The Impact of Myeloid-Derived Suppressor Cells on Gut Bacteria in infectious conditions

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Introduction

- The early gut colonization is a crucial stage for the healthy development of the newborn infant.[1]
- Until recently, it has been thought that newborns are more susceptible to infection due to their underdeveloped immune system.[2] However, our group recently demonstrated that myeloid-derived suppressor cells (MDSCs) are actively immunosuppressive and enriched in neonatal mice (Fig 1).[3]
- It is still not very clear if MDSCs are required for an adaptation to colonization with gut bacteria.

Purpose: The aim of this study is to evaluate the effect of MDSCs on the composition of gut bacteria.

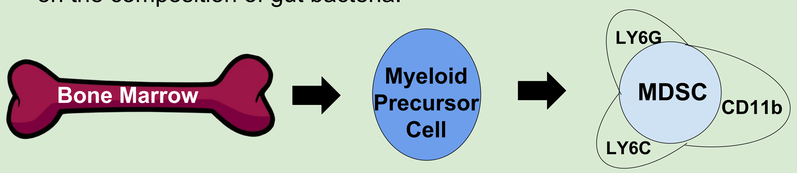

Figure 1: Origin of myeloid-derived suppressor cells (MDSC)

Methods

- Eight day old pups were treated or not with anti-Gr1 antibody for the *in vivo* depletion of MDSCs. One day after the treatment pups were infected with *Bordetella pertussis* (respiratory pathogen). (Fig. 2)
- Spleen samples and small intestine contents were collected for flow cytometric analysis and to study gut bacterial composition, respectively.
- Total bacterial DNA was extracted from the small intestine contents and quantitative PCR was used to measure dominant gut bacterial groups in samples.
- Flow cytometric analysis was performed to determine the percentage of MDSCs among total spleen cells by staining the samples for MDSC markers.

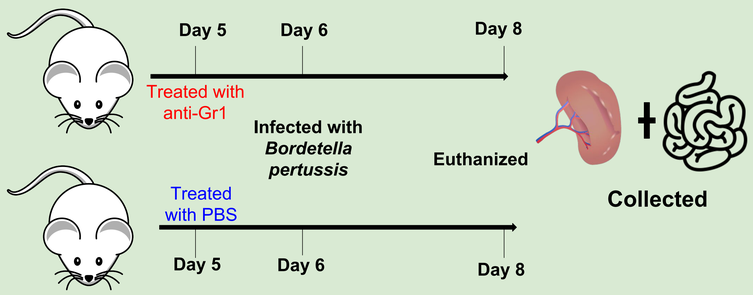

Figure 2: Schematic presentation of experimental setup.

Results

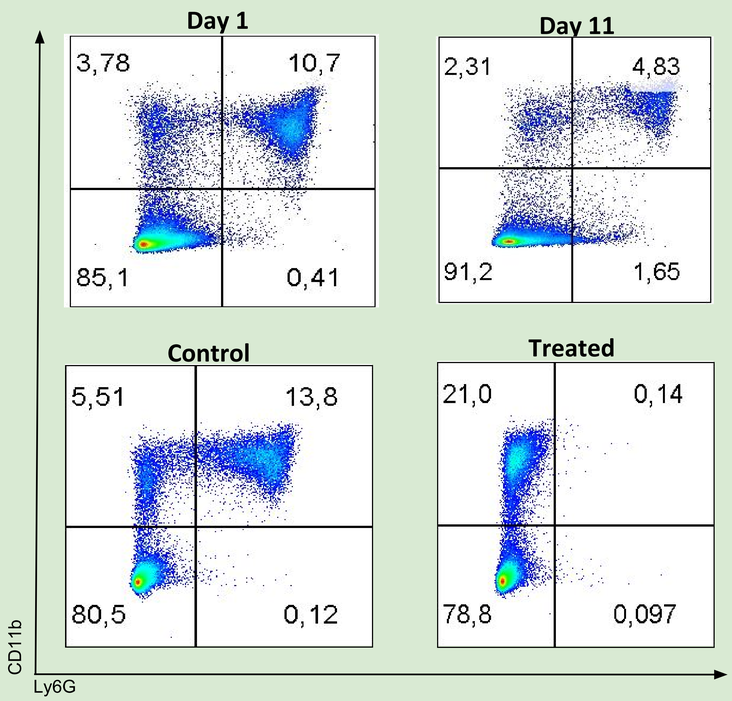

Figure 3: Percentage of MDSCs during neonatal period of mice (day 1 and day 11) and depletion of MDSCs after treatment with anti-Gr1 antibody (control vs treated).
- CD11b - a molecule that regulates leukocytes adhesion and migration to mediate inflammatory response
- Ly6G - a marker for antigen presenting cells (monocytes) and granulocytes and neutrophils

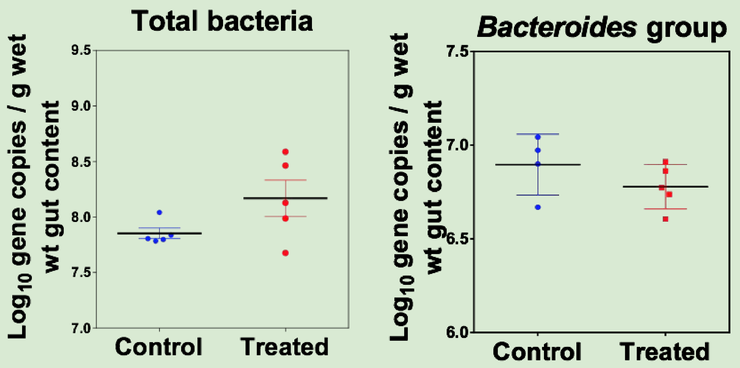

Figure 4: Quantitative PCR analysis of total bacteria and *Bacteroides* group in small intestine contents collected from control animals and pups treated with anti-Gr1 antibody.

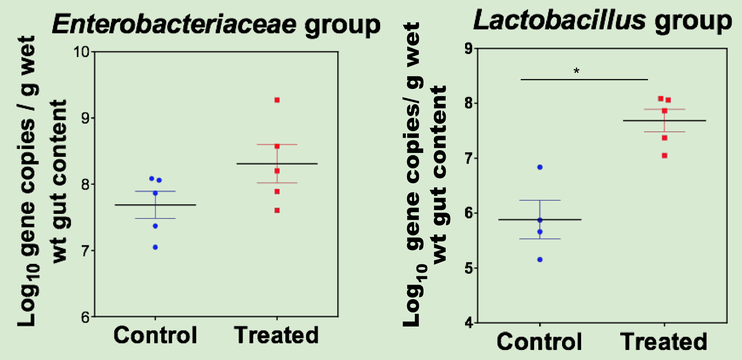

Figure 5: Quantification of *Enterobacteriaceae* group *Lactobacillus* group in small intestine contents of control and treated animals at the end of the experimental treatment period.
- t-test was used to check for significant differences

Key Findings

- The percentage of MDSCs was high during the neonatal period of experimental animals
- Flow cytometric analysis showed that the MDSCs were successfully depleted in the anti-GR1 treated mice
- Gene copy numbers of total bacteria, and microbes belonging to *Bacteroides* and *Enterobacteriaceae* groups did not differ between the control and treated pups.
- **Differences between the two experimental groups were observed in gene copy numbers of *Lactobacillus* group.**

Relevance

- These results provided important preliminary information on the association of gut bacterial groups with MDSCs during infectious conditions.
- Further research needs to be conducted in order to better understand the impact of MDSCs on gut bacteria, and their use as a therapeutic target in cancer, inflammation and infectious.

Acknowledgements

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References

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