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**DIPEPTIDYL PEPTIDASE IV EXPRESSION IN A
CELLULAR AND HUMAN MODEL OF INTESTINAL
INFLAMMATION**

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Introduction Dipeptidyl peptidase IV (DP IV) is a serine protease. It modulates the physiological activity of satiety inducing hormones such as glucagon like peptide 1 (GLP-1) and polypeptide YY (PYY). It also inactivates GLP-2, an enteroendocrine hormone with cytoprotective and reparative properties. By cleaving chemokines essential for the Th-2 inflammatory pathway, DP IV enhances the Th-1 pathway. Reduced serum DP IV activity has been observed in patients with inflammatory bowel disease (IBD) including Crohn's disease (CD). Plasma levels and tissue expression have never been described together. The latter is of particular clinical significance since this is the local site of action of trophic GLP-2 and GLP-1 mediated vagal afferent stimulation.

Methods Experiments were also carried out on a Caco-2 cell line model of intestinal inflammation with TNF α incubation in a graded concentration/time course. DP IV expression was studied at the mRNA level through quantitative PCR (qPCR) and protein level by tissue western blotting and plasma ELISA. DP IV expression was also studied in active small (n=18) and large bowel CD (n=5). A subgroup of patients were restudied when inactive (n=6) and all results were compared to healthy controls (n=17).

Results In Caco-2 cells an ~ 18-fold increase ($p<0.0001$) in DP IV protein expression was seen after incubation with TNF α at a concentration of 25 ng/ μ l for 48 h, as compared to untreated cells. This change is mirrored at the mRNA level with a two-fold increase in DP IV expression at similar TNF α concentration and time course. Similar changes were noted in human tissue with a significant 4.5-fold DP IV upregulation ($p=0.02$) in CD compared to normal controls. However, results at the protein level in human tissue showed an opposite trend, with a ~2.7-fold decrease in DP IV expression in CD tissue compared to controls ($p=0.05$). The highest DP IV fasting plasma levels were noted in the control group (558.5 ± 39.98 ng/ml). Levels in CD were significantly less ($p=0.0028$) both in large bowel CD (406.2 ± 48.10 ng/ml) and more so in the small bowel CD group (361.3 ± 38.83 ng/ml; $p<0.01$). There was no significant difference in plasma DP IV between active and inactive disease.

Conclusion Results in the reductionist cellular model of intestinal inflammation support an increase in DP IV in an inflammatory milieu. However, in the complex, chronic human disease DP IV expression is decreased, as observed in other inflammatory states such human inflammatory arthritis and systemic lupus erythematosus. It is possible that a decrease in DP IV would preserve more biologically active GLP-2, enhancing trophic activity and promoting repair. DP IV may present a potential therapeutic target in IBD.

Competing interests None.

Keywords dipeptidyl peptidase IV, inflammation.