SBR 2019
36º CONGRESSO BRASILEIRO DE REUMATOLOGIA
CENTRO DE EVENTOS DO CEARÁ
04 A 07 DE SETEMBRO
FORTALEZA 2019
PROMOÇÃO
70 anos Sociedade Brasileira de Reumatologia
REALIZAÇÃO
SCR SOCIEDADE CEARENSE DE REUMATOLOGIA

THE ROLE OF GASTRIN-RELEASING PEPTIDE IN MYOFIBROBLAST ACTIVATION OF COLON FIBROBLASTS

Mirian Farinon (Laboratório de Doenças Autoimunes, Serviço de Reumatologia, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brasil), Patrícia Gnieslaw Oliveira (University of California, San Diego, Estados Unidos), Monica Guma (University of California, San Diego, Estados Unidos), Ricardo Machado Xavier (Serviço de Reumatologia, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brasil)

BACKGROUND

Intestinal fibrosis is a common complication of inflammatory bowel diseases (IBD), with a prevalence of 2-12% in ulcerative colitis and 10-30% in Crohn's disease. The fibrotic process is characterized by an excessive accumulation of extracellular matrix components produced primary due to activation of intestinal fibroblasts into myofibroblasts and the therapeutic management of this condition remains a challenge. Gastrin-releasing peptide (GRP) and its receptor (GRPR) play an important role in the immune and inflammatory response and a GRPR antagonist reduced disease severity in an acute rat model of colitis. However, the involvement of GRP-GRPR pathway in fibrosis and fibroblasts activation remains unclear. Based on that, we aimed to evaluate the role of GRP in the phenotype change of fibroblasts isolated from colon of mice.

MATERIALS AND METHODS

Fibroblasts were isolated from colon of healthy C57BL/6 mice. The viability of cells treated with GRP (10µM) was analyzed by MTT assay after 4 and 7 days. Migration was assessed by wound healing assay in the presence of GRP (10µM), PDGF-BB (10 ng/ml) or a combination of both. IL-6 production was assessed by ELISA after 24h of GRP (10µM) or TNF-α (10 ng/ml) stimulation. Gene expression of α-SMA, collagen 1A, collagen 4, fibronectin, IL-1 and IL-6 was analyzed by qPCR after 48h of GRP (10µM), TNF-α (10 ng/ml), TGF-β (5 ng/ml) stimulation or a combination between the stimuli. Statistical analysis was performed by one-way ANOVA followed by Tukey.

RESULTS

GRP treatment did not affect colon fibroblast viability. Exposure to GRP increased fibroblast migration (1419 ± 410 inches) compared with untreated cells (2045 ± 473.6 inches) ($p<0.001$) and PDGF-BB stimulated cells (1678 ± 512.2 inches) ($p<0.05$). GRP treatment increased α-SMA, collagen 1A and fibronectin expression compared with untreated cells ($p<0.05$), without a synergic effect with TNF-α or TGF-β. Exposure to GRP did not affected collagen 4, IL-1 and IL-6 gene expression, as well as IL-6 secretion.

CONCLUSION

Although GRP had no effect over inflammatory markers in colon fibroblasts, it enhanced the migration of these cells and induced the differentiation to myofibroblasts through the induction of α-SMA, fibronectin and collagen 1A expression. Our results suggest that the GRP-GRPR pathway may play an important role in the progress and maintenance of fibrosis in IBD and could be a relevant target in the development of anti-fibrotic therapies. In this sense, further analyses are needed for a better understanding of the mechanisms involved in this process.