Abstract of the Project of Prof. Dr. Mathias Heikenwälder

The causal relationship between chronic inflammation, tissue damage, fibrosis and carcinogenesis is well established by epidemiological studies. Various etiologies, including chronic alcohol consumption, chronic drug abuse, autoimmune disorders, toxins, infections with viruses (e.g. Hepatitis B and Hepatitis C virus) bacteria (e.g. Helicobacter pylori) can lead to chronic inflammation, tissue damage and carcinogenesis. The aberrant expression of cytotoxic cytokines by immune but also non-immune cells is thought to be critically involved in the initial induction of inflammation and its progression towards a chronic state.

In this project we aim at understanding the signaling pathways of inflammation (e.g. cytokines and chemokines), apoptosis and proliferation. Moreover, we aim at unraveling the cellular mechanisms responsible for induction and maintenance of chronic inflammation, finally leading to tissue destruction and cancer.

One main focus of this project is to elucidate the patho-mechanisms of Hepatitis B (HBV) and Hepatitis C (HCV) viruses, by far the most common cause of chronic hepatitis in humans. HBV and HCV infections are frequently associated with hepatocellular carcinoma, the most prevalent primary human liver cancer and fifth most frequent cause of cancer related death. However, the cellular and molecular mechanisms driving hepatitis-induced liver cancer remain elusive.

We have generated transgenic mice that resemble the situation of HBV or HVC infected individuals and that develop liver cancer based on chronic inflammation. Our aim is to understand the exact mechanisms of how inflammation induces the liver cancer on cellular and molecular level: Which cells are involved? What molecules are needed?

These experiments should help finding new targets and approaches to treat inflammation induced liver cancer.

Moreover, we are also interested in an in-detail analysis and characterization of hepatocellular carcinoma and other solid tumors by combining and correlating immunohistological with genetic (array comparative hybridization analysis) and transcriptional changes (micro-array).

Another focus of the laboratory is to understand the mechanisms how tumor cells leave the primary tumor (e.g. in liver cancer) and how they metastasize in the liver or to distinct organs and how this process is controlled on a cellular and molecular level.