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Identification of differentially IgA-coated bacteria in inflammation-induced colorectal cancer

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Introduction

IgA is produced in high amounts by gut-resident B cells and secreted into the intestinal lumen where it coats bacteria to various degrees dependent on the bacterium's previous encounter with the immune system[1].

Thus, identification of IgA-coated bacteria in feces is a mean to determine which intestinal bacteria that previously have engaged with the immune system[2]. Here we studied the taxonomical distribution of IgA-coated bacteria in fecal samples from a mouse model of Dextran sodium sulfate/Azoxymethane (DSS/AOM)-induced inflammation-associated colorectal cancer[3].

Methods

Murine fecal samples were collected from a group DSS/AOM-treated group (n = 5) and a control group
(n = 5). The DSS/AOM was administered through the drink water. We performed the fecal sampling after 7 days of mutagen exposure to identify possible taxa associated with the early stages of disease-induction, and to avoid potential bias induced by the host's inflammatory status.

In order to identify potential disease-associated taxa, we used magnetic bead-based enrichment and flow cytometry-based sorting to isolate highly IgA-coated bacteria, followed by 16S rDNA amplicon sequencing.

To identify the minor changes in the microbiota composition, we used a linear discriminant analysis (LDA) effect size (LEfSe) algorithm. The algorithm helps identify which taxa in each sample that consistently explain the differences between samples.

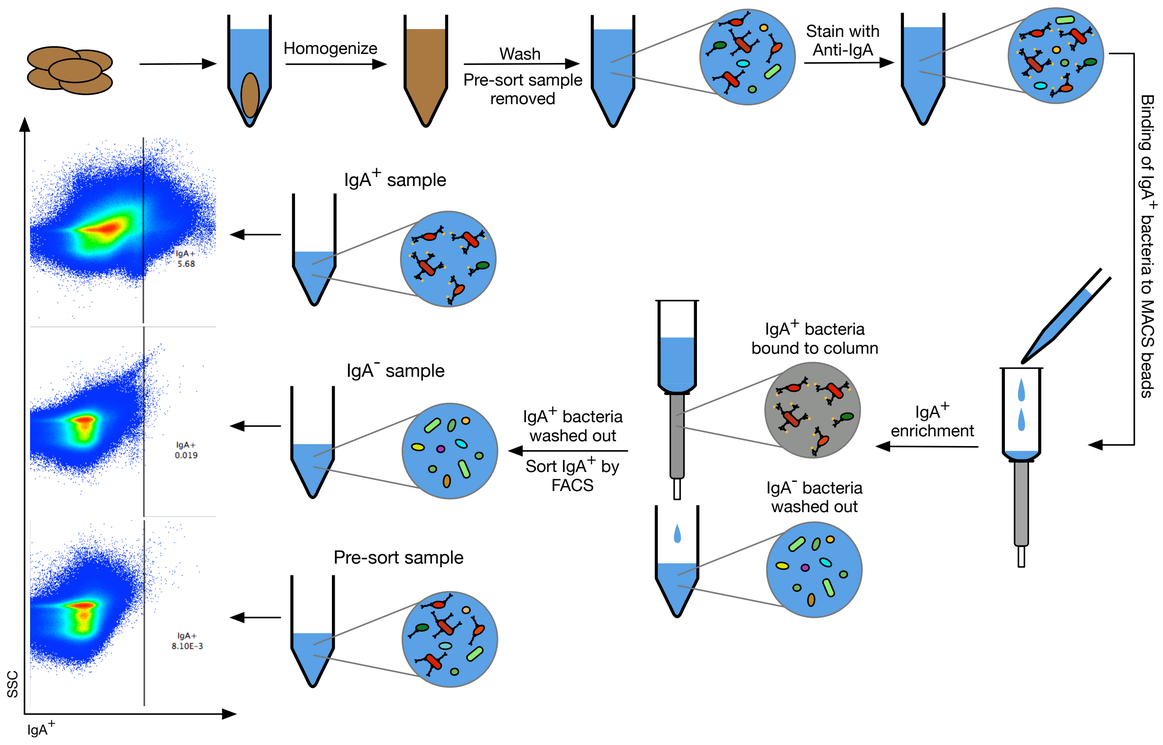

Figure 1: Graphical representation of the purification and sorting of bacteria from murine fecal samples

Literature

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Results

By the use of principal coordinates analysis we found a clear clustering based on the treatment (DSS/AOM vs. control group), and the degree of IgA-coating (IgA-coated vs. uncoated samples), as shown in figure 2.

When taking a closer look at the individual taxa, we identified 21 highly IgA-coated bacterial families of which 11 were detected only in the DSS/AOM-treated mice as shown in figure 3.

Among the most significantly enriched families were: *Erysipelotrichaceae*, *Bacteroidaceae*, *Rikenellaceae* and *Odoribacteraceae*. which previously have been shown to be associated with DSS/AOM-induced colorectal cancer[4].

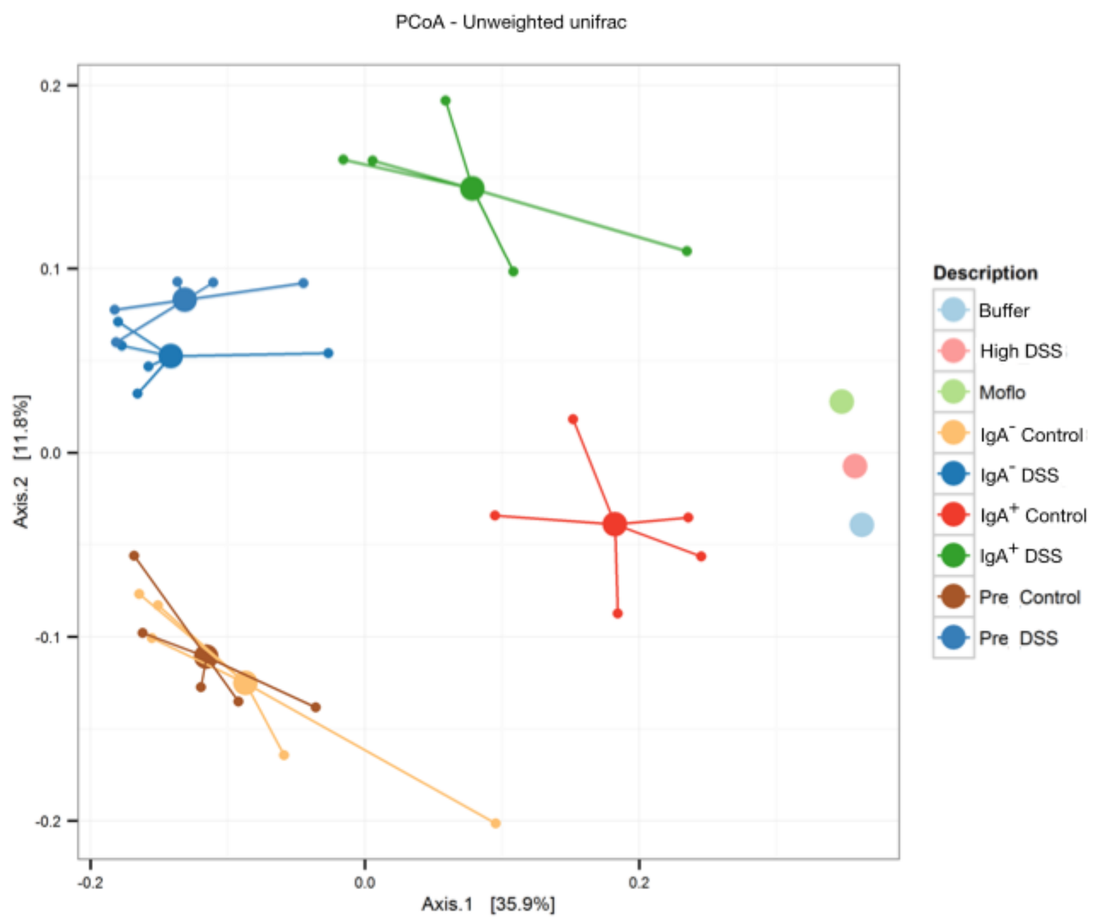

Figure 2: Principal Coordinates Analysis of unweighted UniFrac distances of the samples.

Conclusion and Future perspectives

This study confirms that specific members of the intestinal microbiota can be separated based on their IgA-coating, and demonstrates that different taxa are coated depending on inflammatory status and colorectal cancer progression of the host.

We have further refined the method in order to optimise the speed and sample handling and introduced several steps of quality control.

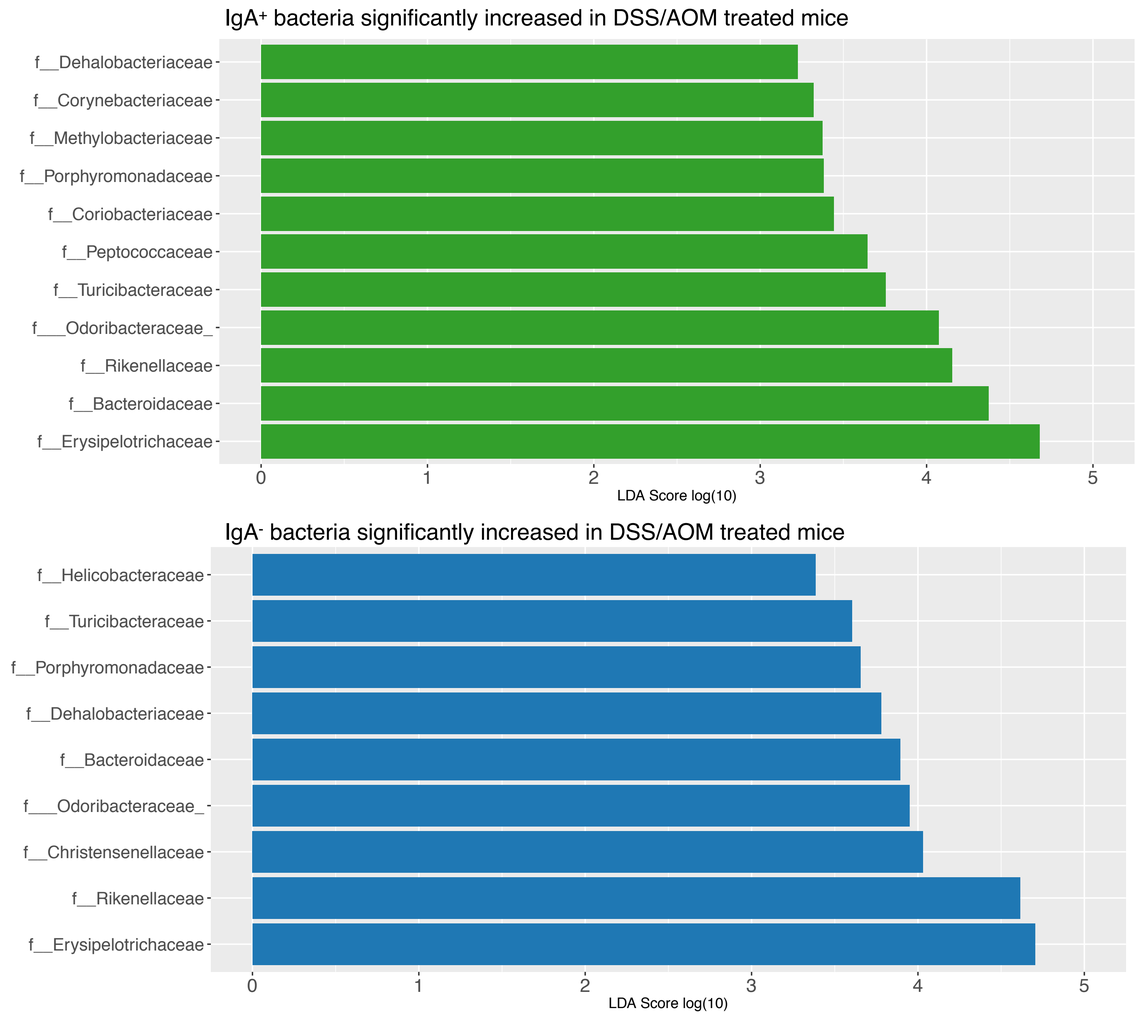

Figure 3: LEfSe comparisons between the effects of DSS on the microbiota composition of the IgA$^+$ (top panel) and IgA$^-$ samples (bottom panel)