#60: Innate immune protein lipocalin-2 and iron mitigate EGCG-mediated inhibition of myeloperoxidase

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Green tea *(Camellia sinensis*, Theaceae) contains a plethora of antioxidant polyphenols that may promote health. Amongst these polyphenols, the (-)-epigallocatechin-3-gallate (EGCG) is extensively studied for its potential therapeutic properties in models of inflammatory bowel disease (IBD), although its molecular mechanism is not completely understood. Here, we demonstrate that EGCG can inhibit the activity of myeloperoxidase (MPO; a pro-oxidant neutrophil enzyme associated with IBD flares) in a dose-dependent manner in vitro. By using spectral analysis, we show that EGCG prevents the MPO-catalyzed reaction by reverting the reactive peroxidase heme back to its native inactive ferric state. Oral administration of EGCG to dextran sodium sulfate (DSS)-induced colitic mice significantly reduced the colonic MPO activity and alleviated pro-inflammatory mediators associated with gut inflammation, confirming that our findings extend to in vivo conditions as well. In light of previous reports that EGCG can complex with innate immune protein lipocalin-2 and iron, we next tested whether these factors can affect the bioactivity of EGCG. Intriguingly, the presence of lipocalin-2 or iron significantly mitigate the ability of EGCG to inhibit MPO in vitro. Further, the efficacy of EGCG against DSS-induced gut inflammation is diminished when orally co-administered with iron. These findings indicate that EGCG-mediated inhibition of MPO could be one of the mechanisms by which EGCG exerts its mucoprotective effects. However, counter-regulatory factors such as host lipocalin-2 and dietary iron could explain why EGCG does not ameliorate gut inflammation in some IBD patients.