

Increased inflammation and lipid peroxidation in GHRHKO mice colon

S. Leone¹, A. Chiavaroli¹, C. Di Nisio¹, L. Recinella¹, R. Shohreh¹, A. Ricciuti¹, G. Orlando¹, C. Ferrante¹, R. Salvatori², M. Vacca¹, L. Brunetti¹

¹Dept. of Pharmacy, G. d'Annunzio University, Chieti, Italy

²Dept. of Medicine, Division of Endocrinology, Johns Hopkins University School of Medicine, Baltimore

In addition to activating the hypothalamic-pituitary-adrenal axis, inflammatory processes are also known to be modulated by the somatotrophic axis. Both anti- and pro-inflammatory effects have been attributed to growth hormone-releasing hormone (GHRH) and growth hormone (GH). The aim of this study was to elucidate the consequences of GHRH deficiency on the responsiveness to acute inflammatory stimuli in a dextran sodium sulfate (DSS)-induced colitis mouse model [Laroui et al., 2012]. Responsiveness to inflammation induced by DSS (2%, for 7 days) was evaluated by histological examinations of distal colon specimens in wild type (+/+, n = 12) controls and GHRH gene knocked out (GHRHKO) mice (-/-; n = 12). Prostaglandin (PG)E₂ and 8-iso-prostaglandin (PG)F_{2α} levels were evaluated in colon samples, as stable biomarkers of inflammation and lipid peroxidation, respectively [Morrow et al., 1997; Roberts et al., 2000; Brunetti et al., 2010]. Differences between groups were analyzed by Student-test; p < 0.05 was considered statistically significant. Compared to +/+ controls, -/- mice showed increased inflammation in slides stained with hematoxylin-eosin, together with higher PGE₂ and 8-iso-PGF_{2α} tissue levels (P < 0.005 and P < 0.05, respectively). We hypothesize that generalized GHRH ablation is associated with increased sensitivity to inflammatory stimuli, consistent with increased PGE₂ and 8-iso-PGF_{2α} production in the colon. Whether this is the result of lack of GHRH or due to GH deficiency remains to be established.

Laroui H, Ingersoll SA, Liu HC, Baker MT, Ayyadurai S, Charania MA, Laroui F, Yan Y, Sitaraman SV, Merlin D. Dextran sodium sulfate (DSS) induces colitis in mice by forming nano-lipocomplexes with medium-chain-length fatty acids in the colon. *PLoS One*. 2012;7(3):e32084.

Roberts LJ, Morrow JD. Measurement of F(2)-isoprostanes as an index of oxidative stress in vivo. *Free Radic Biol Med*. 2000;28(4): 505-13.

Morrow JD, Roberts LJ. The isoprostanes: unique bioactive products of lipid peroxidation. *Prog Lipid Res*. 1997;36(1):1-21.

Brunetti L, Leone S, Chiavaroli A, Orlando G, Recinella L, et al., Cafeteria diet increases prostaglandin E₂ levels in rat prostate, kidney and testis. *Int J Immunopathol Pharmacol*. 2010;23(4):1073-8.