Myeloperoxidase Loss of Function Leads to Intestinal Inflammation and Dysbiosis

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Background: Myeloperoxidase (MPO), a peroxidase predominantly expressed in neutrophils, uniquely catalyzes a two-electron oxidation of chloride anions to produce hypochlorous acid (HOCl), a potent microbicidal oxidant. Due to the redundancy of the immune system in critical functions, the lack of MPO function only results in mild infections, often by fungal pathogens. The significance of MPO in host defense and overall health remains incompletely understood. In this report, we have investigated how the MPO gene-knockout (MPO-/-) in mice affects their intestinal microbiota, inflammation state, and transit function.

Methods: MPO-/- and WT mice, co-housed in the same environment for 4 weeks, were sacrificed to harvest their intestines (large and small). Then, the tissues were homogenized for microbial DNA isolation using the QIAamp DNA Microbiome kit. The purified and enriched bacterial DNAs were subjected to PCR amplification and sequencing of the 16S ribosomal DNA hypervariable V3 and V4 regions. Microbiome compositions and diversities were analyzed and compared. Furthermore, MPO-/- and WT mice were investigated for their immune cell composition in the small intestines via flow cytometry, level of fecal inflammatory marker (calprotectin) via ELISA, and bowel movement via carmine red passing assay.

Results: A total of 13 families of bacteria were found in the intestinal microbiota, of which 2 families (Peptostreptococcaceae and Erysipelatoclostridiaceae) were unique to MPO-/- mice, while 7 families were unique to WT mice, including Ruminococcaceae, Desulfovibrionaceae, and Bifidobacteriaceae. Alpha diversity metrics (Shannon entropy, Observed features, Faith PD) were significantly higher in the WT samples than in the MPO-/- ones. Pielou evenness showed no difference between the genotypes. Beta diversity metrics demonstrated a significant difference between the genotypes. Moreover, the small intestines of MPO-/- mice were inflamed, reflected by significantly greater infiltration of neutrophils and T cells in the mucosa. Fecal calprotectin was significantly higher in MPO-/- mice. Physiologically, MPO-/- mice had a significantly slower bowel movement rate.

Conclusions: MPO loss of function induces intestinal dysbiosis, inflammation, and slow intestinal movement. Thus, MPO functions as a protective factor against infection and inflammation in normal intestinal health.