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Endogenous Fibroblast Growth Factor 2 is Cardioprotective in an *In Vivo*, Closed-Chest, Murine Model of Regional Cardiac Ischemia-Reperfusion Injury

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Fibroblast growth factor 2 (FGF2) has been shown to be cardioprotective in *ex vivo* and chronic ischemia models. Limited data is available on the ability of FGF2 to protect the heart from ischemia-reperfusion injury *in vivo*. We have utilized a clinically relevant, *in vivo*, closed-chest model of regional cardiac ischemia-reperfusion (IR) injury. Mice with a targeted ablation of the *Fgf2* gene (*Fgf2*-/-) and wildtype controls were subjected to 90 minutes of occlusion of the left anterior descending artery followed by reperfusion for 7 days. *Fgf2-/-* mice do not show any baseline abnormalities in cardiac morphometry or function. When subjected to closed-chest, regional cardiac IR injury, *Fgf2-/-* mice have significantly increased myocardial infarct size as measured by echocardiography compared to wildtype mice at both 1 day and 7 days post-IR injury ($p<0.05$). In addition, *Fgf2-/-* mice show significantly worsened cardiac function at 1 day and 7 days post-IR injury ($p<0.05$). Scar length, detected by trichrome and picosirius red staining, is significantly increased in *Fgf2-/-* hearts ($p<0.05$). Myocyte cross-sectional area measurement shows an impaired cardiac hypertrophic response in the *Fgf2-/-* hearts in the peri-infarct area ($p<0.05$) but not in remote myocardium. *Fgf2*-/- mice have normal vessel density compared to wildtype controls in the non-injured state, but after cardiac IR injury, *Fgf2-/-* hearts showed significantly decreased vessel density (both capillaries and smooth muscle actin containing vessels) in the peri-infarct area compared to wildtype controls ($p<0.05$), suggesting a defect in vascular remodeling in the *Fgf2-/-* mice after IR injury. Endogenous FGF2 improves cardiac function, reduces myocardial infarct size, and mediates cardiomyocyte hypertrophy and vascular remodeling after cardiac IR injury. These data show the cardioprotective potential of endogenous FGF2 in a clinically-relevant, *in vivo*, closed-chest, regional cardiac ischemia-reperfusion model which mimics acute myocardial infarction.