

## **Neuronal Nitric Oxide Synthase (nNOS) Is Not Involved In Fibroblast Growth Factor 2 (FGF2) – Induced Cardioprotection In A Murine Model of Ischemia-Reperfusion Injury**

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**Introduction.** Ischemic heart disease caused 20% of all deaths in 2003 and is the single largest killer of Americans. Our laboratory showed previously that over-expressing FGF2 is cardioprotective during ischemia-reperfusion injury. There are three isoforms of NOS (all three are found in heart), and nNOS is implicated in modulating cardiac function. Since certain biological actions of FGFs can occur via NO signaling, we investigated the potential link between FGF2-induced cardioprotection and activation of nNOS during ischemia-reperfusion injury. **Methods.** Wild type (Wt) and two lines of transgenic (Tg) mouse hearts which over-express FGF2 were connected to a work-performing heart apparatus and perfused with an oxygenated Krebs-Henseleit solution. After 30 minutes equilibration, hearts were subjected to ischemia (60 minutes) followed by reperfusion (120 minutes). nNOS activity was inhibited with 1-(2-trifluoromethyl-phenyl) imidazole (TRIM, 100 $\mu$ M) dissolved in ethanol (Vehicle) prior to ischemia and reperfusion. Functional data, perfusate gases, and coronary effluent were obtained at specific time points. Nitrite concentrations in effluents were measured with a fluorometric assay. **Results.** No significant differences were observed in recovery of contractility between vehicle-treated or TRIM-treated hearts in either group (Wt-Veh 69.5%, Tg-Veh 68.0%, Wt-TRIM 51.8%, Tg-TRIM 76.5%). No differences in rates of relaxation were observed between the groups. No differences in NO levels were observed in Wt hearts. NO levels were significantly lower after 120 minutes reperfusion for vehicle and TRIM-treated Tg hearts. Preliminary data indicate that blocking nNOS leads to improved recovery of contractile function in Wt and Tg male hearts. **Conclusions.** FGF2-induced cardioprotection does not rely on nNOS-associated pathways. nNOS-derived NO may be deleterious to male hearts during ischemia-reperfusion injury.