

3200**Topic Category:** 4073-ASIP Liver injury and inflammation**First Author:** Elizabeth Stahl

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First Author is a: Graduate Student**First Author is a member of:** American Society for Investigative Pathology**First Author Degree:** BA, BS, or equivalent**Presentation Preference:** Oral**Sponsor:** Andrew Duncan**Sponsor Phone:** 412-624-5302

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Sponsor's Society: Pathology - American Society for Investigative Pathology (ASIP) - Host Society**Keywords:** 1. Aging 2. Inflammation 3. Liver Pathology**Awards:** ASIP Trainee Travel Award, HCS-Sponsored Trainee Travel Award

Age-induced Hepatic Steatosis and Inflammation of Murine Livers is Influenced by MCP-1

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Aging is linked to the onset and severity of several chronic liver diseases, including non-alcoholic fatty liver disease, alcoholic liver disease, and hepatitis, which correlate with high levels of macrophage infiltration, inflammation, and immunosenescence. Recent findings suggest that liver macrophages can be divided into two unique subsets: CD68⁺ embryonically-derived Kupffer cells and CD11b⁺ bone marrow derived cells, which exhibit specific cell functions. It is currently unclear how the macrophage populations residing in the liver are phenotypically and functionally impacted by the natural aging process, which may have implications for the onset and progression of inflammatory disease and liver pathology in elderly populations.

The aim of this study is to characterize the liver macrophage compartment from young (8-10 week) and aged (18-20 month) C57BL/6 wild-type mice. First, we identified a significant increase in the total number of F4/80⁺ macrophages residing in aged livers. Preliminary in vitro studies showed that aged macrophages were primed towards inflammatory reaction, including increased phagocytosis and nitric oxide production, in response to LPS and interferon-gamma. In addition, the aged macrophage population contained a greater proportion of CD11b⁺ cells, which are most likely derived from circulating monocytes. To confirm this, we determined that aged hepatocytes secrete enhanced levels of monocyte chemoattractant protein-1 (MCP-1), an important signaling molecule for monocyte recruitment following injury. Although aged livers do not show signs of injury or damage, we determined that hepatocytes from aged livers have increased triglyceride content and a shifted fatty acid profile. Of note, the aged mice received the same diet as young controls, and do not show signs of glucose intolerance. Future studies will examine how inhibition of MCP-1 signaling will impact macrophage recruitment, inflammation, and steatosis in aged livers towards a better understanding of age-related liver pathology.

Support or Funding Information

NIH-NIBIB Training Grant (T32-EB001026); NIH-NIDDK NRSA Fellowship (F31-DK112633-01A1); Pittsburgh Liver Research Center Pilot & Feasibility Grant