

Mdr1a knockout rat



MODEL	Mdr1a knockout rat
STRAIN	HsdSage: SD - <i>Mdr1a</i> ^{em1Sage}
LOCATION	U.S.
AVAILABILITY	Live colony

CHARACTERISTICS/HUSBANDRY

- Biallelic 20 bp deletion within *Abcb1a* gene
- Increased oral bioavailability of P-gp-specific substrates
- Homozygous knockout rats display total loss of protein via Western blot
- Background strain: Sprague Dawley

ZYGOSITY GENOTYPE

- Homozygous

RESEARCH USE

- DMPK assay
- PK-PD efflux assay
- Neurotoxicology
- Formulation drug-drug interactions
- Drug resistance
- Blood brain barrier efflux
- Efficacy

ORIGIN

The Mdr1a 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

P-glycoprotein (P-gp) plays a critical role in efflux for both brain and liver. Homozygous null Mdr1a rats display increased exposure to CNS drugs in the brain, as well as increased bioavailability in the plasma for P-gp-specific substrates. MDR1 encodes for P-gp and is a membrane-bound drug transporter expressed in the brain and intestine. It effectively blocks drugs from crossing the blood-brain barrier. P-gp can confer multiple drug resistance to tumor cells. Absence of P-gp creates a functional deficiency in the blood-brain barrier and results in elevated drug levels in many tissues, making this a useful model for efflux assay, efficacy, formulation, tissue distribution, studying neurotoxicology and chemotherapeutic agents.

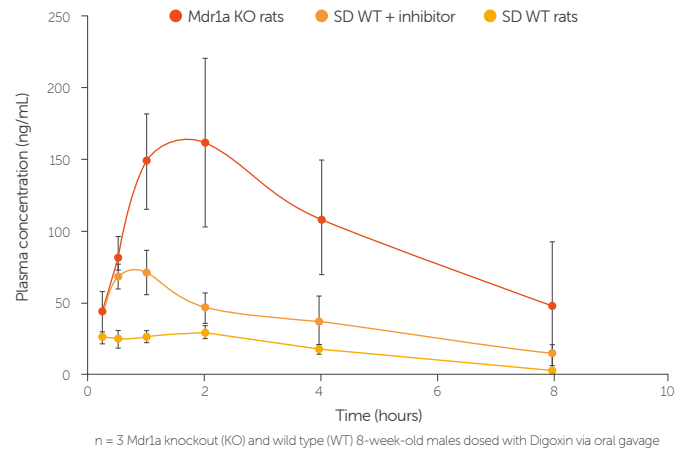


Figure 1: Oral absorption of Digoxin in the absence and presence of Quinidine

	BRAIN	PLASMA	BRAIN:PLASMA
Wild type	0	25.5	N.d.
Knockout	339	236	159

Note: Digoxin concentrations are in units of ng/mL

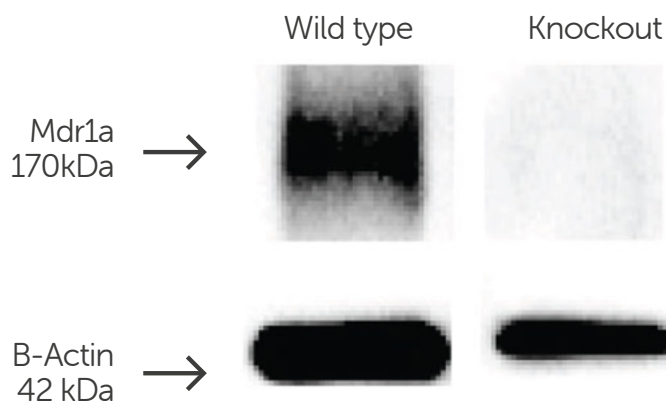


Figure 2: Western blot using proximal colon tissue isolated from both wild type and Mdr1a homozygous knockout tissue

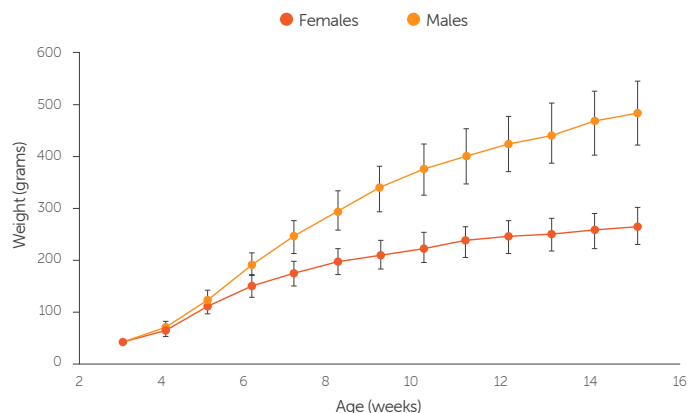


Figure 3: Age/Weight/Curve chart

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