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THE CHALLENGE

When the immune system senses invading bacteria, viruses or cancer cells, it has to act quickly to fend off the threat. Proteins begin to bind or modify each other to activate immune cells. During this activation, many proteins are reorganized: This includes protein movements on a molecular scale or from one part of the cell to another. Understanding how the spatial arrangements of proteins affect the immune response will help scientists to develop new ways to control and modulate the immune system to fight infections, autoimmune diseases or cancers. However, tracking changes in molecular arrangements is difficult, as molecule and cluster sizes are below the resolution of traditional light or fluorescence microscopy.

THE APPROACH

Björn Lillemeier has developed and adapted cutting-edge microscopy techniques for imaging proteins embedded in the outer membranes of cells. His super-resolution imaging approaches have allowed him to see the exact placement of these proteins in the membranes of immune cells, specifically T cells. He has shown that T cells have distinct clusters of crucial proteins in different areas of their membranes. When the cells are activated—in response to an infected or diseased cell—these clusters dramatically rearrange. Clusters of proteins move to different locations in the plasma membrane, break apart or combine to form distinct molecular niches that are essential for appropriate T cell activation. Lillemeier's observations of the spatial

arrangements of proteins in immune cells, and how they change during an immune response, are the most detailed descriptions yet. And he's continuing to improve his imaging techniques so he can watch multiple proteins move in real time. His findings could lead to a better understanding of how protein arrangements are dysregulated during immune system disorders and how scientists might be able to control their physiological functions.

THE INNOVATIONS AND DISCOVERIES

- Lillemeier and his colleagues described techniques for arranging flat sheets of plasma membranes on grids that can be visualized under an electron microscope. This allows researchers to see the arrangement of proteins on the membrane, and how that arrangement changes under different conditions.
- Using super-resolution microscopy, he also discovered that T cell proteins, which allow the immune system to recognize infected or cancerous cells, are arranged in specific patterns. This organization allows different protein types to coordinate their interaction and to maximize the immune system's response against a pathogen.
- He continues to work on understanding how the spatial and temporal arrangement of proteins in immune cells mediates their function. The research has implications for treating autoimmune diseases, infections and cancer by changing immune responses.

For more information, please visit:
WWW.SALK.EDU/SCIENTIST/BJORN-LILLEMEIER

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