

**Development of a Genetically-modified Mouse Model of Renal Cell Carcinoma**

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Renal cell carcinoma (RCC), a relatively common malignant form of kidney cancer in humans, has been associated with environmental and occupational exposure to certain chemicals. In rodents, renal cell tumors are one of the most frequent neoplastic findings noted in safety assessment bioassays of chemical agents. Although there are a number of similarities between human and rodent renal tumors, some important phenotypic and genetic differences are evident. The relatively common occurrence of renal cell tumors in rodent carcinogenesis bioassays underscores the importance of understanding the comparative biology of renal cancer in people and in laboratory animal models. CIIT Centers for Health Research scientists in collaboration with scientists at the MD Anderson Cancer Center (MDACC), were engaged in studies that utilize genetic engineering approaches to develop a mouse model of RCC biologically similar to its human counterpart. This model is based upon the Von Hippel-Lindau (VHL) tumor suppressor gene, a gene controlling development of human RCC. The project had a goal of developing a mouse in which loss of the VHL gene function will be targeted specifically to the kidney. It was believed that this murine model will be predisposed to the development of RCC that will have phenotypic and genetic characteristics of the human condition. In addition to the development of a conditional VHL knock out mouse with targeting to the kidney, the project was examining the effects of known murine carcinogens dimethylnitrosamine and streptozotocin in VHL +/- mice that have already been developed. It was hypothesized that exposure of these mice to kidney carcinogens will induce alterations in the remaining wild-type VHL allele and lead to the subsequent development of renal cancer in these mice. In contrast to humans, in the mouse alterations in the VHL gene did not increase susceptibility to renal carcinogenesis. Lack of expected human phenotype in VHL knockout mice underscored limitations of using the mouse to model human renal carcinoma.

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**Presentation(s):**

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**Peer-reviewed publication(s):**

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