(WT: −15.6±2.1, PPAR-α−/−: −28.0±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 m ice (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±3.0%; p<0.05), whereas LV contractile dysfunction (echocardiographic fractional shortening) was accentuated in PPAR-α−/− mice