Drug Discovery & Development

Targeted Disruption of the Murine NADPH Cytochrome P-450 Oxidoreductase Gene

WARF: P01355US

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in a mouse line in which one or both alleles of the NADPH-cytochrome-P450 oxidoreductase gene have been disrupted.

Overview

Cytochrome P450 (CYP) is a family of predominantly hepatic enzymes known to be important in the metabolism of many drugs, carcinogens and other chemicals of pharmacologic and toxicologic significance. To help determine the role of CYP enzymes in metabolism and toxicity, UW-Madison researchers discovered a method to bioengineer animal models lacking the ability to express NADPH-cytochrome-P450 oxidoreductase (CYPOR), an enzyme required for activity of all CYP isozymes.

The Invention

The UW-Madison researchers have created a mouse line in which one or both alleles of the CYPOR gene have been disrupted. The knockout of both alleles is lethal, while heterozygotes show only 60 to 75 percent of the enzyme activity of controls and therefore display increased sensitivity to factors affecting cytochrome P450- and other CYPOR-dependent metabolic pathways. These animal models can be used to directly assess the potential risks of new, xenobiotic compounds.

Applications

- Studies of efficacy, toxicity, teratogenicity and carcinogenicity of xenobiotic compounds

Key Benefits

- Mice with reduced NADPH-cytochrome-P450 oxidoreductase enzyme activity may show increased sensitivity to drugs, displaying beneficial or adverse effects sooner and more often.
- These mice serve as a model for inborn errors of metabolism (including that of sterols, steroids, vitamin D and retinoids).
- Cell lines generated could be used to investigate relative contributions of P450-dependent versus P450-independent systems.

Tech Fields

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

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854