ENVIGO

Genetically engineered models (GEMS)

BCRP knockout rat

Model	BCRP knockout rat
Strain	HsdSage: SD-*Abcg2*^{tm1Sage}
Location	U.S.
Availability	Live colony

Characteristics/husbandry

+ Background strain: Sprague Dawley
+ Biallelic 588 bp deletion within Abcg2 gene
+ Homozygous knockouts display total loss of protein via Western blot
+ Increased oral bioavailability of BCRP-specific substrates

Zygosity genotype

+ Homozygous

Research use

+ Neurotoxicology
+ DMPK efflux assay
+ Formulation blood brain barrier efflux
+ Drug-drug interactions
+ Tissue distribution
+ Efficacy assay

Origin

The Bcrp 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

BCRP plays a protective role in neurotoxicity by limiting the efflux of xenobiotics into the brain. Homozygous null rats demonstrate increased exposure in the brain and plasma when dosed with BCRP-specific substrates. Loss of function of Bcrp leads to improper transport of drugs across epithelial cells and increased bioavailability of Bcrp substrates. This model is useful for studying metabolism of xenobiotic compounds, tissue distribution, DMPK, efficacy, formulation, and blood brain barrier efflux.

Citations

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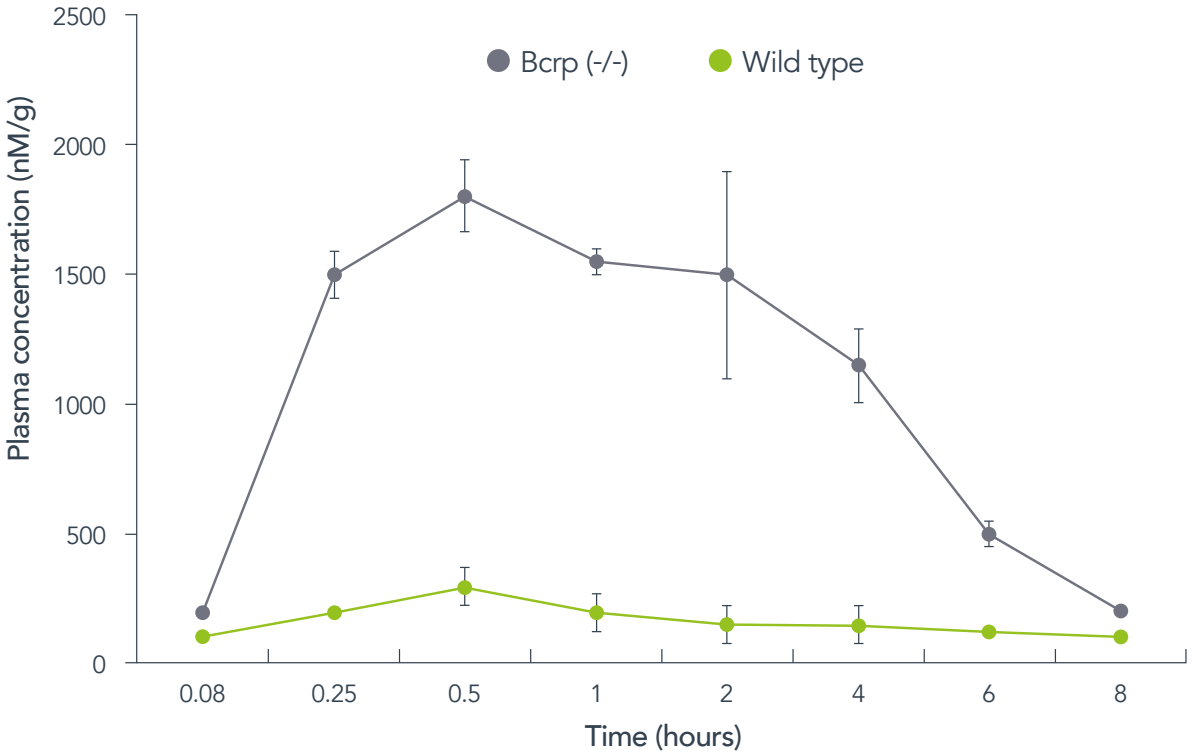
Figure 1: Dantrolene level of Bcrp (-/-) and wild type rats 2 hours after treatment (nM/g)



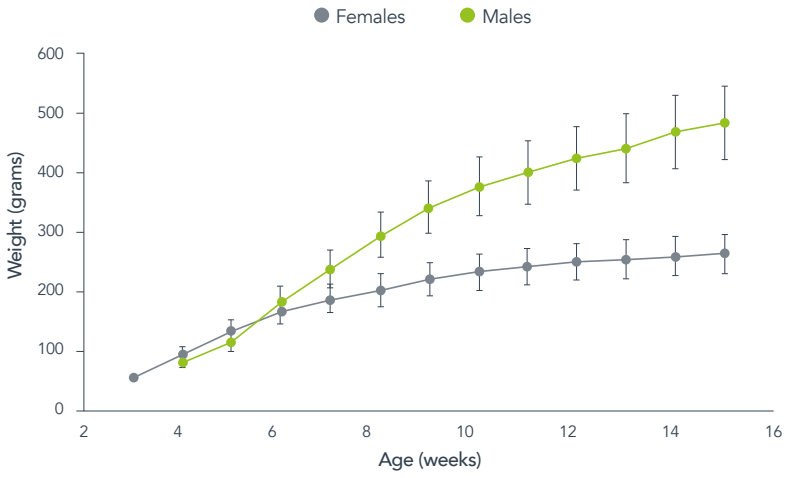
n = 3, 8-week old male Bcrp (-/-) and wild type Sprague Dawley rats

Figure 2: Oral absorption of sulfasalazine

Tissue	Bcrp (-/-) Mean	Wild Type Mean	Ratio of WT to KO
Brain Homogenate	16.0	3.3	0.2
Plasma	421	319	0.8

n= 2, 8-week old male Bcrp (-/-) and n=3 wild type littermates

Figure 3: Age/Weight/Curve chart



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