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# Regulation of miR-34a-SIRT1 axis reduced breast cancer stemness

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**Introduction:** Recent studies showed that enforced expression of miR-34a resulted in elimination of cancer stem cells in many tumors, including prostate, pancreatic cancers. In this study, we aim to understand regulatory mechanism of miR-34a in breast cancer stemcells (BCSCs).

**Methods:** CD44+/CD24− breast cancer stem cells (BCSCs) were isolated from MCF-7 cell line. Total RNA and protein was extracted from BCSCs and xenograft tissues. Levels of miR-34a, Sirtuin1 (SIRT1), ALDH1, BMI1 and Nanog, were measured by using q RT-PCR and Western blot. Cell proliferation and differentiation were measured by assays of CCK-8, colony formation and mammosphere formation. Cell apoptosis was measured by flow cytometry. Four groups of mice (n=5), lentivirus-hsa-miR-34a, shRNA-SIRT1, lentivirus-hsa-NC, and shRNA-Control, were used for study on tumor formation and growth.

**Results:** Lower endogenous level of miR-34a and higher level of Sirtuin1 (SIRT1) gene in CD44+/CD24- BCSCs than in breast cancer cells was identified. Further study demonstrated that miR-34a directly targeted SIRT1 gene leading to reduced SIRT1expression in the BCSCs. Either ectopic expression of miR-34a or silenced SIRT1 inMCF-7 cells inhibited cellular proliferation, and led to cell apoptosis. Over expression of miR-34a also suppressed expression of ALDH1, BMI1 and Nanog, and decreased-capacity of mammosphere formation of the BCSCs significantly, suggesting thereduced stemness of BCSCs. Studies in vivo showed that stable expression of miR-34a reduced tumor burden significantly in nude mice xenografts.

**Conclusion:** Our results showed that anti-synergetic regulation of miR-34a-SIRT1 axis affected proliferation, colony formation, and mammosphere formation in BCSCs, suggesting that miR-34a-SIRT1 axis may play an important role in self-renewal and stemness maintenance of BCSCs. This study may provide a novel BCSCs specific therapeutic strategy to improve breast cancer treatments.

## Biography

Gary Guishan Xiao is a Professor and the scientific Director in School of Pharmaceutical Sciences and Technology at Dalian University of Technology, and the Director of the Functional Genomics and Proteomics Laboratories at the Creighton University School of Medicine, and an internationally recognized expert in the field of genomics and proteomics of cancer. Dr. Xiao earns his Ph.D. in molecular computational biology at Chinese Academy of Sciences. He had his postdoctoral research trained in Baylor College of Medicine and UCLA, focusing on pharmacokinetics and biochemistry of non-steroid inflammatory drugs, and cell cycle regulation. He has been regular reviewer or ad hoc reviewer for several medical journals, different funding agency and several journal Editorial Board members and senior Editors.

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