

**Supplemental Data**

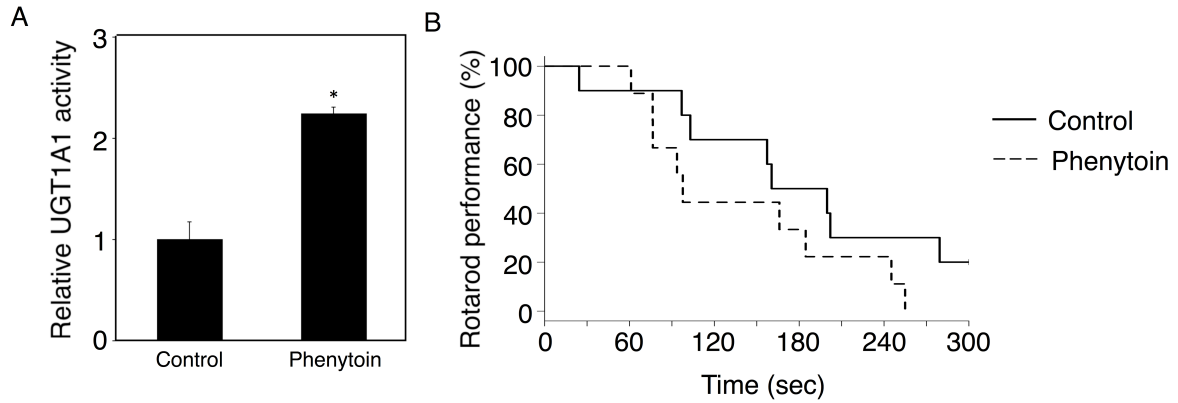
**Induction of the UDP-glucuronosyltransferase 1A1 during the perinatal period can cause neurodevelopmental toxicity**

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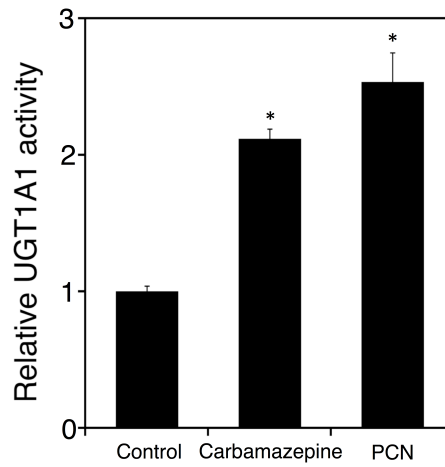
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Supplemental Figure: 3

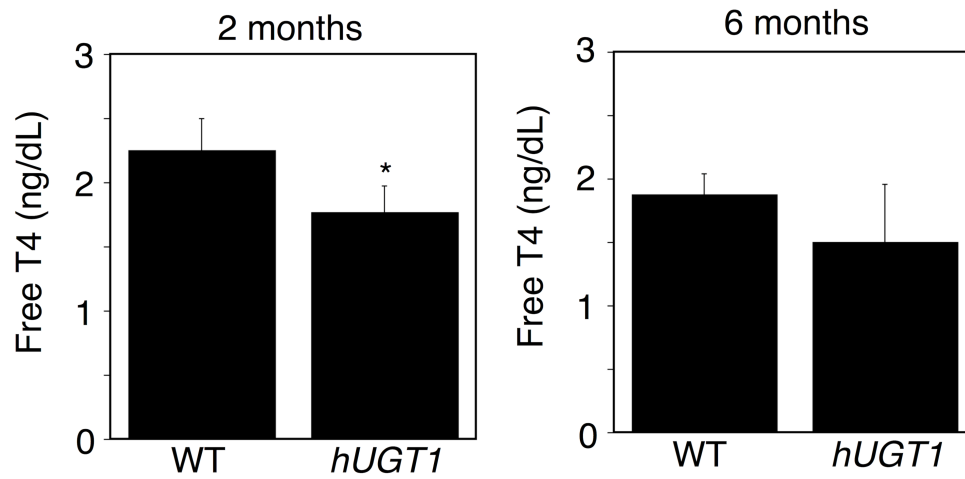
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**Supplementary Figure 1. Effects of postnatal phenytoin treatment on UGT1A1 activity and rotarod performance in wild-type mice.** Phenytoin (s.c. 35 mg/kg) was administered to pups daily from postnatal day 1 to day 14. Liver was collected on postnatal day 14. Pooled liver microsomes were prepared from three wild-type mice and UGT1A1 activity toward estradiol was measured (A). On postnatal day 56, rotarod analysis was performed. Prior to the rotarod study, control mice (solid line,  $n = 10$ ) and phenytoin-treated mice (dashed line,  $n = 9$ ) were trained on rotarod at a fixed speed of 6 rpm for 5 minutes. In the rotarod study, the speed of the rotarod was accelerated from 6 to 20 rpm over 5 minutes. The time to fall off the rod was measured (B). Each column is the mean  $\pm$  S.D. of three technical replicates. \*,  $P < 0.05$ .



**Supplementary Figure 2. Effects of postnatal phenytoin, carbamazepine, and PCN treatments on UGT1A1 activity in liver microsomes of *hUGT1* mice.** Carbamazepine (35 mg/kg) and PCN (10 mg/kg) were subcutaneously administered to pups daily from postnatal day 11 to day 14. Livers were collected on postnatal day 14 and pooled liver microsomes were prepared from three *hUGT1* mice each. UGT1A1 activity toward estradiol was measured. Each column is the mean  $\pm$  S.D. of three technical replicates. \*,  $P < 0.05$ . PCN, Pregnenolone-16- $\alpha$ -carbonitrile.



**Supplementary Figure 3. Comparison of free serum T4 levels between wild-type mice and *hUGT1* mice.** Serum free T4 levels and total T4 levels were determined in 2-month-old (left) and 6-month-old (right) wild-type mice (WT) and *hUGT1* mice. Each column is the mean  $\pm$  S.D. of three biological replicates. \*,  $P < 0.05$ .