**ADVANCING IL-22-BASED THERAPIES FOR INTESTINAL BOWEL DISEASES WITH HUMAN INTESTINAL ORGANOIDS**

**INTRODUCTION**

In an effort to address unmet medical need in IBD of achieving greater efficacy and more durable disease remission than current therapies, recent studies suggest that IL-22 regulates epithelial homeostasis and promotes repair of epithelial damage, thus making IL-22 a promising target for IBD therapy. In an effort to better understand IL-22 biology we have used human colon organoids to strengthen our understanding of the mechanisms by which IL-22 regulates mucosal healing.

**METHODS**

Human colon organoids derived from healthy and Crohn’s disease colonic biopsies were cultured using a standard protocol and treated with recombinant IL-22 alone or in combination with butyrate at multiple concentrations and time points. Cell viability, organoid forming capacity, epithelial cell function, as well as gene expression analysis of markers of epithelial barrier integrity and repair were assessed. To recapitulate the intestinal microbiota, organoids were co-cultured with primary human gut microbiota and treated with recombinant IL-22. Primary human IBD and healthy colon biopsies were snap-frozen to isolate RNA and subjected to RNAseq experiments. To recapitulate the intestinal microbiome, human organoids were co-cultured with primary human gut microbiota and treated with recombinant IL-22. To recapitulate the intestinal microbiome, organoids were co-cultured with primary human gut microbiota and treated with recombinant IL-22.

**RESULTS**

IL-22 selectively regulates the expression of genes involved in epithelial barrier integrity and repair, while inhibiting the expression of genes involved in inflammation and immune cell activation. IL-22 treatment increases the expression of genes involved in mucosal barrier integrity and repair, while decreasing the expression of genes involved in inflammation and immune cell activation. IL-22 treatment also increases the expression of genes involved in mucosal barrier integrity and repair, while decreasing the expression of genes involved in inflammation and immune cell activation. IL-22 treatment further increases the expression of genes involved in mucosal barrier integrity and repair, while decreasing the expression of genes involved in inflammation and immune cell activation.

**CONCLUSIONS**

Our data strongly supports clinical relevance of IL-22 as a mucosal healing therapy in IBD and suggests that IL-22 acts directly on the gut epithelium of both healthy and IBD individuals to promote epithelial homeostasis and repair of epithelial damage.

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