Host transcriptome signatures in human fecal-washes predict histological remission in IBD patients

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Background & objectives

Background:

Colonoscopy is the gold standard for evaluation of inflammation in inflammatory bowel diseases (IBD), yet entails cumbersome preparations and risks of injury. Existing non-invasive prognostic tools are limited in their diagnostic power. Moreover, transcriptomics of colonic biopsies have been inconclusive in their association with clinical features.

Objective:

To assess the utility of host transcriptomics of fecal wash samples of IBD patients compared to controls.

Methods

In this prospective cohort study, we obtained biopsies and fecal-wash samples from IBD patients and controls undergoing lower endoscopy. We performed RNAseq of biopsies and matching fecal-washes, and associated them with endoscopic and histological inflammation status. We inferred cell compositions using computational deconvolution and used classification algorithms to identify informative genes.

Results

We analyzed biopsies and fecal washes from 39 patients (19 IBD, 20 controls). Host fecal-transcriptome carried information that was distinct from biopsy RNAseq and fecal proteomics. Transcriptomics of fecal washes, yet not of biopsies, from patients with histological inflammation were significantly correlated to one another ($p=5.3*10^{-12}$). Fecal-transcriptome was significantly more powerful in identifying histological inflammation compared to intestinal biopsies (150 genes with area-under-the-curve >0.9 in fecal samples versus 10 genes

in biopsy RNAseq). Fecal samples were enriched in inflammatory monocytes, regulatory T cells, natural killer-cells and innate lymphoid cells.

Conclusion

Fecal wash host transcriptome is a powerful non-invasive biomarker reflecting histological inflammation. Furthermore, it opens the way to identifying important correlates and therapeutic targets that may be obscure using biopsy transctriptomics.