

Creation of Mouse Models for Fibrolamellar Hepatocellular Carcinoma

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Abstract: We have recently demonstrated that the genome of the liver cancer fibrolamellar hepatocellular carcinoma (FL-HCC) has very few changes relative to the adjacent normal tissue, with one critical exception. In 30 out of 30 patients examined, the tumor has a single deletion of approximately 400 kb, resulting in a novel fusion protein, an activated kinase. This proposal will generate different mouse models for FL-HCC, specifically to determine if this chimera is sufficient to induce transformation or, if not, to which extent expression of the chimera recapitulates the changes in the transcriptome and proteome in the human tumor. Moreover, the models will determine if the chimera can drive and maintain the cancer. In future studies, the mice will be used for preclinical studies to test both genetic and small molecule approaches for treatment of FL-HCC.