Scientists discover a population of macrophages that participate in alveolar regeneration

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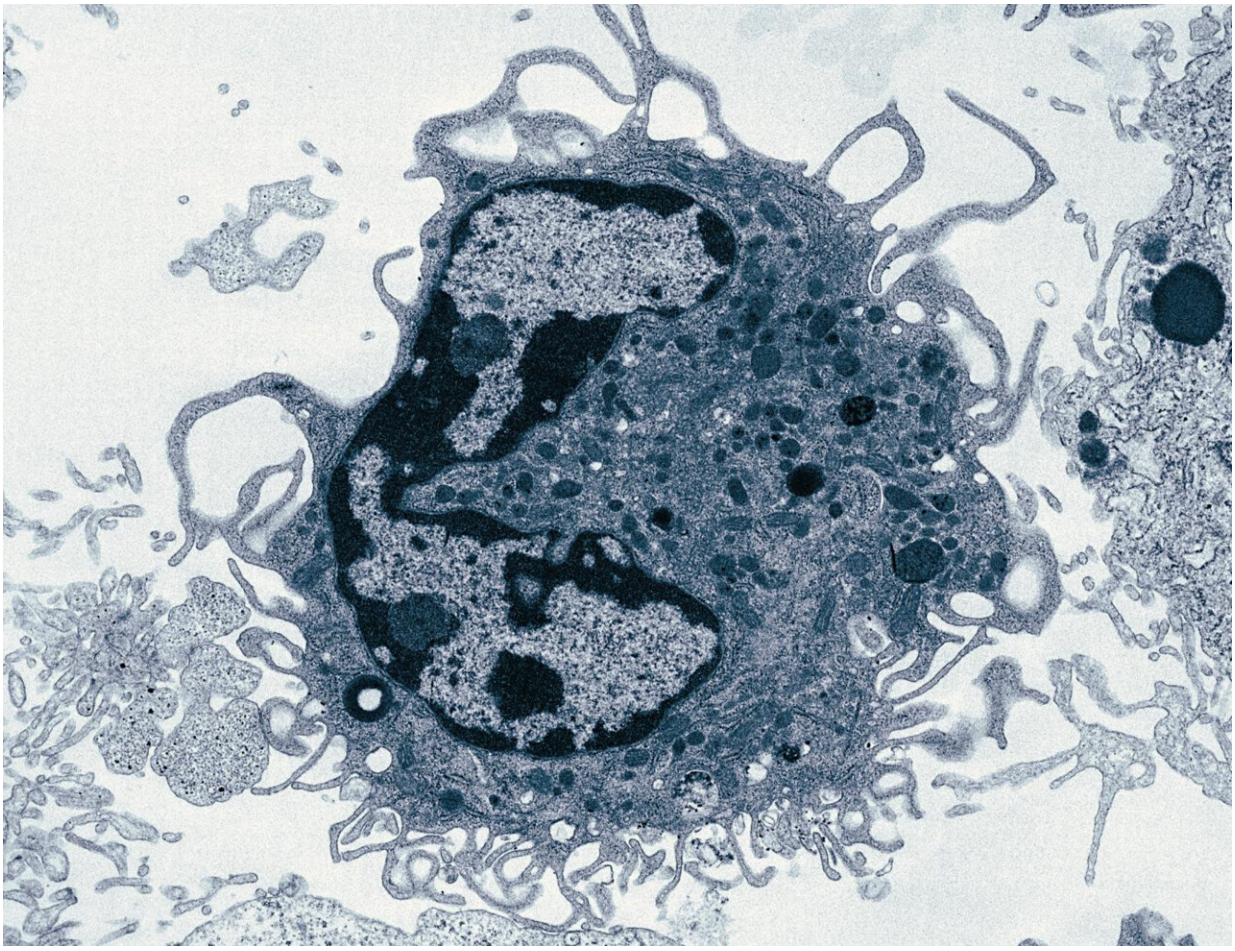


The newly discovered macrophage observed by electron microscopy. Credit: ULiège/Marc Thiry

Researchers at the University of Liège (Belgium) have discovered a new population of macrophages, important innate immune cells that populate the lungs after injury caused by respiratory viruses. These macrophages are instrumental in repairing the pulmonary alveoli.

This groundbreaking discovery promises to revolutionize our understanding of the post-infectious immune response and opens the door to new regenerative therapies. The study is published in the journal *Science Immunology*.

Respiratory viruses, typically causing mild illness, can have more serious consequences, as shown during the COVID-19 pandemic, including severe cases requiring hospitalization and the chronic sequelae of "long COVID."

These conditions often result in the destruction of large areas of the lungs, particularly the alveoli responsible for gas exchanges. Ineffective repair of these structures can lead to ARDS or a permanent reduction in the lungs' ability to oxygenate blood, causing chronic fatigue and exercise intolerance.

While the role of macrophages during the acute phase of respiratory viral infections is well known, their function in the post-inflammatory period has been largely unexplored.

A study by the GIGA Institute at the University of Liège reveals that atypical macrophages, characterized by specific markers and transiently recruited during the early recovery phase, play a beneficial role in regenerating pulmonary alveoli.

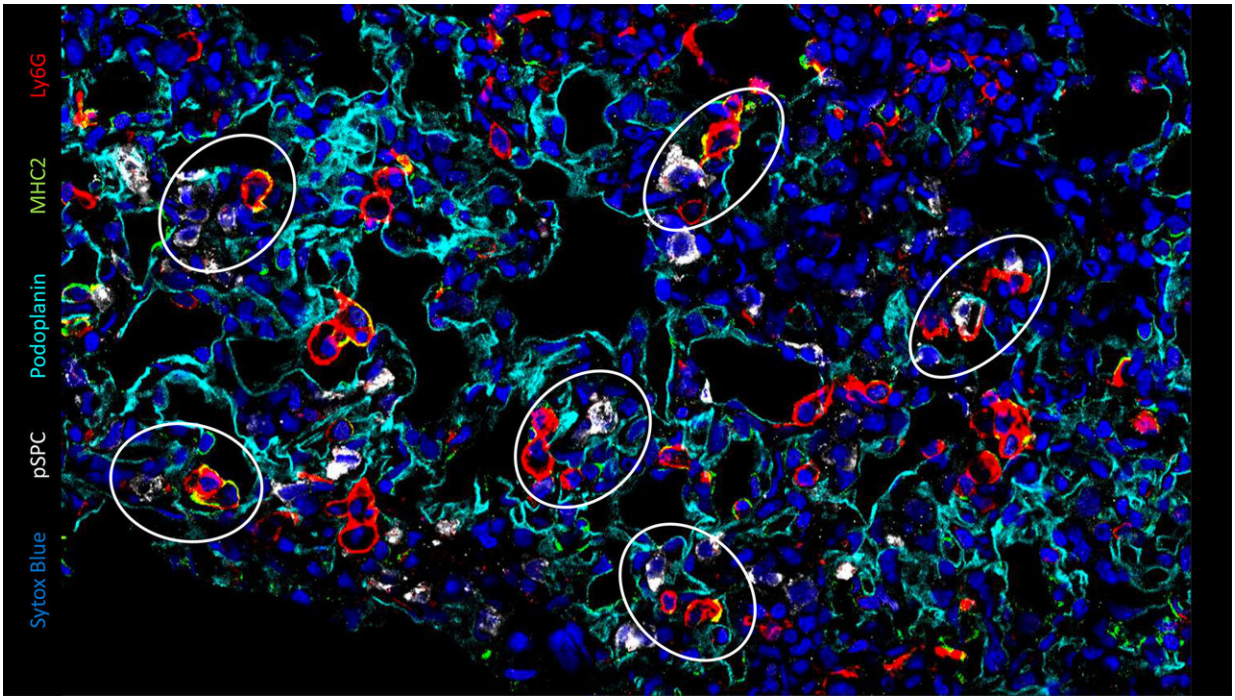
Led by Dr. Coraline Radermecker and Prof. Thomas Marichal from the Immunophysiology Laboratory, the study was conducted by Dr. Cecilia Ruscitti and benefited from the ULiège's advanced technological

platforms, including flow cytometry, fluorescence microscopy, and single-cell RNA sequencing.

"Our findings provide a novel and crucial mechanism for alveolar repair by these atypical macrophages," explains Coraline Radermecker.

"We have detailed their characteristics, origin, location in the damaged lung, the signals they require to function, and their role in tissue regeneration, specifically acting on type 2 alveolar epithelial cells, the progenitors of alveolar cells."

The scientific community had overlooked these macrophages because they express a marker previously thought to be specific for another immune cell population, the neutrophils, and because they appear only briefly during the repair phase before disappearing.



Following infection, in areas of the lung undergoing repair, atypical macrophages

(in orange) are located close to type 2 alveolar cells (in white). Credit: ULiège/Cecilia Ruscitti

"Our study highlights the reparative role of these macrophages, countering the prevailing idea that macrophages following respiratory viral infections are pathogenic," adds Thomas Marichal.

"By targeting the amplification of these macrophages or stimulating their repair functions, we could develop therapies to improve alveolar regeneration and reduce complications from serious respiratory infections and ARDS."

To illustrate, consider the lungs as a garden damaged by a storm (viral infection). These newly-discovered macrophages act like specialized gardeners who clear debris and plant new seeds, enabling the garden to regrow and regain its vitality.

This scientific breakthrough opens new avenues for treating respiratory diseases.

More information: Cecilia Ruscitti et al, Recruited atypical Ly6G+ macrophages license alveolar regeneration after lung injury, *Science Immunology* (2024). DOI: 10.1126/sciimmunol.ado1227. www.science.org/doi/10.1126/sciimmunol.ado1227

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