

## O12 HEMIN ATTENUATES IL-17 PRODUCTION AND EXPERIMENTAL COLITIS

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Th17 lymphocyte activation and regulatory T cell defect are responsible for the pathogenesis of IBD (1). Heme oxygenase-1 (HO-1) plays an anti-inflammatory role in many diseases (2). In this study, we used a dextran sulfate sodium (DSS) -induced colitis model to investigate the effect of up-regulating HO-1 by hemin on the development of colitis. Mice were intraperitoneally administered with hemin for 2 days. Hemin treatment markedly induced HO-1 expression in the colon epithelium. The up-regulation of HO-1 was further correlated with attenuation of DSS-induced colitis. Next, we examined if hemin enhanced the proliferation of FoxP3<sup>+</sup> regulatory T cells (Treg) and suppressed the production of interleukin (IL) -17. Flow cytometry analysis revealed that hemin did not notably alter peripheral CD4<sup>+</sup>CD25<sup>+</sup>FoxP3<sup>+</sup> Treg cell population. In contrast, hemin significantly attenuated IL-17 and its downstream cytokine, IL-6. This coincided with reduced colonic inflammation. Finally, real time-PCR showed that hemin suppressed an array of IL-17-related gene expression, indicating that hemin exerts a broad modulatory effect on IL-17 induction. In summary, these results demonstrate that up-regulation of HO-1 by hemin ameliorated experimental colitis. Moreover, our study suggests that the inhibition of IL-17 is a novel anti-inflammatory mechanism of hemin.