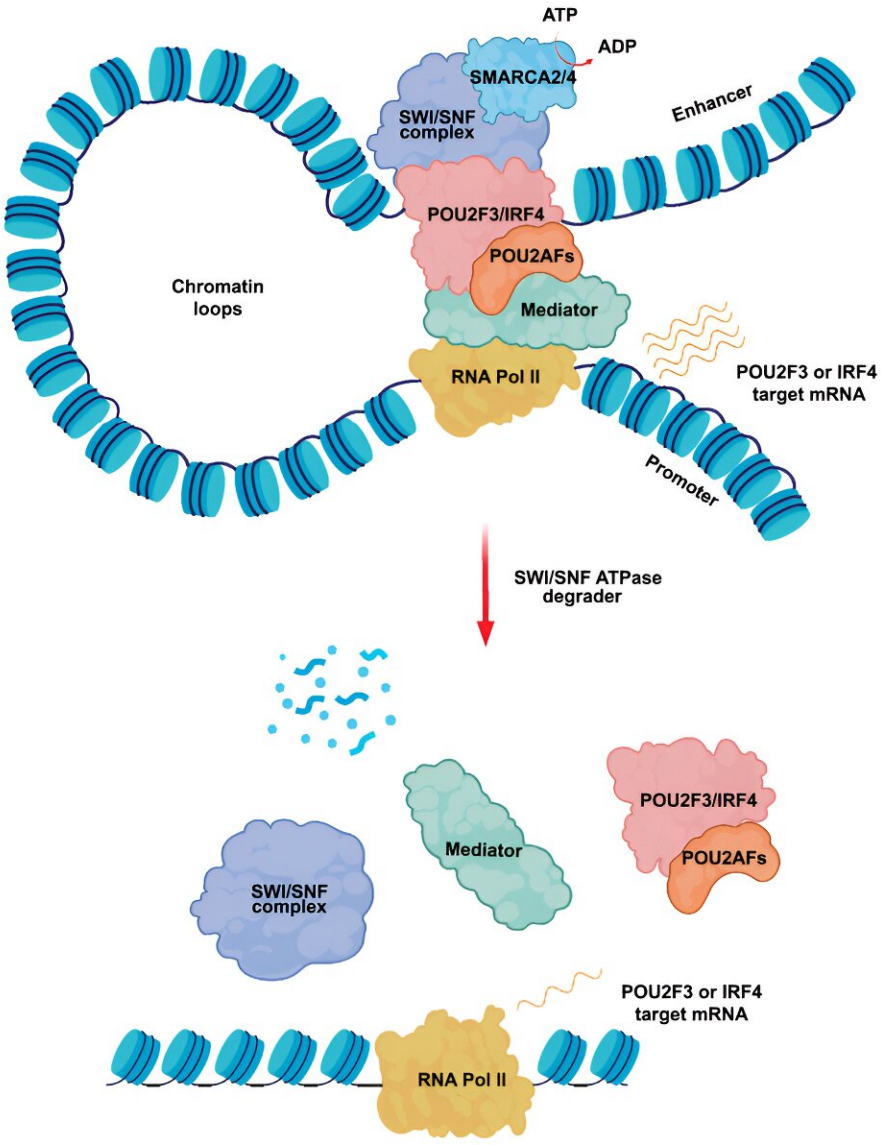
New findings on possible therapies to target oncogenic transcription factors in multiple cancer types

July 30 2024, by Anna Megdell



Credit: *Cancer Cell* (2024). DOI: 10.1016/j.ccell.2024.06.006

A new study from the University of Michigan Health Rogel Cancer Center furthers research that suggests the potential of developing new cancer treatments to target oncogenic transcription factors by indirectly affecting their ability to access enhancer DNA in chromatin.

The findings appear in *Cancer Cell*.

Led by Arul Chinnaiyan, M.D., Ph.D., S.P. Hicks Professor of Pathology and director of the Michigan Center for Translational Pathology at Michigan Medicine, the research builds on previous work to find genetic vulnerabilities to treat transcription factor-driven cancers like prostate cancer.

"These cancers have been challenging to target therapeutically because it's hard to find drugs or small molecules that can bind to transcription factors. They lack a 'druggable' pocket," Chinnaiyan explained. "These findings will hopefully drive forward the clinical development of SWI/SNF degraders or inhibitors to treat transcription factor-driven cancers."

Further, this new research shows that principles Chinnaiyan and his team learned in prostate cancer may apply to other oncogenic transcription factor-driven cancers such as small cell lung cancer and multiple myeloma.

In previous work, Chinnaiyan's team found that it's possible to inhibit key components of nucleosomal remodeling factors of the SWI/SNF

pathway by using PROTAC degrader molecules. In disabling the pathway, oncogenic transcription factors can't access chromatin to bind to the enhancer elements in DNA that drive the overexpression of oncogenic gene programs.

Chinnaiyan previously presented this research at the American Association for Cancer Research 2024 Annual Meeting in San Diego, California.

More information: Tongchen He et al, Targeting the mSWI/SNF complex in POU2F-POU2AF transcription factor-driven malignancies, *Cancer Cell* (2024). DOI: 10.1016/j.ccell.2024.06.006

Provided by University of Michigan