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Specialized white blood cells coordinate 'first responders' to viral infection

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Just as fire engines arrive quickly at the scene to save people and property, the cells that fight viruses have to reach the site of an infection promptly to mount a protective response.

According to recent studies by University of Washington (UW) scientists, specialized types of white blood cells, a category called regulatory T cells, seem to help orchestrate this timely reaction to a virus invasion. Their findings appear in the April 24 edition of *Science Express*, a Web edition of selected *Science* papers published in advance of the print edition. The authors of the study, "Coordination of Early Protective Immunity to Viral Infections by Regulatory T Cells," are Jennifer M. Lund, senior fellow in immunology; Lianne Hsing, immunology graduate student; Thuy T. Pham, senior biology major; and Alexander Y. Rudensky, professor of immunology.

The Rudensky laboratory is noted for many contributions to the superhot field of regulatory T cells. These cells are important in controlling autoimmunity, a cellular self-attack that can lead to diseases like reactive arthritis. UW researchers and other scientists have shown that young mice deficient in regulatory T cells die from an aggressive form of autoimmunity that damages several organs.

Rudensky noted the great clinical interest in the therapeutic potential of regulatory T cells. Evidence is growing on the role of regulatory T cells in keeping the body's immune responses in check. Studies in lab animals suggest these cells might be harnessed to treat autoimmune diseases or

reduce rejection of transplanted organs.

Researchers think that regulatory T cells might call a halt to immune responses as the body nears success in eliminating an infection. This suppression as the fight draws to an end would reduce tissue damage from robust immune responses.

But what happens early in infection? Does the immunity-suppressing function of regulatory T cells form an obstacle to organizing an attack on germs that have just invaded the body? Do regulatory T cells temporarily lose their suppression ability in reaction to viral-sensing mechanisms or other signals? In the recent Science Express study, researchers looked for a role for regulatory T cells during the start of a herpes simplex virus infection in mucus membranes.

When regulatory T cells are deficient in mice, the herpes simplex virus replicates rapidly in the mucus membranes and spreads to the spinal cord. Upon closer examination of these mice that lack regulatory T cells, the researchers found very little interferon, an anti-viral chemical that also boosts the immune response, at the infection site, even though it was found in the draining lymph nodes.

Also in the lymph nodes they noticed a sharp increase in certain chemokines, chemicals that stimulate immune cells to move in and cause inflammation. The presence of chemokines appeared to encourage the entry and retention of certain infection-fighting cells in the lymph nodes draining the site of infection, an ineffective place for the infection-fighting cells to be during the start of a viral attack.

The researchers also noticed a delay in killer cells, dendritic cells (the cells that capture and present foreign proteins to other immune cells), and T cells arriving at the site of infection, where they were supposed to go earlier to fulfill their virus-fighting roles. The researchers suggested

that a possible reason for this tardiness is an alteration in the chemical cues necessary for these cells to migrate to the site of infection.

The authors described the finding of an immune-response promoting role for regulatory T cells during the early stages of a local infection as "unexpected," considering the cells' suppressor roles during later stages of an immune response.

Source: University of Washington