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GI Pathology

**Immunohistochemical comparison between duodenal and colonic polyps in familial adenomatous polyposis.**

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*Background:* Familial adenomatous polyposis (FAP) is characterized by innumerable adenomatous polyps throughout the colorectum and inevitable development of invasive carcinoma by the fifth decade of life. It is caused by a germ line mutation in one of the *APC* alleles and is inherited in an autosomal dominant fashion.

Although screening and prophylactic surgery have significantly improved the survival of FAP patients, life expectancy remains lower than the general population. Upper gastrointestinal and, in particular, duodenal cancer is the leading cause of death in patients with FAP already treated by colectomy. Many different studies strongly suggest a favorable effect of NSAIDs on colorectal cancer development in both normal and FAP patients. However, the chemopreventive effects of NSAIDs on duodenal tumorigenesis appears to be less than in the colon.

Colorectal cancer develops through the adenoma-carcinoma sequence. Mutations in the *APC* gene can be regarded as the first step in the adenoma-carcinoma sequence. Then, additional mutations in tumor suppressor genes (e.g. *TP53* and *SMAD4*) and oncogenes (e.g. *K-Ras*) are necessary for further progression of the adenoma-carcinoma sequence. Also, the expression of some important cell regulatory proteins is changed. One of these is COX-2, which is increasingly expressed in consecutive stages of the adenoma-carcinoma sequence and can be inhibited by non-steroidal anti-inflammatory drugs (NSAIDs). Little is known about molecular changes in the duodenal adenoma-carcinoma sequence.

*Aims:* to investigate differences between duodenal and colonic adenomas in FAP and to give insight in possible mechanisms underlying the lower response to NSAIDs chemoprevention of duodenal adenomas compared to colonic adenomas.

*Methods:* 23 duodenal polyps and matched normal duodenal mucosa from 19 different FAP patients are compared to 50 colonic polyps and matched normal colonic mucosa from 27 different FAP patients using immunohistochemistry on  $\beta$ -catenin, three of its target genes (Cyclin D1, c-myc and CD44), COX-2, EGFR, SMAD4 and p53.

*Results:* data not yet available, will be ready in time.