



CAR knockout rat

Model	CAR knockout rat
Strain	HsdSage: SD-NR113 ^{tm1Sage}
Location	U.S.
Availability	Cryopreserved

Characteristics/husbandry

- + Biallelic 8bp deletion within the Abcb11 gene
- + Homozygous Knockouts exhibit complete loss of protein via Western blot
- + Background strain : Sprague Dawley

Zygoty genotype

- + Homozygous

Research use

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

Origin

The CAR 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

CAR is involved in the induction of cytochrome p450s 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: Lack of cyp induction by TCPOBOP in CAR knockout rats. CAR knockout and wild-type control rats were injected (i.p.) with 12.5 mg/kg TCPOBOP. Twenty-four hours later, animals were euthanized, livers harvested, and RNA extracted. A qPCR array was then performed assessing the relative expression of several cytochrome p450 family members and related genes.

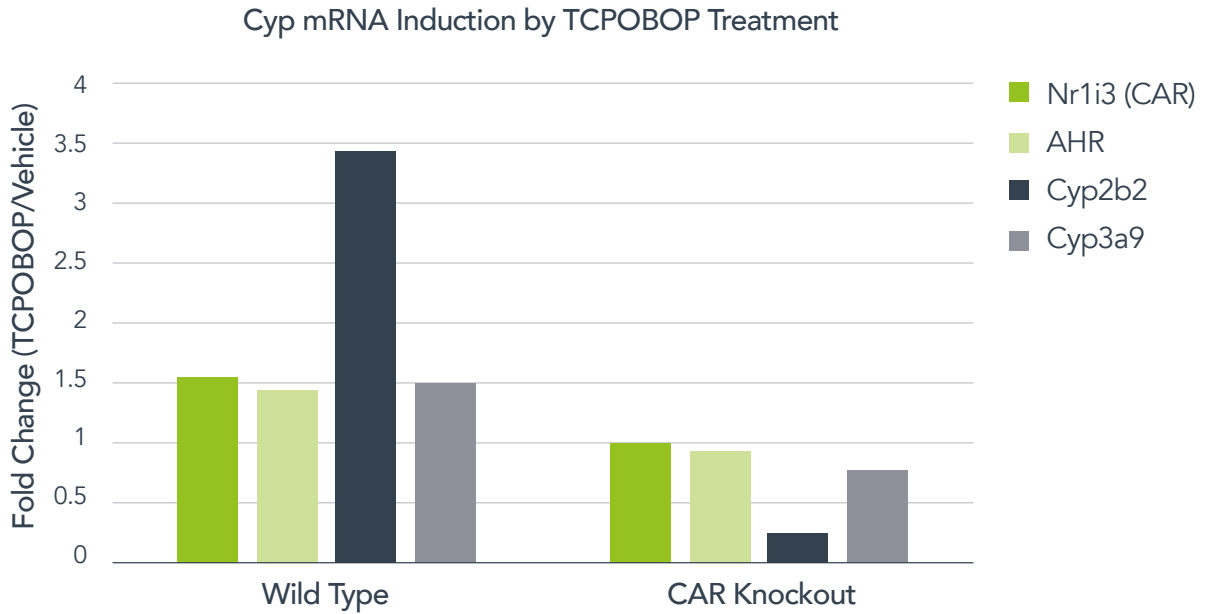
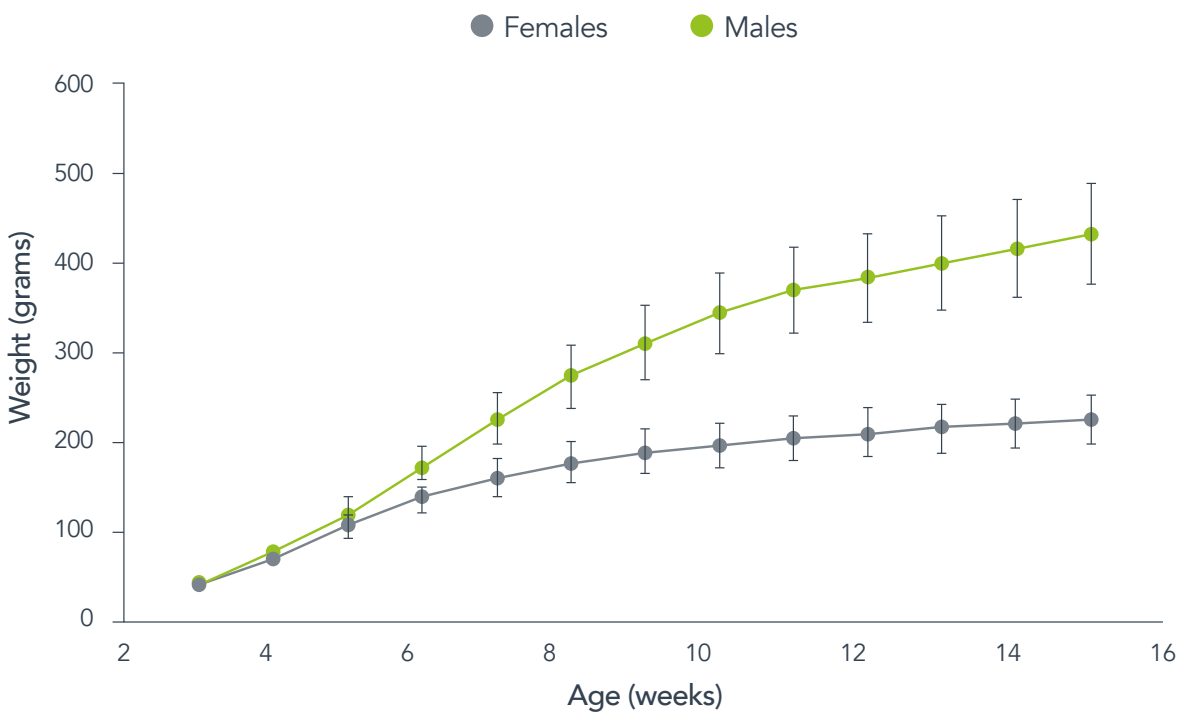


Figure 2. Weight and age comparison chart



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