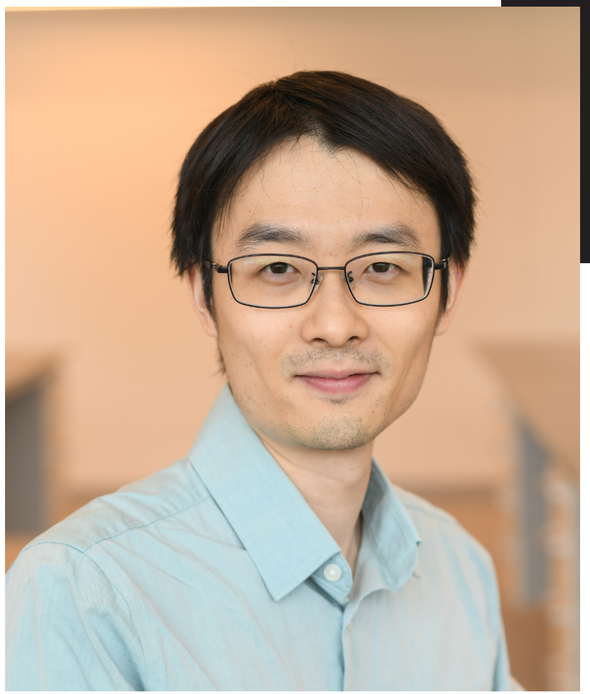
PURDUE UNIVERSITY | Department of Basic Medical Sciences

TARGETING TRANSCRIPTION IN CANCER



Monday, March 31 | 1:00 PM

Hansen Life Sciences Building | Room 103

SEMINAR 1:00 PM | CHALK TALK 2:00 PM

Breast cancer remains the most commonly diagnosed cancer in women, with estrogen receptor-positive (ER+) breast cancer accounting for the majority of cases. ER functions as a transcription factor that drives oncogene expression, including MYC, to promote cancer cell proliferation and survival. While endocrine therapies targeting ER have improved patient outcomes, resistance remains a significant challenge, highlighting the need for new therapeutic strategies. BET inhibitors (BETi) were developed to target bromodomain and extra-terminal (BET) proteins (BRD2, BRD3, and BRD4), which recognize acetylated histones via their bromodomains and facilitate oncogene transcription. By blocking the bromodomains of BET proteins, BETi aim to disrupt their chromatin binding and suppress oncogene expression. While BETi have shown promise in clinical trials for some cancers, they have failed to demonstrate efficacy in ER+ breast cancer, and the underlying mechanisms remain unclear.

Our recent findings reveal that the ER-driven oncogene transcription, including MYC, is intrinsically resistant to BETi due to an unexpected bromodomain-independent mechanism of transcriptional regulation by BRD4. In this seminar, I will discuss how our insights into BRD4's role in transcription redefine our understanding of these "epigenetic readers," uncover new mechanisms of drug resistance, and inform novel therapeutic strategies. These findings challenge the conventional view of BET protein function and highlight alternative approaches to targeting transcriptional dependencies in ER+ breast cancer.

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