Docket #: S20-218

First-in-class isoform-specific aldehyde dehydrogenase (ALDH1B1 and ALDH1A3) inhibitors for cancer

Every year, 1.4 million new cases are reported for colorectal cancer but existing treatments are not effective. This represents an estimated $1 billion market annually in the US. Some subtype of colorectal cancer is attributed to aldehyde dehydrogenase and high activity interferes with several chemotherapies. Stanford researchers have discovered two classes of isoform-specific aldehyde dehydrogenase inhibitors. These imidazolium and guanidine based inhibitors present the only known selective inhibitor of ALDH1B1?an essential enzyme for colorectal and pancreatic cancer stem cell?with nanomolar potency and almost 100-fold selectivity in IC50. A subset of these inhibitors has high selectivity for ALDH1A3 that is related to breast cancer and melanoma. These new molecules have great therapeutic potential and can be further developed into combination therapies and other drug-conjugate applications for a broad range of cancers.

Applications

- ALDH1B1 inhibitor: colorectal cancer, pancreatic cancer
- ALDH1A3 inhibitor: breast cancer, melanoma, and glioblastoma

Advantages

- First-in-class: there are currently no ALDH1B1 inhibitors on the market.
- High nanomolar potency and high isoform selectivity

Publications

- Feng, et al. Targeting colorectal cancer with small-molecule inhibitors of ALDH1B. 2022. Nat Chem Biol.

Patents

- Published Application: WO2021257696
- Published Application: 20230174537

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