Molecular mechanisms underlying control of renal epithelial proliferative homeostasis

Von 2010-12-01 bis 2015-11-30, Abgeschlossenes Projekt

Ziel

This research grant has two major aspects. The first seeks to understand the molecular and cellular basis of the evolution of clear cell renal cell carcinoma (ccRCC), the most frequent form of kidney cancer. We will utilise an integrated approach based on mouse genetics, the use of primary kidney epithelial cell culture systems, genetic screening approaches using RNA interference libraries and analysis of the genetic and molecular changes that arise in human kidney tumours. The rationale behind these studies is that by better understanding the molecular causes of ccRCC it will be possible to identify new molecules or signaling pathways that could serve as appropriate therapeutic targets. The second aspect of this grant relates to the development of a flexible experimental platform that will allow the rapid and simultaneous up- and down-regulation of gene expression in the mouse kidney in a manner in which the affected cells are marked by a luminescent marker. This system will be based on the injection of modified lentiviral gene overexpression and gene knockdown vectors, allowing us to exploit recently-developed genome-wide cDNA libraries and RNA interference libraries. This experimental system should be equally applicable to other organ systems and will allow for the first time a systematic approach to the manipulation of gene expression in living mice, additionally bypassing the time limitations associated with conventional mouse genetic approaches. We aim to develop this system within the biological context of this grant and will combine it with live-animal imaging approaches to generate a series of mouse models of ccRCC. These will ultimately serve as invaluable tools for testing novel therapeutic approaches against this currently untreatable disease.

Verwandte Informationen

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To know more

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