Role of Immature Red Blood Cells in Neonatal Immunity

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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]

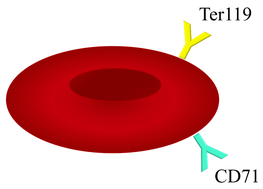


Figure 1: Immature red blood cells have two markers

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.

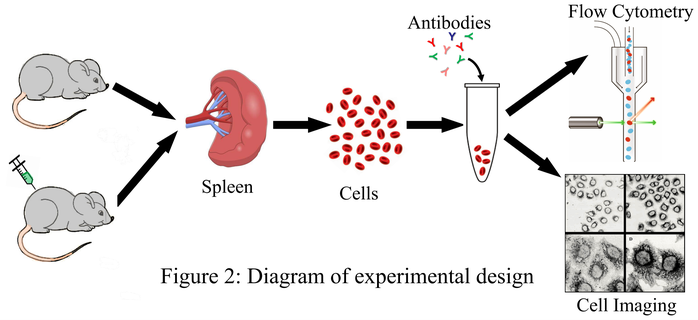


Figure 2: Diagram of experimental design

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.

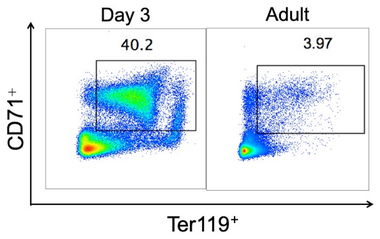


Figure 4: The CD71$^+$ cell count in different ages of mice. Overall the percentage of CD71$^+$ cells decreased as the age increased.

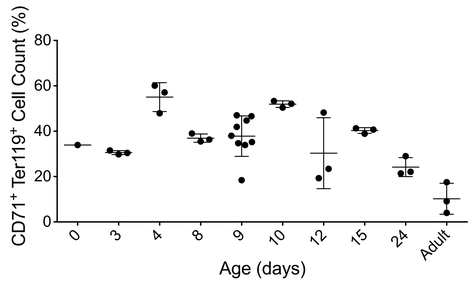


Figure 5: Image of the plate in which the *Listeria* bacteria was cultured. The colonies can be seen as white dots in the corner of the plate.

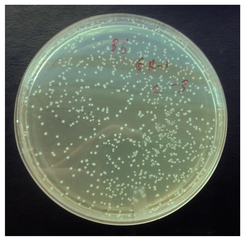


Figure 6: Comparison of CD71$^+$ cell count in healthy and *Listeria* infected adult mice. When infected, there was no significant change in the percentage of CD71$^+$ cells.

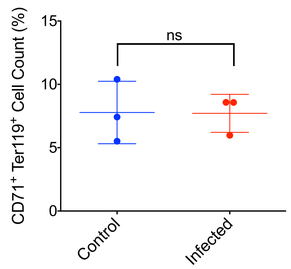
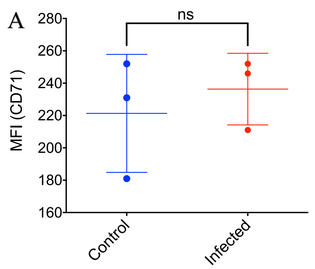


Figure 7: Mean Fluorescent Intensity (MFI) of CD71 (A) and Ter119 (B) in healthy and *Listeria* infected adult mice. There was no significant change in CD71 and Ter119 when infected with *Listeria.*



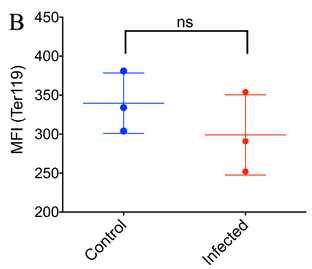
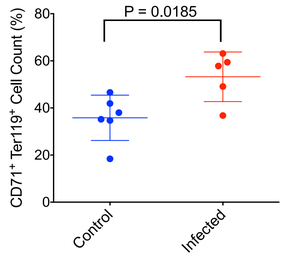


Figure 8: Image of the plate in which the *Bordetella pertussis* bacteria was cultured. The colonies can be seen as white dots on the plate.

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.



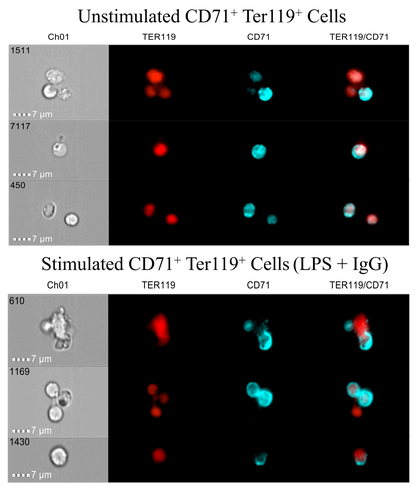


Figure 10: Cell imaging comparison of stimulated and unstimulated CD71$^+$ Ter119$^+$ spleen cells of healthy day 9 mice. The red fluorescence indicates the presence of Ter119 and the blue fluorescence indicates the presence of CD71. Capping of CD71 occurred in the stimulated spleen cells.

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

1. Elahi, S., Frontiers of Immunology, 2014, 5:1-7
2. Badurdeen, S., *et al.* Pediatric Research, 2014, 77(2): 290–297.
3. Elahi, S., Trends in Immunology, 2019, 40(3):181-185

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