**Docket #:** S08-154

# Mitochondrial aldehyde dehydrogenase 2*2 (ALDH2*2) knock-in gene targeting mice-an experimental model for a prevalent human genetic disorder in East Asians

A common dominant negative allele, Aldh2*2, exists in the human population. The ALDH2*2 mutant retains only about 1-3% of the enzymatic activity of a corresponding wild-type ALDH2 and affects >40% of the East Asian population (including Japanese, Chinese, Taiwanese and Koreans with an estimated > 1 billion affected individuals). Reduced ALDH2 activity has been associated with a range of human metabolic disorder and diseases. Accumulation of biogenic/xenogenic aldehydes in ALDH2*2 individuals are known to cause sensitivity to alcohol intoxication (hangover), ischemic tissue damage, free-radical induced damage in an organ, such as acute myocardial infarction, heart failure, stroke, Alzheimer disease, Parkinson's disease, other neurodegenerative diseases, alcohol-induced liver cirrhosis, cancers of upper digestive track, insensitivity to nitroglycerin treatment, and hyper-sensitivity to certain drug metabolism.

This invention creates an identical genetic model for animal research specifically for human subjects carrying the ALDH2*2 allele. No such genetically engineered animal exists currently. This mutation affects an estimated >1 billion people.
This invention offers an innovative idea for testing of drug/pharmaceuticals sensitivity and treatment in human ALDH2*2 carriers. Currently the usage of most of the prescribed pharmaceuticals does not take into account of human genetic polymorphism. This is an important aspect in research and application of pharmaco-genetics. We also provide in vitro data to indicate that ALDH2*2 enzyme may be

sensitive to some drugs that are previously unknown or have not yet been described in the literature.

## Applications

- To provide a proper human analog of the E487K (ALDH2*2) using a genetic mouse strain.
- Ideal animal model for commercial drug testing, treatment and drug discovery.

## Advantages

- The knock-out mice represents complete inactivation of the ALDH2 gene (via gene interruption) and the naturally occurring ALDH2*2 allele in the large human population.
- The ALDH2*2 knock-in mice are completely identical to the human ALDH2*2 carries. The mice segregate to both heterozygous and homozygous genotypes as in the human population
- It is a superior experimental system and innovation for the valuable research purposes. In addition, the partially inactive enzyme offers the opportunity for the discovery of small drug molecules.

## Innovators

- Daria Mochly-Rosen
- Che-Hong Chen

## Licensing Contact


### Brenda Martino

Biological Materials Specialist

Email