

## A unique inducible mouse model of hepatocellular carcinoma (HCC, P-1245)

### Key facts:

- mouse model faithfully mimics clinical conditions in HCC
- allows evaluation of novel therapeutic strategies like immuno- or antiangiogenic therapy or vaccination
- tumor induction is tightly controlled by cre/loxP-system in a dose-dependent manner

### Abstract

Hepatocellular carcinoma (HCC) is one of the deadliest and most common cancer in the world. For studying HCC mainly tumor transplants in rodents are used. However, these xeno-transplant models do not display the clinical conditions, since they are not focal primary tumors. Therefore DKFZ scientists developed a transgenic mouse model using the hepatocyte-specific albumin promoter, a loxP-flanked stop cassette, and the SV40 large T-antigen (Tag) named iAST=inducible albumin-floxstop-Tag. After excision of the stop-cassette by Cre recombinase, Tag oncogene expression is initiated leading to the formation of HCC.

### Applications

(a) Tumorigenesis could be triggered by intravenous adenoviral delivery of Cre recombinase. Somatic excision of the flox-stop cassette is monitored by genotyping and reveals recombination activity mainly in the liver due to the natural liver tropism of adenovirus. Within three months Cre adenovirus-treated animals develop liver tumors in a dose dependent manner. Low dose adenovirus injection leads to the formation of dysplasia and small nodular adenoma or carcinoma while high dose inoculation results in multinodular HCC.

(b) Alternatively, iAST mice can be crossed with Cre-deleter mice, which express Cre recombinase ubiquitously. Cre recombinase activity leads to Tag expression already two days after birth. Tag expression results in the development of liver dysplasia at the age of four weeks, proceeding over nodular adenoma and carcinomata into multinodular

HCC accompanied by a dramatically decreased life span of about 12 weeks. Tumor formation is observed exclusively in the liver, whereas AST single transgenic animals show no signs of tumor growth in the liver or other organs at the age of twelve months as examined by histology.

### Commercial Opportunity

DKFZ is seeking for commercial partners and collaborations interested in using this unique model system.

### Inventors

The model was established by scientists of the division of Molecular Immunology headed by Prof. Dr. Bernd Arnold from DKFZ.

### Reference

Tumor agonist peptides break tolerance and elicit effective CTL responses in an inducible mouse model of hepatocellular carcinoma. [Immunol. Lett. 2009 Mar 24;123\(1\):31-7](#)

An inducible hepatocellular carcinoma model for preclinical evaluation of anti-angiogenic therapy in adult mice. [Cancer Res. 2014 Aug 1;74\(15\):4157-69](#)

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