New Targeted Curcumin Nanoparticles to Prevent Breast Cancer Progression and Metastasis

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Breast cancer (BC) is the most prevalent cancer in women worldwide and the leading cause of cancer death.[1] Metastasis is one of the key contributors to the high mortality rate among BC patients. The most common metastatic site for breast cancer is the bone[2] to which the probability of developing metastasis depends on the subtype of BC.[3] Once BC metastasizes to the bone there is no cure and the current clinically proven approaches include palliative care mainly to relieve symptoms and improve patient's survival to a limited extent.[4] Hence, there is an urgent demand for targeted safe preventative modalities for BC bone metastasis. Breast cancer-associated fibroblasts (BCAF) are the most abundant type of cells in the tumour microenvironment (TME).[5] BCAFs are involved in the progression, invasion, and metastasis of BC.[6] Curcumin is a naturally occurring compound that has been shown to prevent the proliferation, invasion and metastasis of various cancers in *in vitro* studies.[7] Recent studies have demonstrated that curcumin has an inhibitory effect on cancer-associated fibroblasts in various cancers.[8,9] However, the major challenge for its clinical application is the poor drug-like properties of this compound due to poor water-solubility, low metabolic stability and bioavailability. Curcumin is a safe compound, hence, can be used in the long term to prevent bone metastasis in BC patients. In this project, we developed a nanocarrier system to achieve the selective delivery of curcumin to the bone to prevent bone metastasis in BC, bone seeker drug, alendronate, was conjugated with the curcumin nanoparticles (Cur-NPs). We hypothesized that the developed bone-targeted curcumin NPs (Aln-Cur-NPs) can prevent bone metastasis by two mechanisms, 1) targeting the potential of alendronate to localize curcumin in the bone and directly destruct attacking cancer cells, 2) inhibiting BCAFs in the TME in the primary tumour to cause progression and metastasis.

In this study, we investigated the antiproliferative activities of the Cur-NPs and Aln-Cur-NPs, in 2D and 3D BC models. Both Cur-NPs and Aln-Cur-NPs showed improved cellular penetration compared to raw curcumin in timelapse IncuCyte live cell imaging, with IC_{50} values at 10.11±0.60 and 10.80±0.31, respectively, in 2D BC cell culture. Furthermore, in the 3D culture, we observed a significant disintegration in BC monoculture (MDA-MB-231) and coculture (MDA-MB-231 and BCAFs) spheroids by targeted and untargeted nanoparticles as an indication of their anticancer activity. In conclusion, we have developed a nanocarrier system that can effectively overcome the challenges associated with the delivery of curcumin and deliver curcumin to cancer cells and prevent their proliferation in BC cells.

*A talk is preferred

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