hypomethylation, p=0.009) despite modest but significant upregulation of expression (0.24, p=8.20E-03).

Conclusions Our findings could be the first to suggest that the up- and downregulation of BAG3 and EIF6 expression in MC could be due to hypo- and hypermethylation, however, their specific roles in MC tumourigenesis remains to be elucidated. Beyond mucin genes, upregulation of genes rarely associated with CRC was also observed, suggesting new insight into the aetiology of MC resistance to therapies and their roles as a potential target for MC treatment may be worth investigating.

Background Mesenchymal stem cells (MSCs) have become a promising approach for inflammatory bowel disease (IBD). MSCs derived from human induced pluripotent stem cells (iPSC-MSCs) have increased expandability and prolonged stemness, but the therapeutic effects need to be further investigated. Tumour Necrosis Factor-stimulated Gene-6 (TSG6) released from MSCs have been shown to accelerate intestinal repair in IBD. And only CD44 acts as a TSG6 receptor. Therefore, we want to investigate the potential role and mechanism of the iPSC-MSCs on murine colitis via the regulation of TSG-6 and CD44.

Methods Murine colitis was induced by intrarectal TNBS administration. The expression of TSG6 in iPSC-MSCs was assayed with immunocytochemistry and Western blot. To study the role of TSG-6 secreted by iPSC-MSCs in alleviating murine colitis, iPSC-MSCs (2 × 10⁶ cells/mouse) transfected with or without siRNA targeting TSG6 were infected intraperitoneally on the next day after TNBS administration. Body weight and disease activity index were recorded daily. Cell proliferation, apoptosis and the expression of CD44 were analysed by immunohistochemistry or qRT-PCR. In addition, the role of CD44 was studied by applying either control peptide or CD44 signalling inhibitor, PEP-1 to TNBS-induced murine colitis. Mice symptoms and mucosal healing were analysed as well.

Results iPSC-MSC produced and released TSG6. And the injection of iPSC-MSC intraperitoneally attenuated murine colitis accompanied by increasing body weight and reducing the size of the ulcer. However, the therapeutic effects were largely decreased by knockdown of TSG6 in iPSC-MSC. In addition, iPSC-MSC accelerated the ulcer healing by promoting the proliferation (Ki67) of colonic epithelial cells and increasing expression of CD44, but not in mice given iPSC-MSCs with TSG-6 knockdown. And then we assessed the possible mechanism of TSG6 in promoting mucosal healing by CD44, and we found that the therapeutic effects of TSG-6 itself were similar to iPSC-MSC. But the protecting effects of TSG-6 were diminished by inhibition of CD44 via injection of PEP-1 to TNBS induced colitis mice.

Conclusions iPSC-MSCs alleviate murine colitis by releasing TSG-6 and then activating CD44.