

Cancer Therapeutic Based on Hypoxia Inducible Factor 1 (HIF-1) Inhibitors

Summary (1024-character limit)

Researchers at the National Cancer Institute (NCI) have developed small molecule compounds that inhibit activity of hypoxia inducible factor 1 (HIF-1). The HIF-1 inhibitor compounds are designed around the scaffold of naturally occurring metabolite eudistidine. The invention compounds have demonstrated activity against cancer and malaria in vitro.

NIH Reference Number

E-115-2015

Product Type

- Therapeutics

Keywords

- Hypoxia Inhibitor, Cancer, Malaria, Small Molecule

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

Hypoxia is a characteristic of many solid tumors resulting from accelerated cellular proliferation and inadequate vascularization. HIF-1 is a transcription factor critical for maintaining cellular homeostasis in, and adaptively responding to, low oxygen environments. HIF-1 becomes activated through binding to the transcriptional co-activator protein p300. Disruption of the HIF-1/p300 interaction could potentially modulate HIF-1 activity.

Researchers at the National Cancer Institute (NCI) have developed small molecule compounds that inhibit the activity of HIF-1. The HIF-1 inhibitor compounds are designed around the scaffold of naturally occurring metabolite eudistidine. Compounds eudistidine A and C have been shown to disrupt the HIF-1/p300 interaction in vitro. Eudistidine C has also inhibited growth of malaria at low micromolar concentrations.

Potential Commercial Applications

- Therapeutic against cancer that may leave normal cells unaffected. While the HIF-1 α protein occurs in a wide range of human primary tumors, it is only produced at very low levels in normal tissue.
- Therapeutic against malaria – especially at the liver-infection phase. Malaria remains one of the most severe global health issues. According to the World Health Organization, 3.2 billion people (half the world's population) live in areas at risk of malaria transmission in 106 countries and territories. In 2012, malaria caused nearly 207 million clinical episodes and 627,000 deaths – primarily (91%) in the African Region.

Competitive Advantages

- Lack of general cytotoxic effects
- Novel molecular scaffolds and chemotypes
- Attractive molecular target
- Concise and high-yielding synthesis of compounds
- Potent at low micromolar concentrations

Inventor(s)

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Development Stage

- Basic (Target Identification)

Publications

Chan S, et al. Structural Elucidation and Synthesis of Eudistidine A: An Unusual Polycyclic Marine Alkaloid that Blocks Interaction of the Protein Binding Domains of p300 and HIF-1 α . [PMID: 25892103]

S. Chan S et al. Characterization and Synthesis of Eudistidine C, a Bioactive Marine Alkaloid with an Intriguing Molecular Scaffold. [PMID: 27934476]

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/144,182, Filed 07 Apr 2015
- **Foreign Filed:** Foreign Filed - Patent Application PCT/US2016/026145, Filed 06 Apr 2016

Therapeutic Area

- Cancer/Neoplasm