



GASTROINTESTINAL IMMUNOPATHOLOGY

Project title

“The impact of the diet in modulating IBD and CRC development”

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Laboratory name: Gastrointestinal Immunopathology

Abstract

Although the etiopathogenesis of inflammatory bowel disease (IBD) is still unknown, the severity, extent of disease and the duration of inflammation represent the major risks associated with the development of colorectal carcinoma (CRC) in these patients. Unfortunately, the molecular mechanisms underlying the connection between intestinal inflammation and CAC are still unclear. Diet has a major impact on human healthy. The consumption of a westernized diet containing excessive amounts of refined and processed foods, red meats, and sugar beverages, accompanied with a low consumption of fibers, fruits, and vegetables is associated with the increased development of metabolic and inflammatory diseases, and cancer.

Some studies have reported an increased risk for developing IBD with a diet high in polyunsaturated fatty acids, ω -6 fatty acids, saturated fats, and meat. However, there are no direct evidences that identify dietary components as drivers of intestinal chronic diseases and CRC. Therefore the aims of this project is to:

Aim1. To assess the role and the molecular mechanisms triggered by Western diet in promoting intestinal inflammation and CRC development.

Aim2. To explore the impact of diet on early stage of colorectal cancer. Aim3. To study the impact of diet on epigenetic changes in CRC patients.

Main technical approaches

Experimental models of IBD and CRC; patient-derived xenograft tumor model; immunocharacterization by FACS and immunohistochemistry of tumors. RNA-sequencing analysis of xenograft tumors. Analysis of cell metabolism assessed by Seahorse XF Technology. To address whether a specific diet drives epigenetic changes conferring advantages to tumor development, ChIP experiments will be carried out.

Scientific references

E Sala et al. Mesenchymal Stem Cells Reduce Colitis in Mice via Release of TSG6, Independently of Their Localization to the Intestine. *Gastroenterology*. 2015 Jul;149(1):163-176.e20.

C Correale*, M Genua*, S Vetrano*, et al. Bacterial Sensor Triggering Receptor Expressed on Myeloid Cells-2 Regulates the Mucosal Inflammatory Response *Gastroenterology*. 2012 Oct 26 *equal contributors.



S Vetrano, S Danese. Colitis, Microbiota, and Colon Cancer: an Infernal Triangle. Gastroenterology. 2012 Dec 19

S Vetrano, VA Ploplis, E Sala, M Sandoval-Cooper, DL Donahue, C Correale, V Arena, A Spinelli, A Repici, A Malesci, FJ Castellino, S Danese Unexpected role of anticoagulant protein C in controlling epithelial barrier integrity and intestinal inflammation. Proc Natl Acad Sci U S A. 2011 Dec 6;108(49):19830-5.

S Danese, A Malesci, S Vetrano. Colitis-associated cancer: the dark side of inflammatory bowel disease. Gut. 2011 Dec;60(12):1609-10.

S Vetrano et al. The lymphatic system controls intestinal inflammation and inflammation-associated Colon Cancer through the chemokine decoy receptor D6. Gut. 2010 Feb;59(2):197-206.