

Title: Inflammation and Cancer: histologic and molecular studies of precancerous changes in coeliac and Crohn's disease.

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Research Theme/Topic: Anatomic Pathology, Gastroenterology, Oncology, Immunology.

Abstract: Inflammation is a recognized driving factor in carcinogenesis in several sites, including the small bowel. Particularly, coeliac (CD) and Crohn's disease (CrD), two common inflammatory disorders, have a significantly higher risk of developing small intestine adenocarcinoma (SBA) compared to the general population. Nevertheless, both in CD and CrD, very scarce knowledge is available in regard to either molecular mechanisms underlying mucosal changes, metaplastic or dysplastic, and, with particular reference to CrD, the histologic and immunophenotypic features of non-canonical epithelial lesions. Furthermore, to date, the microenvironment surrounding small bowel dysplastic and neoplastic growths in such cancer-predisposing inflammatory disorders has been poorly characterized, although its pivotal role as both negative and positive regulator of cancer development has been long established.

The aims of this project are: i) to characterise precancerous lesions, histologically and molecularly, in CD and CrD and, thus, to define CD- and CrD-associated SBA's natural history; ii) to study the interplay between the microenvironment and dysplasia/neoplasia in CD and CrD patients.

These data will help better understand the molecular pathways leading inflamed and remodelled small bowel mucosa to adenocarcinoma, as well as the role of inflammation in both early and late carcinogenetic processes in CD and CrD.

Techniques: molecular, histologic and translational, including immunohistochemistry, light microscopy, RT-PCR, NGS, flow cytometry.

Graphical abstract. A simplified model illustrating the molecular pathways leading to small bowel invasive adenocarcinoma and the main interactions between cancer and immunity in coeliac (left side) and Crohn's disease (right side).

