MRNA ENCODED ANTIBODIES IMPROVE BIODISTRIBUTION AND EFFICACY OF CHECKPOINT INHIBITORS FOR LIVER CANCER

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Background Lipid nanoparticle (LNP) encapsulated mRNA is emerging as a powerful new modality to deliver protein therapeutics to specific tissues. Of particular interest for hepatocellular carcinoma (HCC) is liver tropic delivery of therapeutic proteins to improve safety and efficacy of current standard of care. Here we describe preclinical in vitro screening, characterization, in vivo PK, biodistribution and efficacy of a novel liver targeted, mRNA encoded bispecific antibody.

Methods We report on the cell based in vitro assessment of the bispecific antibody that combines checkpoint inhibition with anti-angiogenesis. In vivo biodistribution and pharmacokinetics (PK) were examined from liver, peripheral blood, and various tissues in the naïve C57BL/6J mice. Anti-tumor efficacy and survival were assessed in C57BL/6J mice subcutaneously inoculated with hPDL1.MC38 cells or Balb/c mice bearing hepatocellular syngeneic H22 cells orthotopically.

Results Our results show that LNP delivered mRNA encoded antibodies have favorable PK and biodistribution profile compared to systemically administered recombinant antibodies. Furthermore, we measure significant anti-tumor efficacy and survival benefit in the syngeneic orthotopic HCC tumor model as compared to recombinant benchmarks.

Conclusions Our results demonstrate that liver-targeted antibody expression has superior in vivo efficacy compared to systemic delivery for hepatic cancer and supports further development of mRNA/LNP antibodies for the treatment of human hepatocellular carcinoma (HCC).

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