Altered Expression of G Protein-Coupled Receptor Kinases 2 and 6 in Rat Experimental Colitis

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Crohn's disease is a chronic relapsing inflammatory disease of the gastrointestinal tract. Altered G protein-coupled receptor kinase (GRK) activity and/or expression has been reported to occur in tissues and/or lymphocytes isolated from human patients with immunological disorders (Métayé et *al.*, 2005). Therefore, we analyzed GRK2 and GRK6 expression in rat 2,4,6-trinitrobenzene sulphonic acid (TNBS)-induced colitis, an experimental model of intestinal inflammation that most closely resembles Crohn's disease. Colitis was induced in male Wistar Han rats (250-300 g, n=6) by a single rectal administration of 30 mg of TNBS dissolved in 50% ethanol (Morris et *al*., 1989). Control rats received either 50% ethanol in saline (0.9% NaCl) (n=6) or saline (n=5). Seven days after induction animals were sacrificed, blood and tissues were collected. Immunodetection of GRK2/GRK6 was performed by Western blot in whole-cell lysates. Data are means ± S.E.M and $p < 0.05$ (ANOVA) was considered significant. Protein expression levels are presented as percentage of GRK/GAPDH expression of the saline group. GRK2 expression was significantly increased in distal (inflamed) colonic mucosa from TNBS-treated rats (298.51±29.04) compared to vehicle- (154.88±14.81) and saline-treated (100±11.3) animals. In proximal colonic (non-inflamed) mucosa, GRK2 levels were increased only in the TNBS-treated group (170.72±11.26). Decreased GRK2 expression was found in isolated peripheral blood mononuclear cells (PBMC) from both vehicle- and TNBS-treated rats (71.18±11.3 and 70.50±7.09, respectively) compared to the saline group. No differences in GRK2 levels were detected in the ileum, jejunum and spleen between the 3 groups. GRK6 expression markedly increased in distal colonic mucosa from TNBS-treated rats (1523.60±14.81) compared to vehicle and saline groups. Increased levels of GRK6 have been also observed in the splenic tissue from TNBS rats (262.29±36.89). No significant changes were observed for the other tissues in all the 3 groups. In conclusion, colonic inflammation is associated with increased expression of GRK2 and GRK6 which may underlie a mechanism attempt to control inflammation with functional consequences in GPCR signaling. Métayé et *al*. *Cell Signal* 17, 917-928, 2005. Morris et *al*. *Gastroenterology* 96, 795–803, 1989. Supported by Portuguese Foundation for Science and Technology (SFRH/BPD/26665/2006).

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