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**Br Ormeloxifene regulates epithelial to mesenchymal transition by targeting miR200a and  $\beta$ -catenin in cervical cancer**

Mohammed Sikander<sup>1</sup>, Shabnam Malik<sup>1</sup>, Sonam Kumari<sup>1</sup>, Pervez Khan<sup>2</sup>, Hassan Mandil<sup>1</sup>, Bilal Bin Hafeez<sup>1</sup>, Sheema Khan<sup>1</sup>, Abdulrhman Alsayari<sup>3</sup>, Fathi T. Halaweish<sup>4</sup>, Meena Jaggi<sup>1</sup> and Subhash C. Chauhan<sup>1</sup>

<sup>1</sup>University of Tennessee Health Science Centre, USA

<sup>2</sup>Jamia Millia Islamia University, India

<sup>3</sup>King Khaled University, Saudi Arabia

<sup>4</sup>South Dakota State University, USA

Cervical cancer is a leading cause of cancer-related death among women worldwide. Current standards of care for cervical cancer include radiation, chemotherapy, and surgery. Thus, an utmost need exists to discover novel therapeutic modalities that would enhance therapy outcomes of this disease with minimal side effects. Ormeloxifene, a synthetic, non-steroidal molecule that has potent anti-cancer effects through inhibition of important oncogenic signaling pathways. We have synthesized novel analogue Br-ormeloxifene (Br-ORM), which showed an enhanced therapeutic efficacy as compared to parent compound ormeloxifene. Molecular docking analysis showed, Br-ORM proficiently docked with  $\beta$ -catenin. Furthermore, bioinformatics analysis identified  $\beta$ -catenin (CTNNB1) as a direct and functional target of miR-200a. In the current study, we observed the underlying mechanism of miR-200a and epithelial to mesenchymal transition by interacting with  $\beta$ -catenin. Br-ORM treatment inhibited epithelial to mesenchymal transition as evident by downregulation of  $\beta$ -catenin, ZEB 1, N-cadherin, slug, snail, vimentin, MMPs and restore the expression of tumor suppressor miR-200a and E-cadherin. Moreover, Br-ORM arrested cell cycle in G2-S phase and induced apoptosis. Furthermore, it showed remarkable inhibition of migratory and invasive potential of cervical cancer cells. *In vivo* orthotopic mouse model demonstrated the regressed tumor growth by Br-ORM treatment. We observed upregulated expression of miR-200a by fluorescent in situ hybridization in excised tumor tissues. The expression of the potential miR-200a target gene/s  $\beta$ -catenin and other EMT markers were detected in similar tissues as shown by immunohistochemistry. For the first time, our findings exhibited Br-ORM restored tumor suppressor miR-200a, inhibited  $\beta$ -catenin signaling and the EMT process. These pre-clinical data suggest that Br-ORM may be an effective therapeutic agent for cervical cancer treatment.

msikande@uthsc.edu