

## SUPPLEMENTARY INFORMATION

### **Orphan nuclear receptor Nur77 affects cardiomyocyte calcium homeostasis and adverse cardiac remodelling.**

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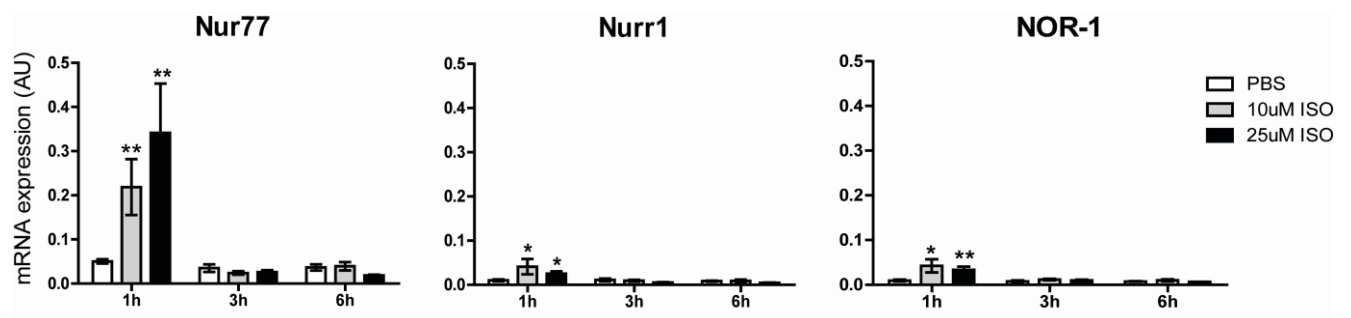
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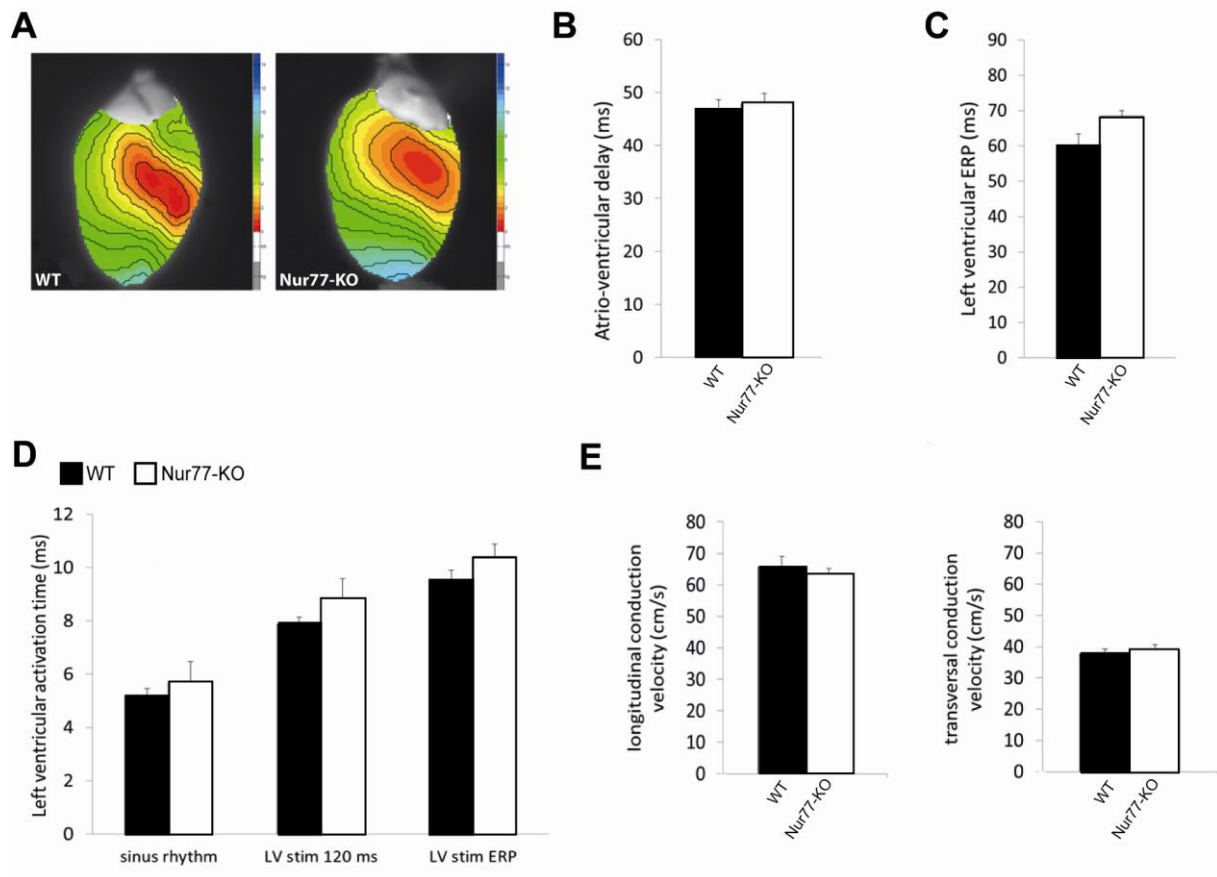
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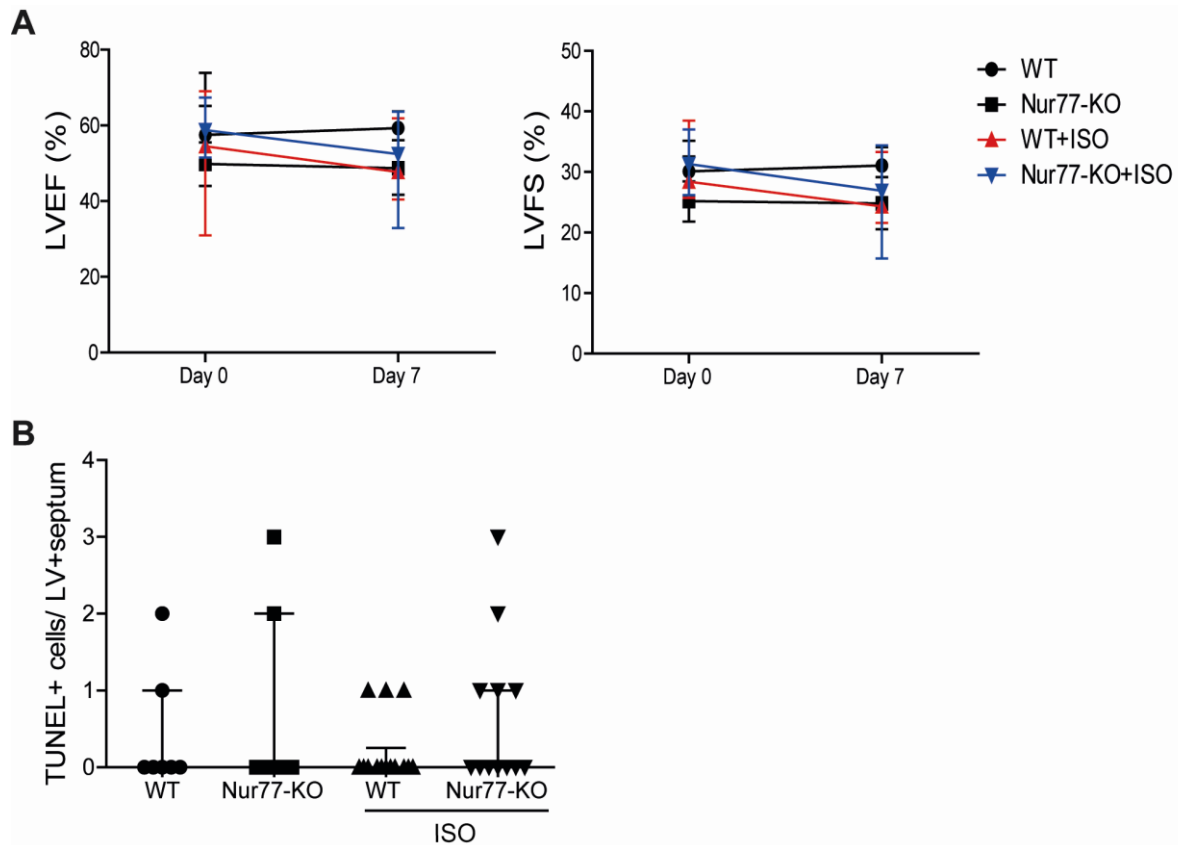
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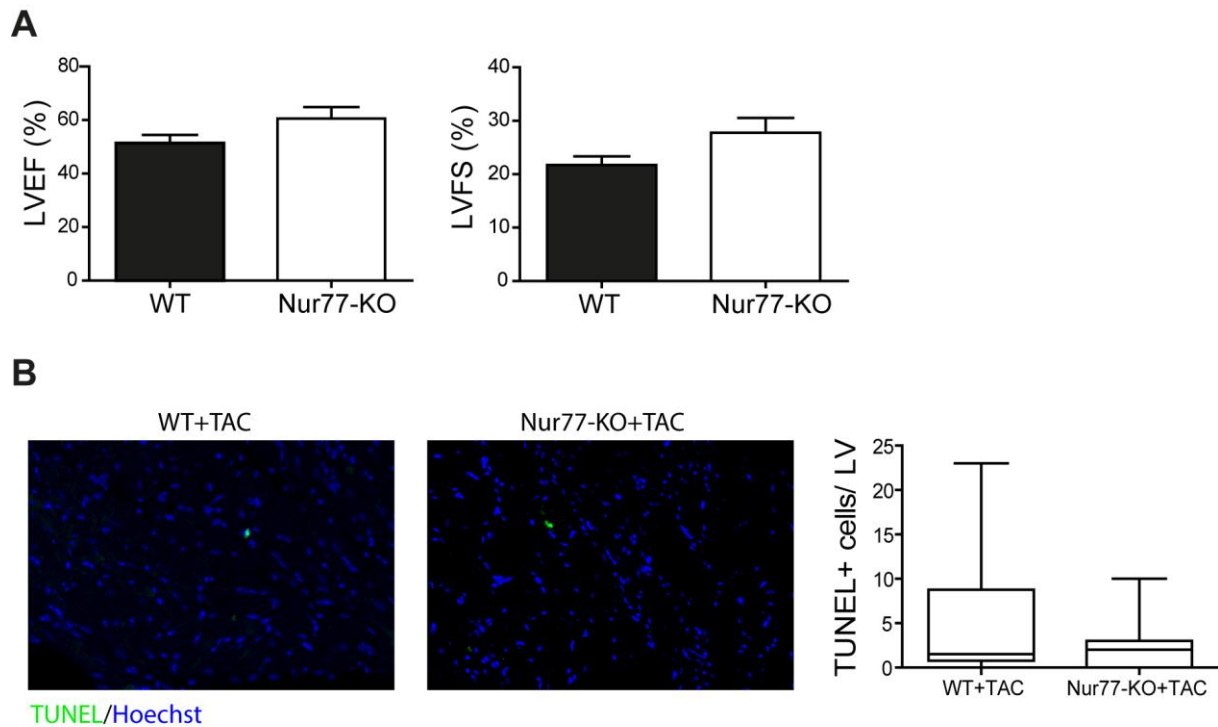
**Supplementary Figure S1. NR4A gene expression in cardiomyocytes after isoproterenol stimulation.** Expression of all three members of the NR4A subfamily of nuclear receptors is significantly up-regulated after 1h of isoproterenol stimulation, with Nur77 mRNA being most abundant. After 3 and 6h of stimulation, expression of all three NR4As is decreased to control levels. Data presented as median and minimum/maximum values.



**Supplementary Figure S2. Unaltered conduction in Nur77-KO hearts.** Optical mapping experiments were performed in WT (n=8) and Nur77-KO (n=7) hearts. **A.** Typical examples of left ventricular (LV) activation maps of a WT and Nur77-KO heart during central LV stimulation at a cycle length of 120 ms. No differences were observed between WT and Nur77-KO in atrio-ventricular conduction delay during right atrial stimulation at 120 ms (**B**) LV effective refractory period (ERP; **C**; trend  $p=0.06$ ), total LV activation times during sinus rhythm, LV central stimulation at 120 ms and during LV central stimulation at the ERP value (**D**) or LV longitudinal and transversal conduction velocities during LV central stimulation at 120 ms. Data presented as mean+SEM.



**Supplementary Figure S3. Cardiac function and apoptosis after chronic isoproterenol stimulation.** **A.** Cardiac function after 1 week of isoproterenol stimulation as assessed in all WT mice (n=16), the surviving 13 Nur77-KO mice and control groups (n=9 each). Although a hypertrophic response is established in both WT and Nur77-KO mice after 1 week of isoproterenol stimulation, no difference in left ventricular ejection fraction (LVEF) and fractional shortening (LVFS) was evident compared to baseline or between groups. **B.** Apoptotic cells as assessed by TUNEL staining. No significant difference between the numbers of apoptotic cells in left ventricles of WT and Nur77-KO mice after 1 week of isoproterenol stimulation was observed (median is 0 in all groups). Data presented as median and minimum/maximum values.



**Supplementary Figure S4. Cardiac function and apoptosis after TAC.** **A.** Cardiac function after 28 days of transverse aortic constriction. Left ventricular ejection fraction (LVEF) and fractional shortening (LVFS) were assessed in all WT (n=13) and Nur77-KO (n=11) mice. Nur77-KO mice exhibit a trend towards enhanced cardiac function. Data presented as mean+SEM. **B.** Apoptotic cells as assessed by TUNEL staining. No significant difference between the numbers of apoptotic cells in left ventricles of WT and Nur77-KO mice after 28 days of aortic constriction was observed. Data presented as median and minimum/maximum values.