Histone Transferase Inhibitors to Treat and Target Drug-resistant Cancer Stem Cells

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BACKGROUND

The fact that histone methyl- and acetyl-transferases modify the structure of euchromatin and gene transcription has invited the development of drugs against these enzymes. And while histone transferase inhibitors have been touted as potential cancer therapeutics, there have been challenges to realizing their potential. Recent studies suggest a more specific utility for targeting cancer stem cells and enables therapeutic options not previously available.

TECHNOLOGY DESCRIPTION

An appreciation for mechanisms that underlie the progression from a cancer cell to a cancer stem cells (see references) has yielded therapeutic options to retard disease progression and the development of resistance. UC researchers have found that histone acetyl- and methyl-transferase inhibitors may prevent the appearance of αVβ3 and thereby abrogate the development of the “stem” phenotype in a cancer cell and facilitate treatment of such cells that become refractory to standard chemotherapeutic regimens. This approach can be used alone or in combination with other cancer therapeutics to decrease the development of cancer stem cells and also increase the susceptibility of cancer stem cells to cancer therapeutic drugs.

APPLICATIONS

Cancer therapeutic options are enabled by development of stand-alone drugs and combination therapies, which can:

- suppress tumor progression and the development of cancer stem cells
- sensitize tumor cells to first-line chemotherapeutic drugs, particularly tyrosine kinase inhibitors

ADVANTAGES

In addition to providing a new means of targeting a refractory cell population, this approach tackles the clinical challenge of patients developing resistance to chemotherapeutics currently on the market.

STATE OF DEVELOPMENT

Earlier work (see references, below) showed that β3 expressions correlates with “stemness” as assessed in vitro and in vivo (xenograft mouse model). New data demonstrate that this may be regulated by epigenetic genes identified.

INTELLECTUAL PROPERTY INFO

Worldwide rights available; pending patents available under confidentiality.

RELATED MATERIALS

- Sequin et al., Targeting the Achilles' heel of drug-resistant cancer stem cells, Cell Cycle, (2014), 13(13):2017-8 - 06/06/2014
- Desgrosellier, J.S., et al., Integrin avß3 drives slug activation and stemness in the pregnant and neoplastic mammary gland, Dev Cell, (2014) 11;30(3):295-308 - 06/05/2014
- Seguin L, et al. An integrin ß3-KRAS-RalB complex drives tumour stemness and resistance to EGFR inhibition., Nat Cell Biol. 2014 May;16(5):457-68. doi: 10.1038/ncb2953. Epub 2014 Apr 20 - 04/20/2014

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OTHER INFORMATION

KEYWORDS

oncology, cancer, therapeutic, therapy, kinase, tumor, combination therapy, avß3, alpha v, alpha-v, beta 3, beta-3, integrin, kinase, inhibitor, resistance, chemoresistance

CATEGORIZED AS

- **Biotechnology**
  - Health
- **Medical**
  - Disease: Cancer
  - Therapeutics

RELATED CASES

2015-103-0, 2015-203-0

▶ Seguin, L., et al., An integrin ß3-KRAS-RalB complex drives tumour stemness and resistance to EGFR inhibition, Nat Cell Biol. (2014) 16(5):457-68 - 07/08/2013

▶ Alber, M. and K. Helin, Histone Methyltransferases in Cancer, Semin Cell Dev Biol. 2010 Apr;21(2):209-20 - 04/01/2010

▶ Desgrosellier JS, et al., An integrin alpha(v)beta(3)-c-Src oncogenic unit promotes anchorage-independence and tumor progression, Nat Med. (2009) 15(10):1163-9. - 09/06/2009

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20180000821	01/04/2018	2015-103

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