

Molecular evolution and progression of liver cancer: from tumor-prevention to therapeutic approaches

Initiative: Lichtenberg - Professuren

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Projekt-Website: www.unimedizin-mainz.de/1-med/patienten/mitarbeiter/portraits/marquardt.html

Despite recent technological progress, the understanding of the molecular complexity and intra-tumoral heterogeneity in hepatocellular carcinoma (HCC) remains limited. This lack of information represents a major challenge for both, preventive strategies as well as therapeutic approaches in HCC. The goal of the professorship is to define the multi-stage molecular evolution of HCC. First, the impact of preventive modulation of the tumor-microenvironment for liver cancer development will be tested. Therefore, inhibition of key pro-oncogenic factors such as insulin signaling, inflammation as well as stem cell activation will be performed in mice followed by induction of liver cancer. By using hydrodynamic injections, the relevance of IGFALS (Insulin-like growth factor binding protein, acid labile subunit) for tumor-initiation will be evaluated. Next, the sequential epigenetic evolution of liver cancer will be characterized by applying whole epigenome sequencing to the complete spectrum of early and advanced lesions. The most abundant genetic alterations of HCC will then prospectively assessed by a target next-generation sequencing approach. Finally, the key mechanisms responsible for chemoresistance will be unraveled by using the ex-vivo precision-cut liver slice tool as well as freshly isolated liver cancer cells.

Projektbeteiligte

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