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Title: A Novel Oxygen Carrier Sensitized Cisplatin Based Chemotherapy in Hepatocellular Carcinoma

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Body: Background and Objective

Our previous study showed that acute phase liver graft injury not only promotes tumor recurrence, but also induces chemoresistance in recurrent HCC after liver transplantation [1]. Recently, we found that the oxygen carrier "YQ23" significantly ameliorates hepatic IR injury and prevents tumor recurrence [2]. Here, we intended to explore the novel therapeutic strategy using oxygen carrier "YQ23" to sensitize chemotherapy in HCC.

Methods

To investigate the role of YQ23 treatment combined with Cisplatin, the proliferation of HCC cells was examined by MTT and colony formation assay. To explore the effect of YQ23 on sensitization of Cisplatin based chemotherapy, the orthotopic xenograft liver cancer model was established. In order to characterize the delivery of YQ23 in tumor tissue, the real-time intravital imaging system was applied for longitudinal observation in ectopic xenograft liver cancer model using dorsal window chamber. The distribution of YQ23 in the whole body was examined by IVIS spectrum.

Results

YQ23 administration significantly suppressed the proliferation of HCC cells under Cisplatin treatment in a dose and time dependent manner. Moreover, YQ23 significantly inhibited colony formation of HCC cells under Cisplatin treatment. The YQ23 administration significantly sensitized Cisplatin based chemotherapy in orthotopic xenograft liver cancer model (Fig. 1A). More necrotic area and apoptotic cells were induced by YQ23 combined with Cisplatin therapy. Real-time intravital imaging showed that YQ23 accumulated in the tumor tissue (Fig. 1B) and maintained as long as 3 days in ectopic xenograft liver cancer model using dorsal window chamber. The IVIS spectrum showed that YQ23 distributed mainly at liver and bladder within the first 6 hours after administration and gradually excreted through bladder afterwards in orthotopic xenograft liver cancer model.

Conclusion

YQ23 treatment may be a potential therapeutic strategy to sensitize chemotherapy in recurrent HCC after liver transplantation.

[1] Geng et al, Oncotarget, 2015

[2] Li et al, BMC Cancer, 2014