Scientists show how body determines optimal amount of germ-fighting B cells

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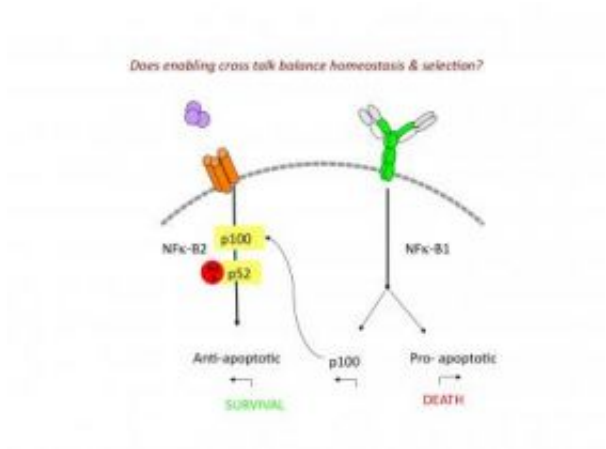

Molecular crosstalk between two B-cell surface receptors (green, Y-shaped B-cell receptor and orange cylinder-shaped BLyS receptor) balances the need to have enough B cells to drive a healthy immune response while at the same time guarding against autoimmunity. Credit: Michael P. Cancro, Ph.D., University of Pennsylvania School of Medicine

Researchers at the University of Pennsylvania School of Medicine can now explain how the body determines whether there are enough mature B-cells in the blood stream at any one time. These are the cells that produce antibodies against germs to fight infections.

"There is a steady state number of B cells that is considered normal for humans," says senior author Michael P. Cancro, PhD, Professor of Pathology and Laboratory Medicine. "We found that molecular crosstalk

between two receptors on the surface of B cells balances the need to have enough B cells to make good immune responses, while at the same time guarding against autoimmunity."

The B-cell crosstalk paper appeared online this week in *Nature Immunology*. This and other work from the Cancro lab has important implications for transplantation science and battling autoimmune diseases.

Cancro, first author Jason E. Stadanlick, a PhD student in the Cancro lab, and others found that when more of a protein called BLyS, which binds to a receptor on B-cell surfaces is circulating, more mature B cells can be kept alive. By adding more BLyS to the system, the "brakes" governing how many immature B cells are allowed to become mature B cells are relaxed. On the other hand, the body guards against autoimmune diseases such as lupus by preventing the survival of B cells via the other receptor in this equation.

The research from the Cancro lab reveals a complicated interplay between these two receptors that allows them to integrate their signals, which are at odds with one another. "One receptor sends signals to the cell nucleus that says, 'yes stay alive, the body needs more B cells,' while the other says 'wait a minute, be careful which B cells are allowed to live.'"

The Cancro lab also described in a recent *Proceedings of the National Academy of Sciences* (*PNAS*) paper that if BLyS is neutralized, most B cells die, but the ones in charge of remembering what the body has already been vaccinated against or has been exposed to, remain alive.

Together, these findings should eventually lead to interventions that alter or adjust B cell behavior in the prevention, diagnosis, and treatment of autoimmune diseases.

Source: University of Pennsylvania School of Medicine