Is transforming growth factor-beta involved in intestinal wound healing?

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Migration of colonic lamina propria fibroblasts (CLPF) plays an important role during the progression of fibrosis and fistulae in Crohn's disease. Transforming growth factor- beta (TGF- beta) is involved in the regulation of cell migration, cell differentiation, extracellular matrix deposition, and immune responses. Since the regulation of migration and differentiation of intestinal fibroblasts is an important mechanism during intestinal wound healing and fibrosis, it is important to investigate the effect of TGF- beta 1 on these processes and on fibronectin (FN) and FN isoform production.

A research team led by Dr. Julia Brenmoehl from University of Jena addressed this issue and their study will be published on March 28, 2009 in the World Journal of Gastroenterology.

In their study, primary CLPF cultures were incubated with TGF-beta 1 and analyzed for production of alpha-smooth muscle actin (alpha-SMA), FN and FN isoforms. Migration assays were performed in a modified 48-well Boyden chamber. Levels of total and phosphorylated focal adhesion kinase (FAK) in CLPF were analyzed after induction of migration.

They found that incubation of CLPF with TGF-beta 1 for 2 days did not change alpha-SMA levels, while TGF-beta 1 treatment for 6 day significantly increased alpha-SMA production. Short term incubation (6 hours) with TGF-beta 1 enhanced CLPF migration, while long term treatment (6 day) of CLPF with TGF-beta 1 reduced migration to

15%-37% compared to untreated cells. FN and FN isoform mRNA expression were increased after short term incubation with TGF-beta 1 (2 days) in contrast to long term incubation with TGF-beta 1 for 6 days. After induction of migration, TGF-beta 1-preincubated CLPF showed higher amounts of FN and its isoforms and lower levels of total and phosphorylated FAK than untreated cells.

Their results indicated long term incubation of CLPF with TGF-beta 1 induced differentiation into myofibroblasts with enhanced alpha-SMA, reduced migratory potential and FAK phosphorylation, and increased FN production. In contrast, short term contact (6 hours) of fibroblasts with TGF-beta 1 induced a dose-dependent increase of cell migration and FAK phosphorylation without induction of alpha-SMA production. This study adds to the understanding of the role of TGF- beta in intestinal wound healing and stricture formation.

More information: Brenmoehl J, Miller SN, Hofmann C, Vogl D, Falk W, Schölmerich J, Rogler G. Transforming growth factor-beta 1 induces intestinal myofibroblast differentiation and modulates their migration. World J Gastroenterol 2009; 15(12): 1431-1442
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