

Docket #: S23-242

Molecules and methods for treatment of cancer with TCIPs

Researchers in the laboratories of Nathanael Gray and Gerald Crabtree at Stanford University have developed and synthesized new small molecule chemotherapeutics for targeted (and potentially less toxic) treatment of cancers having high BCL6 levels including lymphomas and other human hematopoietic cancers. These small bifunctional molecules engage the cancer driver, BCL6 on one side and a molecule binding a histone acetylase transferases (HAT) on the other side of the molecules; and rewire the cancer driver (BCL6) to activate cell death genes such as P53, BIM, NOXA, PUMA and others that then kill the cancer cell using its own driver. These Transcriptional/Epigenetic Chemical Inducers of Proximity, or TCIPs, function at picomolar concentrations to kill human cancer cells specifically that express both the anchoring transcription factor and the histone modifying enzyme and have little toxicity to other human cells. Preliminary studies demonstrate good pharmacologic features and feasibility for human safety studies. These HAT-BCL6 TCIPs could provide a targeted treatment of Diffuse Large Cell B Cell Lymphoma (DLBCL) having mutations in the BCL6 gene. In addition, these molecules may be useful for treatments of other cancers and hematologic malignancies having high BCL6 levels or mutations.

Stage of Development

Pre-clinical: The Gray and Crabtree Labs continue pharmacologic optimization, animal safety and efficacy studies, and future human safety studies.

Applications

- **Cancer treatment** – in particular Diffuse Large Cell B Cell Lymphoma (DLBCL), and other malignancies expressing BCL6 and histone acetyltransferases.

Advantages

- **More targeted and effective** (and potentially less toxic) – especially for Diffuse Large Cell B Cell Lymphoma (DLBCL) that is commonly treated with RCHOP, a combination chemotherapy which often causes permanent neurologic damage, anemia, and bone marrow repression, and leads secondary malignancies.
- Possible treatment for tumors that have metastasized and spread beyond surgical resection.

Innovators

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