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“While signal transduction is traditionally seen as a sequence of protein interactions and modifications, it has become clear that these events are also spatially controlled through plasma membrane compartmentalization. To further understand this, my lab studies the architecture of the plasma membrane in general, as well as its contribution to signal transduction in T cells.”

In eukaryotes, the plasma membrane—a double layer of lipid molecules that encloses all cells—not only segregates the cell from its environment but also serves as the principal interface for communication between cells. Not surprisingly, the plasma membrane’s structure and properties impact many biological processes. T cells, whose main job is to fight infection, for example, utilize and reorganize their plasma membrane constantly during activation and effector functions. This is most dramatically seen in the establishment of signaling microclusters and the formation of the immunological synapse between T cells and antigen-presenting cells upon activation of the former by the latter.

Despite a lot of interest in the precise architecture of the plasma membrane in the past, studies of plasma membrane-associated signaling had been hampered by technical barriers such as cell lysis and limited resolution in microscopy. Lillemeier overcame these limitations through the use of novel high-resolution imaging techniques such as photo-activated localization microscopy (PALM) and dual color fluorescence cross-correlation spectroscopy (dcFCCS), which allowed him to observe directly the spatial and temporal distribution of membrane-associated molecules on a nanometer scale.

He discovered that all membrane-associated proteins in the cells that he examined are clustered into what he refers to as “protein islands,” which led him to postulate a novel concept for the general architecture of plasma membranes. Lillemeier also found that the T cell receptor signaling cascade is spatially and temporally controlled through the segregation and association of distinct membrane microdomains (protein islands) that contain specific subsets of T cell signaling molecules. He believes that this type of signal control may be a general feature of membrane-associated signaling and is probably used in a variety of signaling processes.

In the future, Lillemeier will expand his research to understand how this higher order in the plasma membrane is achieved and what molecular mechanisms are in place to utilize it during signal transduction. His studies will help to expand knowledge of spatio-temporal signaling control, which will suggest new approaches in manipulating the response of the immune system to pathogens and diseases.

For more information, please visit
salk.edu/faculty/lillemeier.html

