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Intestinal microbiota: A source of novel biomarkers in inflammatory bowel diseases?

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A B S T R A C T

The human intestine harbours a complex microbial ecosystem that performs manifold functions important to the nutrition and health of its host. Extensive study has revealed that the composition of the intestinal microbiota is altered in individuals with inflammatory bowel disease (IBD). The IBD associated intestinal microbiota generally has reduced species richness and diversity, lower temporal stability, and disruption of the secreted mucus layer structure. Multiple studies have identified certain bacterial taxa that are enriched or depleted in IBD including *Enterobacteriaceae*, *Ruminococcus gnavus*, and *Desulfovibrio* (enriched) and *Faecalibacterium prausnitzii*, *Lachnospiraceae*, and *Akkermansia* (depleted). Additionally, the relative abundance of some taxa appears to correlate with established markers of disease activity such as *Enterobacteriaceae* (enriched) and *Lachnospiraceae* (depleted). Signature shifts in fecal microbial community composition may therefore prove to be valuable as diagnostic biomarkers, particularly for longitudinal monitoring of disease activity and response to treatments.

Introduction

The field of intestinal microbiology has recently experienced a major burst of activity charged by advances in deoxyribonucleic acid (DNA) sequencing technologies that enable high-throughput

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metagenomics and the large-scale efforts of the Human Microbiome Project and MetaHIT consortium [1,2]. The intestinal microbiota is species-rich, with each person hosting at least 160 bacterial species from an estimated 40,000 different species identified across human cohorts (Fig. 1) [1,3]. It is also numerically abundant, with the intestines sheltering approximately 10^{14} microorganisms packed so densely that feces is roughly half microbial biomass [3]. The microbiota collectively contains about 100 times the number of genes as the human genome, which has prompted a view of humans as meta-organisms and the gut microbiota as our second genome [4]. A major focus thus far has been to define the characteristics of the baseline, or 'healthy' intestinal microbiota (see, among others, the following reviews: [5,6]), though molecular techniques have also been applied to describe the intestinal microbiota of individuals with inflammatory bowel diseases (IBD), including the major IBD phenotypes ulcerative colitis (UC) and Crohn's disease (CD). The goal of this review is to describe characteristic alterations in the composition of the microbiota in IBD that may prove useful as diagnostic biomarkers.

Methods to study the intestinal microbiota

Methods to study the intestinal microbiota can be divided into cultivation-based and cultivation-independent techniques. Cultivation-based methodologies involve the isolation of an organism with either non-selective or selective media and subsequent characterization in pure culture, in co-culture

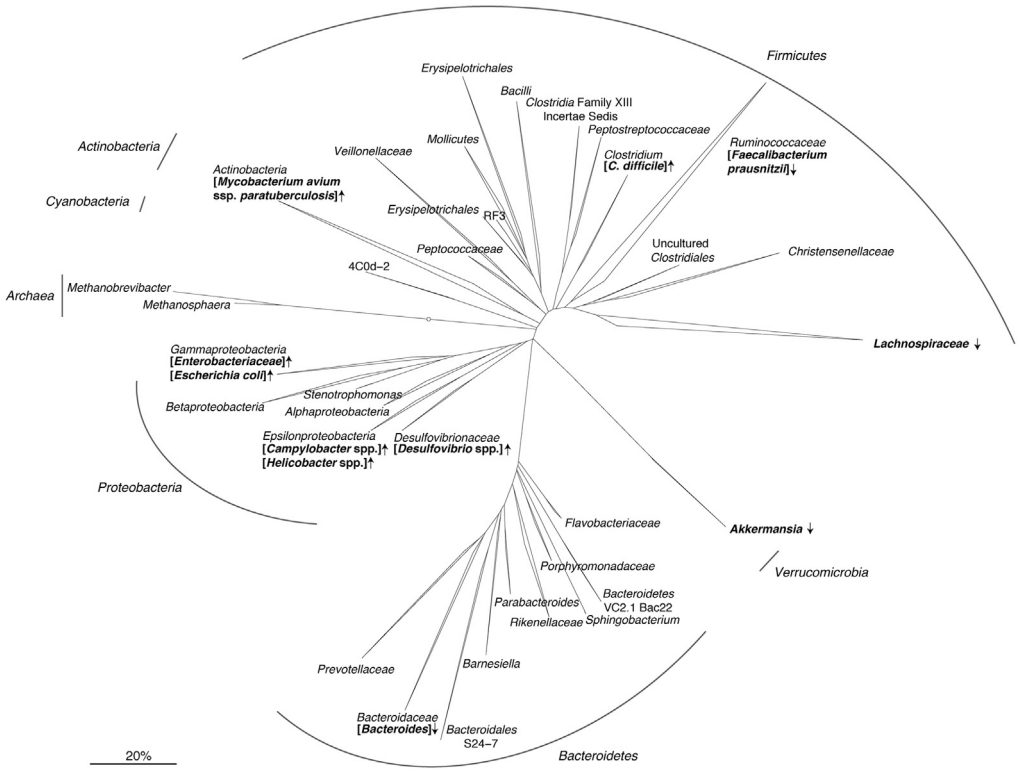

Fig. 1. 16S rRNA gene-based phylogenetic tree of *Bacteria* and *Archaea* identified in the human intestinal microbiota. The tree is composed of all sequences retrieved from human intestinal or fecal samples and based on the parsimony-generated guide tree and taxonomic assignments in the SILVA SSU Ref NR Release 111 database. Sequences are clustered into taxonomic groups and phylum (or domain) affiliations are indicated by the outer lines. Taxa that are altered in relative abundance in the intestinal microbiota of individuals with IBD are indicated in bold and with an arrow indicating whether they are enriched or depleted in IBD (see Table 1). When these taxa are part of a larger grouping they are shown in brackets beneath the cluster in which they are located. The branch length indicates the strength of the maximum parsimony branching and is standardized using a sequence distance matrix to estimate percent sequence divergence.