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Fatty Acid Synthase Inhibition in Colorectal Cancer Peritoneal Carcinomatosis

Introduction
Peritoneal carcinomatosis (PC) in colorectal cancer (CRC) remains a major therapeutic challenge. We previously identified elevated fatty acid metabolism in PC-derived cancer stem cells (CSCs) compared to liver metastases (LM) and primary tumors (PT) from a murine stage IV CRC model. Western blot analyses confirmed significantly higher expression of fatty acid synthase (FASN) and acetyl-CoA carboxylase (ACC) in epithelial cells from PC. These findings suggest a metabolic vulnerability that may be targeted therapeutically.

Methods
We evaluated the therapeutic potential of FASN inhibition in a CRC PC mouse model treated with the FASN inhibitor Fasnall. The peritoneal carcinomatosis index (PCI), liver, and primary tumor burden were assessed. Organoid re-seeding assays from PC, LM, and PT were performed to analyze CSC function and proliferation following Fasnall treatment. Apoptosis was quantified using Annexin V FACS analysis.

Results
Fasnall treatment significantly reduced PCI in vivo, without affecting liver or primary tumor burden. In organoid re-seeding assays, Fasnall treatment markedly decreased organoid formation, particularly in PC organoids, indicating impaired CSC function. Fasnall treatment resulted in increased apoptosis and reduced proliferation in organoid cultures.

Conclusion
Our results indicate that fatty acid metabolism represents a promising therapeutic target in CRC PC. FASN inhibition by Fasnall impairs PC growth and may disrupt CSC function, highlighting its potential for innovative treatment strategies in this difficult-to-treat disease subset.

Preferred type of presentation

Poster Presentation only

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