inotiv
analyze. answer. advance.

Genetically engineered models **(GEMS)**

PXR/CAR knockout rat

MODEL	PXR/CAR knockout rat
STRAIN	HsdSage:SD-*Nr1i2*^{em1Sage}*Nr1i3*^{em1Sage}
LOCATION	U.S.
AVAILABILITY	Live colony

CHARACTERISTICS/HUSBANDRY

- Biallelic 20 bp deletion within Nr1i2 gene
- Biallelic 10 bp deletion within Nr1i3 gene
- Background strain: Sprague Dawley

ZYGOSITY GENOTYPE

- Homozygous

RESEARCH USE

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

ORIGIN

The PXR/CAR knockout rat model was originally created at SAGE Labs, Inc. in St. Louis, MO. The animal inventory was acquired by Envigo in 2019 and then by Inotiv in 2021. The line continues to be maintained through the original SAGE Labs animal inventory and is distributed out of the Boyertown, PA facility.

DESCRIPTION

PXR and CAR are 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.

This double knockout model was generated by crossing together the single PXR and Car knockout rat lines.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 knockout rats.

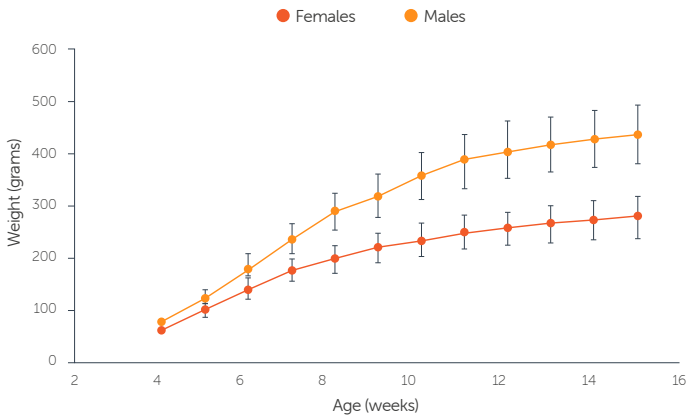

Figure 1: Age and weight chart