**Abstracts**

**PMO-50**  **FACTORS INDEPENDENTLY ASSOCIATED WITH FATIGUE IN IBD: RESULTS FROM THE PREDiCCt STUDY**

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Introduction Fatigue is one of the most common symptoms in IBD resulting in decreased quality of life, impaired work productivity, and higher societal costs. However, little is known about its etiology and pathophysiology. We aimed to estimate the prevalence of fatigue and to identify predictive factors for fatigue.

Methods The PREdiCCt study is the largest prospective study of the causes of IBD flare. 2629 patients in clinical remission were recruited from 48 UK sites. 1946 (74%) patients completed the baseline questionnaires. We assessed the prevalence of fatigue at baseline using a single item from the IBD Control questionnaire. To identify predictors for fatigue, we performed univariable and multivariable analyses including demographic, biochemical, environmental and psychosocial factors.
Introduction The gut selective oral beclomethasone dipropionate (Clipper) is approved for use in mild-to-moderate ulcerative colitis (UC), with a better safety profile compared to conventional systemic corticosteroids. We reviewed the efficacy and response rates at 4 weeks. 83% of those in remission remained in steroid-free clinical remission at 6 months. Overall 53% were in remission at 6 months, 4 of whom had their background medications escalated over the review period. 12 patients had paired faecal calprotectin results showing a mean reduction of 981ug/g (p=0.036).

Conclusions Clinical remission can be effectively induced with Clipper in patients with UC, with significantly higher remission in mild disease. It is useful as bridging therapy during a change or escalation in background therapy. It has the potential to reduce the need for systemic steroid therapy. Clipper seems to also have a similar effect in patients with colonic CD.

Liver

PWE-1 ALKBH5-MODIFIED HMGB1-STING ACTIVATION CONTRIBUTES TO RADIATION INDUCED LIVER DISEASE VIA INNATE IMMUNE RESPONSE

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Introduction Radiation therapy (RT) is vital for the therapy of primary liver cancer, but inevitable liver injury limits the implement of RT. N6-methyladenosine (m6A) methylation is involved in many molecular functions; however, its role in radiation-induced liver diseases (RILD) remains unknown. Hence, we intend to investigate the role of m6A methylation in RILD.

Methods Methylated RNA-immunoprecipitation sequencing (MeRIP-seq) and RNA transcriptome sequencing (RNA-seq) were used to reveal the methylation pattern of human hepatic stellate cells with exposure to irradiation. C3H/HeN mice and STING-deficient mice underwent X-ray irradiation of 24 Gy in three fractions. The m6A methylation of HMGB1 transcript was validated using MeRIP, RIP, luciferase assay and mRNA decay assays.

Results Human hepatic stellate cells showed significant difference of methylation pattern after 8 Gy of X-ray irradiation. Irradiation recruits ALKBH5, an eraser of m6A methylation, and then demethylated HMGB1 transcript at m6A residues in the 3’UTR, following activation of STING-IRF3 signaling. Inserting of the HMGB1 3’UTR into a luciferase reporter resulted in regulation of luciferase activity by ALKBH5 knockdown, which was lost after m6A residue mutation. Strikingly, ALKBH5 deficiency or HMGB1 silencing both attenuated type I interferon production, resulting to less hepatocyte apoptosis. In vivo depletion of ALKBH5 abolished the upregulation of HMGB1-mediated STING signaling, leading to slightly liver inflammation, which was consistent to STING+/− mice in response to irradiation. Notably, the m6A reader protein YTHDF2 directly binds to m6A-modified site of HMGB1 transcript, which consequently promotes its degradation.

Conclusions ALKBH5-dependent HMGB1 expression mediates STING-IRF3 innate immune response in RILD.