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Metatranscriptomics of colonic lesions in inflammatory bowel disease

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Crohn's disease (CD) and ulcerative colitis (UC) are inflammatory bowel diseases (IBD) characterized by chronic and relapsing inflammation of the gastro-intestinal tract (GIT). They cause lifelong suffering, as well as considerable drainage of health care resources. Although their aetiology is still unclear there is a growing body of evidence for a significant microbial factor. Previous research in this area has focused on examining the microbiota composition in stool and in the GIT producing conflicting and inconclusive results. Here, we adapt a new approach and focus on the meta-transcriptome through RNA sequencing of colonic biopsies. Biopsies were collected from inflamed and non-inflamed colonic mucosa from 6 CD and 12 CD patients and sequenced using RNA-Seq using Illumina HiSeq at 15Gb/sample. Raw reads were quality filtered and trimmed using Trimmomatic before aligning to the human genome (hg20) with STAR. The SILVA database along with Bowtie2 was used for identifying and removing rRNA sequences. Remaining reads were aligned using Bowtie2 against a non-redundant gene catalogue constructed from multiple previously published meta-genomic studies of the human GIT. DESeq2 was subsequently used to analyse the count data and identify differentially expressed genes. This led to the finding of microbial genes which are significantly differentially expressed between inflamed and non-inflamed mucosa in bacterial species. Furthermore the count data from these samples show a clear distinction between bacterial gene expression of UC and CD. Thus, our analysis has revealed a clear difference in the gene expression of bacteria in the colon of IBD patients and demonstrated that novel approaches are required in order to understand complex multi-factorial diseases.

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