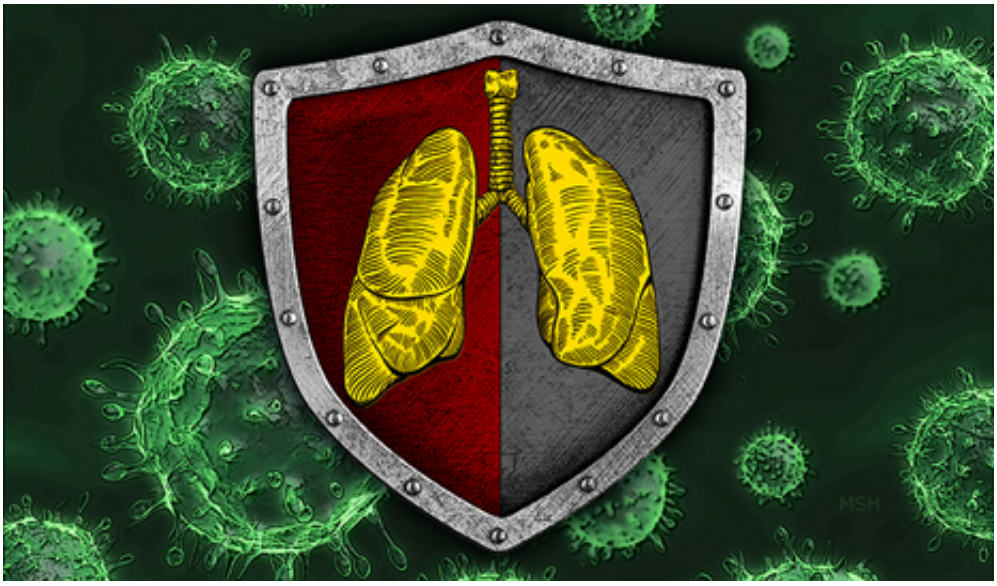
Researchers describe how lungs stand guard against the flu

October 10 2014, by Jim Shelton



Credit: Michael S. Helfenbein

Influenza viruses mutate annually, making it difficult to produce vaccines that induce antibodies capable of recognizing the changing proteins on the surface of the flu virus and conferring long-term immunity.

Researchers at the Yale School of Medicine describe in the Oct. 9 online edition of the journal *Immunity* how different types of immune system cells interact to generate cells in the lungs capable of mounting an effective counterattack on the invading virus, regardless of the types of

proteins on the virus' surface.

"This gives us a leg up in designing vaccines which don't lose effectiveness seasonally," said Brian Laidlaw, an immunobiology graduate student researcher in the labs of professors Susan Kaech and Joseph Craft and lead author of the study.

As the immune system responds to influenza infection in the lungs, "killer" $CD8^+$ T cells migrate to where they destroy infected cells to combat viral infection. A few of these T cells remain lodged in the lung, even after the infection dissipates, providing long-term immunity. These lung-resident "memory" T cells are ideally located to remember the prior influenza infection and respond vigorously upon reinfection. Unlike antibodies unleashed by most vaccines, these killer T cells can recognize proteins within an influenza virus that are largely unchanged season after season. However, protection wanes if the numbers of these cells in the lungs decline, so Yale researchers looked for ways to bolster this defense system.

The Yale team discovered that the formation of protective lung-resident killer $CD8^+$ T cells is impaired in the absence of "helper" $CD4^+$ T cells. They also identified factors produced by the $CD4^+$ T cells that promote formation of these T cells that stand guard at the frontline of our lungs.

The annual "flu shot" that we take every year does not generate these types of memory T cells in our lungs but instead produces antibodies—but only to specific strains of flu.

"But the problem is that the flu virus changes rapidly from year to year, and often the antibodies that we have from the prior year are not protective," Laidlaw said. "Hopefully, elucidating the steps that are taken to generate these types of memory T cells that live in our lungs will move us one step forward towards making a universal flu vaccine."

Primary funding for the study was provided by the National Institutes of Health and the Howard Hughes Medical Institute.

Craft, the Paul Beeson Professor of Medicine (Rheumatology) and professor of immunobiology, and Kaech, associate professor of immunobiology, are senior co-authors of the paper.

Provided by Yale University