

2nd International ge Cancer Study & Therapy Conference

February 20-22, 2017 Baltimore, USA

KDM4/JMJD2 histone demethylase inhibitors block prostate tumor growth by suppressing the expression of AR and BMYB-regulated genes

Lingling Duan and Zhi-Ping Liu*

Departments of Internal Medicine and Molecular Biology, UT Southwestern Medical Center, USA

Haistone lysine demethylase KDM4/JMJD2s are overexpressed in many human tumors including prostate cancer (PCa). KDM4s are co-activators of androgen receptor (AR) and are thus potential therapeutic targets. Yet to date few KDM4 inhibitors that have anti-prostate tumor activity in vivo have been developed. Here, we report the anti-tumor growth effect and molecular mechanisms of three novel KDM4 inhibitors (A1, I9, and B3). These inhibitors repressed the transcription of both AR and BMYB-regulated genes. Compound B3 is highly selective for a variety of cancer cell lines including PC3 cells that lack AR. B3 inhibited the in vivo growth of tumors derived from PC3 cells and ex vivo human PCa explants. We identified a novel mechanism by which KDM4B activates the transcription of Polo-like kinase 1 (PLK1). B3 blocked the binding of KDM4B to the PLK1 promoter. Our studies suggest a potential mechanism-based therapeutic strategy for PCa and tumors with elevated KDM4B/PLK1 expression.

Biography:

Dr. Zhi-Ping Liu obtained her PhD in Biophysics and post-doctoral training in Molecular Biology at UT Southwestern Medical Center. She is now an associate professor in the department of internal medicine, UT Southwestern. Her research focuses on the transcriptional regulation of genes involved in cancer and cardiovascular diseases.