factors such as anxiety and depression (HADS), sleep quality (PSQI) and physical exercise (GPAQ).

Results 759/1919 IBD patients in clinical remission (39.6%) reported fatigue in the past 2 weeks, while 1034 patients (53.9%) did not report fatigue. Patients who reported fatigue were more frequently female, had more frequently CD, and were more frequently smokers (Table 1). Univariable comparisons showed higher inflammatory markers in the fatigued group, with fewer patients in clinical remission. Multivariable analyses identified female sex (OR 2.4), CRP >5 (OR 2.1), bad sleep quality (OR 2.5), anxiety (OR 1.8) and depression (OR 6.2) as independent factors associated with fatigue.

Conclusion We show the significant burden of fatigue in IBD patients and describe putative causes which demonstrate both the impact of residual gut inflammation and the relationship between fatigue and mental health.

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 shown 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.