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Secretion of angiopoietin-like 4 protein from intestinal cells

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ABSTRACT

Background: Angiopoietin-like 4 (ANGPTL4) has been suggested to play a role in lipid metabolism as a regulatory protein of lipoprotein lipase activity. Intestinal secretion of ANGPTL4, which is regulated by fatty acids, may inhibit the activity of circulating lipoprotein lipase; but, recent studies suggest that it could also inhibit pancreatic lipase in the gut and thereby reduce intestinal uptake of lipids. Secretion of the ANGPTL4 protein to either the lumen or tissue/blood side of the intestinal epithelial layer would indicate possible modes of action.

Methods: Caco-2 cells were grown on permeable membranes and cultured for 21 days to spontaneously differentiate into an intact monolayer of intestinal cells, mimicking the epithelial cell layer lining the intestinal wall. Cells were treated with 9 mM butyrate and the time dependent gene expression and protein secretion to the apical and basolateral side was analysed over a time-course of 24 hours. Possible feedback from ANGPTL4 protein was investigated by adding 0.25 ng/ml recombinant ANGPTL4 protein to culture media.

Results: Butyrate-induced *ANGPTL4* gene expression increased in Caco-2 cells after 2 hours, reaching a plateau of approximately 6 fold after 6-24 hours, while the ANGPTL4 protein secretion to both the apical and basolateral sides was increased 18-24 hours after stimulation. A negative feedback on apical and basolateral secretion was observed in the presence of recombinant ANGPTL4 on the apical and basolateral sides, respectively.

Conclusion: The present study indicates that, upon exposure to butyrate, the monolayer of epithelial cells secretes the ANGPTL4 protein to both the tissue/blood (basolateral) side and the luminal (apical) side of the monolayer which, in an *in vivo* situation, may be interpreted as potential inhibition of both the circulating and pancreatic lipase.

Keywords: Angiopoietin-like 4, Caco-2, Permeable membrane, Protein, Secretion, Intestine, Negative feedback.