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Verification of the efficacy of targeting peptides linked liposomal nanoparticles for therapy of hepatocellular and nasopharyngeal carcinomas and breast cancer

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The efficacy of systemic cytotoxic chemotherapy has been widely assessed in patients with advanced hepatocellular carcinoma (HCC). For example, doxorubicin is the most commonly studied chemotherapeutic agent for HCC. However, it has been shown to have a response rate of only 10-20% in clinical trial. In addition, its potential benefit has been reduced by the related adverse effect. So far, the multikinase inhibitor sorafenib is considered to provide survival benefit over supportive care. However, the long term prognosis of those cancer patients still remains poor. Therefore, in the present experiment, we proposed to use the so-called peptide targeting chemotherapy to overcome the adverse event in the conventional targeted chemotherapy. In order to perform this experiment, we have constructed some peptides which can bind specifically to the cancer cells and cancer vascular endothelia by using a phage displayed 12-mer random peptide library. We obtained three different peptides and one control peptide. Each contains 12 amino acids: a. L-peptide: RLLDTNRPLLPY (anti-different cancer cell membrane); b. control peptide: RLLDTNRGGGGG; c. SP-94-peptide: SFSHHTPILP (anti-NPC tumor cell and hepatoma cell membranes) and d. PC5-52-peptide: SVSVGMKPSPRP (anti-tumor endothelia). The L-peptide (L-P), SP-peptide (SP-P), PC5-52-peptide and the control peptide (C-P) were linked to liposomal iron oxide nanoparticles; and also to liposomal doxorubicin (L-D). Using peptide linked liposomal iron oxide, we can localize the peptide targeted tumor cells and tumor endothelia, and then we used those peptides linked liposomal doxorubicin to treat SCID mice bearing different cancer xenografts. Our results showed that when L-P-L-D containing 2mg/kg of SCID mouse body weight was used to treat xenografts bearing SCID mice, the tumor could be well controlled, and no specific adverse event was seen. However, when the control peptide was used to replace the specific peptide, the xenograft size was also decreased, but the visceral organs revealed marked apoptotic change. In conclusion, the specific peptides linked liposomal doxorubicin nanoparticles can be used for treatment of SCID mice bearing cancer xenografts with minimal adverse event, especially in the SCID mice γ species (NGS), which shows remarkable tumor suppression.

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