DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

No. 43 August 26, 2008 (Koh)

Gaining a Better Understanding of Kidney Diseases

By introducing a genetic switch in mice it is possible to increase or decrease the production of specific protein molecules in their kidneys. Thus, researchers can study the influence of specific proteins on disease development. Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), Heidelberg University Hospitals and other research institutes have published this model of investigating severe kidney diseases in the latest issue of *Nature medicine*.

Cystic kidney disease, renal fibrosis, or renal cell carcinoma: Many diseases of the excretory organs are characterized by overproduction or – on the contrary – absence of characteristic proteins in the renal cells. An international research team under the leadership of scientists from DKFZ and Heidelberg University Hospitals has now developed an animal model to better investigate these conditions.

The researchers introduced a genetic switch into the genome of mice. This switch allows to selectively turn on and off the production of disease-typical proteins in renal tissue. It is activated simply by adding the antibiotic tetracycline to the animal food.

To find out whether it is possible to study the development of kidney diseases in the genetically modified (transgenic) animals, the investigators stimulated the production of c-Myc in the renal tissue of the mice. Numerous tumors have been reported to be associated with elevated levels of this transcription factor. Shortly after activation of the c-Myc gene the animals started developing cysts that led to organ failure. Pathologists also discovered renal cell carcinomas in some of the mice. As a reaction to the overexpression of another signaling molecule, the mice developed renal fibrosis.

Earlier attempts to study disease development using transgenic animals have often failed because the proteins to be studied are overproduced in the murine embryos already. As a result, the animals often develop severe malformations that make meaningful conclusions impossible. “A particular advantage of our model is that we can switch on and off disease-typical renal proteins at any given time,” explained Associate Professor (PD) Dr. Robert Kösters of the Institute of Human Genetics of the University of Heidelberg and Professor Dr. Hermann-Josef Gröne of the German Cancer Research Center. “Thus, we are able to simulate the natural course of disease development and also of healing processes.”

Milena Traykova-Brauch, Kai Schönig, Oliver Greiner, Tewfik Miloud, Anna Jauch, Manja Bode, Dean W Felsher, Adam B Glick, David J Kwiatkowski, Hermann Bujard, Jürgen Horst, Magnus von Knebel Doeberitz, Felix K Niggli, Wilhelm Kriz, Hermann-Josef Gröne and Robert Koesters: An efficient and versatile system for acute and chronic modulation of renal tubular function in transgenic mice. Nature medicine, 24 August 2008