How does the immune system of newborns tolerate gut bacteria?

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Introduction

- It is believed that the colonization of the infant's gut starts at birth and continues during the first year of life.[1] This process is a crucial stage for the healthy development of newborns and has profound influence on lifelong health.[2]
- Recently, our research group has provided evidence that the infant's immune system adapts to the bacterial colonization due to the presence of immunosuppressive CD71+ erythroid cells. These are nucleated immature red blood cells that are highly abundant in the spleen of newborn mice, but decrease significantly overtime. [1,2]
- However, the presence of CD71+ cells in the gut and their relationship with the gut bacteria are still unclear.

Objective

- The purpose of this research project is to study the presence of immature red blood cells in the small intestine of a mouse animal model and examine its relationship with the gut bacteria.

Methods

- Gut tissues were collected at day 3, 7, 21, and adulthood, and processed in order to isolate gut immune cells. Then, cells were stained to measure the percentage of immature red blood cells in the small intestines.
- A second experiment was conducted where 5 day old pups were treated to deplete immature red blood cells. All animals were euthanized one day after treatment and gut tissue samples were collected for further analysis.
- Gut tissues were used for RNA extraction, and quantitative PCR was applied to check the expression levels of TLR-3 and TLR-4 (TLR, toll-like receptor).

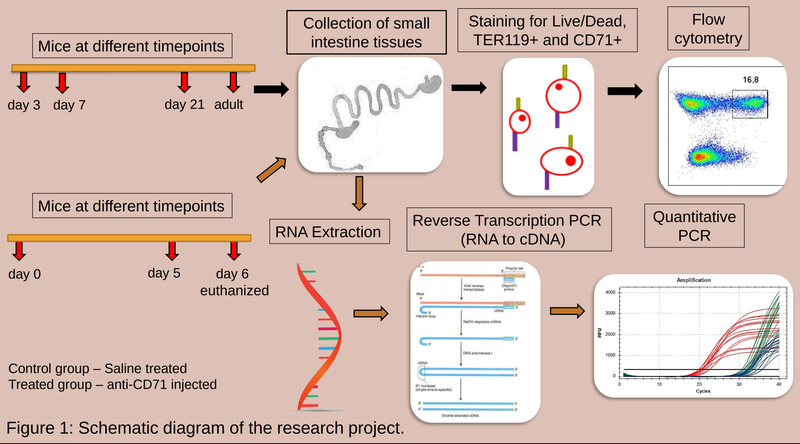

Figure 1: Schematic diagram of the research project.

Results

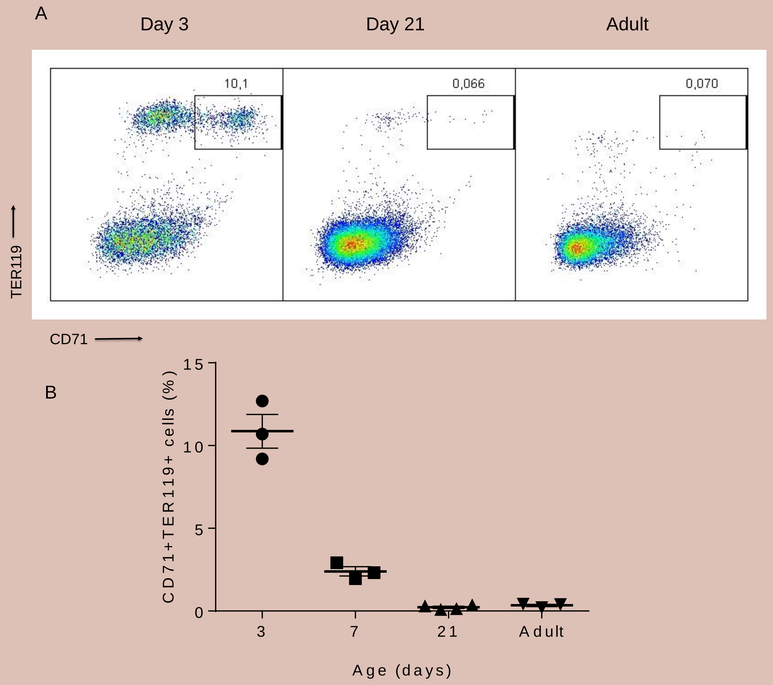

Figure 2: Presence of immature red blood cells in the gut tissues of mice overtime; A) Representative flow cytometry plots of the immature red blood cells in the small intestine; B) Accumulative data of the percentage of immature red blood cells.

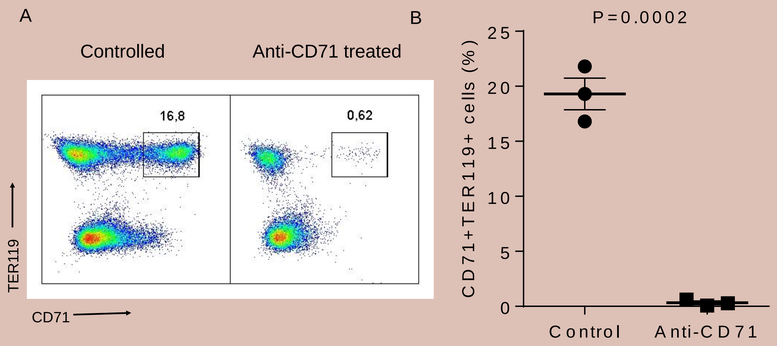

Figure 3: Depletion of immature red blood cells in the small intestine of pups that are treated with Anti-CD71+ antibody.
A) Representative flow cytometry plots of the immature red blood cells after the depletion; B) Accumulative data of the percentage of immature red blood cells in the small intestines.

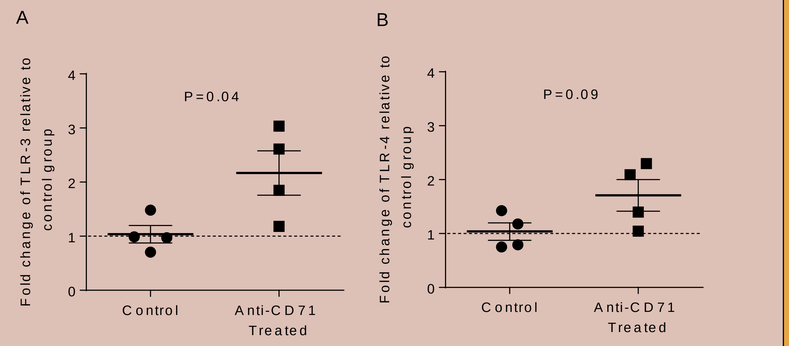

Figure 4: Expression levels of TLR-3 and TLR-4 in treated with anti-CD71 antibody pups or not.
A) TLR-3 gene expression (it recognizes double-stranded RNA); B) Expression levels of TLR-4 gene (it recognizes a component of the cell wall of Gram-negative and some Gram-positive bacteria).

Key Findings

- The percentage of immature red blood cells in the mice small intestines was high during the infancy period but gradually decreases towards adulthood.
- Upon injection with anti-CD71 antibody, the immature red blood cells were successfully depleted in the small intestines.
- Depletion of immature red blood cells leads to significant increase in the gene expression of TLR-3 and TLR-4, which are surface receptors used by the host cells to communicate with gut bacteria.

Relevance

- These results provides proof of the presence of immature red blood cells in the gut tissues of mice.
- This study provides pilot evidence about the indirect interaction between immature red blood cells and gut bacteria.
- This research can lay the foundations of future research questions and potential development of new immunotherapies about the important role of these cells in the gut health.

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Literature cited

[1]Elahi S, *et al.* 2013, Nature, 504:158;
[2]Dunsmore G, *et al* 2017, Journal of Immunology, 199:2081