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Gut microbiome contributes to impairment of immunity in pulmonary tuberculosis patients by alteration of butyrate and propionate producers

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Summary

Tuberculosis (TB) is primarily associated with decline in immune health status. As gut microbiome (GM) is implicated in the regulation of host immunity and metabolism, here we investigate GM alteration in TB patients by 16S rRNA gene and whole-genome shotgun sequencing. The study group constituted of patients with pulmonary TB and their healthy household contacts as controls (HCs). Significant alteration of microbial taxonomic and functional capacity was observed in patients with active TB as compared to the HCs. We observed that *Prevotella* and *Bifidobacterium* abundance were associated with HCs, whereas butyrate and propionate-producing bacteria like *Faecalibacterium*, *Roseburia*, *Eubacterium* and *Phascolarctobacterium* were significantly enriched in TB patients. Functional analysis showed reduced biosynthesis of vitamins and amino acids in favour of enriched metabolism of butyrate and propionate in TB subjects. The TB subjects were also investigated during the course of treatment, to analyse the variation of GM. Although perturbation in microbial composition was still evident after a month's administration of anti-TB drugs, significant changes were observed in metagenome gene pool that pointed towards recovery in functional capacity. Therefore, the findings from this pilot study suggest that microbial dysbiosis may contribute to pathophysiology of TB by enhancing the anti-inflammatory milieu in the host.

Introduction

Mycobacterium tuberculosis, the causative agent of Tuberculosis (TB), latently infects one-third of the world's population, with predilection mainly for lungs (World Health Organization report, 2014). Extensive research over the years has increased our knowledge immensely about *M. tuberculosis* and its interaction with the host (Sachdeva *et al.*, 2010; O'Garra *et al.*, 2013; Stanley and Cox, 2013; Maji *et al.*, 2015; Sajid *et al.*, 2015), yet we are unable to fully understand the complexities of the disease process such as latency and reactivation. Epidemiological studies have revealed that socioeconomic conditions play an important role in the progression of the disease (Dye *et al.*, 2009). Various factors, which are effectively associated with immune surveillance breakdown, such as malnutrition, human immunodeficiency virus (HIV) infection or administration of immunosuppressive medication, contribute to the manifestation of the active form of the disease. To better comprehend the TB disease process, it is imperative to

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