Assessing the role of innate immune cells in the control of primary infection with Mycobacterium tuberculosis

Eduardo Ibarguen-Mondragon

Universidad de Nariño

Tuberculosis (TB) is an infectious disease caused by the Mycobacterium tuberculosis (Mtb). It is both preventable and generally curable. However, in 2022, TB was the second leading cause of death worldwide due to a single infectious agent, following coronavirus disease (COVID-19) [1]. After an individual is infected with Mtb, the risk of developing TB disease is highest in the first 2 years (approximately 5%), after which decreases. Without treatment, the mortality rate from TB is high (approximately 50%). With the treatments currently recommended by WHO (a 4- to 6-month course of anti-TB drugs), approximately 85% of people with TB can be cured [1]. The above allows us to assume that one in two sick people not treated with any medication overcomes the disease thanks to their immune system (a complex network of cells, tissues, organs, and substances they produce, which help the body fight infections and other diseases). Defense mechanisms against substances that are considered harmful or foreign are divided into innate immune response and acquired immune response. The role of adaptive or acquired immunity in controlling Mtb infection is well-studied and the protective role of T and B lymphocytes in anti-tuberculosis immunity is widely recognized [2]. However, following exposure to Mtb, it typically takes 4 to 6 weeks for a human host, and 2 to 3 weeks for mice, to develop antigen-specific T-cell responses in the lymph nodes [3]. Therefore, the non-specific innate immune response plays a pivotal role in protecting the host before the onset of adaptive immunity and even leads to early clearance of bacteria [3]. Mathematical models had been used to gain insights in within-host dynamics of TB; mainly, related to adaptive immunity [4, 5]. Currently, it is known

MCA 2025 internal code: SS64-T08

that the innate immune response is critical to the outcome of Mtb infection, since it can control bacterial progression or substantially influence the subsequent adaptive response of the host. This issue has been investigated less thoroughly from the perspective of mathematical modeling. In the talk, It will present results from models describing the interaction between innate immune cells and Mycobacterium tuberculosis during primary infection with Mtb. They suggest that macrophages are on the front of primary protective response against Mtb. Also highlight the importance of other innate cells in the outcome of infection. Specifically, our findings suggest that, in addition to macrophage activity, the involvement of other innate immune cells is essential for eliminating or controlling bacterial progression, ultimately leading to an adaptive immune response.

References

[1] World Health Organization, Global tuberculosis report 2023, 1 Eds., Genove: Licence CC BY-NC-SA3.0 IGO, 2023. Available from: `https://www.who.int/publications/i/item/9789240083851`

[2] D. D. Chaplin, Overview of the Immune Response, J Allergy Clin Immunol., 125 (2010), S3-S23.

[3] P. Sankar, B. B. Mishra, Early innate cell interactions with Mycobacterium tuberculosis in protection and pathology of tuberculosis, Front. Immunol., 14 (2023), 1_x0015_21.

[4] D. Kirschner, E. Pienaar, S. Marino, J. J. Linderman, A review of computational and mathematical modeling contributions to our understanding of Mycobacterium tuberculosis within-host infection and treatment, Curr. Opin. Sys Biol., 3 (2017), 170_x0015_185.

[5] D. Chakraborty, S. Batabyal, V.V. Ganusov, A brief overview of mathematical modeling of the within-host dynamics of Mycobacterium tuberculosis, Front. appl. math. Stat., 10 (2024), 1355_x0015_373.