Supplemental Table 6: Diff gene expression

Key Event	Male CD-1 Mouse	Female CD-1 Mouse
Baseline differences in drug metabolism and transporters, osmotic regulation and oxidative stress handling	• Exclusive expression: Cyp2j13, Cyp4a12a, Cyp7b1. • Exclusive expression: Slc7a13, Slco1a1 • ↑ ROS generation: Cyp2e1	• ↑ Cyp4a14 and Cyp2d12 • ↑ ABC transporters; exclusive expression: Slc17a2, Slc7a12 • ↑ Osmotic stress regulation: Aqp4, Aqp2, Ces1d, Cryab, Hspa1b, Hspa2, Prlr, Serpina6 • ↑ Glutathione-mediated detoxification: Gsta1, Gsta2 , Gsta4, Gsto1, Mgst1, Gsta3, Gstm2 • ↑ Oxidative stress protection: Cbr1, Ephx1
Pharmacology and compound related renal stress (1000 mg/kg/day, Wk 1-4)	• ↑ Osmoregulation: Aqp2, Slc6a12 • ↑ Lipid metabolism and oxidative stress response: Cyp4a14 • ↑ Urea transporter: Slc14A2 • ↑ Cell cycle (Wk 4): Cdkn1a	

Supplemental Table 6: Diff gene expression

Exhaustion of stress handling reserve (1000 mg/kg/day, Wk 8-13)	• 186 genes with changed expression (Wk 13) • ↑ Cell cycle: Cdkn1a, Gdf15, Ccng1, Cdk1, Ccnb2, Trp53inp1, Btg2 • ↑ p53 pathway: Gdf15, Mdm2, Ephx1, Mki67, Nek6 • ↑ Cell adhesion, cytoskeleton structure: Tubb2a, Ckap2, Nef1, Gdf15, Mybpc2 • ↑ Fibrosis, cystogenesis: C3, Sulf2, Ltbp2, Col19a1 • ↑ Oxidative stress and renal injury: Ephx1, Aldh1a1, Aldh1a7, Nqo1, Lcn2, Havcr1, Ltbp2, Mki67	• 16 genes with changed expression (Wk 13) • ↑ Aldh1a7: Fold change less than male
	• No notable changes in DNA damage/repair pathway genes	