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STUDY OFFERS INSIGHTS ABOUT DEVELOPMENT OF THE HUMAN IMMUNE SYSTEM

A UCSF study has found that a surprisingly high number of maternal cells enters the fetus during pregnancy, prompting the generation of special immune cells in the fetus that suppress a response against the mother.

Such peaceful co-existence represents a form of "tolerance," or the way in which the immune system of one individual is able to live side-by-side with foreign objects (or "antigens") that come from elsewhere. The new finding may be important for areas of medical research ranging from stem cell transplantation to the way in which the body can adapt to the presence of chronic infectious agents.

In previous studies, the same UCSF research team found that the human fetal immune system is made up of many special immune cells, known as regulatory T cells. In the new study, the researchers focused on trying to understand why this might be so. They found that cells from the mother cross the placenta into the fetus during the course of pregnancy, inducing the generation of so-called "regulatory T cells" that help to enforce a state of tolerance between the fetus and the mother.

"These results provide one potential explanation for the longstanding observation that many individuals demonstrate some level of immunological tolerance towards unshared maternal HLA antigens," said lead author, Jeff Mold, a biomedical sciences graduate student in the UCSF Division of Experimental Medicine.

The findings, published in the December 5th issue of *Science*, are important because they define a previously-unrecognized pathway for the development of tolerance in humans, according to the research team. This is an active area of current medical research because the mechanisms governing tolerance are important for understanding and managing autoimmune diseases, in which the body attacks its own cells, and organ transplant rejection, in which the body rejects the transplanted tissue, they add.

The findings also raise an intriguing question in regard to HIV, said senior study author Joseph M. McCune, MD, PhD, chief of the UCSF Division of Experimental Medicine: if cells from the mother can move across the placenta and induce fetal tolerance during pregnancy, what would happen if infectious agents such as HIV did the same thing?

"Only 5 to 10 percent of babies born to untreated HIV-infected mothers in the absence of antiretroviral interventions are born infected with HIV. Perhaps some aspect of the

immunological tolerance of the fetal immune system explains how the baby could avoid HIV infection in utero,” McCune noted.

In this respect, he added, the study opens up new research directions that could be important for the creation of effective HIV vaccines.

Co-authors include Jakob Michaelsson from the Karolinska University Hospital, Stockholm; Trevor D. Burt from the UCSF Department of Pediatrics; Marcus O. Muench, Michael P. Busch, and Tzong-Hae Lee from Blood Systems Research Institute; Karen P. Beckerman from the Albert Einstein College of Medicine; and Douglas F. Nixon from the UCSF Division of Experimental Medicine.

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The UCSF Division of Experimental Medicine is affiliated with the AIDS Research Institute (ARI) at UCSF. UCSF ARI houses hundreds of scientists and dozens of programs throughout UCSF and affiliated labs and institutions, making ARI one of the largest AIDS research entities in the world.

UCSF is a leading university dedicated to defining health worldwide through advanced biomedical research, graduate level education in the life sciences and health professions, and excellence in patient care.