

CrI:CF1-*Abcb1a*^{mds} mutant mouse A p-glycoprotein-deficient mouse model

Summary

The PGP-deficient mouse is a model of disrupted blood-brain barrier function on a CF-1™ (non-Swiss) albino outbred background.

Gene Synonyms

Evi32, mdr-3, Mdr1a, MDR3, multiple drug resistant 1a, p-glycoprotein, P-gp, Pgp, Pgy-3, Pgy3

Origin and History

In 1995, a number of CF-1™ mice with an anomalous response to certain compounds were identified by the Department of Safety Assessment, Merck Research Laboratories, West Point, PA.

Characterization of the mice and cloning of the spontaneously mutated gene resulted in the identification of animals with a mutation in the *Abcb1a* gene. The mutation is known as *mds* (multiple drug sensitive). This led to the development of two populations of CF-1™ mice; those with the mutation and those without. These stocks were developed by Charles River Genetically Engineered Models and Services in conjunction with Merck.

The CF-1™ is an albino outbred, non-Swiss stock of mice.

Strain Characteristics

Deficient in p-glycoprotein in the intestinal epithelium and brain capillary endothelium, as well as in the placenta.

Applications

- Central nervous system research
- Transport/excretion involving *mds* (multiple drug sensitive) for neurobiology and chemotherapy

- Toxicology (especially sensitive to avermectins and vinblastine)
- Teratology
- Altered intestinal intraepithelial lymphocyte development

References

Abbott, NJ, et al. Drug Resistance in Epilepsy: The Role of the Blood-Brain Barrier. *Novartis Found Symp.* **243**, 38-53, 180-5 (2002).

Bihorel, S., Camenisch, G., Lemaire, M., & Scherrmann, J.M. Influence of breast cancer resistance protein (*Abcg2*) and p-glycoprotein (*Abcb1a*) on the transport of imatinib mesylate (Gleevec) across the mouse blood-brain barrier. *J. Neurochem.* **102**, 1749-57 (2007).

Dagenais, C., Rousselle, C., Pollack, G.M., & Scherrmann, J.M. Development of an *In Situ* Mouse Brain Perfusion Model and Its Application to *mdr1a* P-Glycoprotein-Deficient Mice. *J. Cereb. Blood Flow Metab.* **20**, 381-6 (2000).

de Lange, E.C., et al. BBB transport and P-glycoprotein functionality using MDR1A(-/-) and wild-type mice. Total brain versus microdialysis concentration profiles of rhodamine-123. *Pharm. Res.* **15**, 1657-65 (1998).

Kwei, G.Y., et al. Disposition of Ivermectin and Cyclosporine A in CF-1 Mice Deficient in *mdr1a* P-Glycoprotein. *Drug Metab. Dispos.* **27**, 581-7 (1999).

Vautier, S., et al. Interactions between the dopamine agonist, bromocriptine and the efflux protein, P-glycoprotein at the blood-brain barrier in the mouse. *Eur. J. Pharm. Sci.* **27**, 167-74 (2006).