Oxidative Stress and Redox-Modulating therapeutics in Inflammatory Bowel Disease

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Inflammatory bowel disease (IBD) is associated with the production of reactive species. However, there is still insufficient understanding of the redox architecture that defines the pathogenic mechanisms that link oxidative stress to IBD. In addition to reactive oxygen species (ROS), there are reactive nitrogen species (RNS) and reactive sulfur species (RSS). Interactions among themselves and with downstream biological targets are defined by the recently introduced concept of the 'Reactive Species Interactome' (RSI). At a cellular level reactive species can target cysteine redox switches in proteins, thereby affecting gene regulation, DNA damage, ion transport, intermediary metabolism, and mitochondrial function. Precursors of reactive species are derived from organic and inorganic compounds and their cofactors, including amino acids, vitamins, oxygen, nitrite, and sulfate. Nutrition and the gut microbiome fuel this process to a significant extent. Whereas cellular cysteine free thiols (-SH) are the major biological constituents of the RSI that fulfill important redox switch functions, free thiols in plasma/serum are a central readout of the whole-body redox status. The production of reactive species in IBD is reflected by a reduction in systemic free thiols, the major components of the antioxidant machinery. Systemic free thiols are amenable to nutritional or therapeutic intervention. This opens up future avenues for therapeutic modulation of the redox status in IBD. Also, redox metabolomics, in conjunction with other multi-omics technologies, may be a promising approach to improve our understanding of the pathophysiology of IBD.