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Promotionsverfahren von **Frau M.Sc. Paula Rita Anna Augusta Follert**
Auslage der Dissertation und Gutachten sowie Termin der mündlichen Prüfung
Anlage: Einseitige Zusammenfassung der Dissertation

Sehr geehrte Damen und Herren,

in dem oben genannten Promotionsverfahren wird die Annahme der Dissertation

The role of myeloid-derived growth factor (MYDGF) as an angiocrine signal for hepatocyte proliferation

von den Berichterstattenden Prof. Dr. E. Lammert und Prof. Dr. A. Gödecke beantragt. Sie kann zusammen mit den Gutachten in der Zeit

vom 29.06.2024 bis 10.07.2024

eingesehen werden. Bitte wenden Sie sich zur Einsicht an das Promotionsbüro (promotionmnf@hhu.de).

Einsprüche gegen diese Dissertation können nur zwei Tage nach der vorgenannten Frist geltend gemacht werden. Erfolgt kein Einspruch, so gilt die Dissertation als angenommen (§ 7 Ziffer (5) PO).

Sofern die Dissertation angenommen wird, findet die mündliche Prüfung am

15.07.2024 um 13:30 Uhr

im **Raum 26.44.02.028** statt. Als Prüferinnen bzw. Prüfer sind vorgesehen:
Prof. Dr. H. Al-Hasani, Prof. Dr. S. Prömel und Prof. Dr. G. Groth.

Die Öffentlichkeit ist bei der Befragung nicht zugelassen.

Mit freundlichen Grüßen
im Auftrag

Amina Diekmann

Paula Follert – Summary – PhD thesis

The liver is the largest detoxifying organ in the human body and has a remarkable ability to regenerate. When two-thirds of the liver is surgically dissected, a process called partial hepatectomy (PHx), the liver mass restores within 5-7 days in mice and within 14 days in humans. The process of liver regeneration is initiated by increased blood flow in the remaining one third of the liver. This causes vasodilation of hepatic blood vessels, which results in mechanical stretching of hepatic endothelial cells (hepatic ECs) that line the inside of the blood vessels and triggers the secretion of angiocrine signals. The latter promote the proliferation and survival of hepatocytes to restore the original liver mass.

In this study, we described the role of myeloid-derived growth factor (MYDGF) as an angiocrine signal for hepatocyte proliferation and thus liver regeneration. Previous experiments in our laboratory have shown that MYDGF is secreted by mechanically stretched primary human hepatic ECs and has a proliferation- and survival-promoting effect on primary human hepatocytes. Here we demonstrated that our stretching conditions, which have been shown to trigger the release of MYDGF, do not lead to increased cell death of mechanically stretched primary human hepatic ECs. Subsequently, we verified our previous results that MYDGF induces proliferation and prevents apoptosis of 2D cultured primary human hepatocytes. We also showed that daily MYDGF treatment triggers the growth and proliferation of primary human hepatocyte organoids. In addition, we reported that phosphorylation of mitogen-activated protein kinase (MAPK) and signal transducer and activator of transcription 3 (STAT3) is involved in MYDGF-induced hepatocyte proliferation. Next, we analyzed the expression kinetics of MYDGF in humans and mice and revealed that MYDGF levels are elevated at an earlier timepoint after liver surgery compared to the known angiocrine signal: hepatocyte growth factor (HGF). Finally, we investigated the effect of MYDGF on liver regeneration after two-thirds PHx. Our results showed that overexpression of MYDGF in the liver significantly increased hepatocyte proliferation and improved liver regeneration after two-thirds PHx in mice, and a knockout (KO) of MYDGF significantly abolished hepatocyte proliferation after two-thirds PHx.

In conclusion, our results showed that MYDGF is an angiocrine signal that enhances the proliferation and survival of primary human hepatocytes *in vitro*. *In vivo*, MYDGF increases in the first hours after liver surgery and represents a promoting factor for liver regeneration. Thus, our results provide a basis for further investigation of MYDGF as a potential therapeutic drug to stimulate liver regeneration after liver surgery.