MAYO CLINIC

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Dear IHPBA Research Committee,

I am truly honored to have been selected as the recipient of the Kenneth Warren Fellowship for 2024/ 2025. This prestigious research fellowship allows me to dedicate a full year to research at Mayo Clinic Rochester, under the mentorship of Dr. Patrick Starlinger. This experience is not only a once-in-a-lifetime opportunity but also a pivotal milestone that will significantly shape my career path.

At the halfway mark of my fellowship at Mayo Clinic Rochester, I have been actively engaged in a diverse range of projects, including translational and clinical studies on cholangiocarcinoma and liver surgery outcomes, as well as laboratory research on posthepatectomy liver failure and regeneration. Additionally, I have regularly participated in academic meetings and grand rounds, further enhancing my clinical education in HPB surgery.

Elucidating the Role of Immune Cell Interactions During Human Liver Regeneration Using Single Nuclear Sequencing

Over the past six months, we have made significant progress in our project investigating cell-cell interactions during liver regeneration using single-nuclear sequencing. Our focus has been on understanding gene expression changes by comparing different baseline liver samples with the regenerative state and exploring their involvement in post-hepatectomy liver failure (PHLF). So far, we have analyzed 30 liver samples from patients with different liver conditions, including healthy, PHLF, steatosis, and steatohepatitis, to identify key molecular drivers of liver regeneration/ dysfunction and potential therapeutic targets.

One of the key comparisons we have been working on is between baseline healthy liver and baseline PHLF samples. Our preliminary analysis reveals distinct differences in several key cellular mechanisms: In baseline PHLF, genes related to cell-cell interaction and proliferation are downregulated in cholangiocytes and hepatic stellate cells, while those involved in cellular remodeling are upregulated in endothelial, hepatic stellate, and myeloid cells. Metabolic pathways, particularly cytochrome P450 enzymes, show a trend of reduced expression in hepatocytes, whereas immune-related genes are upregulated in cholangiocytes, hepatocytes, and immune cells. These findings highlight early molecular alterations in PHLF and their impact on liver function.

As a next step, we are planning to compare differentially expressed genes across regeneration, steatosis, and steatohepatitis to identify key molecular pathways involved in liver dysfunction. Furthermore, we are expanding our approach by comparing both single-nuclear and single-cell sequencing. In parallel, we have developed a preclinical model to explore liver regeneration in metabolic dysfunction. Using NASH mouse models and age-matched controls, we apply a 70% partial hepatectomy to replicate human regeneration phases. Single-cell sequencing will analyze

gene expression in healthy and NASH-affected livers, providing insights into how metabolic dysfunction impacts recovery. These next steps will be essential in strengthening our findings and expanding our understanding of liver regeneration in both healthy and pathological liver conditions.

30-Year Review of De Novo pCCA: Transplantation vs. Resection

This project examines a 30-year dataset from Mayo Clinic Rochester, comparing liver transplantation and resection – with and without vascular reconstruction – for de novo pCCA. The primary aim is to evaluate long-term survival and refine surgical decision-making based on tumor resectability.

Neoadjuvant Gemcitabine, Cisplatin, and Durvalumab in Borderline Resectable CCA

We also investigated the feasibility and efficacy of neoadjuvant gemcitabine, cisplatin, and durvalumab in anatomically and biologically borderline resectable cholangiocarcinoma. The aim of this retrospective analysis is to assess treatment response and the potential for conversion to resectability following neoadjuvant chemoimmunotherapy.

Predictive Value of Circulating vWF-Ag for PHLF

This study evaluates preoperative von Willebrand Factor Antigen (vWF-Ag) as a predictor of PHLF in over 500 liver resection patients. The objective is to combine vWF-Ag with other established liver function parameters to enhance perioperative risk assessment.

Retrospective Analysis of Cholangiocarcinoma Database

Moreover, I have been compiling data for a comprehensive cholangiocarcinoma database, including intrahepatic and perihilar CCA cases, to evaluate long-term outcomes and treatment efficacy across surgical and oncological strategies, with the goal of generating meaningful clinical insights.

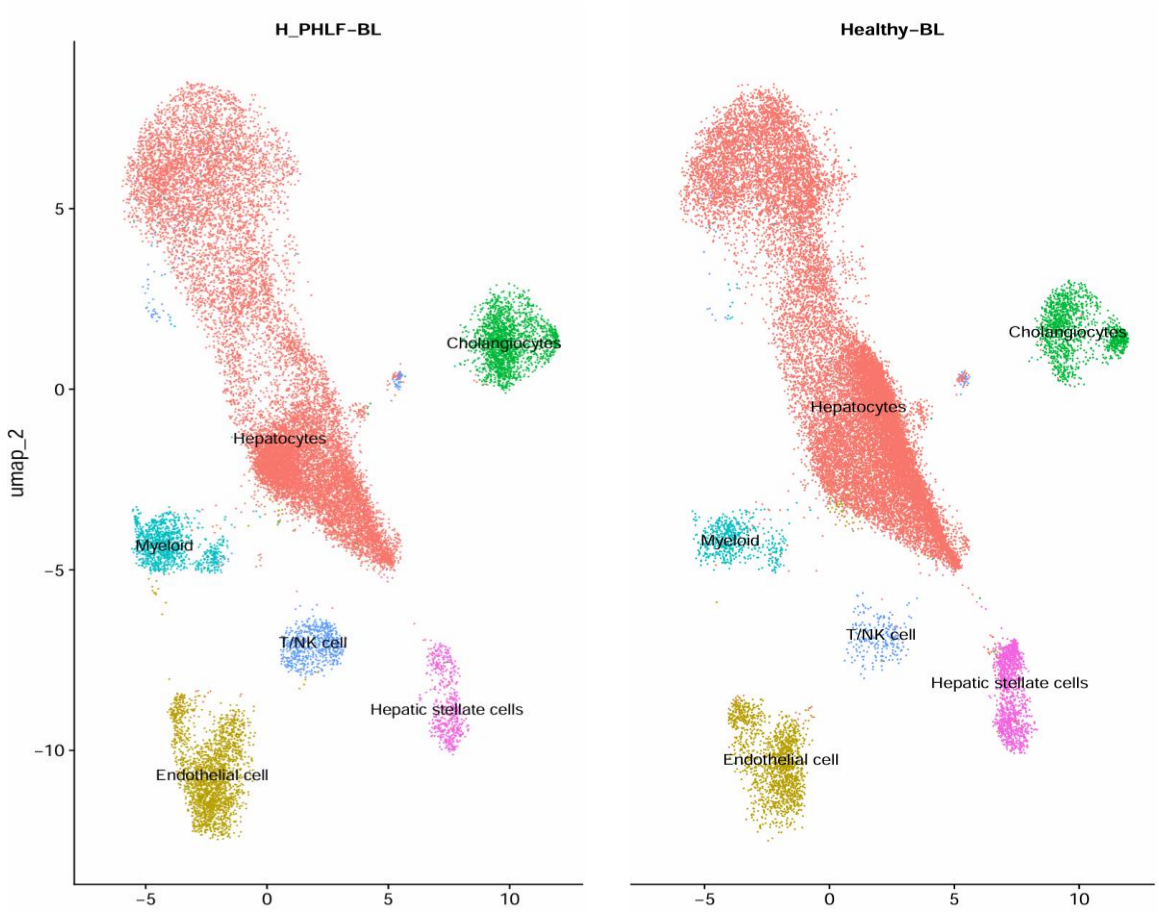
Future Directions and Follow-Up Projects

The second half of my fellowship will be dedicated to exploring several follow-up projects, including recurrence patterns in perihilar CCA, risk assessment in intrahepatic CCA and the evaluation of liver function and hypertrophy after augmentation procedures such as portal vein embolization or double embolization.

My research fellowship has been truly rewarding and productive so far, allowing me to engage in translational, preclinical, and basic research. As I continue, I am excited to further advance these projects and contribute to HPB surgery and surgical oncology. I am very grateful for Dr. Patrick Starlinger's mentorship and the opportunities at Mayo Clinic Rochester, and I look forward to participating in the IHPBA 2026 conference in Singapore.

Best regards,

Yawen Dong, M.D.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Hepatic stellate cells
Endothelial cell