Ironing out the details of intestinal repair

Intestinal inflammation, such as occurs in inflammatory bowel disease (IBD), infections and colorectal cancers, often results in intestinal bleeding and hence anaemia. Given the function of liver-derived hepcidin as a master regulator of systemic iron homeostasis, Bessman et al. looked at the role of hepcidin in iron regulation in the gut. They describe a new pathway by which dendritic cell (DC)-derived hepcidin promotes intestinal repair.

Hepcidin‐deficient (Hamp–/–) and wild-type (Hamp+/+) mice had similar levels of intestinal tissue damage after dextran sodium sulfate (DSS) administration, but the Hamp–/– mice had persistent weight loss, disruption of intestinal architecture and reduced colon lengths compared with Hamp+/+ mice after DSS withdrawal. By contrast, the recovery of Hamp+/+ mice, which lack hepatocyte‐derived hepcidin, from DSS exposure was comparable with that of wild‐type mice. Therefore, a non‐hepatocyte source of hepcidin is required for mucosal repair.

Bessman et al. showed that type 2 conventional DCs (cDC2s) are the main myeloid source of hepcidin in the mouse colon after DSS administration and that intestinal cDCs are important producers of hepcidin also in patients with IBD. Furthermore, cDCs were shown to produce hepcidin in vitro in response to microbial stimulation. Hamp+/+ mice, which lack hepcidin expression in cDCs, had a similarly impaired recovery phenotype to Hamp–/– mice after DSS withdrawal, which shows that cDC‐derived hepcidin is required for intestinal repair.

As liver-derived hepcidin promotes degradation of the cellular iron efflux transporter ferroportin...