Nature: CNIC scientists discover a type of immune cell that produces defensive "shields" in the skin

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The discovery, published in Nature, opens the path to new strategies for treating skin diseases and immunological disorders, with special potential for the treatment of inflammation, diabetes, and age-related conditions

A team at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) led by Dr. Andrés Hidalgo has discovered a specialized population of neutrophils in the skin that produce extracellular matrix, helping to maintain the skin's resistance and integrity. The study, published in *Nature*, demonstrates that the immune system not only targets pathogens, but also physically strengthens the skin to prevent them entering the body.

Neutrophils are an important type of circulating immune cell. The specialized neutrophils described in the new study populate the skin, where they produce collagen and other matrix proteins that strengthen the skin barrier. The discovery broadens understanding of the immune system and may

lead to new strategies for treating skin diseases, inflammation, diabetes, and age-related conditions.

Although neutrophils are best known for their microbicidal properties, the new study reveals an unexpected role for these cells in the generation and remodeling of the subepidermal extracellular matrix. Hidalgo explains that, “The extracellular matrix is critical for maintaining the structure and function of the skin and other tissues, acting as a barrier to the entry of microorganisms and toxins.”

First author Tommaso Vicanolo adds that the study, “demonstrates that these neutrophils help to maintain skin integrity under normal conditions and are activated in response to injury to generate protective structures around wounds that prevent the entry of bacteria and toxins.”

The study further shows that this structural function of skin neutrophils is regulated by the TGF-β signaling pathway. By genetically deleting this pathway in mice, the authors showed that the deposition of extracellular matrix was diminished, resulting in skin that was more fragile and permeable. Hidalgo notes that, “This suggests that the interaction between the immune system and the body’s structural components is much more direct than previously believed.

Another fascinating result emerging from the study is that the activity of these skin neutrophils follows a day-night pattern, adjusting the production of extracellular matrix according to the body’s circadian cycle. As a result, the skin of mice is more resistant at night than during the day, thanks to the nocturnal peak in neutrophil activity. Hidalgo underlines that, “This finding opens new avenues for investigating how internal body rhythms influence tissue defence, regeneration and repair.”

For Hidalgo, now at Yale University School of Medicine, the discovery of matrix-producing neutrophils not only broadens knowledge about innate immunity, but also suggests new treatment strategies for skin diseases and immunological disorders. He explains, “These findings will help develop treatments to strengthen the skin barrier in patients with inflammatory diseases or immunological alterations, including patients with diabetes and older adults.”

The authors conclude that this advance—the fruit of collaboration between various CNIC groups and laboratories in Germany, the United States, Singapore, and China, “signals a change in the way we view the immune system’s protective role in the body.”

Dr. Hidalgo is currently investigating the possible implications of the study findings for fibrotic processes and cancer.

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- *Vicanolo, T., Özcan, A., Li, J. L. Y., Huerta-López, C., Ballesteros, I., Rubio-Ponce, A., Dumitru, A. C., Nicolás-Ávila, J. Á., Molina-Moreno, M., Reyes-Gutierrez, P., Johnston, A. D., Martone, C., Greto, E., Quílez-Alvarez, A., Calvo, E., Bonzon-Kulichenko, E., Álvarez-Velez, R., Chooi, M. Y., Kwok, I., ... Hidalgo, A. (2025). Matrix-producing neutrophils populate and shield the skin. Nature. https://doi.org/10.1038/s41586-025-08741*

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