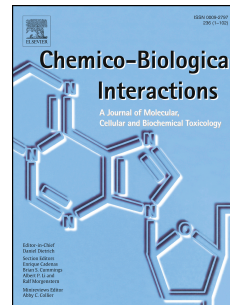


# Accepted Manuscript

ALDHs in normal and malignant hematopoietic cells: Potential new avenues for treatment of AML and other blood cancers

Maura Gasparetto, Clayton A. Smith



PII: S0009-2797(17)30666-X

DOI: [10.1016/j.cbi.2017.06.020](https://doi.org/10.1016/j.cbi.2017.06.020)

Reference: CBI 8033

To appear in: *Chemico-Biological Interactions*

Received Date: 3 November 2016

Revised Date: 28 April 2017

Accepted Date: 19 June 2017

Please cite this article as: M. Gasparetto, C.A. Smith, ALDHs in normal and malignant hematopoietic cells: Potential new avenues for treatment of AML and other blood cancers, *Chemico-Biological Interactions* (2017), doi: 10.1016/j.cbi.2017.06.020.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

**ALDHs in normal and malignant hematopoietic cells: potential new avenues for treatment of AML and other blood cancers**

Maura Gasparetto<sup>1</sup> and Clayton A Smith<sup>1</sup>

<sup>1</sup>University of Colorado Medical Center, Aurora, USA

Communicating Author:

Maura Gasparetto, MD

Division of Hematology, University of Colorado

Mail Stop B170, 12700 E.19<sup>th</sup> Ave, Room P15-10440A, Aurora, CO 80045

Phone: 720-724-7415

Fax: 720-724-4087

Email: [Maura.Gasparetto@ucdenver.edu](mailto:Maura.Gasparetto@ucdenver.edu)

Text word count: 2741

*Abstract*

Multiple studies have demonstrated that ALDH1A1 is elevated in hematopoietic stem cells (HSCs). As a means to better characterize such cells, we previously developed the fluorescent ALDH1A1 substrate Aldefluor to facilitate HSC identification and isolation. This has proven useful for counting and isolating HSCs from human bone marrow, peripheral blood and cord blood as well as stem cells in other tissues and organisms. Given the high level expression of ALDH1A1, we explored its biology and that of other ALDHs in HSCs and found that ALDH1A1 and ALDH3A1 were important in metabolizing reactive aldehydes (RALDs) and reactive oxygen species (ROS). In murine models, loss of these two isoforms resulted in a variety of effects on HSC biology, increased DNA damage and predisposition to leukemia formation when combined with a genetic driver of HSC proliferation and self-renewal. Loss of ALDH activity may also predispose to marrow failure and AML in Fanconi's anemia (FA). ALDHs also have importance in mediating drug resistance in AML, may be useful in the identification of leukemia stem cells (LSCs) and ALDH activity levels may have prognostic significance. Together these findings suggest that further studying ALDH biology in AML and other blood cancers may provide important insights into malignant transformation and may point the way to the development of novel diagnostics and therapies.

Download English Version:

<https://daneshyari.com/en/article/8545510>

Download Persian Version:

<https://daneshyari.com/article/8545510>

[Daneshyari.com](https://daneshyari.com)