Matrix Metalloproteinases and Their Tissue Inhibitors as Biomarkers in Ulcerative Colitis and Crohn's Disease

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Laura Mäkitalo, MD, defended her PhD thesis in Helsinki on September 17th 2010. The thesis was supervised by Docent Kaija-Leena Kolho from Hospital for Children and Adolescents, Helsinki University Central Hospital, and Professor Ulpu Saarialho-Kere, Department of Dermatology, Allergology and Veneorology, University of Helsinki, Finland. The opponent was Docent Katri Kaukinen from University of Tampere. The thesis is available at: http://www.doria.fi/handle/10024/63351.

Matrix metalloproteinases (MMPs) represent a family of 23 metalloendopeptidases, collectively capable of degrading all components of the extracellular matrix. MMPs have been implicated in several inflammatory processes such as arthritis, atherosclerosis, and even carcinomas. They are also involved in several beneficial activities such as epithelial repair. MMPs are inhibited by endogenous tissue inhibitors of matrix metalloproteinases (TIMP).

In this study, MMPs were investigated in intestinal mucosa of inflammatory bowel diseases (IBD), chronic intestinal disorders. The main focus was to characterize mucosal inflammation in the intestine, but also cutaneous pyoderma gangrenosum (PG), to assess similarites with IBD inflammation. MMPs and TIMPs were mainly examined in colonic mucosa, in adult Crohn's disease (CD), and paediatric CD, ulcerative colitis (UC), and indeterminate colitis (IC). Ileal pouch mucosa of proctocolectomized paediatric onset IBD patients was also investigated to characterize pouch mucosa. The focus was on finding specific MMPs that could act as markers to differentiate between different IBD disorders, and MMPs that could be implied as markers for tissue injury, potentially serving as targets for MMP-inhibitors. All examinations were performed using immunohistochemistry.

The results show that immunosuppressive agents decrease stromal expression of MMP-9 and -26 that could serve as specific targets for MMP-inhibitors in treating CD. In paediatric colonic inflammation, MMP-10 and TIMP-3 present as molecular markers for IBD inflammation, and MMP-7 for CD. MMP expression in the pouch mucosa could not be classified as strictly IBD- or non-IBD-like. For the first time, this study describes the expression of MMP-3, -7, -9, -12, and TIMP-2 and -3 in pouch mucosa. The MMP profile in PG bears resemblance to both intestinal IBD inflammation and cutaneous inflammation.

Fig. 1. Laura Mäkitalo, MD, defended her PhD thesis on Matrix Metalloproteinases and Their Tissue Inhibitors in Helsinki in September 2010.

Based on the results, MMPs and their inhibitors emerge as promising tools in the differential diagnosis of IBD and characterization of the disease subtype, although further research is necessary. Furthermore, the expression of several MMPs in pouch has been described for the first time. While further research is warranted, the findings contribute to a better understanding of events occurring in IBD mucosa, as well as pyoderma gangrenosum.