morphology independent of IMI exposure suggesting a basal role of CAR in maintaining overall SI morphology. Car-/-mice also exhibited increased SI weight and length and shorter villi height. AB-PAS staining showed IMI reduced ileal mucin production in WT mice but not Car-/-mice. To further examine CAR's role in the xenobiotic metabolism in the ileum, we will compare microbial diversity and bile acid pools with and without IMI exposure. Our results suggest IMI is not overtly toxic, but the absence of xenobiotic nuclear receptor CAR allows increased accumulation of IMI in the liver and disrupts the structure and Cyp gene expression in the intestine.

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Steroid Hormones and Receptors

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Examining the role of Constitutive Androstane Receptor during Imidacloprid exposure

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Imidacloprid (IMI) is a neonicotinoid pesticide used for pest control and seed treatments. It mimics nicotine and selectively targets insect nicotinic acetylcholine receptors to induce paralysis and death. Popularly used worldwide, IMI residue is readily detectable in crops, the environment, and human samples. Gastrointestinal symptoms in patients as well as defective gut barrier and hepatoxicity in animal models have been reported subsequent to IMI exposure. However, the mechanism underlying IMI toxicity in mammals is unclear. Pesticide exposure frequently activates xenobiotic nuclear receptors, like constitutive androstane receptor (CAR), to induce detoxification phase I and phase II genes. We found that IMI exposure in wild-type (WT) mice induced hepatic expression of Cyp2b10, a bona fide target of CAR. This data led us to investigate the role of CAR in alleviating IMI toxicity. We dosed wild-type (WT) and Car-/- mice with 50mg/kg BW IMI, twice daily for 21 days and collected serum, liver, and intestine tissues. The absence of CAR resulted in a three-fold increased accumulation of IMI within the liver as well as a 6% increase in body weight. Intriguingly, IMI exposure resulted in hepatic inflammatory pockets in WT mice but did not induce serum liver injury markers (ALT and AST) in either WT or Car-/-mice. We quantified the expression of genes involved in detoxification and oxidative stress within the liver and ileum using qRT-PCR. We found Car-/-mice had significantly blunted expression of Cyp-P450 enzymes in the ileum. To compare gut function, we measured organ coefficient and examined ileal histology using Alcian Blue/PAS staining. We found the absence of CAR altered small intestine (SI)