Inflammatory bowel disease free papers

OC-161 INVESTIGATION OF THE ACTION OF HISTONE DEACETYLASE INHIBITORS IN EX VIVO AND IN VITRO MODELS OF INFLAMMATORY BOWEL DISEASE

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Introduction The management of inflammatory bowel disease (IBD) has evolved rapidly with anti-TNFα agents and the more appropriate use of immunomodulators. Despite this, a large therapeutic gap remains to be filled. Histone deacetylase (HDAC) inhibitors (HDI) preserve acetylation of core histones which prevents chromatin from condensing thus facilitating gene transcription. HDI have been approved for the treatment of sub-cutaneous T-cell lymphoma and recent work has shown that HDI may have a protective anti-inflammatory effect in murine models of UC (Tao et al 2007). We hypothesise that HDI have anti-inflammatory effects in human IBD and aim to investigate this using a human ex vivo model of IBD.

Methods Carefully phenotyped patients with active UC (n=7) and CD (n=10) undergoing lower GI endoscopy had 8 pinch biopsies (∼3 mm²) taken for these experiments. Biopsies were cultured ex vivo at an air liquid interface for 8 h±FK228 or SAHA. Additionally, gut fibroblasts isolated from resection tissue were used to model mucosal plasticity in vitro±TNFα and FK228 and a monocytic cell line (U937) was differentiated in vitro with GMCSF±FK228. Supernatants, RNA and tissue were collected for analysis by qRT-PCR, mesoscale assay, western blotting and histology.

Results Nanomolar levels of FK228 significantly reduce mRNA expression and protein secretion of Th1 and Th2 cytokines and pro-inflammatory mediators (IL-8, MMP-1, -3, -9 and -12) in the ex vivo UC and CD biopsy models. Data suggest that FK228 can decrease mRNA expression of Th1 and Th17 signalling molecules in the ex vivo models. FK228 significantly decreases IL-8, MMP-3 and MMP-12 mRNA expression as well as IL-8 and MMP-3 protein secretion by gut fibroblasts and decreases GMCSF induced MMP-12 protein production by U937 cells.

Conclusion This human ex vivo biopsy culture model is relevant for pre-clinical study of drug action in IBD as it utilises small amounts of tissue in a human system. FK228 produces significant anti-inflammatory effects at low doses by reducing cytokines and MMPs in this model. FK228 is able to act upon specific cells found in the gut such as lymphocytes, fibroblasts and monocytes to elicit anti-inflammatory effects. Based upon our initial findings, further investigation of the role of FK228 in IBD is warranted.

Competing interests None declared.

REFERENCE


OC-162 THE ROLE OF MICRORNAS MIR-31 AND MIR-155 IN THE DEREGULATION OF THE IL-13 PATHWAY IN ULCERATIVE COLITIS

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Introduction IBD patients are of working age and have access to web based and smartphone technologies that could be used in the management of their IBD. IBD patients desire e-health access and the use of technology for communication regarding their disease management as well as web-based monitoring and self management of their IBD. Patients with IBD are ready for telemedicine systems to be employed as an adjunct in the management of their disease.
OC-160 Telemedicine systems in IBD management—are patients ready?

J Landy, S T Peake, A Akbar and A L Hart

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