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**TRANSCRIPTION FACTORS SOX2 AND PDX-1 IN ULCERATIVE COLITIS AND ASSOCIATED NEOPLASIA - ARE THEY RELATED TO GASTRIC APOMUCIN EXPRESSION AND INVOLVED IN CARCINOGENESIS?**

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**Introduction:** Ulcerative colitis (UC) provides a well documented preneoplastic condition in colonic mucosa where carcinogenesis pathways remain poorly understood. Our previous work on apon mucin expression in UC suggested the probable involvement of gastric metaplasia on UC malignant transformation. Homeobox genes SOX2 and Pdx-1 are reported as important in the control of gastric apon mucin expression.

**Aim:** To evaluated expression of transcription factors SOX2 and Pdx-1 in colonic mucosa of patients with UC, its relationship with gastric apon mucin production and with neoplasia.

**Material and Methods:** Ninety patients with UC were selected. The duration, the extent of disease and the use of therapeutic drugs were registered in all the cases. Colonic mucosa from all the patients was histologically and immunohistochemically assessed by using monoclonal antibodies against the apon mucins MUC5AC and MUC6 and the transcription factors SOX2 and Pdx-1.

**Results:** Neoplasia was observed in 16 patients, 8 non-invasive (dysplasia) and 8 invasive (adenocarcinoma). MUC5AC was detected in 63 and 16 out the 90 cases, 70.0% and 17.8%, respectively. Expression of SOX2 was detected in 20.2% cases and Pdx1 in 74.1%, (both in areas of regenerative mucosa and neoplasia). Correlation between SOX2 and MUC6 (R=0.436, p<0.000) and Pdx1 and MUC5AC (R=0.562, p=0.000) was observed. SOX2 expression correlated with dysplasia (R=0.385, p<0.000) and showed a negative correlation with the use of therapeutic agents (R = -0.297, p = 0.007), Pdx1 correlated with distortion (R=0.324, p<0.003) and inflammation (R = 0.229, p = 0.046).

**Conclusions:** Our study: 1) demonstrates the aberrant expression of gastric transcription factors in UC; 2) supports the involvement of SOX2 and Pdx-1 in UC carcinogenic pathway. Our study: 3) suggests the involvement of SOX2 in UC carcinogenic pathway.

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**ABERRANT GASTRIC APOMUCIN IN ULCERATIVE COLITIS AND ASSOCIATED NEOPLASIA - AN IMMUNOHISTOCHEMICAL DEMONSTRATION**

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**Introduction:** Ulcerative colitis (UC) provides one well documented preneoplastic condition in the colon. As in other models in the context of chronic inflammation, the presence of metaplastic mucosa may precede the development of dysplasia and invasive neoplasia.

**Aim:** To evaluate the presence of gastric metaplasia in colonic mucosa of patients with UC and its relationship with dysplasia/neoplasia.

**Material and Methods:** Ninety patients with UC were selected. The duration and the extent of disease were registered in all the cases. Biopsies were histologically and immunohistochemically assessed. No significant differences were reported in the carcinogenesis of IBD-associated CRC (I-CRC) compared to sporadic CRC (S-CRC): e.g. whereas p53 mutations occur early in I-CRC, they appear late in S-CRC. Additionally, in S-CRC, Cdx2 expression (a homeotic gene with anti-oncogenic properties) is decreased, possibly resulting of an inhibitory beta-catenin-SOXV-dependent pathway. Our objectives were to confirm p53 accumulation, and to investigate Cdx2 and beta-catenin expression in I-CRC compared to S-CRC. We investigate p53, Cdx2, and beta-catenin expression by immunohistochemistry in 10 normal and 10 S-CRC colonic mucosal specimens, as well as in IBD specimens without any dysplasia or CRC (CD: n=10, UC: n=10), and I-CRC (CD: n=10, UC: n=10). In I-CRC, p53 expression was strongly and homogeneously expressed compared to non-inflamed, non-dysplastic, non-CRC IB patients. However, p53 expression was detected in the normal colon of UC patients, showing the probable involvement of gastric metaplasia on UC malignant transformation.

**Conclusions:** Our study demonstrates the aberrant expression of gastric apoptosis in UC and Ulcerative colitis (UC) and Crohn’s disease (CD). Several differences were reported in the carcinogenesis of IBD-associated CRC (I-CRC) compared to sporadic CRC (S-CRC): e.g. whereas p53 mutations occur early in I-CRC, they appear late in S-CRC. Additionally, in S-CRC, Cdx2 expression (a homeotic gene with anti-oncogenic properties) is decreased, possibly resulting of an inhibitory beta-catenin-SOXV-dependent pathway. Our objectives were to confirm p53 accumulation, and to investigate Cdx2 and beta-catenin expression in I-CRC compared to S-CRC. We investigate p53, Cdx2, and beta-catenin expression by immunohistochemistry in 10 normal and 10 S-CRC colonic mucosal specimens, as well as in IBD specimens without any dysplasia or CRC (CD: n=10, UC: n=10), and I-CRC (CD: n=10, UC: n=10). In I-CRC, p53 expression was strongly and homogeneously expressed compared to non-inflamed, non-dysplastic, non-CRC IB patients. However, p53 expression was detected in the normal colon of UC patients, showing the probable involvement of gastric metaplasia on UC malignant transformation.

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**IMMUNOHISTOCHEMICAL EXPRESSION OF P53, CDX2 AND BETA-CATELIN IN INFLAMMATORY BOWEL DISEASE (IBD)-ASSOCIATED, COMPARED TO SPORADIC, COLORECTAL CANCER: FURTHER EVIDENCE FOR DIFFERENT CARCINOGENIC PATHWAYS**

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**Conclusion:** In ulcerative colitis (UC) and Crohn’s disease (CD), several differences were reported in the carcinogenesis of IBD-associated CRC (I-CRC) compared to sporadic CRC (S-CRC): e.g. whereas p53 mutations occur early in I-CRC, they appear late in S-CRC. Additionally, in S-CRC, Cdx2 expression (a homeotic gene with anti-oncogenic properties) is decreased, possibly resulting of an inhibitory beta-catenin-SOXV-dependent pathway. Our objectives were to confirm p53 accumulation, and to investigate Cdx2 and beta-catenin expression in I-CRC compared to S-CRC. We investigate p53, Cdx2, and beta-catenin expression by immunohistochemistry in 10 normal and 10 S-CRC colonic mucosal specimens, as well as in IBD specimens without any dysplasia or CRC (CD: n=10, UC: n=10), and I-CRC (CD: n=10, UC: n=10). In I-CRC, p53 expression was strongly and homogeneously expressed compared to non-inflamed, non-dysplastic, non-CRC IB patients. However, p53 expression was detected in the normal colon of UC patients, showing the probable involvement of gastric metaplasia on UC malignant transformation.