

TECHNOLOGY OFFERS

A Unique Inducible Mouse Model of Hepatocellular Carcinoma (HCC) (P-1245)

A transgenic mouse model that faithfully mimics HCC clinical conditions and allows evaluation of novel therapeutic strategies.

EXECUTIVE SUMMARY

DKFZ scientists have 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. 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.



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Category

Research
Tools

Indication

Hepatocellular
carcinoma
(HCC)

Development stage

Prototype

Seeking

Licensing, Commercial partner

BENEFITS

- 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

TECHNOLOGY BACKGROUND

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.

DEVELOPMENT STAGE

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

APPLICATIONS

Alternatively, iAST mice can be crossed with Cre-deleted 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.

INTELLECTUAL PROPERTY

- No patent filed; mice model is know-how based.

PUBLICATIONS & REFERENCES

- Simone Stahl, Torsten Sacher, Astrid Bechtold, Ulrike Protzer, Ruth Ganss, Günter J. Hämmerling, Bernd Arnold, Natalio Garbi, "Tumor agonist peptides break tolerance and elicit effective CTL responses in an inducible mouse model of hepatocellular carcinoma", *Immunology Letters*, Volume 123, Issue 1, 2009, Pages 31-37, ISSN 0165-2478, <https://doi.org/10.1016/j.imlet.2009.01.011>.
- Anja Runge, Junhao Hu, Matthias Wieland, Jan-Philip Bergeest, Carolin Mogler, André Neumann, Cyril Géraud, Bernd Arnold, Karl Rohr, Dorde Komljenovic, Peter Schirmacher, Sergij Goerdts and Hellmut G. Augustin, "An Inducible Hepatocellular Carcinoma Model for Preclinical Evaluation of Antiangiogenic Therapy in Adult Mice", *Cancer Res August 1 2014 (74) (15) 4157-4169*, DOI: 10.1158/0008-5472.CAN-13-2311

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ABOUT THE DKFZ INNOVATION MANAGEMENT

Working at the interface of research and industry, the Innovation Management of the German Cancer Research Center (DKFZ) helps to get new cancer medications, diagnostic tests, and research instruments onto the market as quickly as possible.

The DKFZ with its more than 3,000 employees is the largest biomedical research institution in Germany. At the Center more than 1,300 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg