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Role of TGFβ1/Smads pathway in the pathogenesis of intestinal fibrosis in Crohn's disease

Roberta Sferra[1], Nadia Pallotta[2], Enrico Corazziari[2], Giuseppe Ricciardi[1], Annunziata Scirocco[2], Carola Severi[2], Simona Pompili[1] and Antonella Vetuschi[1]

[1] Department of Experimental Medicine, University of L'Aquila, L'Aquila, Italy
[2] Department of Internal Medicine and Medical Specialties, "Sapienza" University of Rome, Rome, Italy

Inflammatory bowel diseases (IBD) are characterized by an intestinal fibrosis that may lead to stenosis and obstruction (Burke et al., 2007) and by disfuntions of gastrointestinal (GI) motility associated with altered functions of enteric nerves, interstitial cells of Cajal or smooth muscle (Vetuschi et al., 2006). In experimental model TGFβ1/Smad3 signalling plays a major role in tissue fibrogenesis (Latella et al, 2009). Aim of this study was to evaluate the potential role of the TGFβ1/Smads pathway in intestinal fibrosis and to explore the possible mechanisms by which fibrogenesis induces alterations of GI motility in patients affected by CD. Evaluation of TGFβ1, CTGF, collagen I-III, Smad3/7, PDGF, C-Kit, α-SMA, and a neuronal cocktail expression and a morphometrical analysis were performed in human CD terminal ileum samples; human smooth muscle cells (HSMC) were cultured for morphofuncional and mRNA expression (RT-PCR). Histo-morphometrical evaluation of stenotic fragments showed a significantly increase of a) both intestinal fibrosis and inflammation; b) mucosa, submucosa and muscle layer thickness and c) expression of TGFβ1, CTGF, collagen I-III, Smad3, PDGF, C-Kit and α-SMA staining. HSMC obtained from stenotic tracts showed an increase of PDGF-β and collagen I-III types mRNA and an inhibition in contractile response to acetylcholine compared to pre-stenotic tracts. These data support the hypothesis that TGFβ1/Smads pathway play a central role in development and differentiation of intestinal mesenchymal cells in sustaining intestinal fibrosis in CD and could be responsible for alteration of GI motility.

References

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