Drug Discovery & Development

Controllable Murine Models of First Pass Metabolism

WARF: P04330US

Inventors: Christopher Bradfield, Jacqueline Walisser, Tami Thomae

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing mutant mouse lines with an open ductus venosus for more effective drug testing and development.

Overview

The liver detoxifies many of the drugs and toxins in blood, which poses a problem in drug development and testing because drugs are rapidly cleared from the system. In the mammalian fetus, the liver is not needed to detoxify blood, so a large shunt called the ductus venosus carries blood quickly through the fetal liver to the heart.

The Invention

UW-Madison researchers have developed mutant mouse lines that display an open (patent) ductus venosus. They also developed a way to control the closure of the ductus venosus so that some mice have first pass clearance while others do not.

The researchers used embryonic stem cell targeting to create alleles of the transcriptional regulators AHR and ARNT with reduced gene expression. Because AHR and ARNT play a role in vascular development in the fetus, mutations affecting these genes alter blood vessel formation. The particular mutations developed by the researchers result in an open ductus venosus.

Applications

- Drug testing and development

Key Benefits

- Allows researchers to more effectively assess toxicity and biological efficacy of test compounds
- Particularly useful for the pharmaceutical industry
- Results in a 50 percent reduction in blood flow to the liver
- Blood flow to the liver can be restored in these animals, allowing the development of control and test groups of animals with the same genetic background.

Additional Information

For More Information About the Inventors

- Christopher Bradfield

Tech Fields

- Drug Discovery & Development : Preclinical testing
- Research Tools : Animal & disease models

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847