Abundance of Secondary Metabolites in Human Microbiome

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Abstract

Human body harbors the most complicated microbial ecosystem. Bacteria that have co-evolved within a human context have barely been explored for secondary metabolites. These secondary metabolites are hypothesized to possess biological activities significant within the human host context.

In our study, we studied conservation profiles of 203 secondary metabolite gene clusters across 16 human body sites and found that gastro intestinal tract and oral sites show the highest conservation for secondary metabolic gene clusters. We observed that majority of highly conserved metabolites belong to pathway type NRPS. Our phylogenetic analysis of highly conserved stool and oral samples revealed abundance of firmicutes,bacteroidetes and actinobacteria phylum

Introduction

- Human body sites are colonized by an enormous diversity of Bacteria . These microbial communities are thought to play an important role in human physiology. Human Microbiome Project (HMP) aims to characterize the microbial communities found at multiple human body sites
- Microbial derived secondary metabolites have the potential to bind to therapeutically relevant human targets. Genes which encode for secondary metabolite biosynthesis are present in most of the sequenced microorganisms. Secondary metabolitic gene clusters can be broadly classified as polyketide synthetases (PKS), non-ribosomal peptides synthetases (NRPS) and Hybrids. Many recent studies investigated the diversity of secondary metabolite gene clusters by mining genomic and metagenomic data.
- Currently, there are no comprehensive surveys studying the diversity and conservation of secondary metabolites in the human microbiome which hosts trillions of bacteria.

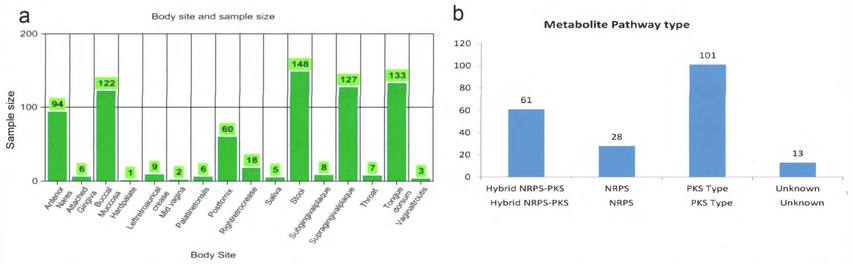


Figure 1.a showing number of samples in 16 different human body sites. **Figure 1.b** represents the classification of 203 secondary metabolites according to their functional pathway type

Methods

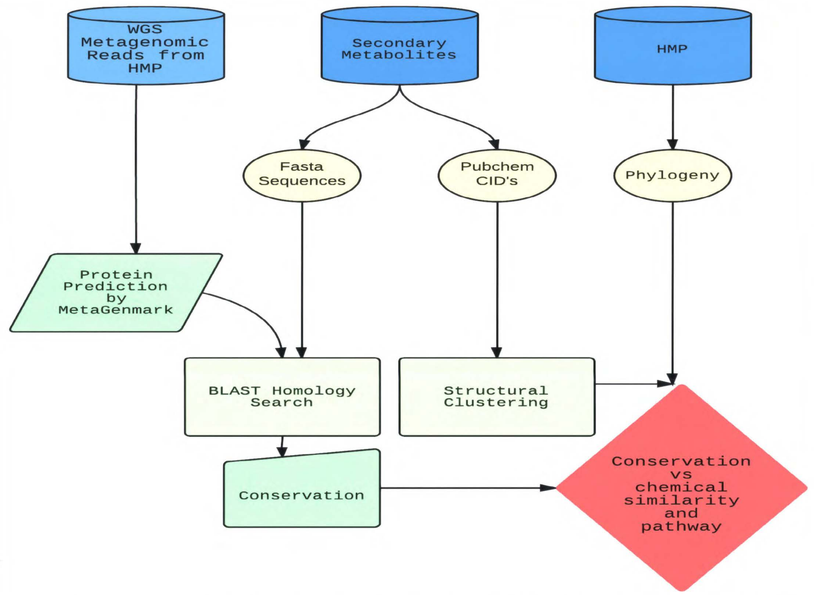


Figure 2. Flowchart showing the methodology to investigate the abundance of sec -ondary metabolites in human microbiome

Results and Discussion

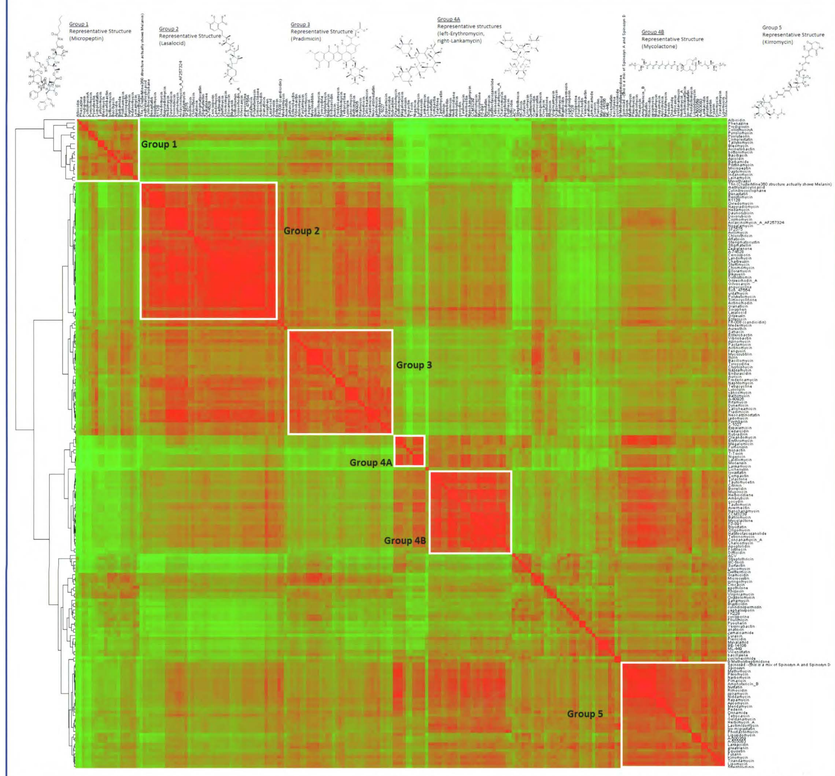
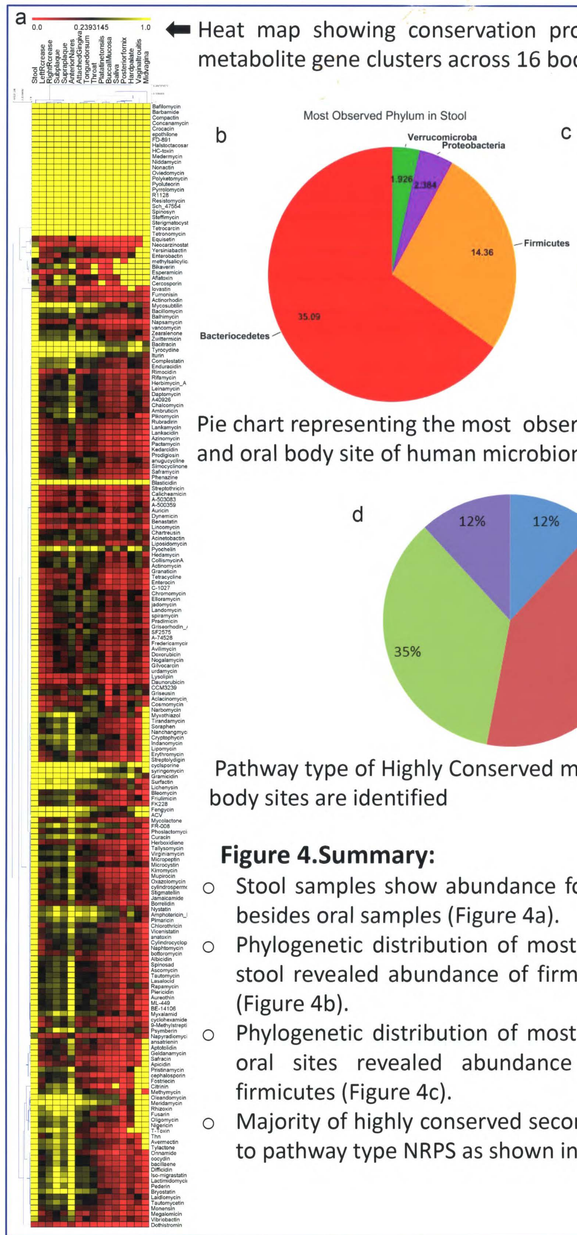


Figure 3. Clustering and heat map of 203 secondary metabolites by their Tanimoto chemical similarity



Heat map showing conservation profiles of 203 secondary metabolite gene clusters across 16 body sites

Pie chart representing the most observed phylum in the stool and oral body site of human microbiome

Pathway type of Highly Conserved metabolites across all body sites are identified

Figure 4.Summary:

- Stool samples show abundance for secondary metabolites besides oral samples (Figure 4a).
- Phylogenetic distribution of most conserved sequences in stool revealed abundance of firmicutes and bacteroidetes (Figure 4b).
- Phylogenetic distribution of most conserved sequences in oral sites revealed abundance of actinobacteria and firmicutes (Figure 4c).
- Majority of highly conserved secondary metabolites belong to pathway type NRPS as shown in Figure 4d.

Conclusion

Our study establishes quantitative relationship between structural similarity and biosynthetic pathway type of secondary metabolites. We found that gastrointestinal and oral sites show high conservation of secondary metabolites indicating their role in the context of human. Phylogenetic analysis revealed an abundance of firmicutes and bacteroidetes phylum in stool while actinobacteria and firmicutes were prevalent in oral sites.

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