ENVIGO

Genetically engineered models (GEMS)

PXR/CAR/AHR knockout rat

Model	PXR/CAR/AHR knockout rat
Strain	HsdSage:SD-NR1i2/NR1i3/AHR^{tm1Sage}
Location	U.S.
Availability	Cryopreserved

Characteristics/husbandry

+ Biallelic 20 bp deletion within Nr1i2 gene
+ Biallelic 10 bp deletion within Nr1i3 gene
+ Biallelic 760 bp deletion within Ahr gene
+ Background Strain: Sprague-Dawley

Zygosity genotype

+ Cryopreserved as heterozygous embryos

Research use

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

Origin

The PXR/CAR/AHR knockout 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, CAR, and AHR are involved in the induction of cytochrome p4503A (Cyp3a) and are abundantly expressed in the liver and intestine. This model is useful for studying metabolism of xenobiotic compounds and hepatotoxicity. This triple knockout model was generated by crossing together the three single PXR, Car, and AHR knockout rat lines.

PXR Citations

Forbes KP, Kouranova E, Tinker D, Janowski K, Cortner D, McCoy A, Cui X. Creation and Preliminary Characterization of Pregnane X Receptor and Constitutive Androstane Receptor Knockout Rats. Drug Metab Dispos. 2017 Oct;45(10):1068-1076.

Haines C, Chatham LR, Vardy A, Elcombe CR, Foster JR, Lake BG. Comparison of the hepatic and thyroid gland effects of sodium phenobarbital and pregnenolone-16-carbonitrile in wild-type and constitutive androstane receptor (CAR)/pregnane X receptor (PXR) knockout rats. Xenobiotica. 2019 Feb;49(2):227-238.

Haines C, Chatham LR, Vardy A, Elcombe CR, Foster JR, Lake BG. Comparison of the hepatic and thyroid gland effects of sodium phenobarbital in wild type and constitutive androstane receptor (CAR) knockout rats and pregnenolone-16□carbonitrile in wild type and pregnane X receptor (PXR) knockout rats. Toxicology. 2018 May 1;400-401:20-27.

Hunter SR, Vonk A, Mullen Grey AK, Riddick DS. Role of Glucocorticoid Receptor and Pregnane X Receptor in Dexamethasone Induction of Rat Hepatic Aryl Hydrocarbon Receptor Nuclear Translocator and NADPH-Cytochrome P450 Oxidoreductase. Drug Metab Dispos. 2017 Feb;45(2):118-129.

PXR/CAR Citations

Forbes, Kevin P; Kouranova, Evguenia; Tinker, Daniel; Janowski, Karen; Cortner, Doug; McCoy, Aaron; Cui, Xiaoxia; Creation and Preliminary Characterization of Pregnane X Receptor and Constitutive Androstane Receptor Knockout Rats. Drug metabolism and disposition: the biological fate of chemicals Vol.45, 2017

AHR Citations

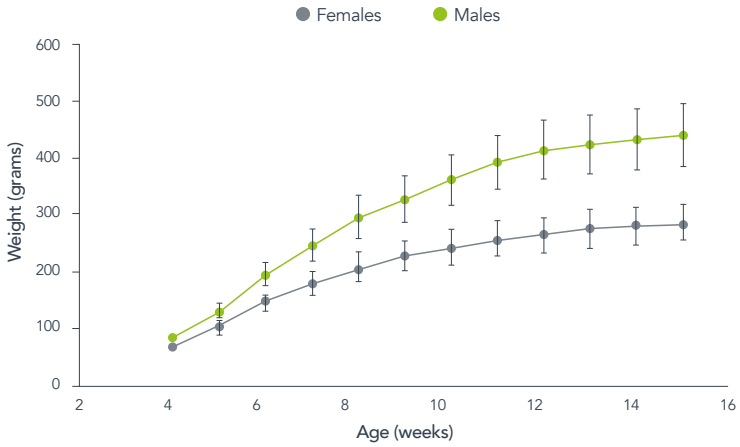
Harrill JA, Hukkanen RR, Lawson M, Martin G, Gilger B, Soldatow V, Lecluyse EL, Budinsky RA, Rowlands JC, Thomas RS. Knockout of the aryl hydrocarbon receptor results in distinct hepatic and renal phenotypes in rats and mice. Toxicol Appl Pharmacol. 2013 Oct 15;272(2):503-18

Harrill JA, Layko D, Nyska A, Hukkanen RR, Manno RA, Grassetti A, Lawson M, Martin G, Budinsky RA, Rowlands JC, Thomas RS. Aryl hydrocarbon receptor knockout rats are insensitive to the pathological effects of repeated oral exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. J Appl Toxicol. 2016 Jun;36(6):802-14.

Phadnis-Moghe AS, Chen W, Li J, Crawford RB, Bach A, D'Ingillo S, Kovalova N, Suarez-Martinez JE, Kaplan BL, Harrill JA, Budinsky R, Rowlands JC, Thomas RS, Kaminski NE. Immunological characterization of the aryl hydrocarbon receptor (AHR) knockout rat in the presence and absence of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Toxicology. 2016 Aug 10;368-369:172-182.

Pohjanvirta R, Mahiout S. Aryl hydrocarbon receptor is indispensable for β-naphthoflavone-induced novel food avoidance and may be involved in LiCl-triggered conditioned taste aversion in rats. Physiol Behav. 2019 May 15;204:58-64.

Figure 2. Weight and age comparison chart



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