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Judging Dept.

**Xin Zhou**

Student

**BMS****3****Xinxin Ding**

Dept or Program Years in program

Mentor

## An exploration of the mechanisms for increased resistance of lateral nasal gland to acetaminophen toxicity in Cyp2g1-null mice

Author (s)

**Xin Zhou, Jun Gu, Xinxin Ding**

CYP2G1 is a cytochrome P450 monooxygenase expressed uniquely in the olfactory mucosa (OM). The lateral nasal gland (LNG), the largest anterior gland in the nasal cavity, is an important organ for the production of odorant binding proteins. Cyp2g1-null mouse was recently found to have an increased resistance to acetaminophen (AP) cytotoxicity in the LNG, even though CYP2G1 is not expressed in that organ. The aim of this study is to identify mechanisms that link CYP2G1 expression in the OM to AP toxicity in the LNG. We found that the increased resistance of LNG to AP toxicity was accompanied by reduced AP levels, and decrease in AP-induced non-protein thiol (NPT) levels depletion, in the LNG. However, in vitro metabolic activation of AP by LNG microsomes was found previously to be unaltered in the Cyp2g1-null mouse. Subsequent microarray analysis identified 20 genes that are differentially expressed in the LNG of Cyp2g1-null and wild-type mice. Among the up-regulated are three genes encoding secretory carrier proteins, including prostaglandin D2 synthase (L-PGDS), androgen binding protein A (Abpa), and androgen binding protein B (Abpb). We propose that the increased expression of these proteins in the LNG of the Cyp2g1-null mice contributes to the reduction in target tissue AP levels and increased resistance to AP toxicity. Furthermore, since the expression of both L-PGDS and Abp is relevant to steroid hormones, which are potential Cyp2G1 substrates in the OM, we propose that the loss of CYP2G1 in the OM leads to changes in steroid hormone levels in the LNG, thereby altering the expression of secreted carrier proteins in the LNG. Studies designed to test these hypotheses are underway.