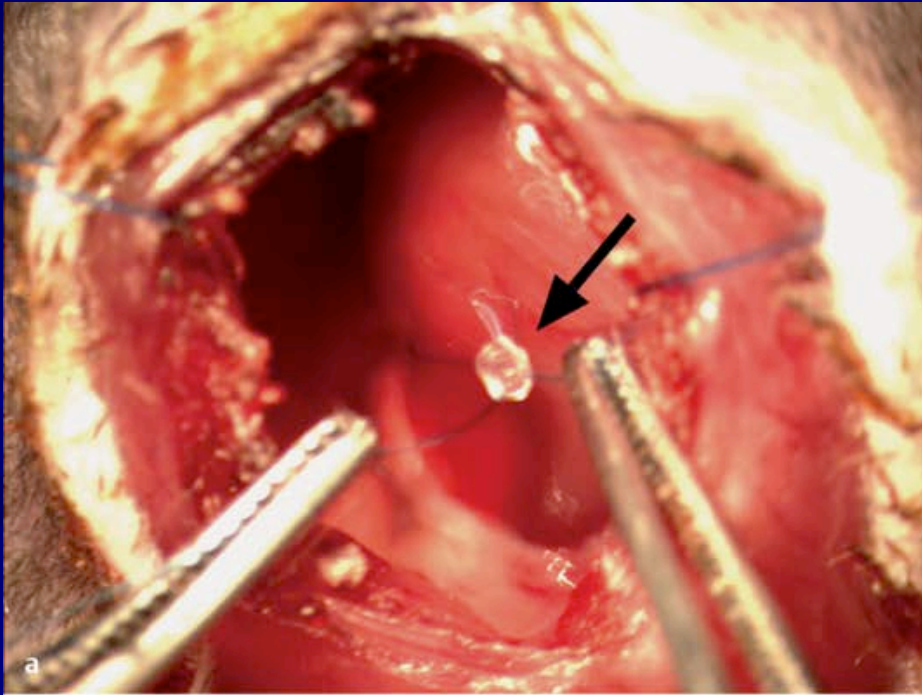
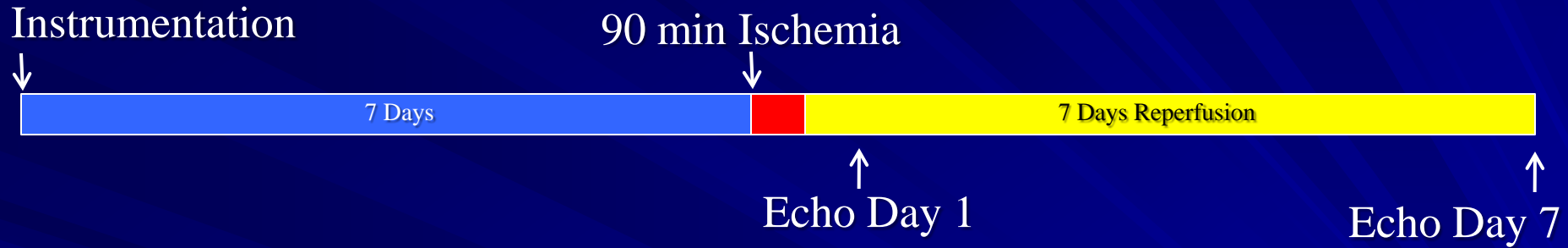
Targeted ablation of all isoforms of FGF2

Viable and fertile

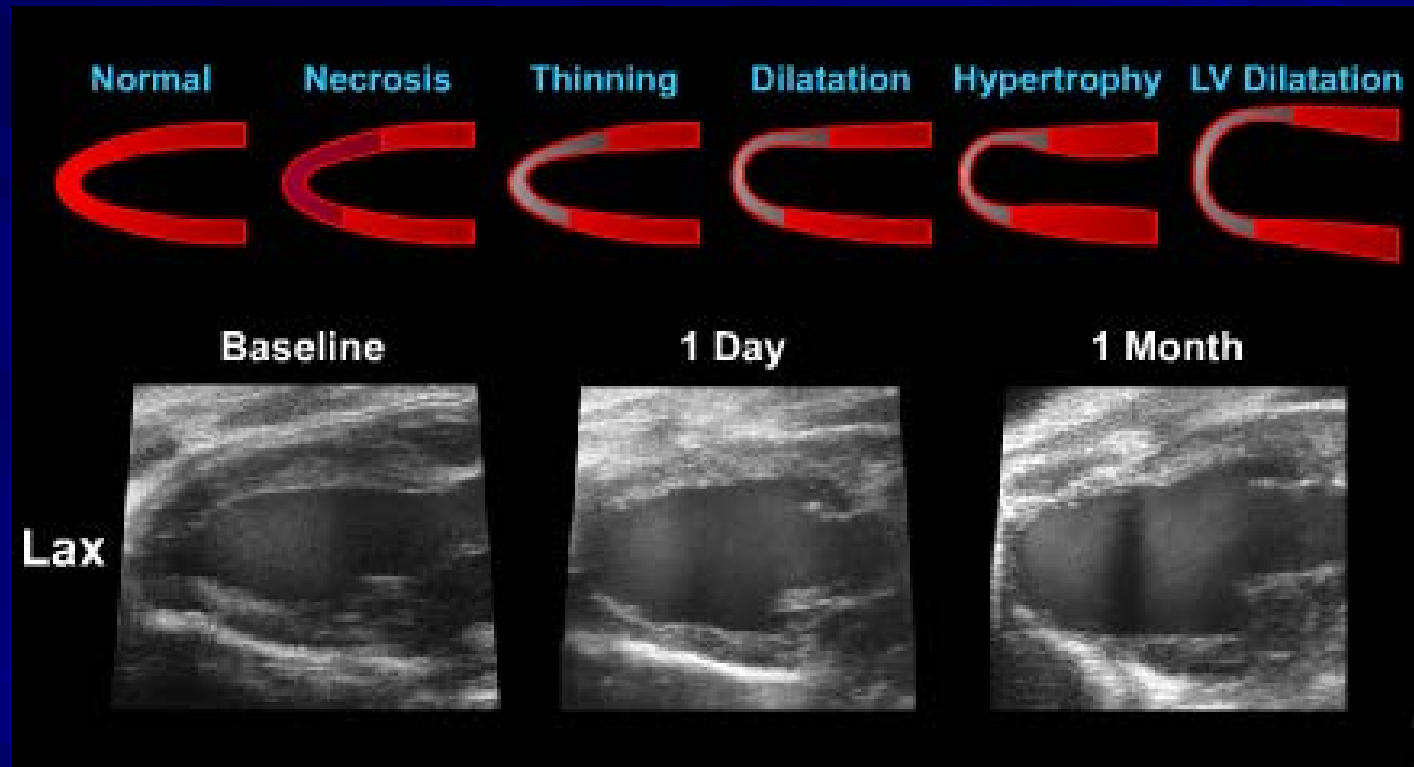
No difference from wildtype with respect to cardiac morphometry, function, or vessel density



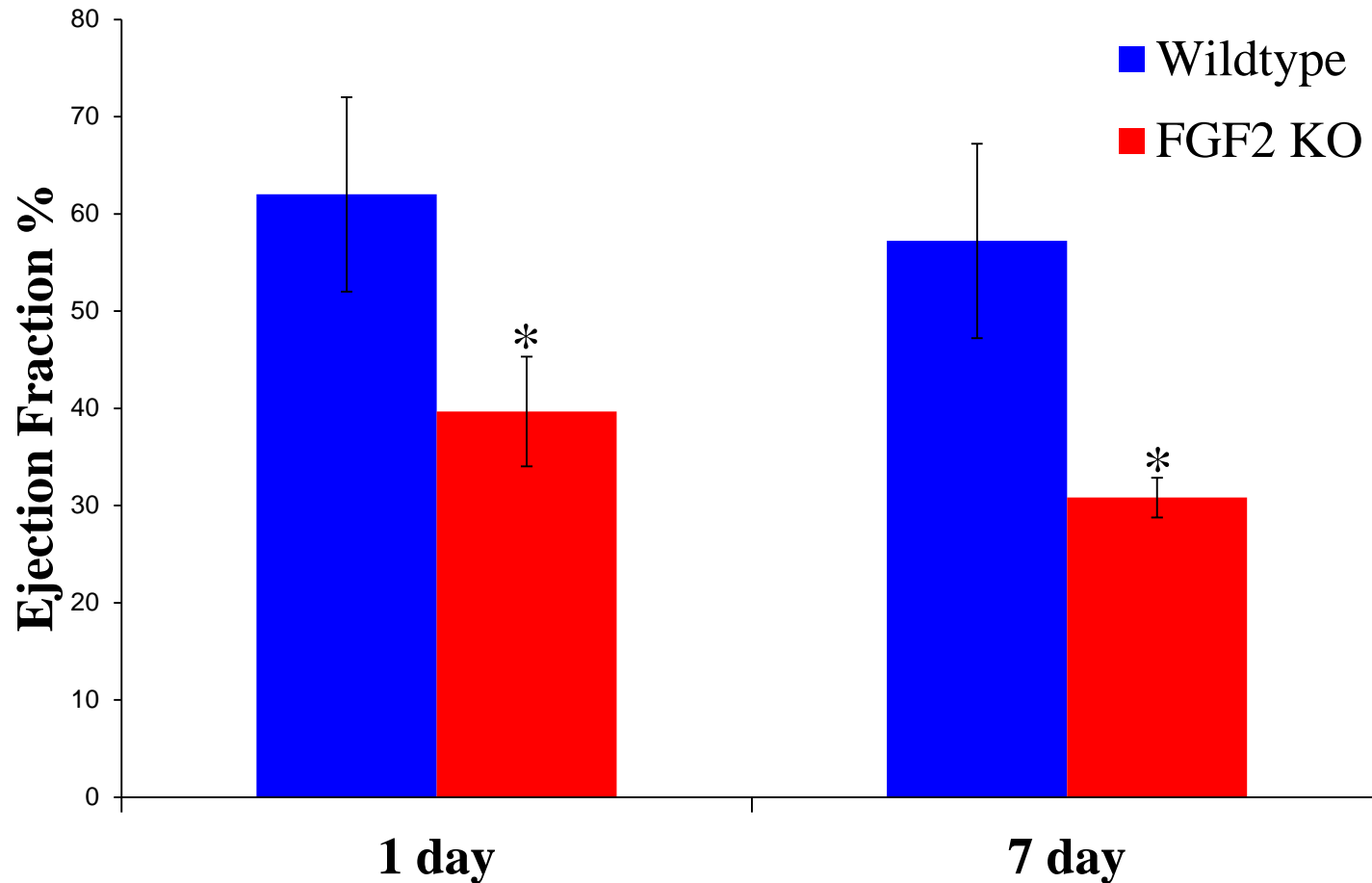
Closed Chest Ischemia-Reperfusion



Echo Determination of Ejection Fraction

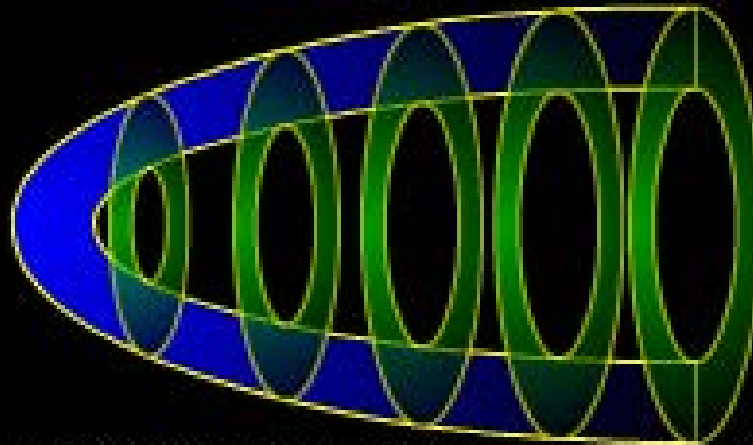


Endogenous FGF2 in Cardiac Function Post IR Injury



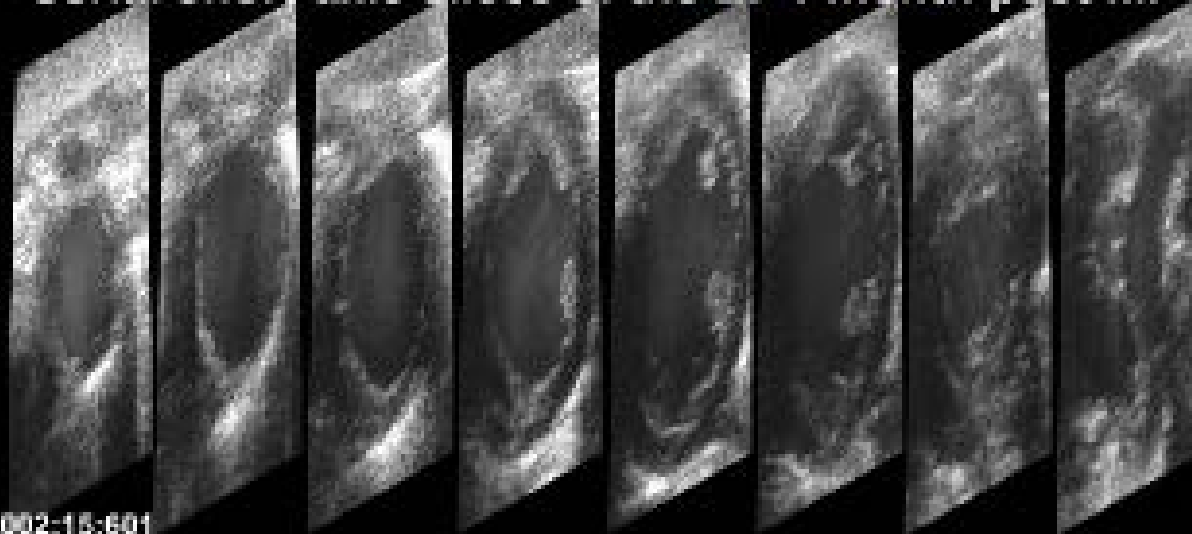
Echo Analysis of LV Wall Motion Abnormalities

Lax



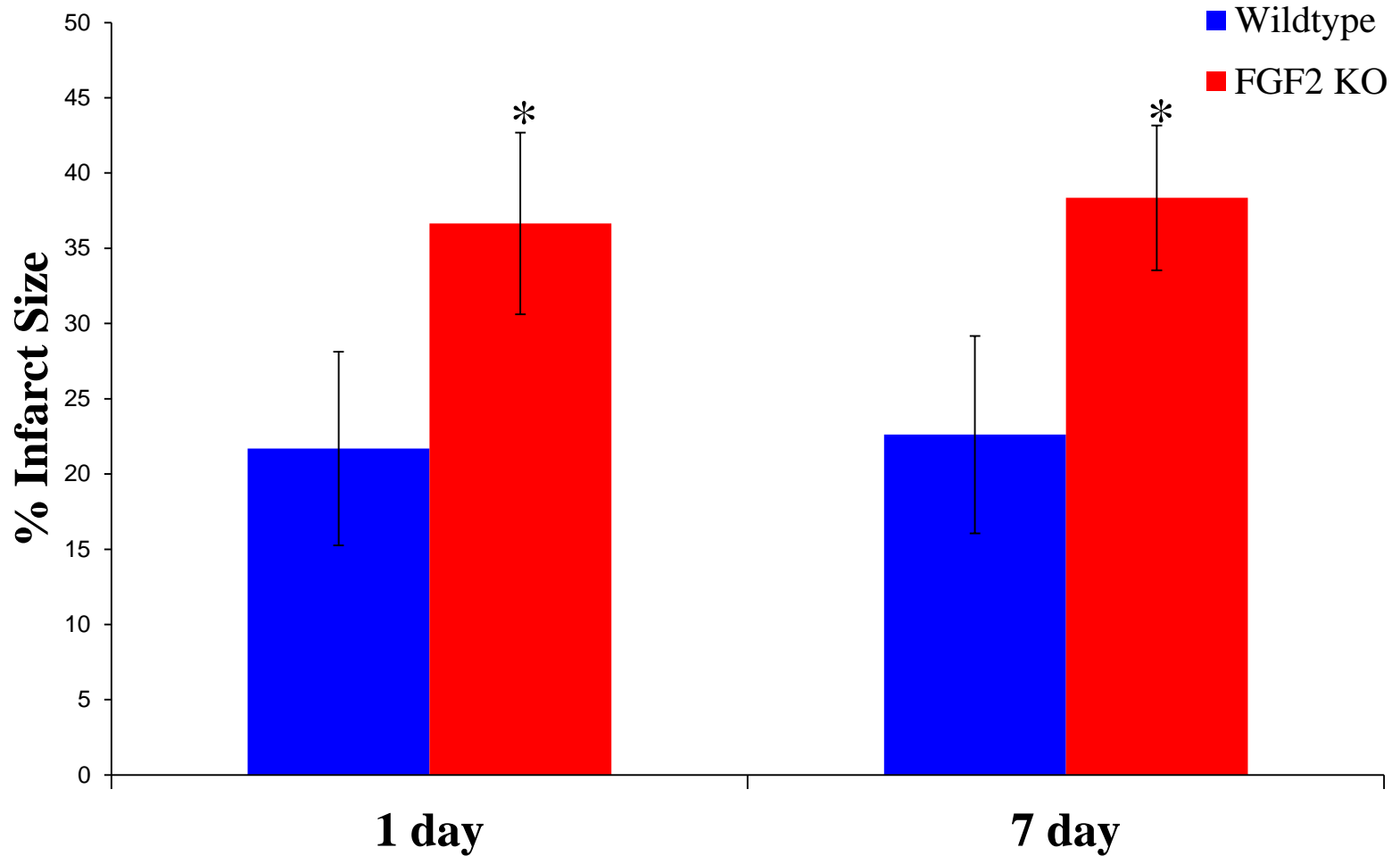
Serial short-axis slices of the LV 1 month post-MI

Apex



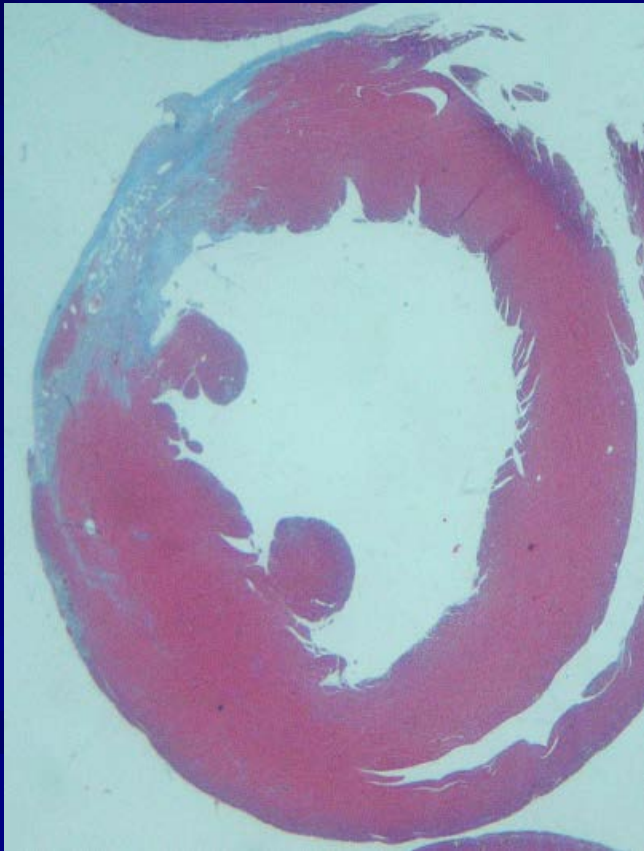
Base

Echo Analysis of LV Wall Motion Abnormalities

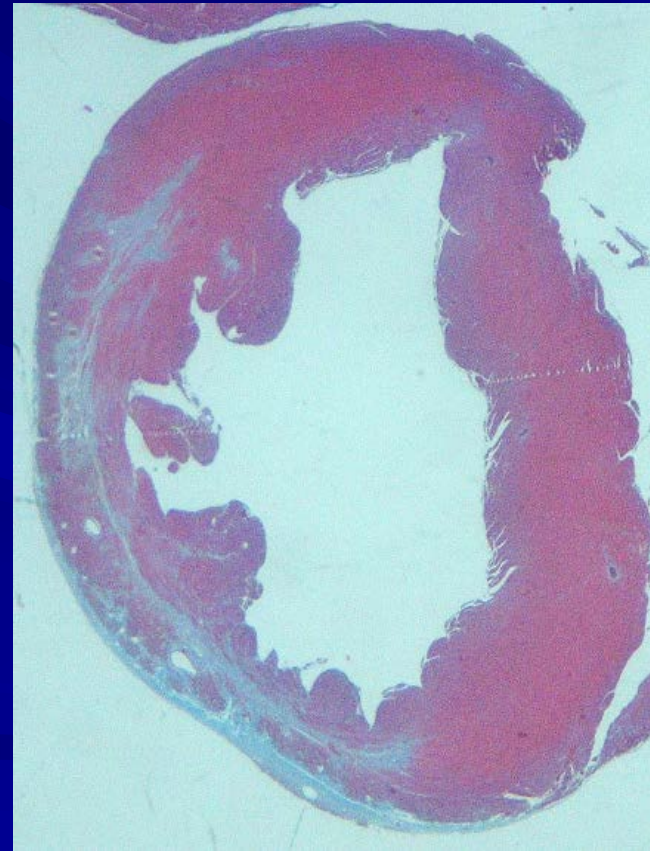


Trichrome Staining of Fibrosis

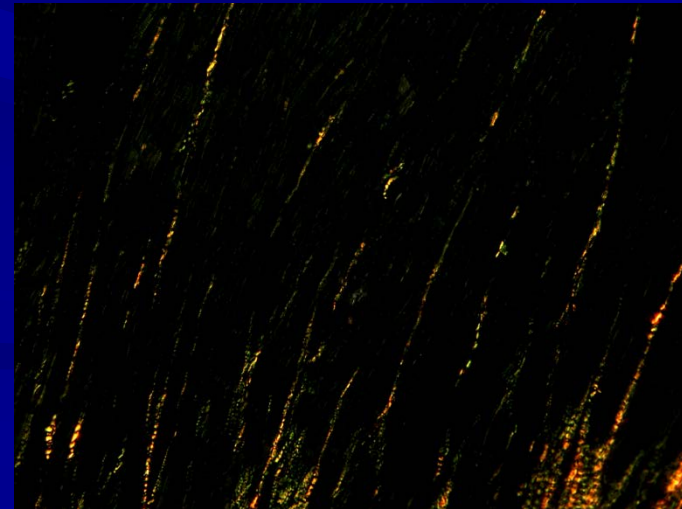
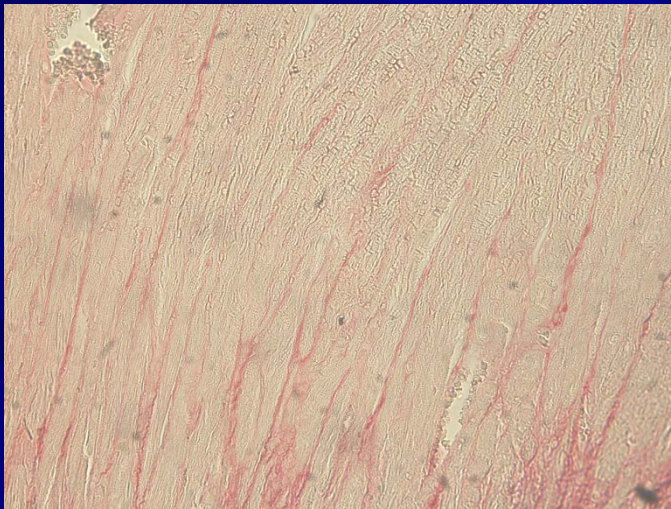
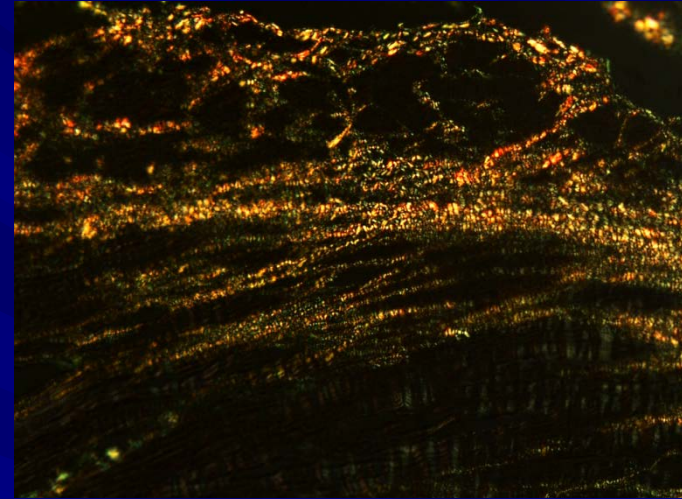
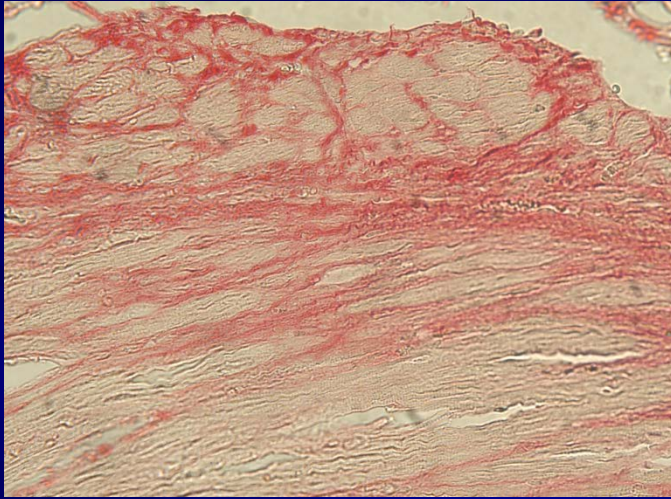
Wildtype



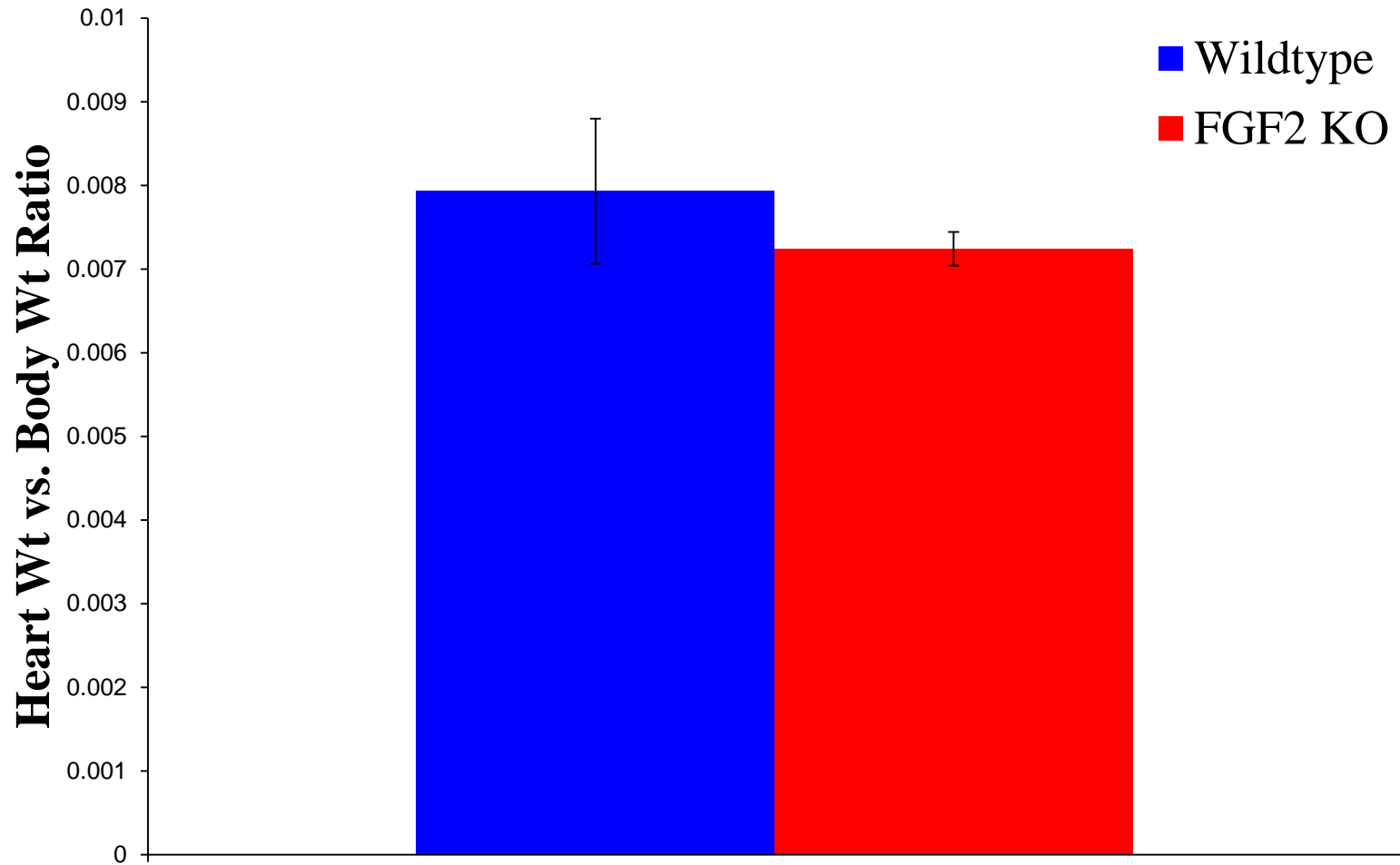
Fgf2 KO



Picosirius Red Stain of Collagen Fibrils

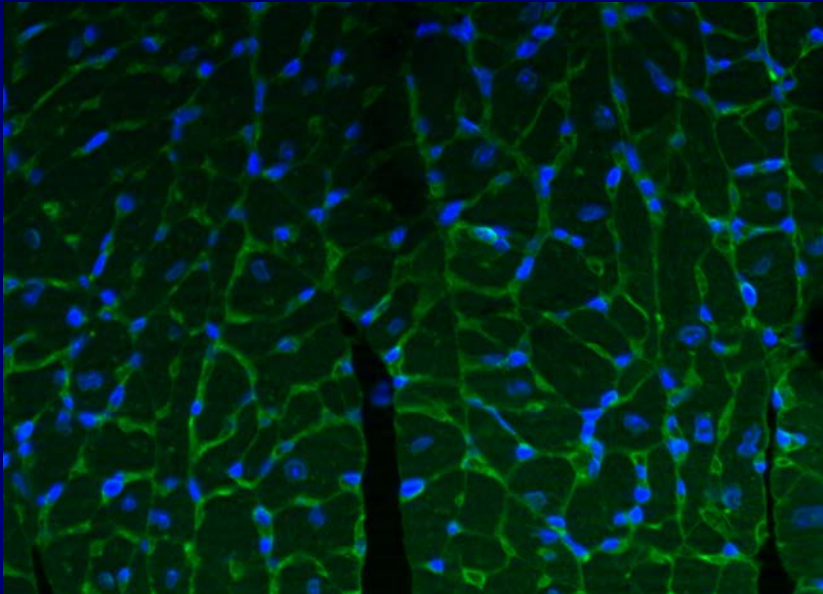


Endogenous FGF2 Effect on Cardiac Hypertrophy

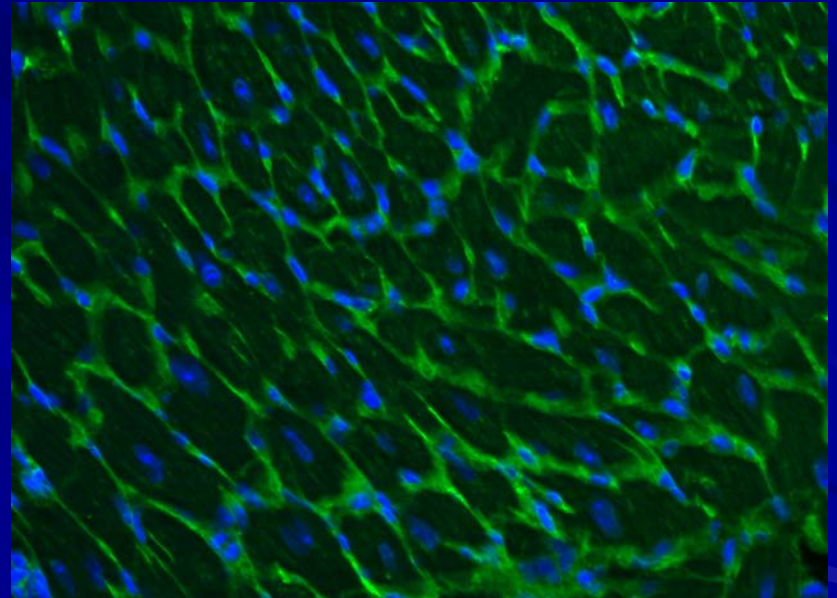


Myocyte Area Staining

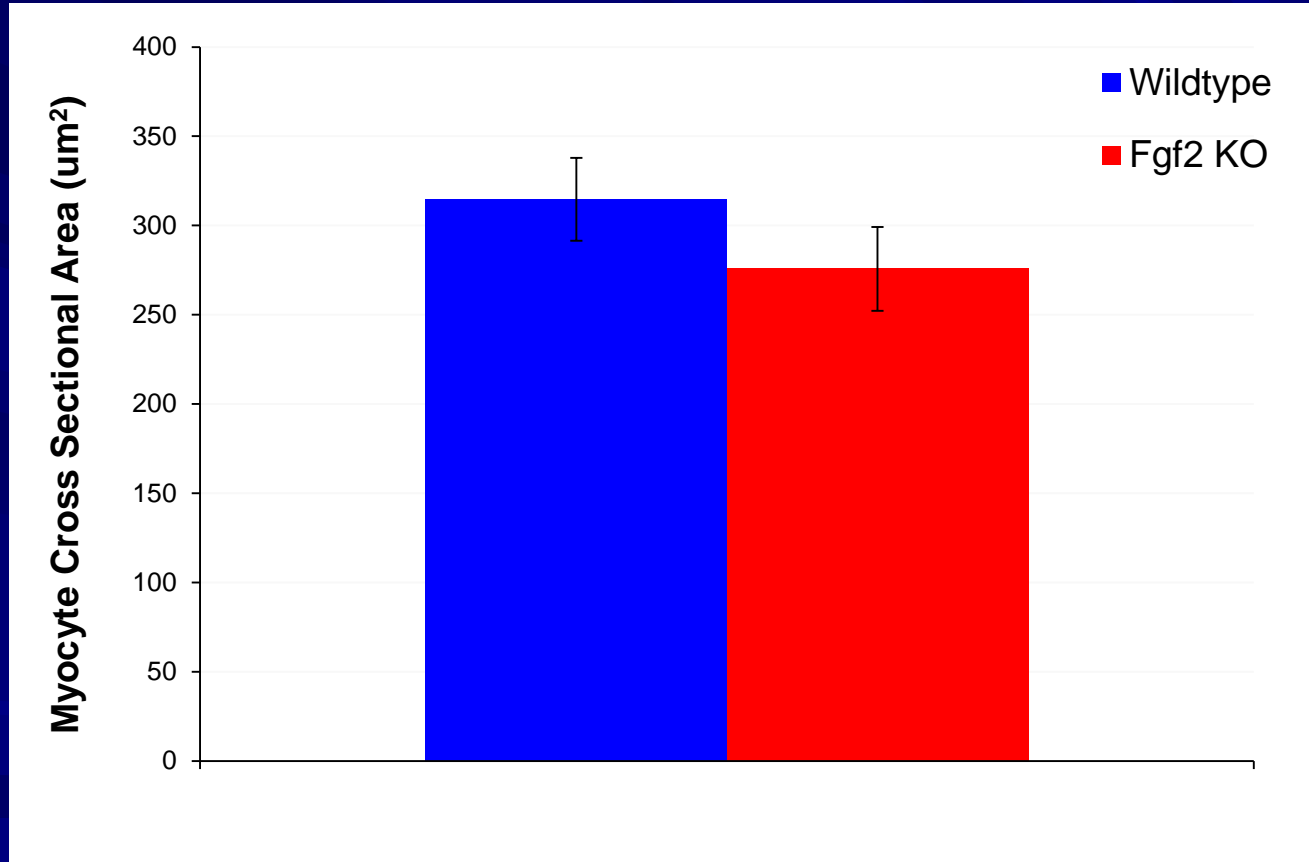
Wildtype



Fgf2 KO

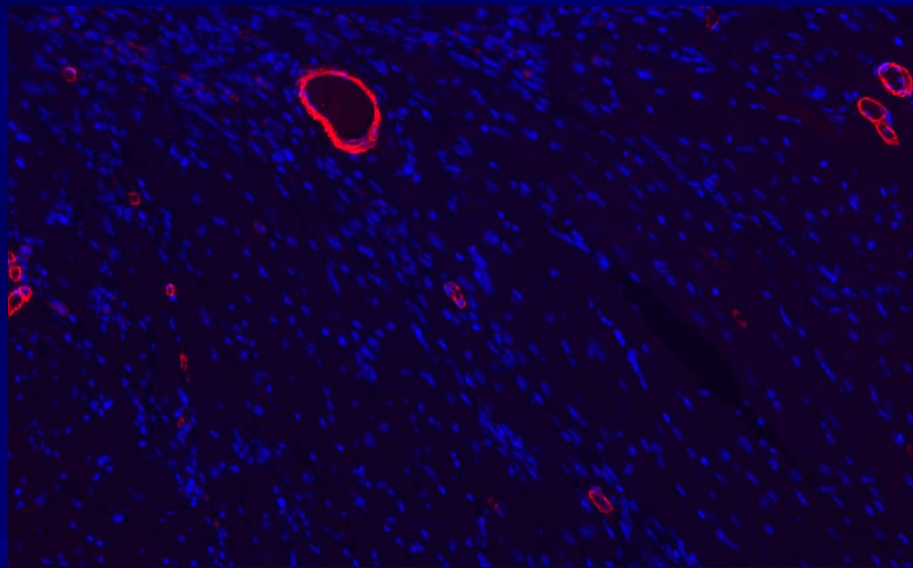


Myocyte Cross Sectional Area Post IR Injury

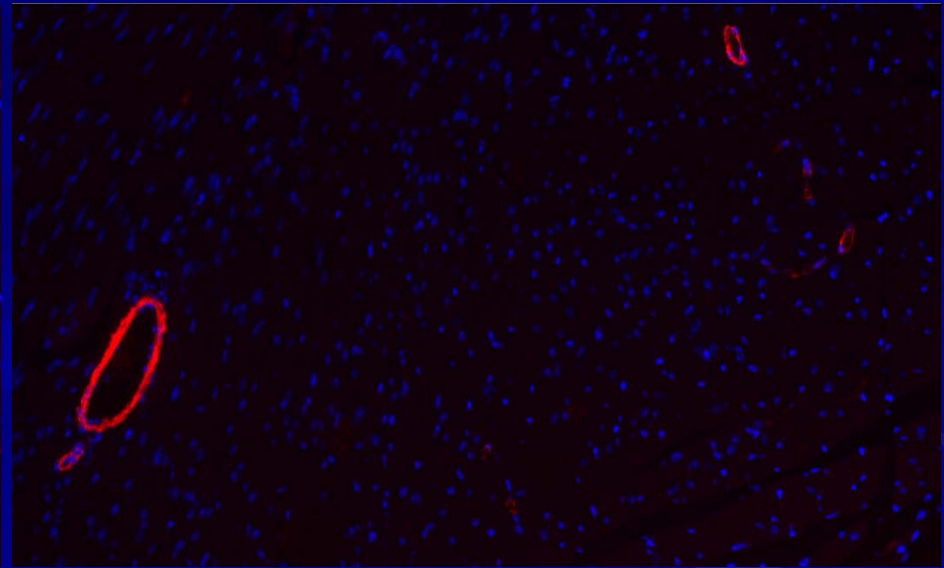


Smooth Muscle Actin Staining

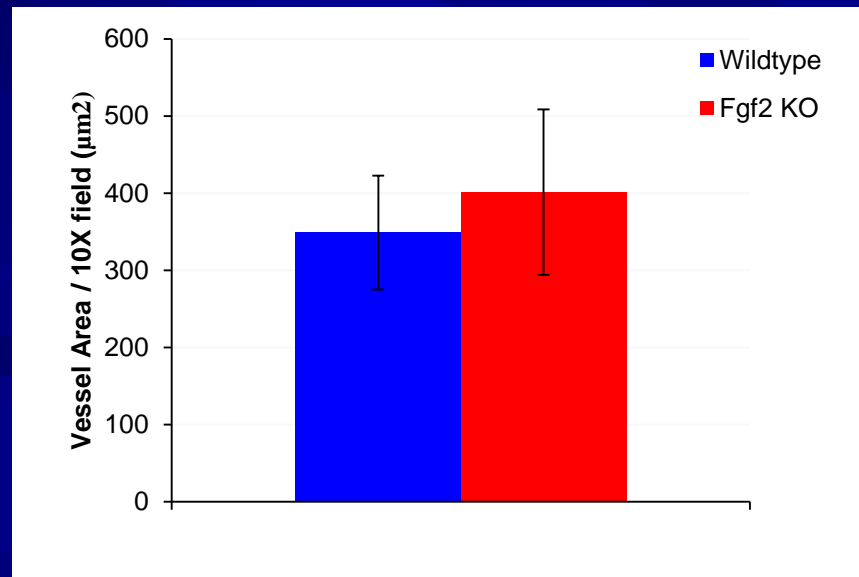
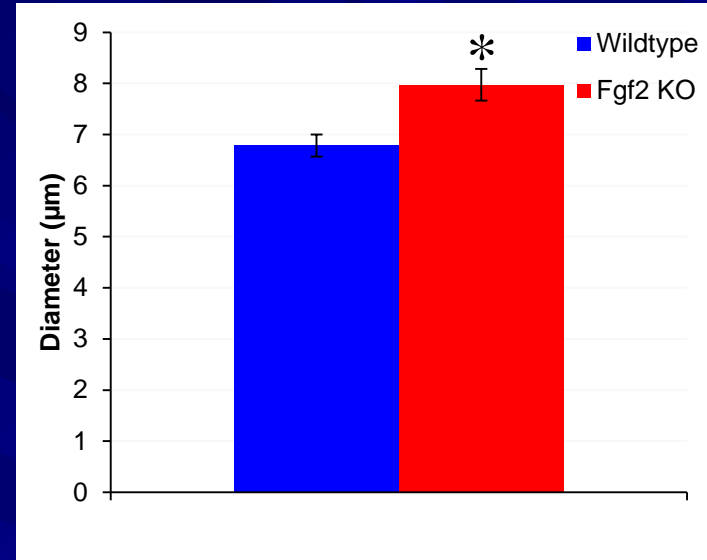
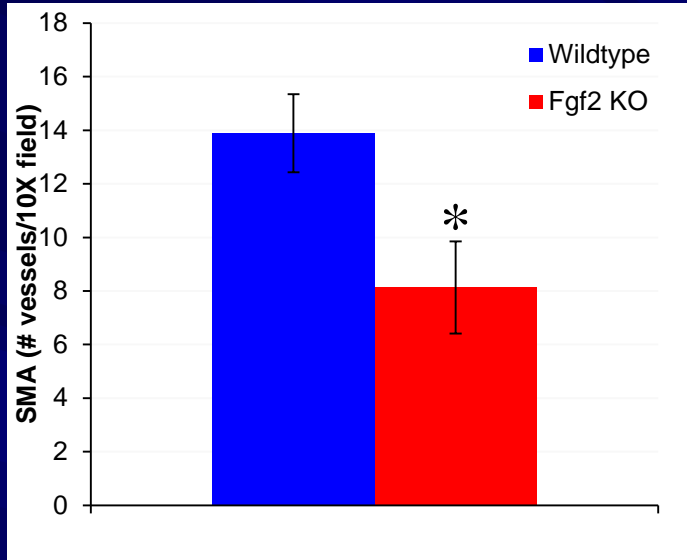
Wildtype



Fgf2 KO



Vessel Density After IR injury



n=6

* $p < 0.05$ vs. wildtype

Future Directions

Analysis of capillary density and vascular remodeling at early time points post IR injury

Analysis of inflammatory response post IR injury

Acknowledgements

Dave Ornitz

Carla Weinheimer

Attila Kovacs

Sarah Davis

Funding Sources

American Heart Association

Emergency Medicine Foundation

Missouri ACEP