Metformin targets mammary/cancer stem cells in breast cancer prevention and treatment

Xiaohe Yang
North Carolina Central University, USA

Increasing evidence suggests that targeting cancer stem cells (CSCs)/tumor-initiating cells (TICs) is a promising approach to treat and prevent cancer diseases. Recent advances indicate that use of metformin, a common anti-diabetes drug, is associated with reduced risk of breast and other types of cancers. However, the mechanisms of metformin mediated anti-cancer activities remain unclear. ErbB2/Her2 amplification in breast cancer has been associated with poor prognosis and therapeutic resistance. It was sought to determine the effect of metformin on CSCs/TICs in ERBB2 tumor models. In vitro results showed that metformin has potent anti-proliferative effects on trastuzumab-resistant breast cancer cells via inhibition of erbB2/IGF-1R interactions. Using mammary tumor virus (MMTV)-ErbB2 transgenic mouse model, it was demonstrated that systemic administration of metformin to these mice during the premalignant risk window selectively inhibited the CD61 (high)/CD49f (high) mammary epithelial cells. Cells with this phenotype had been identified as luminal progenitor cells and may function as TICs during tumor development in MMTV-ErbB2 mice. It was further demonstrated that metformin also inhibited CD61 (high)/CD49f (high) subpopulation in ErbB2 tumor-derived cells in vitro and tumor development in a syngeneic tumor graft model. Mechanistic studies indicated that metformin inhibited the expression and activation of ErbB family members and IGF-1R, AKT/mTOR signaling, and STAT3, c-myc associated activities. In vitro data also showed that low doses of metformin inhibited the self-renewal/proliferation of cancer stem cells (CSCs)/TICs in ErbB2-overexpressing breast cancer cells. Results provide fundamental support for developing metformin-mediated preventive strategies targeting ErbB2-associated carcinogenesis.

Biography

Xiaohe Yang completed his PhD in Microbiology/Immunology from RFUMS/The Chicago Medical School and Postdoctoral studies from Northwestern University. He is currently an Associate Professor of Biology at North Carolina Central University. His research focuses on erbB-2/Her-associated breast cancer etiology, prevention and therapeutics. He has published more than 50 papers in reputed journals. He was a recipient of the Career Development Award from the Department of Defense Breast Cancer Research Program and the AACR Minority-Serving Institution Faculty Scholar in Cancer Research Awards. He is also an American Cancer Society Research Scholar.

xyang@nccu.edu