Small Molecule Inhibitors of STAT3 for the Treatment of AML

Product

STAT3 Inhibitors

Indication

Multiple Cancer Types Including AML

Value Propositions

- STAT3 inhibitors eliminate leukemic stem cells
- Minimal toxicity to normal hematopoietic stem cells

Market

- $1.4 Billion—Global AML Therapeutic Market Size (CAGR of 13.6% through 2026)

Intellectual Property

- Patents pending*
- Available for licensing

Background on CU4899H

Signal transducer and activator of transcription-3 (STAT3) is an attractive target for small molecule inhibitors due to its role in cancer and inflammatory disease. STAT3 has been implicated in cancer types including leukemia, prostate cancer, breast cancer, hepatocellular carcinoma, colorectal cancer, and glioblastoma. While many have tried to target STAT3 at its SH2 dimerization domain, there has been fewer attempts at disrupting the molecule's DNA-binding domain. Targeting STAT3 for AML treatment is appealing since STAT3 plays an essential role in OXPHOS regulation, which is necessary for leukemic stem cells proliferation and AML progression. Many traditional chemotherapies fail to eliminate leukemic stem cells that drive the AML disease process.

Technical Innovation

A team at the University of Colorado, led by Dr. Philip Reigan, synthesized novel analogs of niclosamide that display inhibitory activity at the STAT3 DNA binding domain and induction of apoptosis in leukemic stem cells. STAT3 has two binding sites, based on its crystalline structure, that may be targeted to inhibit DNA binding. Dr. Reigan's nuclosamide analogs can inhibit both targets on the STAT3 molecule. Small molecule inhibition of STAT3 is an intriguing therapeutic for AML treatment since STAT3 plays an integral part in leukemic stem cell expansion and AML development. The lead two molecules included in CU4899H have shown the ability to decrease leukemic stem cell viability and colony formation in primary AML samples, while not affecting the viability of normal hematopoietic stem cells. This novel approach to AML treatment may also have the potential to treat various other cancer sub-types.

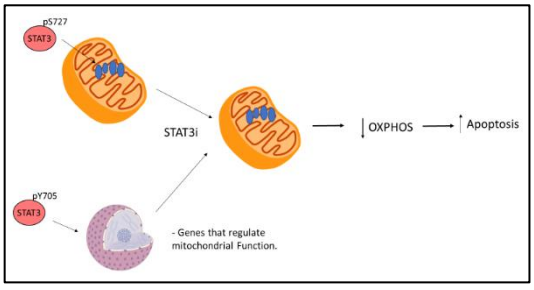

Figure: STAT3 inhibition reduces OXPHOS expression, which causes apoptosis in Leukemic stem cells.

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Resources & Documents:

***US and EU patents pending:** "STAT3 Transcription Factor Inhibitors And Methods Of Using The Same"—Filed 2021.*