ENVIGO

Genetically engineered models (GEMS)

PXR knockout rat

Model	PXR knockout rat
Strain	HsdSage:SD-*Nr1i2*^{tm1Sage}
Location	U.S.
Availability	Cryopreserved

Characteristics/husbandry

+ Biallelic 20 bp deletion within Nr1i2 gene
+ Lacks induction of Cyp3a1
+ Background strain: Sprague Dawley

Zygosity genotype

+ Homozygous

Research use

+ Xenobiotic sensor
+ Cytochrome p450 pathways
+ Drug metabolism
+ Hepatotoxicity
+ Cholestasis

Origin

The PXR KO rat model was originally created at SAGE Labs, Inc. in St. Louis, MO and distributed out of the Boyertown, PA facility. The line continues to be maintained through the original SAGE Labs animal inventory acquired by Envigo.

Description

PXR is involved in the induction of cytochrome p4503A (Cyp3a) and is abundantly expressed in the liver and intestine. This model is useful for studying metabolism of xenobiotic compounds and hepatotoxicity.

The activation of nuclear receptors, including the Pregnane X Receptor (PXR) and the Constitutive Androstane Receptor (CAR), is a common Mode of Action (MoA) for chemicals that exhibit non-genotoxic hepatocarcinogenicity in rodents. Conversely, the activation of the human PXR and/or CAR receptors is not believed to result in a carcinogenic response. Therefore, if a compound causes liver tumors in rodents, or if studies demonstrate that the compound is a nuclear receptor agonist, it is critical to unambiguously demonstrate the role of specific nuclear receptors in the rodent response, for example by using PXR or CAR KO rats.

Figure 1: Cyp mRNA induction in livers of PXR knockout and wild type Sprague-Dawley rats

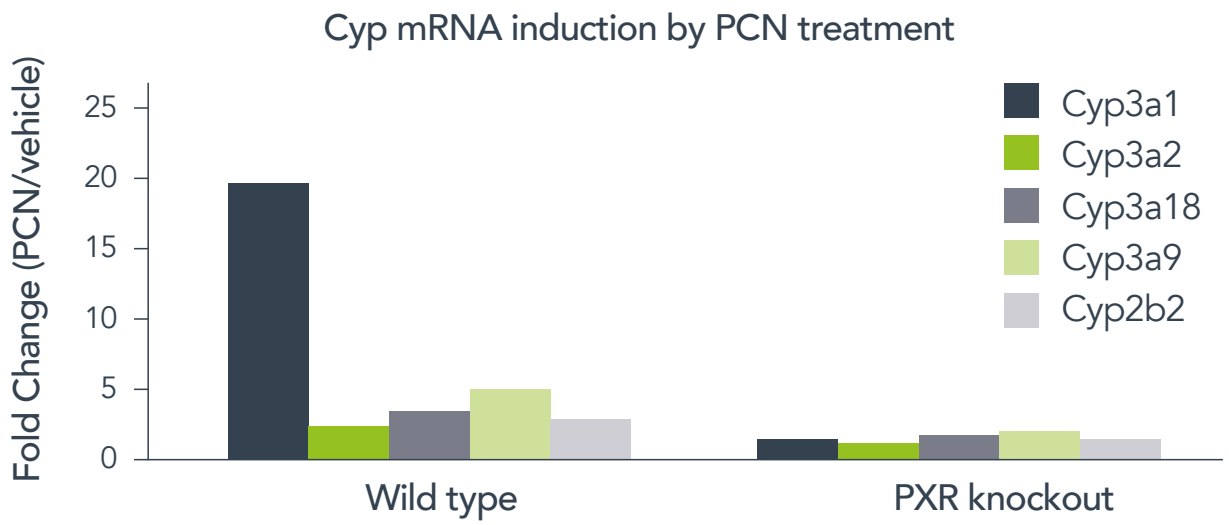
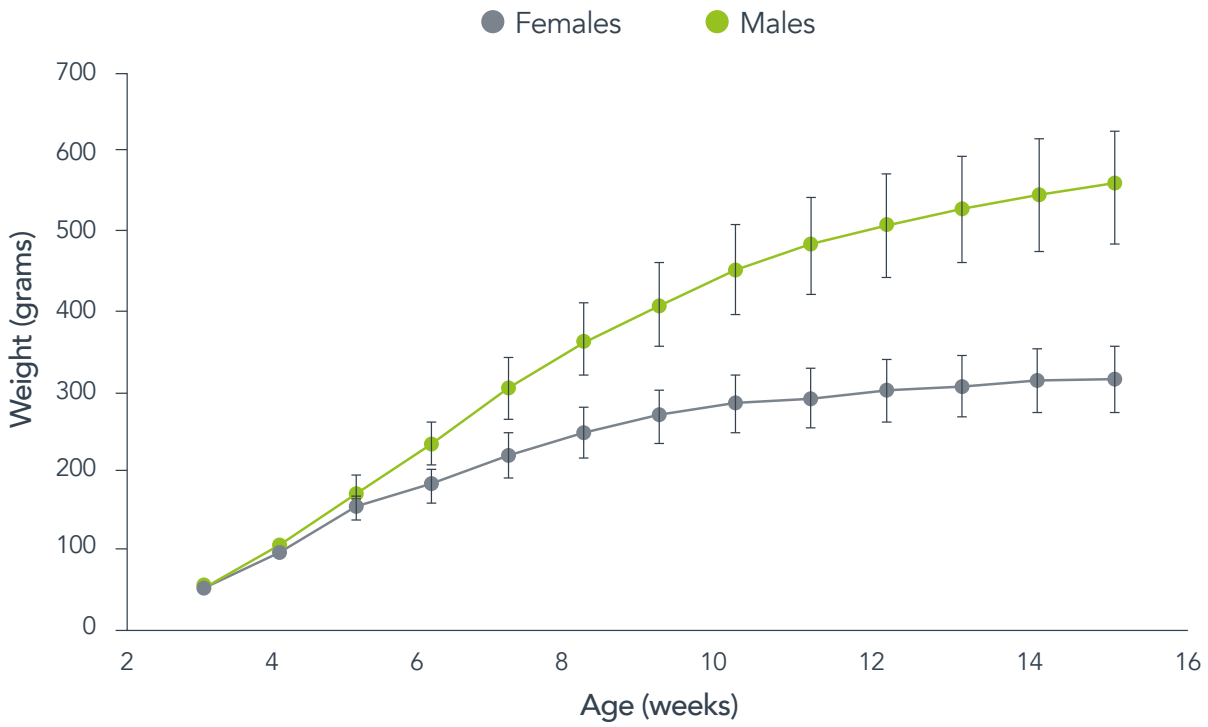


Figure 2. Weight and age comparison chart



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