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Molecular links between inflammation, NAFLD and HCC in the context of Ncoa5 deficiency

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Hepatocellular carcinoma (HCC) is the fifth most common and the third most lethal cancer worldwide with increasing incidence in developed countries including the United States. It is estimated that 15-50% of HCC patients develop HCC in the absence of eminent etiological factors such as hepatitis viral infection and alcohol abuse. Emerging evidence has indicated that metabolic disorders such as non alcoholic fatty liver disease (NAFLD) and type-2 diabetes (T2D) are linked to HCC development, which may account for the increasing incidence of HCC in developed countries. Our laboratory previously reported that male mice bearing heterozygous deletion of *Ncoa5* gene developed glucose intolerance, NAFLD and HCC. This mouse model of HCC offers a genetically defined system for exploring the mechanisms underlying HCC in the context of glucose dysregulation, inflammation and NAFLD. We compared hepatic gene expression between wild type and Ncoa5+/- male mice at a premalignant stage by RNA-seq transcriptome profiling and found differentially expressed genes involved in the pathogenesis of Inflammation, NAFLD and HCC. The HCC development was paralleled with increased expression of several key pro inflammatory cytokines and enzymes involved in inflammation and fatty acid synthesis in livers. We further show that heterozygous deletion of IL-6 rescues phenotypes of hepatic steatosis, aberrant sperm morphology and motility occurring in male mice with Ncoa5 heterozygous deletion, suggesting the importance of Interleukin 6 (IL-6) in the development of these pathogenic conditions. Together, our results provide novel insight into molecular mechanisms underlying HCC development.

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Liver diseases in pregnancy

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Liver diseases in pregnancy occur in up to 10% of pregnant mothers. They are not without complications. Morbidity and mortality happen for both mother and baby and can reach 80% in some cases. Mortality in pregnancy is rising in the US and is the highest among developed country reaching 18% per 100,000. While cardiovascular mortality is the major cause of death, liver disorders are contributing factors and knowledge of the physiology of the liver and the pathophysiology is important for the management of these disorders and the impact they may have on global health. As many liver disorders occur at a young age and liver transplantation is done more often than before during the reproductive years of young women who are continuously seeking to get pregnant, the challenge of maintaining liver health in cirrhosis and after transplantation is also rising. Studies are scant during pregnancy and thus yet knowledge is evolving due to large registries and the task of disseminating this knowledge is essential in preserving the pregnant mother and her child. In this overview presentation, we will differentiate between normal and abnormal liver tests in pregnancy, we will recognize various liver disorders that occur during the different stages of pregnancy and we will understand the management of various liver diseases in pregnancy and recognize safety of drugs in pregnancy.

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