CHRD 2022: Abstract & Poster Submission Form

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Presenter Status

- ○ Undergraduate Students
- ○ Masters Student
- ○ PhD Student
- ○ Post-Doctoral Fellows
- ○ Residents
- ◉ Non-Trainee

Research Category

- ◉ Basic Science
- ○ Clinical
- ○ Community Health / Policy

Role in the project

- ☑ Design
- ☑ Perform Experiments
- ☐ Analyze Data
- ☑ Write Abstract
- ☐

Title

INTESTINAL INTERFERON-LAMBDA RECEPTOR 1 EXPRESSION AND RESPONSES ARE SIGNIFICANTLY DECREASED IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS

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Background

Inflammatory bowel diseases (IBD) affect approximately 300,000 Canadians, with incidence rates in children especially rising. The immune proteins, type III IFNs (IFN-λs), were shown to be critical for mucosal healing and dampening inflammation in gut-damaged mouse models, but IFN-λ activity in human patients with IBD is understudied.

Objective

We hypothesized children with severe IBD would present with lower intestinal IFN-λR levels and responses contributing to IBD pathology.

Methods

We screened 14 novel antibodies through flow cytometry to find the optimal clone that binds IFN-λ receptor subunit (IFN-λR1) protein in human intestinal tissue and IFN-λR1 levels were quantified by immunohistochemistry in biopsy samples from children without IBD, Crohn's disease, or ulcerative colitis (n=9 each). Fresh patient biopsies were also cultured ex vivo for 24hr in media +/- IFN-λ3 and gene expression was quantified by RT-qPCR. Tests used are one-way Anova with Tukey's test for 3 groups and unpaired t-test with Mann-Whitney test for 2 groups

Results

We identified 2 antibodies (mAb 8 and 13) that accurately stained human cell lines and immune cells known to express IFN-λR1 protein (gut epithelial cells and B cells). We found through immunohistochemistry that IFN-λR1 expression is significantly reduced in gut epithelial and immune cells within pediatric IBD intestinal tissue, even at non-inflamed sites ($p<0.01$, 30-50% reduction) and this was even more pronounced when comparing moderate/severe disease compared to children with no disease activity. This led to lower IFN-λ induction of known IFN-λ-dependent genes such as IFI44 and MX1 in IBD compared to non-IBD biopsies ($p<0.05$, 4-7 fold reduction) measured through RT-qPCR.

Conclusion

Together, our findings support our hypothesis that children with IBD have dysregulated IFN-λ receptor responses which could lead to the lower induction of key anti-inflammatory pathways. This work supports the strategy to restore and promote IFN-λ responses as a therapy for pediatric IBD.

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Authors

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