

Unlocking secrets of immune system proteins: A potential path to new treatments

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Researchers peering into the minute workings of cells reveal how immune system proteins interact to mount an immune response. Credit: Jagannath Maharana/IIT Kanpur

In the intricate dance of our body's defenses against harmful invaders, certain immune system proteins play pivotal roles. New research from the Bridge Institute at the USC Michelson Center for Convergent Bioscience, in collaboration with international teams from India,



Australia and Switzerland, has shed light on these proteins.

The work potentially paves the way for innovative treatments for a range of diseases, including severe cases of COVID-19, rheumatoid arthritis, neurodegenerative diseases and cancer.

Central to our immune response is the complement cascade, a series of events activated when potential threats are detected. This process produces protein messengers, C3a and C5a, which in turn activate specific receptors on cells, setting off a cascade of internal signals. The precise mechanisms of these receptors, especially the elusive C5aR1, have remained a mystery.

Using the advanced technique of cryo-<u>electron microscopy</u> (cryo-EM), the researchers captured detailed images of these receptors in action. These images unveil how the receptors interact with molecules, change shape upon activation and transmit signals within the cell.

The study's lead author, Cornelius Gati, assistant professor of biological sciences, chemistry, and quantitative and <u>computational biology</u> at the USC Dornsife College of Letters, Arts and Sciences, remarked on the findings, noting, "This research offers significant and comprehensive insights into a crucial receptor family within the immune system."

The study's revelations suggest potential avenues for the development of drugs targeting these receptors to treat various diseases, added Gati, who heads USC's cryo-EM facility, which is available for use by researchers around the globe.

As the <u>global community</u> continues to grapple with diseases that impact millions, understanding the nuances of our immune system becomes ever more critical. <u>This research</u>, published in the journal *Cell* on Oct. 17, contributes to that understanding, providing a foundation for future



studies aiming to harness the power of our body's natural defenses.

More information: Manish K. Yadav et al, Molecular basis of anaphylatoxin binding, activation, and signaling bias at complement receptors, *Cell* (2023). DOI: 10.1016/j.cell.2023.09.020

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