Minimal Variations of Oral Virome and Microbiome in Human IgA Deficiency

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Short report

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Abstract

Bakcground Immunoglobulin A (IgA) is the dominant antibody found in our mucosal secretions and plays an important role in the protection and homeostatic regulation of intestinal, respiratory and urogenital epithelia by `recognizing´and shapping our human commensal microbiome. Paradoxically, yet selective IgA-deficiency in humans and animal models is often described as asymptomatic and only a few microbiome studies are available, only focused on the mice and human gut microbiome.

Results Here, we broad the view an address the oral microbiome employing a more holistic view integrating in our study for the first time not only microbes but also the frequently neglected commensal viruses of our human virome and measured the impact of IgA deficiency on our microbial and viral communities. Unexpectedly, data from fine 16S rRNA gene profiling and virome and metagenome analysis in human IgA deficiency indicate minimal changes in microbiome and virome composition compared to healthy control group and point out to a rather functional, resilient oral commensal viruses and microbes. However, a significant depletion (2-fold) of number of bacterial cells (p-value <0.01) and virus-like particles (VLPs) was observed in IgA-deficiency.

Conclusions Our results challenge the view of an irreplaceable IgA role for regulating the composition and function of our commensal microbiota and pose the question whether other “ back-up ” Ig-independent mechanisms dicussed here might exist for maintaining a functional commensal microbiome.

Full Text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the latest manuscript can be downloaded and accessed as a PDF.

Figures

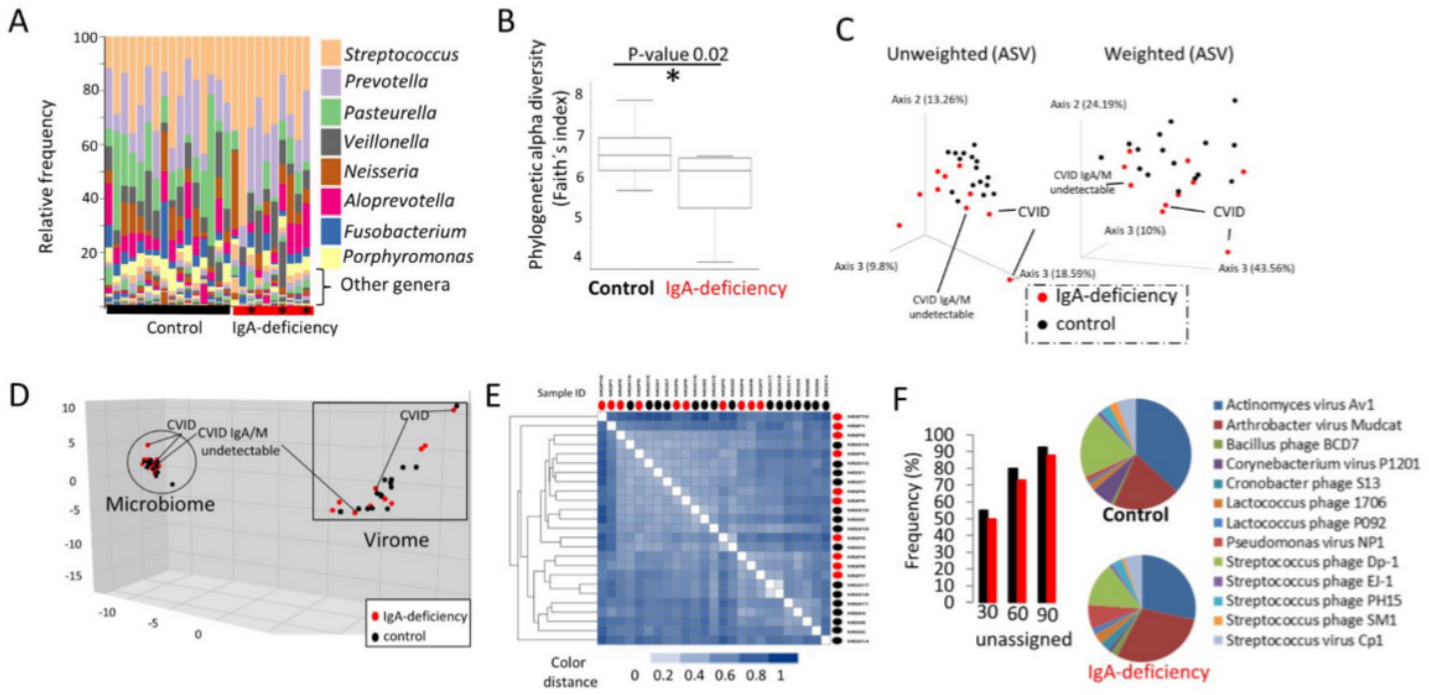

Figure 1

Diversity, composition and metabolic functionality of human oral microbiome and virome from control and IgA deficiency. (A) Taxonomic analysis at the species level based on 16S rRNA gene Illumina sequencing. Relative abundance (%) of the most abundant species (at least >1% of abundance) is displayed. For convenience, these other rare taxa are not depicted in panel enumerating species. Star denotes CVID patients. (B) Comparison of phylogenetic alpha richness diversity by Faith´s index between groups. Other alpha diversity indices used in Qiime program were not conclusive (p- value>0.05). ANCOM test implemented in Qiime2 did not found statistical differences for common abundant bacterial commensalists. (C) PCoA representing Unweighted and Weighted Unifrac distance for controls and IgA-deficiency. Three samples were from CVID patients. (D) PCA representing the analysis and comparison of more than 300,000 annotated genes from each group (control and IgA- deficiency samples) recovered by metagenomics and viral metagenomics. Genes were annotated by COG at the IMG-JGI bioinformatic platform. Similar representation was obtained for pfam and other gene annotation methods. (E) Massive Metagenomic analysis of pairwise comparison of raw reads obtained from control and IgA-deficiency samples. Metafast program was used to compute the analysis. Heat map illustrate relatedness between the pairwise sample comparison. Color distance from 0 (white color) to value 1(dark blue) indicates the distance. A value of “0” or white color indicates that two samples are identical. (F) Metaviromic analysis of assembled viral contigs from viral metagenomes from groups. Viral metagenomes were quality trimmed, assembled, annotated at the IMG-JGI bioinformatic platform, computed the best-hit scoring for each annotated gene using three different thresholds (30, 60 and 90% of amino acid identity). Bar chart represents the fraction of annotated genes with unknown function (named “unassigned”) using the three different identity thresholds. Data indicate that most of the genes were unknown. Results from the taxonomic assignment of viral genes by best-hit scoring are shown in the pie chart.

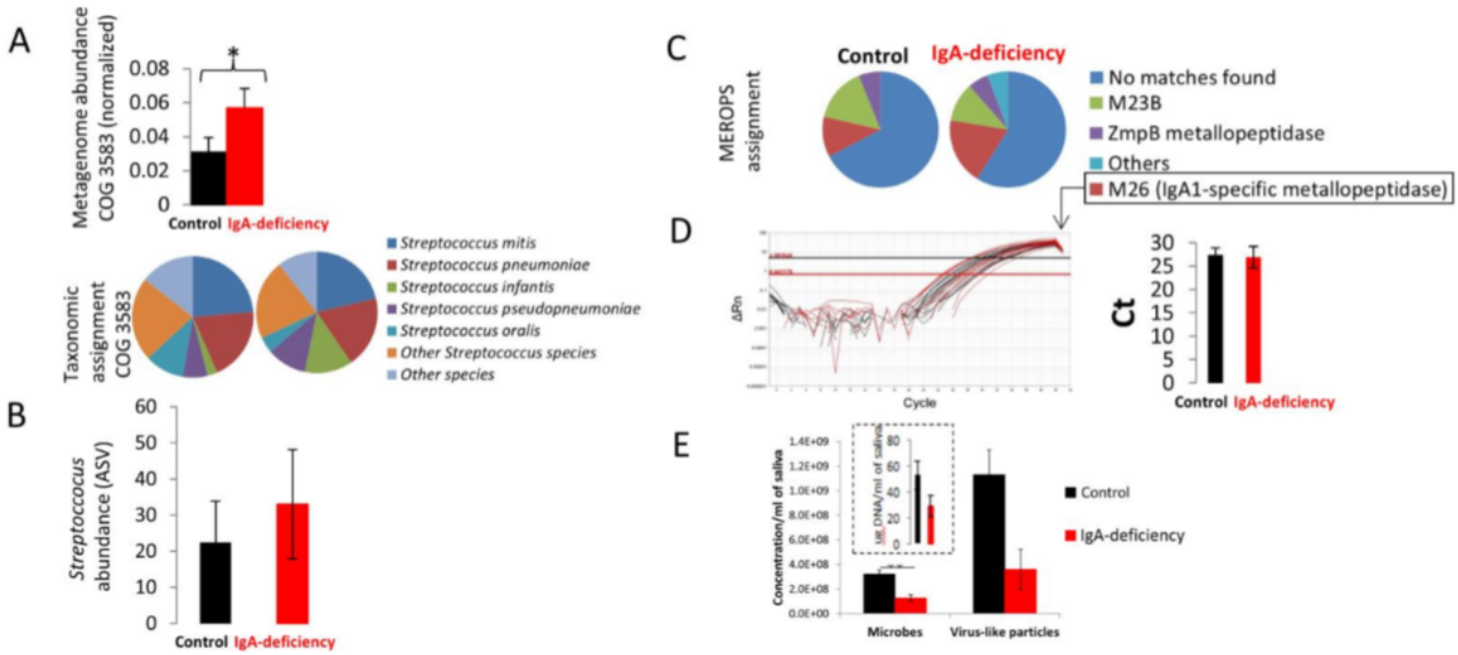

Figure 2

Fine metagenomic analysis and microbial and viral abundance in controls and IgA deficiency. (A) Metagenomic analysis of abundance of genes annotated within COG 3583 involved in the processing and cleavage of IgA (bar chart). An over enrichment is observed from IgA deficiency patients. Taxonomic assignment of bacteria having COG3583 (pie chart) that was clearly dominated by Streptococcus spp. (B) Relative abundance of amplicon sequence variants (ASV) assigned to genus Streptococcus. Although more Streptococcus was found in IgA deficiency samples, differences were not statistically significant. (C) Analysis of active domains found in the analyzed proteins belonging to COG3583. MEROPS database was used to identify active domain. IgA metallopeptidases typically have the protease domain M26. (D) qPCR results of COG 3583 genes encoding proteases with M26 domain involved in IgA cleavage. No differences in abundance were found between the groups. (F) Fluorescence microscopy and microbial and viral abundance obtained by DAPI and SYBR Gold stain, respectively. Small pie chart panel depicts concentration of DNA per ml of saliva obtained from controls and IgA deficiency samples.

Supplementary Files

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- Supplementry.pdf