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Role of Immature Red Blood Cells in Neonatal Immunity

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Abstract

Newborns are highly susceptible to diseases. Infections such as Bordetella Pertussis (i.e. whooping cough) and Listeria (i.e. food poisoning) can result in the death of neonates while causing little harm to older children and adults. Although previously attributed to an underdeveloped immune system, recent research has shown that this susceptibility is due to the high presence of immature red blood cells or CD71+ cells. These cells possess immunosuppressive properties. By interfering with the function of other immune cells, they can prevent an effective pathogenic immune response. In this study, the changes in the amount of CD71+ cells were observed throughout the different age points of mice as well as in mice infected with Bordetella pertussis and Listeria. This study aimed to gain a better understanding of the development of the immune system as to better aid neonates in fighting infection. Flow cytometry was used to determine the amount of CD71+ cells in the spleens of mice at different age points. The results showed that overall the amount of CD71+ cells decreased as the age of the mouse increased, paralleling the decrease in susceptibility of the immune system. Furthermore, the change in CD71+ cells was also observed in the spleens of mice infected with Bordetella pertussis and mice infected with Listeria. There was no significant change for the Listeria infected mice, as CD71+ cells play no immunological role in fighting Listeria, an intracellular bacteria. However, there was a significant increase in CD71+ cells in Bordetella Pertussis infected mice since this infection was extracellular. These results show that CD71+ cells react differently to different infections and play a different immunological role in the presence of different pathogens. Furthermore, the results shows a direct correlation between age and the amount of CD71+ cells present in the spleen. The changes in the amount of CD71+ cells was most likely due to different pathological conditions and requirements at different ages.

Key words:
red blood cells, immature red blood cells, immune system, susceptible, CD71

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Introduction

- Newborns have a highly susceptible immune system. Infections such as *Bordetella pertussis* (i.e. whooping cough) and *Listeria* (i.e. food poisoning) can result in the death of neonates while causing little harm to older children and adults.
- Although previously attributed to an underdeveloped immune system, recent research has shown that this susceptibility is due to the high presence of immature red blood cells in neonates.[1, 3]
- Immature red blood cells, also called CD71$^+$ cells, have immunosuppressive properties. By producing various chemicals, they suppress different immune cells and prevent an effective immune response.[1, 2, 3]

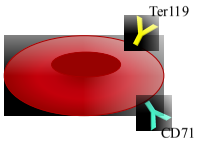


Figure 1: Immature red blood cells have two markers

Purpose: Understanding the changes in the amount of CD71$^+$ cells in healthy and infected mice will improve our knowledge on the development of the newborn's immune system.

Methods

- Spleens from healthy BALB/c mice at different age points were harvested, stained for CD71$^+$Ter119$^+$ and analyzed with flow cytometry.
- Day 9 spleen cells were stimulated with lipopolysaccharides (LPS) and subjected to an image stream.
- Three healthy BALB/c mice were infected with *Bordetella pertussis* (whooping cough) at day 6. Another three healthy BALB/c mice were infected with *Listeria* (food poisoning) at day 21. The mice were euthanized three days post-infection and the spleens were harvested, stained for CD71$^+$Ter119$^+$ and subjected to flow cytometry.

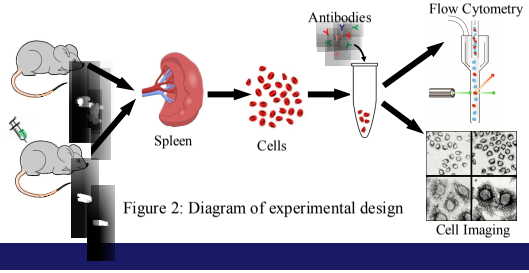


Figure 2: Diagram of experimental design

Results

Figure 3: The percentage of CD71$^+$ cells present in the spleen of day 3 and adult mice. Day 3 mice had a higher percentage of CD71$^+$ cells.

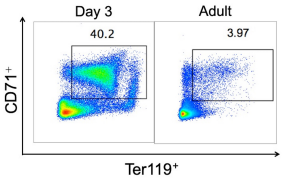


Figure 4: The CD71$^+$ cell count in different ages of mice. Overall the percentage of CD71$^+$ cells decreased as the age increased.

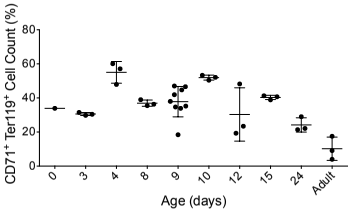


Figure 5: Image of the plate in which the *Listeria* bacteria was cultured. The colonies can be seen as white dots in the corner of the plate.

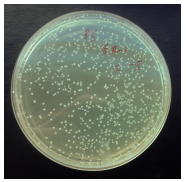


Figure 6: Comparison of CD71$^+$ cell count in healthy and *Listeria* infected adult mice. When infected, there was no significant change in the percentage of CD71$^+$ cells.

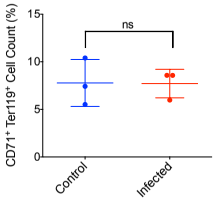
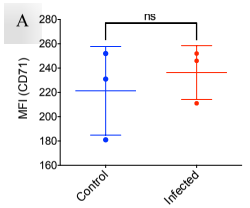


Figure 7: Mean Fluorescent Intensity (MFI) of CD71 (A) and Ter119 (B) in healthy and *Listeria* infected adult mice. There was no significant change in CD71 and Ter119 when infected with *Listeria.*



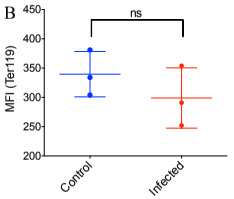
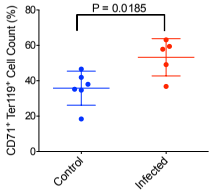


Figure 8: Image of the plate in which the *Bordetella pertussis* bacteria was cultured. The colonies can be seen as white dots on the plate.

Figure 9: Comparison of CD71$^+$ cell count in healthy and *Bordetella pertussis* infected day 9 mice. When infected, the percentage of CD71$^+$ Ter119$^+$ increased significantly.



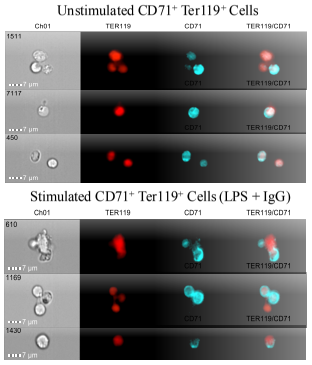


Figure 10: Cell imaging comparison of stimulated and unstimulated CD71$^+$ Ter119$^+$ spleen cells of healthy day 9 mice. The red fluorescence indicates the presence of Ter119 and the blue fluorescence indicates the presence of CD71. Capping of CD71 occurred in the stimulated spleen cells.

Conclusions

- Overall, the percentage of CD71$^+$ cells in the spleen gradually decreased from day 0 to adult, demonstrating that as the age increases, the immune system of the mice becomes less suppressed.
- The amount of CD71$^+$ cells was higher in the *Bordetella pertussis* infected mice than in the healthy mice. This may be due to CD71, a transferrin receptor, depleting the iron resources in order to fight *Bordetella pertussis,* which requires iron to spread and grow.
- When infected with *Listeria,* there was no significant change in the amount of CD71$^+$ cells. A possible explanation is a difference in immune response in adults vs newborns.
- Splenocytes activated with LPS exhibited capping of CD71 because CD71 can directly compete with LPS for iron.

Literature Cited

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3. Elahi, S., Trends in Immunology, 2019, 40(3):181-185

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