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Revving up innate control of viral infection requires a three-cell ignition

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One of the most important cell types for controlling certain viral infections are natural killer (NK) cells. As part of the innate and rapid immune response, NK-cell recruitment and activation was thought to be a straightforward process. New research shows that NK-cell recruitment and activation requires a rather carefully choreographed interaction of three cell types in the headquarters of the slower adaptive immune-activation: the lymph node.

In a new paper published in *Cell Reports,* Luis J. Sigal, Ph.D., Professor Microbiology and Immunology at Jefferson (Philadelphia University + Thomas Jefferson University) and colleagues show that after a mousepox infection in the skin of mice, sentinel immune cells called dendritic cells become infected and rapidly migrate to the draining lymph node carrying the virus along. Within the first 24 hours after the initial infection, these dendritic cells perform at least two tasks in the draining lymph node. First, they produce chemokines that specifically attract inflammatory monocytes to the draining lymph node. Second, the dendritic cells stimulate the few NK cells already in the draining lymph node to produce a cytokine known as interferon gamma that stimulates the recently arrived monocytes to produce other chemokines that attract reinforcements in the form of larger numbers protective NK cells to the draining lymph node.

The work unveils a cascade of events whereby three types of innate immune cell collaborate to recruit protective NK cells, which are essential for resistance to mousepox.

"Although we knew that that cytokines and chemokines are important for NK-cell recruitment to infected tissues," said Dr. Sigal, "we did not know that a single innate cell type—the NK cell—would require the participation of multiple cells, each with a defined task."

This complexity suggests that deficiencies in multiple cell types may affect a single protective mechanism and result in uncontrolled viral infection. The results could have parallels in other virus types and possibly in human immunity.

More information: Eric Wong et al, Migratory Dendritic Cells, Group 1 Innate Lymphoid Cells, and Inflammatory Monocytes Collaborate to Recruit NK Cells to the Virus-Infected Lymph Node, *Cell Reports* (2018). DOI: 10.1016/j.celrep.2018.06.004

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