Molecular Pharmacology

The high affinity cAMP-specific phosphodiesterase 8B (PDE8B) controls steroidogenesis in the mouse adrenal gland

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Supplementary Figure 4

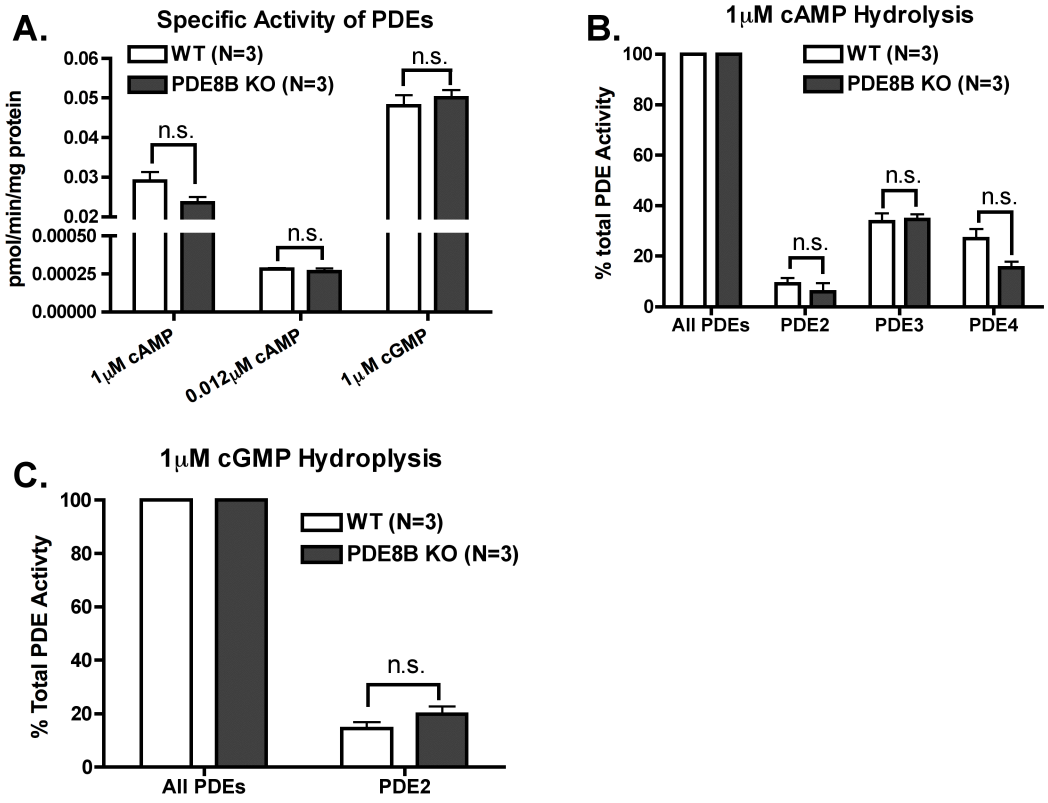

Figure S4. No significant increase in PDE activity as a compensation to the reduction in PDE8B due to the chronic PDE8B ablation was found. (A) Total PDE activity was measured from the adrenal lysate of WT and PDE8B KO mice. The PDE8B KO adrenal lysate did show an apparent small but statistically non-significant reduction (~20%) in total PDE activity with 1 μM cAMP substrate compared to the WT lysate, and no increase in PDE4 activity was seen. (B) The activities of various PDE isoforms were calculated by the percentage of total activity that is sensitive to selective PDE inhibitors against the different PDEs (100nM Bay60-7550 for PDE2, 200nM Cilostamide for PDE3 and 20μM Rolipram for PDE4). (C) The cGMP-stimulated PDE2 activity was determined by measuring Bay60-7550 inhibitable activity in a 1μM cGMP hydrolysis assay. The data are reported as means ± SEM, and the data were analyzed by student's t-test (unpaired, two tailed): no significance (n.s.). Note, we do not believe this reduction in PDE4 activity is responsible for the phenotype of increased urinary corticosterone in PDE8B KO mice since 50μM IBMX treatment, which will nearly completely inhibit PDE4 (and all other PDEs) was unable to elicit the same response as the PDE8-selective inhibitors in Y-1 cells and in the primary adrenal cells (figure 4B and figure 5A).