

Title: Attenuating transcription in cancer

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Abstract: For decades, transcription factors (TFs) have been identified as key biological players in diseases including cancer, diabetes, and autoimmune disorders. However, outside of nuclear receptors, this class of proteins has traditionally been considered “undruggable” by small molecules due to significant structural disorder and lack of defined binding pockets. A renewed interest in the field has been ignited by significant advances in chemical biology approaches to ligand discovery and optimization, especially the advent of targeted protein degradation approaches, along with increasing appreciation of the critical role a limited number of collaborators play in the regulation of key TF effector genes. Dr. Koehler will review recent advances in the lab involving successful targeting strategies, including discussion of compounds that modulate MYC-driven transcription via mechanisms involving the MAX partner protein or the transcriptional kinase CDK9. Finally, new directions for cancer target classes beyond transcription factors will be discussed, including RNA-binding proteins and cytokines.

Biography: Professor Koehler earned her bachelor's degree in biochemistry and molecular biology from Reed College in 1997. In 2003, she finished her doctorate in chemistry from Harvard University and became an institute fellow at the Broad Institute. Professor Koehler joined the Koch Institute in 2014, where she serves as faculty co-director of the Swanson Biotechnology Center High-Throughput Screening Facility. Her lab at MIT is focused on expanding the repertoire of targets accessible for therapeutic intervention with emphasis on target-directed screening approaches. The lab undertakes chemical probe discovery and development for challenging targets such as transcription factors, RNA-binding proteins, and extracellular factors. She has served on the Chemists in Cancer Research Executive Advisory Board for AACR. Awards include being named a Genome Technology Young Investigator and a Broad Institute Merkin Fellow. She has also received the Ono Pharma Foundation Breakthrough Science Award, the Novartis Lectureship in Chemistry, the AACR-Bayer Innovation and Discovery Award, and NSF CAREER Award, and the Junior Bose Award for Excellence in Teaching. Professor Koehler is a founder of Ligon Discovery, Kronos Bio and 76Bio and has served as an advisor to several other pharmaceutical or biotechnology companies.