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SUMMARY & MISSION STATEMENT

Our group studyies pathology-relevant topics of liver and intestinal cancer. Trying to better understand the underlying mechanisms and their implication for pathology, we aim to improve diagnostics and the management of patients with liver and intestinal tumors.

OVERVIEW

We study basic mechanisms of liver and intestinal carcinogenesis by taking advantage of mouse models and correlative studies in human tissues. A major interest is the phenomenon of apoptosis-driven carcinogenesis (Weber et al., 2010, Hepatology). We contributed to the concept of understanding tumorigenesis as a result of persistent apoptotic cell death and regeneration. The significance of theses hallmarks was demonstrated in mouse models and patients` tissue samples with chronic liver diseases which etiology-independently display chronically elevated hepatocyte apoptosis and regeneration (Boege et al., 2017, Cancer Cell). Further projects aim to unravel the cellular and molecular mechanisms underlying epidemically increasing metabolic disorders of the liver, i.e. non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), and NASH-driven HCC (Wolf et al., 2014, Cancer Cell). Moreover, we study the comparability and applicability of murine tumor models to human liver tumors with special interest in HCC intratumor heterogeneity and its implications for tumor classification approaches and molecular targeted therapy (Friemel et al., 2015, Clinical Cancer Research). Finally, we try to translate our findings into routine pathology diagnostics aiming to improve pathology diagnostics, and thus, patient management (Lenggenhager et al. 2017, J Hepatol).

SELECTED CANCER RELATED PUBLICATIONS

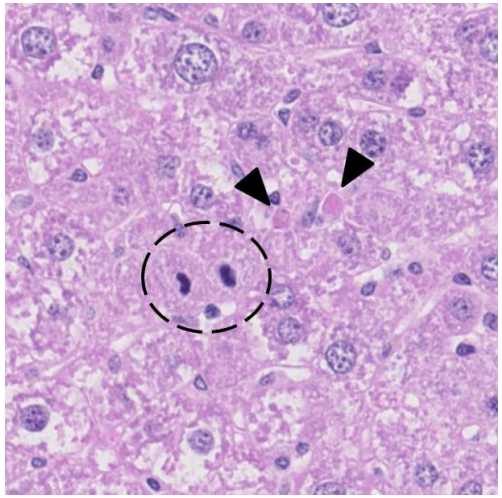
A Dual Role of Caspase-8 in Triggering and Sensing Proliferation-Associated DNA Damage, a Key Determinant of Liver Cancer Development. Boege Y, Malehmir M, Healy ME, Bettermann K,……, Green DR, Lopes M, Lavrik I, Luedde T, Heikenwalder M*, Weber A*. **Cancer Cell.** 2017 32(3):342-359

Visualization of hepatitis E virus RNA and proteins in the human liver. Lenggenhager D*, Gouttenoire J*, Malehmir M, Bawohl M, Honcharova-Biletska H, Kreutzer S, Semela D, Neuweiler J, Hürlimann S, Aepli P, Fraga M, Sahli R, Terracciano L, Rubbia-Brandt L, Müllhaupt B, Sempoux C, Moradpour D, Weber A. **Journal of Hepatology.** 2017 67(3):471-479

Intratumor heterogeneity in hepatocellular carcinoma. Friemel J, Rechsteiner M, Frick L, Böhm F, Struckmann K, Sigg M, Moch H, Heikenwalder M, Weber A. **Clinical Cancer Research.** 2015 21(8):1951-61

Metabolic activation of intrahepatic CD8+ and NKT-cells causes nonalcoholic steatohepatitis and hepatocellular carcinoma via cross-talk with hepatocytes. Wolf MJ, Adili A, Piotrowitz K, Abdullah Z, Boege Y, Stemmer K, Ringelhan M, Simonavicius N, Egger M, Wohlleber D, Lorentzen A, Einer C, Schulz S, Clavel T, Protzer U, Thiele C, Zischka H, Moch H, Tschöp M, Tumanov AV, Haller D, Unger U, Karin M, Kopf M, Knolle P*, Weber A*#, Heikenwalder M*#. **Cancer Cell.** 2014 Sep;37(9):12485-12495

Hepatocyte-specific deletion of the anti-apoptotic protein Mcl-1 triggers proliferation and hepatocarcinogenesis in mice. Weber A*, Boger R*, Vick B, Urbanik T, Haybaeck J, Zoller S, Teufel A, Krammer PH, Opferman JT, Galle PR, Schuchmann M, Heikenwalder M, Schulze-Bergkamen H. **Hepatology** 2010 51(4):1226-36



Liver histology of a Mcl-1$^{\Delta hep}$ mouse. The image displays concomitant increased levels of apoptotic liver cell death (apoptotic hepatocytes, arrow heads) and regeneration (hepatocyte mitosis, dotted circle), histologic hallmarks of both, Mcl-1$^{\Delta hep}$ mice and human chronic liver diseases. Both, patients with chronic liver diseases as well as Mcl-1$^{\Delta hep}$ mice are prone to develop hepatocellular carcinoma.