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Suppressing lung metastasis of breast cancer by inhibition of VCAM-1 expression with nanomedicine

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Cancer metastasis is the leading reason for the high mortality of breast cancer. The prevention and treatment of lung metastasis of breast cancer remain a major challenge. The recent findings of vascular cell adhesion molecule-1 (VCAM-1) provide a potential therapeutic target in lung metastasis. Herein, succinobucol (SCB), a potent and selective VCAM-1 inhibitor, was assembled with triblock polymer poloxamer P188 into nanoparticles. We report that the SCB loaded nanoparticles can greatly improve the oral delivery and suppress the lung metastasis of breast cancer. The cell migration and invasion abilities of metastatic 4T1 breast cancer cells, the VCAM-1 expression on 4T1 cells and the cell-cell binding ratio of RAW 264.7 cells to 4T1 cells was greatly reduced by SN. In particular, in the metastatic breast cancer model, the lung metastasis was notably reduced 90% by SN treatment. Based on these findings, we further designed wormlike micelles loading SCB (PWM) with sequential targeting capability to inhibit lung metastasis of breast cancer, which can be first specifically delivered to the sites of metastases in lung and then enable the intracellular pH-stimuli responsive drug release in cancer cells to improve the anti-metastatic effect. PWM could induce a higher specific accumulation in lung and be specifically delivered to the sites of metastases in lung, thereby leading to an 86.6% inhibition on lung metastasis of breast cancer. Therefore, the nanomedicine of SCB could provide a potential strategy to inhibit the lung metastasis of breast cancer by inhibition of VCAM-1 expression.

Biography

Zhiwen Zhang has completed his PhD from Fudan University. In July 2008, he joined the Center of Pharmaceutics, Shanghai Institute of Materia Medica, Chinese Academy of Sciences. His scientific interest lie in the use of nanotechnology based drug delivery system to improve the therapeutic efficacy on cancer metastasis. He has published more than 25 papers in reputed journals.

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