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Sulforaphane Suppresses the Growth of Triple-negative Breast Cancer Stem-like Cells *In vitro* and *In vivo*

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Abstract

Triple-negative breast cancer (TNBC) represents the poorest prognosis among all of breast cancer subtypes with no currently available effective therapy. In this study, we hypothesized that sulforaphane, a dietary component abundant in broccoli and its sprouts, can inhibit malignant cell proliferation and tumor sphere formation of cancer stem-like cells (CSC) in TNBC. CSC population was isolated using FACS analysis with the combined stem cell surface markers, $CD44^{+}/CD24^{-}/CD49f^{+}$ The effect of sulforaphane on a stem-related embryonic oncogene CRIPTO-1/TDGF1 (CR1) was evaluated via ELISA. *In vivo*, BalbC/nude mice were supplemented with sulforaphane before and after TNBC cell inoculation (daily intraperitoneal injection of 50 mg sulforaphane/kg for 5 and 3 weeks, respectively), and the effects of sulforaphane during mammary tumor initiation and growth were accessed with NanoString gene analysis. We found that sulforaphane can inhibit cell proliferation and mammosphere formation of CSCs in TNBC. Further analysis of gene expression in these TNBC tumor cells revealed that sulforaphane significantly decreases the expression of cancer-specific CR1, CRIPTO-3/TDGF1P3 (CR3, a homologue of CR1), and various stem cell markers including Nanog, aldehyde dehydrogenase 1A1 (ALDH1A1), Wnt3, and Notch4. Our results suggest that sulforaphane may control the malignant proliferation of CSCs in TNBC via Cripto-mediated pathway by either suppressing its expression and/or by inhibiting Cripto/Alk4 protein complex formation. Thus, the use of sulforaphane for chemoprevention of TNBC is plausible and warrants further clinical evaluation.

Figures

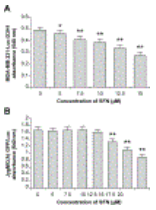

Fig. 1 *In vitro* growth inhibitory effects...

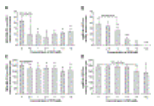

Fig. 2 Effects of SFN on the...

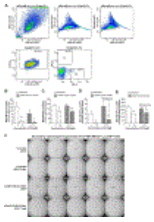

Fig. 3 Inhibitory effects of SFN on...

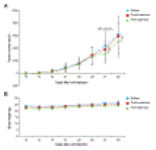

Fig. 4 *In vivo* effects of SFN...

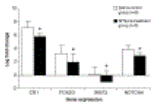

Fig. 5 Selected validation of Nanostring gene...

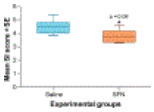

Fig. 6 Box plots for average staining...

All figures (7)

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