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Novel anti-cancer agents that target the epigenetic reader protein

Small-molecule inhibitors target the bromodomain and PHD finger transcription factor (BPTF) for development as anti-cancer therapeutics.

Technology No. 2021-055

IP Status: Provisional Patent Application Filed; **Application #:** 63/089,999

Applications

- Cancer therapeutic
- Cancer research
- Epigenetic regulations in cancer cells

Key Benefits & Differentiators

- **High potency:** The inhibitors targeting BPTF bromodomain are under the submicromolar range and with high ligand efficiency.
  High selectivity against BET family proteins
- **Broad anti-cancer spectrum:** BPTF is implicated in various types of cancer, such as breast cancer, melanoma, lung, bladder, and etc. Therefore, inhibitors targeting this protein could potentially be effective against multiple cancers.
  BPTF has also been shown to play an immunomodulatory role supporting an additional mechanism for anticancer therapy
- **Excellent physicochemical properties:** The inhibitors developed here are highly water soluble, low molecular weight and potent, resembling good drug-like physicochemical properties.

Targeting epigenetics for cancer therapy

Genome instability and mutations is one hallmark of cancer. Epigenetic alterations concern heritable yet reversible changes in histone or DNA modifications that regulate gene activity beyond the underlying sequence. The emerging epigenetic therapy for cancers seek to normalize DNA methylation patterns and post-translational modifications on histones that promote or maintain a malignant phenotype. The Nucleosome Remodeling Factor interacts

with chromatin through its largest subunit, the bromodomain and PHD finger transcription factor (BPTF), resulting in changes to chromatin accessibility and gene expression. BPTF is overexpressed in several cancers and has been shown to promote resistance to several chemotherapeutics. Targeting BPTF using small-molecule inhibitors presents a potential strategy for anti-cancer therapies. While numerous chemical probes have been developed for other bromodomain proteins, inhibitor development for BPTF has lagged behind.

Professor Pomeranz at the University of Minnesota has developed a series of novel small-molecule inhibitors targeting BPTF with excellent potency, good selectivity, and drug-like physicochemical properties. The co-treatment of the lead compound in this series showed enhanced efficacy of doxorubicin, a FDA-approved chemotherapy drug, against a breast cancer cell line. Given the tractable synthesis method, the BPTF inhibitors can serve as useful starting points for chemical tool development to explore the biological roles of BPTF, and present the potential for new anti-cancer drug development.

Phase of Development

TRL: 2-3
In vitro data showed the lead compound of this series of inhibitors, BZ1, enhanced efficacy of doxorubicin when co-administered in the breast cancer cell line 4T1.

Desired Partnerships

This technology is now available for:

- License
- Sponsored research
- Co-development

Please contact our office to share your business' needs and learn more.

Researchers

- **William C. Pomerantz, PhD** Associate Professor, McKnight Land-Grant Professor, McKnight Presidential Fellow, Department of Chemistry