Preface

From January 26 to January 27, 2012, the Falk Workshop on 'Inflammation & Cancer' took place at the University Medical Center Hamburg-Eppendorf, Hamburg, Germany, as a pre-symposium of the 28th annual meeting of the German Association for the Study of the Liver (GASL). Pioneers in the field of inflammation and cancer from several European countries, Israel, and the USA discussed their latest results on this important area of cancer development in the liver and gut.

It was in 1863 when Rudolf Virchow hypothesized in thirty published lectures on 'Die krankhaften Geschwülste' that cancer originates at sites of chronic inflammation. Tumors in the liver and gut seem to originate particularly often from persistent viral infections or other chronic inflammatory disorders. In particular, chronic hepatitis B and C may cause hepatocellular carcinoma (HCC), and colon cancer develops more frequently in patients with inflammatory bowel disease. It is generally accepted that the hepatitis B and C viruses are not cytopathic for hepatocytes but elicit a chronic inflammatory response due to persistent viral infection. Persistent viral infection might result from dampening of the specific anti-viral immune response by the tolerogenic properties of the liver. However, viral proteins can affect the cell cycle control in hepatocytes, thereby directly acting pro-carcinogenically in the target cell. The inflammatory response is characterized by production of pro-inflammatory cytokines such as tumor necrosis factor- α (TNF) and its family members lymphotoxin α and β , which have pro- as well as anti-carcinogenic functions depending on the cell type affected and the respective signaling path-

way. TNF itself induces the pro-apoptotic caspase cascade but also, depending on NF- κ B signaling, inflammation and cell survival. TNF has been shown to play a significant role in hepatic pathology in several models of liver injury and intoxication but also in HCC. IL-6, another pro-inflammatory cytokine which seems to be particularly involved in liver regeneration, uses two different signaling pathways for inflammation or regeneration depending on the particular receptor/ligand complex. In addition, pro- as well as anti-inflammatory adipokines which seem to play a fundamental role in obesity-associated non-alcoholic fatty liver disease (NAFLD) may be involved in the development of HCC. However, pro-inflammatory cytokines induce angiogenic factors and growth factors critical for regeneration and wound healing. If concomitant mutations and gene amplifications cannot be repaired, these mechanisms of inflammation and regeneration favor carcinogenesis. Moreover, immune-regulatory mechanisms are induced in response to inflammation. These include the production of transforming growth factor (TGF)- β which is a central regulator of fibrosis and cirrhosis. It seems that TGF- β can act as a tumor suppressor but also as a tumor promoter depending on the stage of liver damage. TGF- β may also participate in the immunosuppression mediated by regulatory T cells (Tregs). These master suppressors of autoimmunity and inflammation together with tumor-associated macrophages (TAMs) and myeloid derived suppressor cells (MDSCs) accumulate at sites of inflammation and in tumors and suppress the specific immune response to tumor antigens.

All of these mechanisms related to infection and/or chronic inflammation in the gastrointestinal tract which are referred to in the following chapters by contributors of the Falk Workshop seem to be involved in the development and progression of tumors and might have implications for the prevention and treatment of cancer.

The organizers of the Falk Workshop 'Inflammation & Cancer', namely: Ansgar W. Lohse, Hamburg; Robert Thimme, Freiburg; Christian Trautwein, Aachen, and

Gisa Tiegs, Hamburg, are thankful to the excellent speakers who contributed to this workshop and provided manuscripts to be published in these proceedings which give an excellent overview of the field of inflammation and cancer.

Prof. Dr. Gisa Tiegs, Hamburg (Germany)
for the organizers of the Falk Workshop
on 'Inflammation & Cancer', Spring 2012