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"INVESTIGATING THE ROLE OF THE MACROPHAGE FERROPORTIN/HEPCIDIN AXIS IN THE PERITONEAL CAVITY DURING HEALTH, INFLAMMATION, AND METASTATIC DISEASE"

By

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Infection, Immunity and Inflammation
B.S. Cell and Molecular Biology, 2018
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Friday, August 7th, 2026
Cancer Center, G1196
10:30 A.M.

Join Zoom presentation
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Abstract

Iron is an essential nutrient for many biological processes in healthy humans, and its dysregulation is implicated in several chronic diseases. To maintain homeostasis, iron is recycled by the liver and splenic macrophages, which phagocytose damaged or senescent red blood cells, process their breakdown products, and export iron back into circulation via the surface protein, ferroportin (Fpn). Fpn-mediated iron efflux is regulated by hepcidin, a peptide hormone released from the liver that binds to and triggers the internalization of Fpn. The Fpn/Hepcidin axis has been extensively studied in the spleen and liver, but its role outside of the iron recycling pathway is poorly understood. Here, using a macrophage-specific hepcidin-insensitive Fpn mutant mouse model, we investigated the contribution of Fpn-mediated iron export to macrophage function in the context of peritoneal inflammation and metastatic disease. We demonstrate that macrophage Fpn hepcidin insensitivity does not affect systemic iron homeostasis but exacerbates OC disease progression within the peritoneal cavity. We further show that this worsened OC metastasis is improved by exogenous hepcidin treatment, but not iron chelator. Transcriptional analyses of sorted hepcidin-insensitive macrophages from OC ascites revealed significant transcriptional reprogramming, including dysregulation of several immunomodulatory and Type I interferon signaling pathways and subsequently, antitumor immunity, which may explain the observed disease exacerbation. Altogether, these findings identify Fpn-dependent iron export as a critical determinant of macrophage phenotype within the peritoneal microenvironment and suggest that disruption of the hepcidin/Fpn axis contributes to the establishment of a pro-tumorigenic inflammatory niche. Our results provide insight into how iron metabolism influences peritoneal inflammation and metastasis and support macrophage-intrinsic iron regulation as a potential therapeutic target in ovarian cancer and other diseases characterized by peritoneal dissemination.