Increasing degradation of Hypoxia-Inducible Factors impairs cancer stem cell proliferation

Technology #cu16166

This technology describes a method for treating ID2 protein-related diseases through increased degradation of Hypoxia-Inducible Factors (HIFs).

Unmet Need: Therapeutics that inhibit hypoxic cancer stem cell proliferation

Hypoxia is a characteristic feature of many malignant tumors, including glioblastoma, and is associated with poor patient prognosis. The hypoxic microenvironment drives tumor progression by triggering adaptive transcriptional responses, including the Hypoxia-Inducible Factors (HIFs) and tumor suppressor Von Hillel Landau (VHL), which targets HIF2a for degradation by a mechanism that is not well understood. Despite the substantial demand for new therapeutics for glioblastomas, there are currently no therapeutics on the market that target either VHL or HIFs.

The Technology: Increasing degradation of HIFs prevents cancer stem cell proliferation

This technology describes compositions and methods for treating glioblastomas and other ID2 protein-related diseases by increasing the degradation of HIFs. This technology is based on the finding that the DYRK1 kinases target ID2 for degradation through phosphorylation, subsequently preventing it from inhibiting the VHL complex. As a result, HIF2a undergoes increased degradation, thus reducing the cancer cell's ability to survive in a hypoxic environment. Therefore, activating DYRK1 and inhibiting ID2 may prevent the proliferation of hypoxic cancer stem cells. In addition to cancer, this technology may also be used in the treatment of other ID2 protein-related diseases such as metabolic, renal, and vascular diseases. In sum, this technology provides a mechanism-backed method for the specific treatment of ID2 protein-related diseases by increasing degradation of HIFs.

This technology has been demonstrated in a mouse model of human glioma, in which overexpression of DYRK1 led to increased degradation of HIF2a and inhibition of tumor cell proliferation.

Applications:

- Treatment and prevention of glioblastoma and other cancers
- Treatment and prevention of other ID2 protein-related diseases
- Research tool for developing additional targeted therapeutics

**Advantages:**

- Mechanism-backed treatment of ID2 protein-related diseases
- Applicable to multiple types of hypoxia-related cancers
- Provides multiple drug targets for increasing degradation of HIFs, reducing risk of resistance

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**Patent Information:**


**Related Publications:**


**Tech Ventures Reference:**

- IR CU16166
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