Targeting beta-Catenin signaling to induce apoptosis in human breast cancer cells by gugulipid extract of Ayurvedic medicine plant *Commiphora mukul*

Dong Xiao\(^1\) and Guoqin Jiang\(^2\)

\(^1\)Department of Urology, University of Pittsburgh, USA
\(^2\)Department of General Surgery, The Second Affiliated Hospital of Soochow University, China

**Introduction:** Gugulipid (GL), extract of Indian Ayurvedic medicinal plant *Commiphora mukul*, has been used to treat a variety of ailments. We now report anti-cancer effect and mechanism of GL against human breast cancer cells.

**Methods:** Using the human estrogen receptor-positive (MCF-7) and triple-negative (MDA-MB-231) breast cancer cells as well as the normal human mammary epithelial cell line (HMEC), we evaluated the anti-breast-cancer efficacy of GL. We measured the activity of GL on apoptosis inducing. Finally, we determined the cellular and molecular mechanism of GL-inhibited breast cancer cell growth.

**Results:** Treatment with GL significantly inhibited viability of human breast cancer cell line MCF-7 and MDA-MB-231 cells with an IC\(_{50}\)~2 µM (24 h treatment) at pharmacologically relevant concentrations standardized to its major active constituent \(\alpha\)-guggulsterone. The GL-induced growth inhibition correlated with apoptosis induction as evidenced by an increase in cytoplasmic histone-associated DNA fragmentation and caspase 3 activity. Interestingly, a normal human mammary epithelial cell line HMEC is significantly more resistant to growth inhibition and apoptosis induction by GL. The GL-induced apoptosis was associated with down-regulation of \(\beta\)-Catenin signaling pathway. The decrease of Wnt/\(\beta\)-Catenin targeting genes, such as cyclin D1, C-myc and inhibition of transcription factor (T-cell factor4, TCF4) was observed in GL-treated breast cancer cells. The GL treatment caused apoptotic cell death was significantly enhanced by RNA Interference of \(\beta\)-Catenin and TCF-4.

**Conclusion:** The present study indicates that \(\beta\)-Catenin signaling pathway is the target for GL-induced the growth inhibition and apoptosis induction in human breast cancer.

This investigation was supported by USPHS grant R21 CA143104 and RO1-CA157477, awarded by the National Cancer Institute.

dongx@upmc.edu