

Building Immunity: Team recreates a T-cell receptor signaling pathway

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Assembly of a T-cell receptor pathway in vitro using 12 purified components on model membranes. An actin network (red) was induced by LAT clustering



(blue). Credit: Xiaolei Su

The front line of the human immune system is made up of T-cells: white blood cells that circulate in the body and scan for foreign invaders and infections. If a T-cell surface receptor detects a threat during its surveillance, it relays a signal to the interior of the cell and activates it to attack.

Once this crucial "call of duty" is heard in the cell, how the signal is relayed through a series of proteins to activate the cell's immune response is clarified in a new paper in Science by a team working at the Whitman Center of the Marine Biological Laboratory (MBL) in Woods Hole.

By successfully re-creating a T-cell receptor signaling <u>pathway</u> independent of the cell itself, the scientists gained novel insights into how protein signaling works in a complex cellular process.

"We focused on one T-cell receptor signaling pathway involving 12 different proteins, but what we discovered is probably reflective of the way other signaling pathways happen in the cell, as well," said co-author Ron Vale, a Howard Hughes Medical Institute (HHMI) investigator at the University of California, San Francisco and a Whitman Center scientist. The study, supported by HHMI, was performed by scientists from several institutions who convene at the MBL to work collaboratively.

Their study revealed "a very important self-organization of the protein molecules in the signaling pathway, where they end up clustering to form dense structures in which the proteins are talking to one another," Vale said. The <u>protein molecules</u> separate into structures by a process similar



to phase separation of oil and water, he said. "That spatial organization seems to be very important for the efficiency of the <u>signaling pathway</u>."

"It's very important that we could conduct this research at MBL," Vale said. "This reconstitution was a very complicated undertaking that was beyond what any single lab could do. At MBL, we could bring all these labs together with different expertise to make it work."

More information: X. Su et al. Phase separation of signaling molecules promotes T cell receptor signal transduction, *Science* (). <u>DOI:</u> <u>10.1126/science.aad9964</u>

Provided by Marine Biological Laboratory

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