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BRMS1L suppresses breast cancer metastasis by inducing epigenetic silence of FZD10

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BRMS1L (breast cancer metastasis suppressor 1 like, BRMS1-like) is a component of the SIN3A-HDAC co-repressor complex that suppresses target gene transcription. However, the contribution of BRMS1L in cancer development is not well characterized. Here, it was shown that reduced BRMS1L in breast cancer tissues is associated with tumor metastasis and poor patient survival. Functionally, BRMS1L inhibits migration and invasion of breast cancer cells by inhibiting epithelial-mesenchymal transition (EMT). These effects are mediated by epigenetic silencing of FZD10, a receptor for Wnt signaling, by facilitating the recruitment of HDAC1 to its promoter and enhancing histone H3K9 deacetylation. Consequently, BRMS1L-induced FZD10 silencing inhibits aberrant activation of WNT3-FZD10- β -catenin signaling. Furthermore, BRMS1L is a target of miR-106b and miR-106b upregulation leads to BRMS1L reduction, which is responsible for Wnt pathway activation and the ensuing EMT in breast cancer cells. RNAi-mediated silencing of BRMS1L expression promotes metastasis of breast cancer xenografts in immunocompromised mice, while ectopic BRMS1L expression inhibits metastasis. Therefore, BRMS1L provides an epigenetic regulation of Wnt signaling in breast cancer cells and acts as a breast cancer metastasis suppressor.

Biography

Chang Gong started her clinical practice and research career on breast cancer in Sun Yat-Sen University since 2001 and was appointed as an Associate Professor of surgery in Breast Tumor Center of Sun Yat-Sen Memorial Hospital in 2011. Gong focuses on the epigenetic mechanisms of drug resistance and metastasis of breast cancer. She found that non-coding RNAs and BRMS1L, a co-suppressor in HADC complex play a critical role in regulating the trastuzumab resistance and metastasis in breast cancer. She also found that autophagy is required for the tumorigenicity of breast cancer stem cells (BCSCs) and demonstrated that markers of BCSCs predict the chemoresistance of breast cancer. She published articles on the *Journal of Cancer Cell*, *Nature Communications*, *Cancer Research*, *Oncogene*, *Autophagy* and *JBC* et al.

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