CD44 antibody-targeted liposomal nanoparticles for molecular imaging and therapy of hepatocellular carcinoma

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1. Introduction

Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the third leading cause of cancer death [1]. Over 80% of the world’s cases occur in developing countries, with 44% in China alone [1,2]. Advances in treatment, imaging, surgical techniques and liver transplantation have resulted in considerable improvements in therapy of HCC. However, most of these fail to consider the differences in drug sensitivities of cancer stem cells (CSCs) compared to their non-tumorigenic progeny. Chemotherapy and radiotherapy target rapidly proliferating non-tumorigenic cells and spare the relatively quiescent cancer stem cells. Moreover, surgery is directed at reducing the bulk of tumor mass, but cannot sufficiently clear tumorigenic/metastatic cells. Consequently, such treatments are often followed by recurrence of tumor and relapse of diseases in the majority of cases [3].

By contrast, if therapies can directly target against tumorigenic CSCs, even without shrinking tumors, this may render the tumors unable to maintain themselves or grow, thus eventually leading to cures [4]. To date, a number of putative markers for liver CSCs have been reported, including CD133, CD90, CD44, OV6, epithelial cell adhesion molecule (EpCAM) and CD13 [5–8]. It has been shown that activating anti-CD44 monoclonal antibody markedly reduced leukemic repopulation [9] and inhibited proliferation and stimulated apoptosis [10]. Therefore, CD44 is potentially an attractive therapeutic target especially in tumors overexpressing CD44.