The emerging field of morphogens in the adult liver of mice and human – a deep insight into distribution, interaction and regulation

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RESULTS

AIM

For a better understanding of metabolic liver zonation under morphogenic control we aimed at demonstrating mutual impact and zonal distribution of Hh and Wnt-β-Catenin signaling.

METHODS

To investigate the impact of Hh- and Wnt-signaling on liver zonation human liver material was used. In addition different mouse models were bred which allow a hepatocyte-specific modulation of both pathways in adult mice. To depict the pericentral distribution of different pathway marker liver slices were stained by immunohistochemistry and analyzed by the modular software tool TiQuant (6). This tool allows an efficient quantification of biological tissues based on volume data obtained by biomedical image modalities. Gene expression was analyzed on isolated hepatocytes from the different mouse models. Moreover a proteomic analysis from murine liver was used to get a global overview about the impact on metabolic functions of the liver by morphogens.

CONCLUSIONS

Our results indicate a strong relation between Wnt and Hh in the adult liver of mice and human for the first time. The immunohistological analysis indicates how central proteins of the Hh and Wnt pathways are localized and how they influence each other when the pathways are modulated. Activation of the pericentral localized Wnt/β-Catenin pathway leads to a zonal expansion of Hh proteins like IHH and Wnt related proteins like AXIN2.

Further, we found a diverging impact of both morphogenic pathways especially on liver lipid metabolism. Our data suggest that the influence of morphogens regulate lipid metabolism in detail and contribute to a better understanding of the fine tuning mechanism on zonation of the liver and may help to shed light on the underling mechanisms of deregulations in liver like NAFLD and NASH.

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REFERENCES


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