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Thymoquinone inhibits bone metastasis of triple negative breast cancer cells through the suppression of CXCR4 signaling axis

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Several lines of evidence(s) indicate that CXCR4 overexpression has been correlated with distant site metastasis and poor overall survival rate in patient with breast cancer. The tumor metastasis promoting molecule CXCR4 is considered as a potential therapeutic target for inhibiting breast cancer metastasis. Thus, novel agents that can down-regulate CXCR4 expression have potential against breast cancer metastasis. In the present report we investigated the effect of thymoquinone (TQ), derived from the seeds of medicinal plant *Nigella sativa*, on the expression and regulation of CXCR4 in breast cancer cells. In addition, we evaluated the effect of TQ in a metastasis mouse model established by intracardiac injection of luciferase-tagged MDA-MB-231 breast cancer cells that metastasize to the bones. We observed that TQ could inhibit the expression of CXCR4 in MCF-7 and MDA-MB-231 cells in a dose and time dependent manner. TQ (2 mg/kg or 4 mg/kg) treatment for four weeks significantly inhibited tumor growth and significantly reduced metastases to multiple vital organs, including lungs, brain and bone. Immuno-histochemical analysis of the lung and brain tissue showed significant reduction in the expression of CXCR4, Ki67, MMP9, VEGFR2 and COX2 compared to tissues from control mice. TQ treatment also reduced the overall bone tumor burden. Overall, our results show that TQ exerts its antitumor and anti-metastatic effects by downregulation of CXCR4 expression both *in vitro* and *in vivo* thus may have possible potential for the treatment of breast cancer.

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Biography

Muthu K Shanmugam is a senior research fellow in the Department of Pharmacology, National University of Singapore, Yong Loo Lin School of Medicine. He got his PhD in cancer pharmacology and he is currently working as a senior research fellow. He has twelve years of experience in experimental laboratory research and have published in journal papers and presented at international conferences. Muthu K Shanmugam has vast experience in cancer biology, inflammatory diseases, orthotopic, xenograft and transgenic mice models, in molecular biology, cell and tissue culture experiments. In addition, he is trained in high-throughput technology such as cDNA microarray technology, antigen and antibody array technology, two dimensional gel electrophoresis, mass spectrometry, pharmacokinetics and in the development of array based clinical diagnostic tools.

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