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

Carsten Eriksen¹, Jacob Bak Holm², Mohammad Yassin³, Jørgen Olsen³, Anders Elm Pedersen⁴, Karsten Kristiansen² and Susanne Brix¹

¹ DTU Bioengineering, Dept. of Biotechnology and Biomedicine, Technical University of Denmark, Denmark ² Laboratory of Genomics and Molecular Biomedicine, Department of Biology, University of Copenhagen, Denmark ³ Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark ⁴ Department of Immunology and Microbiology, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

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. Thus, identification of IgA-coated bacteria in feces is a means to determine which intestinal bacteria that previously have engaged with the immune system. 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.

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.

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.

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.

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Literature