(WT: -15.6 ± 2.1 , PPAR- α -/-: $-28.0 \pm 3.8\%$; $p < 0.05$), but unaltered in Nox2-/- mice. Interestingly, associated increases in PPAR- α mRNA (real-time RT-PCR) in WT TAC versus sham mice (1.31 ± 0.08 vs 1.01 ± 0.05 arbitrary units; $p < 0.05$) were reversed in Nox2-/- mice (0.83 ± 0.11 vs 1.11 ± 0.10 ; $p < 0.05$), whilst parallel reductions in Nox2 mRNA were evident in WT (0.49 ± 0.03 vs 1.03 ± 0.09 ; $p < 0.05$) but not PPAR- α -/- mice. These data clearly suggest that cross-talk between PPAR- α and Nox2 plays an important role in LVH. To elucidate underlying mechanisms, a combined proteomic/transcriptomic approach using DIGE gel-LC-MS proteomics and Illumina mouse Ref-8 beadchips was employed in LV tissue ($n=4$ /group). Data analysis by DAVID functional annotation tools identified several genes whose TAC-regulated differential expression (proteomics: $FC > 1.2$, $p < 0.05$; transcriptomics: $FC > 1.2$, $p < 0.001$) was significantly altered in the absence of PPAR- α and/or Nox2, including integrin- α - β subunits, desmin, and AP-1 subunits c-Fos and c-Jun. These potential key mediators provide exciting new avenues of investigation which may uncover novel mechanisms underlying important interaction between PPAR- α and Nox2 in LVH.

S5

INVESTIGATION OF MECHANISMS UNDERLYING THE INTERACTION BETWEEN NOX2 NADPH OXIDASE AND PPAR- α IN LEFT VENTRICULAR HYPERTROPHY

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NADPH oxidases and peroxisome proliferator-activated receptor- α (PPAR- α) play key roles in left ventricular hypertrophy (LVH) with emerging evidence supporting an important interaction. To investigate the nature of this interplay, gene-modified mice lacking PPAR- α (PPAR- α -/-) or Nox2 (Nox2-/-), and wild-type (WT) controls underwent thoracic aortic constriction (TAC) or sham surgery ($n > 8$) before study at 7 days. TAC-induced increases in LV/body weight were abolished in both PPAR- α -/- and Nox2-/- mice (WT: 10.8 ± 2.1 , PPAR- α -/-: 1.6 ± 1.8 , Nox2-/-: $1.7 \pm 3.0\%$; $p < 0.05$), whereas LV contractile dysfunction (echocardiographic fractional shortening) was accentuated in PPAR- α -/- mice