Neuropeptide-Y Receptor Y2 Antagonism Attenuates Inflammatory Bowel Disease-like Pathology

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Pharmaceuticals designed to treat inflammatory bowel disease (IBD), an autoimmune disease characterized by a pro-inflammatory and anti-inflammatory cytokine imbalance and chronic histopathological changes in the gastrointestinal (GI) tract, are often inefficient and cause serious side effects, thus necessitating the development of more efficacious forms of treatment. It has been suggested that Neuropeptide-Y (NPY), a 36-amino acid peptide in the GI tract, may play a pivotal role in mediating IBD neuroinflammation by modulating key immune cell functions through its Y1 and Y2 receptors. Therefore, the current study blocked NPY receptor signaling through its Y1 and Y2 receptors in an experimental colitis murine model to determine if this blockade improved IBD-like histopathology and if these histopathological changes are correlated with behavioral and biochemical changes. ImageJ software measurements and blinded severity ratings assessed the histology of the colon, which included quantification of colonic architecture, cell counts, and inflammation. Data revealed that in experimental colitis, Y1 antagonism significantly increased IBD-like pathological effects ($p<0.05$) and strengthened the correlations associated with IBD ($p<0.05$). In contrast to Y1 antagonism, Y2 antagonism significantly decreased IBD-like pathological effects ($p<0.05$) and reversed the correlations associated with IBD ($p<0.05$). Combined, these results identified Y2 receptor antagonism as a novel therapeutic strategy for the treatment of IBD at a pathological and biochemical level, which may lead to a more specific and effective treatment for IBD.

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