J Cancer Sci Ther 2018, Volume 10
DOI: 10.4172/1948-5956-C8-145

EZH2 as a novel therapeutic target for human endometrial cancer

Peixin Dong
Hokkaido University, Japan

EZH2 inhibition and reactivation of tumor suppressor microRNAs (miRNAs) represent attractive anti-cancer therapeutic strategies. Previously, we reported that miR-101 can suppress EC cell proliferation, invasion and stem cell-like features of endometrial cancer (EC) cells by targeting EZH2. We recently found that EZH2-suppressed let 7b and miR-361, two likely tumor suppressors, inhibited EC cell proliferation and invasion, and abrogated cancer stem cell-like properties. In EC cells, EZH2 induced and functioned together with YY1 to epigenetically suppress miR-361, which directly targets Twist. Treating EC cells with GSK343, a specific EZH2 inhibitor, mimicked the effects of siRNA-mediated EZH2 knockdown, upregulating miR-361 and downregulating Twist expression. The treatment with GSK343 also siginificantly decreased tumor size and weight in EC cell xenografted mice. Quantitative real-time PCR analysis of 24 primary EC tissues showed that lower let-7b and miR-361 levels were associated with worse patient outcomes. These results were validated in a larger EC patient dataset from The Cancer Genome Atlas. Our findings suggest that EZH2 drives EC progression by regulating miR-361/Twist signaling, and support EZH2 inhibition as a promising anti-EC therapeutic strategy. .

dpx1cn@gmail.com