Docket #: S11-154

Mitochondrial Aldehyde Dehyrogenase-2 Modulators and Methods of Use Thereof

Stanford researchers in the laboratory of Dr. Daria Mochly-Rosen have developed novel small molecules for modulating ALDH2 (mitochondrial aldehyde dehydrogenase-2). More specifically, this new class of ALDH modulators can be applied to conditions where sustained or increased ALDH2 enzymatic activity is beneficial, or to conditions and diseases that are associated with decreased ALDH2 enzymatic activity.

ALDH2 plays an important role in reducing toxicity of both biogenic and xenogenic aldehydic compounds related to ischemic tissue damage or free-radical induced damage in an organ. Therefore, the ALDH2 activator compounds could potentially be used to preventively to reduce damage from ischemia, Alzheimer's disease, Parkinson's disease, alcohol-induced liver cirrhosis, or to overcome nitroglycerin insensitivity.

ALDH Portfolio
This technology is a part of a larger portfolio that explores the potential applications of the ALDH multi-gene family.
Stanford Docket S03-268 describes ALDH2 activation and screening.
Stanford Docket S07-020 describes novel small molecule modulators of ALDH2 and improved screening techniques.
Stanford Docket S08-073 describes structural studies and rational drug design methods.
Stanford Docket S08-154 is comprised of ALDH2 knock-in mice.
Stanford Docket S08-219 describes ALDH2 and ALDH1 activators.
Stanford Docket S09-430 describes a collection of 48 ALDH cDNA and genomic clones for various ALDH isozymes.
Stanford Docket S11-044 describes a novel ALDH3 activator and potential uses.

Stanford Docket S11-153 describes ALDH1-specific antagonists.
Stanford Docket S12-066 describes ALDH2 as a therapeutic target for pain.

Applications

- **Therapeutic small molecule compounds for possible treatment of:**
  - ischemic myocardial injury in bypass surgery or heart transplantation
  - heart failure
  - cancer (by increasing tumor sensitivity to chemotherapy and radiation)
  - Alzheimer's disease
  - Parkinson's disease
  - ethanol/acetaldehyde toxicity
  - liver cirrhosis
  - nitroglycerin sensitivity
- **High-throughput screen** - for compounds that modulate ALDH2
- **Stem cell therapeutics:**
  - adult - compounds could inhibit injury to cells after isolation and injection
  - embryonic - ALDH2 is a marker for embryonic stem cells

Advantages

- **New structures/analogs:**
  - improved potency of the compounds for both ALDH2 wild type and the ALDH2E487K
  - more desirable chemical and pharmacological properties such as stability and solubility

Publications

- Published Patent Application: PCT/US2014/025993

Patents

- Published Application: WO2014160185

- Published Application: 20160107996
- Published Application: 20170320828
- Issued: 9,670,162 (USA)

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