Specialized natural killer cells in human tonsils pack a punch

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Tonsils are a source of sore throats and an excuse for ice cream. But they also provide an important protective service, their immune-cell-rich tissue acting as the body's first defense against the germs about to be swallowed or inhaled. Researchers have known that tonsils are packed with B cells, which flag invaders for other cells to attack. But a new study by Rockefeller University scientists shows that tonsils also house a different, very specialized cell that helps protect against the Epstein Barr virus (EBV).

EBV is a member of the herpes virus family and can cause a variety of ailments, from infectious mononucleosis to cancers such as Burkitt's lymphoma. It acts by working its way into B cells and transforming them into virus-infected cells that continuously multiply. Some people manage to control the virus with no symptoms whatsoever, while others succumb. New research published in *PLoS Pathogens* may help explain why.

In comparison to peripheral blood, the tonsils contain just a small number of natural killer cells, immune cells named for their ability to recognize something as foreign and destroy it. But Christian Münz, head of the Laboratory of Viral Immunobiology, and Ph.D. student Till Strowig have found that the majority of the tonsils' natural killer cells are a specific kind, called CD56bright cells, and incredibly potent — nearly a hundred times better at preventing EBV from transforming B cells than natural killer cells located in peripheral blood. "These cells are not only enriched in this organ, but they are better than at any other site," Münz says.

In fact, the researchers found that the location of this protective subset of natural killer cells is quite precise, poised at a germ-entry site where they can control incoming pathogens. And surprisingly, the CD56bright cells have something in common with a totally different class of immune cells: Like T cells, they must be activated before they can do their job. This discovery paves the way for future EBV vaccine research, as prompting the activating cells could lead to a higher degree of viral resistance by the natural killer cells. Because there's not yet a mouse model for the virus, Münz, Strowig and postdoc Cagan Gurer are now working to create mice with human immune system components, allowing the mice to be infected with EBV and allowing the researchers to watch what happens during the early stages of infection — stages during which humans have no symptoms, and have therefore never been studied.

"It might allow us, for the first time, to look at very early immune responses to Epstein Barr virus," Münz says. "And it could hopefully be developed to test different vaccine formulations that might make the mice resistant against developing virus-induced tumors." For developing nations, where Burkitt's lymphoma is too costly to treat once it develops, a vaccine that efficiently controls Epstein Barr virus would be invaluable.

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