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Pregnancy generates maternal immune-suppressive cells that protect the fetus

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A new study published online in the journal *Nature* suggests it might be possible to develop vaccines to prevent premature birth and other pregnancy complications. If so, such vaccines would be the first intended to stimulate the subset of regulatory CD4 T cells that suppress the immune response.

Current vaccines are specifically designed to stimulate T cell subsets that activate the immune response.

The study, led by a researcher at Cincinnati Children's Hospital Medical Center, shows the immune system of a pregnant mother stimulates cells that selectively prevent attack and rejection of fetal tissues recognized as being foreign. Importantly, these pregnancy-induced, immune suppressive regulatory T cells are retained after delivery, and rapidly re-accumulate and provide protection in subsequent pregnancy.

Successful pregnancy requires the ability to tolerate antigens inherited from the father. These antigens evoke an immune response by the mother's immune system, which considers these antigens foreign. If the mother gets pregnant again, these T cells remember the first pregnancy and provide additional protection to the fetus from being attacked by the mother's own immune system.

"We show definitively immune suppressive regulatory CD4 cells can form immunological memory," says Sing Sing Way, MD PhD, a physician researcher in Infectious Diseases at Cincinnati Children's and

the study's senior author. "These memory features shown in pregnancy illustrate why complications become reduced in subsequent compared with primary pregnancy, but can also be broadly applied to new ways to better control the stringent balance between immune stimulation and suppression for preventing autoimmune diseases."

Way and his colleagues demonstrate that the protective program during pregnancy is established by the expansion and retention of regulatory T cells that specifically recognize fetal antigens.

"Knowing this, we can design vaccines that specifically target immune suppressive T cells," explains Dr. Way. "Current vaccines exclusively target immune activating T cells. With the polio vaccine, for example, vaccination is designed to induce long-lasting immune-activating cells that eradicate the virus with later infection. A vaccine that targets the expansion and retention of immune suppressive cells would allow selective silencing of undesired responses and prevent them from attacking the body."

Having shown that these cells can generate and retain immunological memory might make it possible to develop vaccines against autoimmune disorders – such as juvenile idiopathic arthritis and type 1 diabetes – in which the body's immune system attacks its own healthy tissues.

More information: DOI: 10.1038/nature11462

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