Docket #: S20-218

Targeting Cancer Stem Cell Metabolism via Isoform-specific ALDH1B1 and ALDH1A3 Inhibitors

Colorectal cancer affects 1.4 million new patients annually, with existing treatments often ineffective. A key factor in treatment resistance is high aldehyde dehydrogenase activity, which undermines several chemotherapies. Stanford University's Chen Lab has developed two groundbreaking classes of inhibitors that selectively target specific aldehyde dehydrogenase isoforms.

These imidazolium and guanidine-based compounds are:

- The first selective inhibitors of ALDH1B1, an enzyme essential for cancer stem cell survival in colorectal and pancreatic cancers
- Selective ALDH1A3 inhibitors targeting breast cancer and melanoma

Recent Chen Lab advancements demonstrate:

- Nanomolar potency against cancer spheroids
- Nearly 100-fold selectivity for specific ALDH isoforms
- Enhanced metabolic stability
- Improved pharmacokinetic properties (reduced clearance, higher maximum concentration) in mice

This approach represents a shift from targeting rapid cell division to addressing the metabolic pathways that sustain cancer stem cells. These inhibitors have significant therapeutic potential for combination therapies and other drug-conjugate applications for a broad range of cancers, potentially improving long-term outcomes for cancer patients.

Stage of Development
Research in vivo

Applications

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

Advantages

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

Publications

- Tarhan, A. K., Feng, Z., Fernandez, D., Kim, A., Bearrood, T., Hinman, A., White, N., & Chen, J. (2025). Development of next-generation ALDH1B1 inhibitors with enhanced pharmacological and functional properties. *ChemRxiv* (2025).
- Feng, Z., Hom, M. E., Bearrood, T. E., Rosenthal, Z. C., Fernandez, D., Ondrus, A. E., ... & Chen, J. K. (2022). Targeting colorectal cancer with small-molecule inhibitors of ALDH1B1. *Nature chemical biology, 18*(10), 1065-1075.

Patents

- Published Application: WO2021257696
- Published Application: 20230174537
- Issued: 12,570,661 (USA)

Innovators

- James Chen
- Toni Kline
- Alison Ondrus
- Cody Marshall
- Marisa Hom
- Zhiping Feng

Licensing Contact

Kimberly Griffin

Technology Licensing and Strategic Alliances Manager

Email