New aging studies improving vaccine efficacy for the elderly

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Making breakthrough discoveries that lead to improved human health, the Trudeau Institute. Credit: The Trudeau Institute

A new study from the Trudeau Institute in Saranac Lake, New York, demonstrates that immune system cells important for both pathogen resistance and vaccine efficacy live longer in older animals but because of this longevity acquire functional defects. The work may provide new targets for boosting immune system function in older individuals.

The well-documented decreases in immune system function that accompany aging leave elderly individuals more susceptible to numerous infectious agents than younger people. Thus many vaccines now in use are not nearly as effective in protecting older people. For example, a *Journal of the American Medical Association* study found that in individuals over the age of 70, influenza vaccination offered only 23

percent protection, and reduced responses have also been seen for tetanus and hepatitis vaccinations.

In previous work, Trudeau Institute Investigator Susan Swain and her colleagues demonstrated that a specific type of immune cells, called CD4 T cells, which are critical to vaccine response, become less effective with age. Robust CD4 activity is necessary for antibody production in response to infection or vaccination. (The immune system contains a number of different cell types including B cells, which manufacture antibodies, and multiple classes of T cells. CD4 T cells are a type of helper cell that stimulates B cell production and many other components of immunity.) Specifically, "naive" CD4 T cells, those that have not come into contact with or become specialized to respond to a particular pathogen, are needed to ensure protection against new pathogens as well as vigorous responses to vaccination.

In the current study, published in the October issue of the Proceedings of the National Academy of Sciences, Swain and her group showed that naďve CD4 T cells from older mice survived longer than the corresponding cells from young mice when transplanted into normal intact hosts. This finding helps to explain how older animals maintain populations of circulating CD4 T cells, even though generation of new cells in the thymus decreases dramatically with age. The Trudeau team demonstrated that the older cells were relatively resistant to cues that trigger a process known as apoptosis (from the Greek "falling leaves"), a type of orchestrated cell death, and that these cells contained lower levels of a molecule that promotes apoptosis.

But even though aged CD4 T cells enjoy longer lives, their function decays. The Swain study shows that this functional decay and longer life-span appear to be linked, with the onset of increased longevity preceding functional defects. Since age exposes cells to increasing levels of stressors such as oxidative damage (aka "free radicals") that promote

changes associated with cancer, the authors speculate that the strategy of maintaining CD4 cell numbers by increasing the life spans of individual cells rather than by promoting proliferation of new cells may be a safeguard of sorts against tumor development. This hypothesis remains to be further examined, however, through future research, which will also be aimed at unraveling the connection between cellular life-span and functional decay in an effort to develop means of boosting CD4 activity, and therefore pathogen resistance and vaccine efficacy, in older individuals.

More information: "Age-associated increase in lifespan of naďve CD4 T cells contributes to T-cell homeostasis but facilitates development of functional defects," *Proceedings of the National Academy of Sciences.*

Source: Trudeau Institute (news : web)