Keck Foundation awards Tulane University $1 million to study why women have stronger immune systems than men

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Women respond more vigorously to infection and vaccination compared to men, but they're also more susceptible to autoimmune diseases. James McLachlan, PhD, and his research team at Tulane University School of Medicine launched a new study to find out why. Photo by Shutterstock.

Do women have an extra line of defense in their immune systems that gives them an advantage over men in fighting infections?

That’s one of the questions Tulane University researchers hope to answer using a $1 million grant from the W. M. Keck Foundation to study how sex differences shape disparate immune responses in men and women. The goal is to learn more about how immune systems evolved differently in the two sexes and to use this information to eventually create more precise treatments for men and women against various diseases.

The grant was awarded to a team of scientists at the Tulane University School of Medicine led by James McLachlan, PhD, associate professor of Microbiology and Immunology. He will work with his father, Weatherhead Professor of Pharmacology John McLachlan, PhD, a national expert in women’s health and estrogen action, and Price-Goldsmith Professor of Nutrition Dr. Franck Mauvais-Jarvis, a leading researcher of sex differences in metabolic diseases.

“One of the most fundamental, unanswered questions in immunology and inflammation is why males and females often exhibit vastly different immune responses,” said James McLachlan. “Females respond more vigorously to infection and vaccination compared to males, but they also exhibit a greater incidence of many autoimmune diseases.”

“We made the surprising discovery that females appear to have evolved an immune system that is distinct and separate from that of males,” McLachlan said. “It is possible that this novel immune system can explain why female immunity is often much more potent across species. To our knowledge, no one has discovered this previously.”

In immunology, it is well accepted that almost all immune responses are initiated in distinct “immune” organs, called lymphoid tissues. These include the lymph nodes, which are familiar to any person who has ever had “swollen glands” when they feel sick. These organs behave like immunological train stations where immune cells converge and meet up to respond to various infections or challenges. For example, when a person’s lung becomes infected with influenza virus, the immune response starts in nearby lymph nodes, not in the lungs.

The team wanted to find out if immune responses could be induced in non-lymphoid tissues without the help of lymphoid tissues. To test this, they infected mice with Salmonella bacteria. Typically, one of the most important immune cells in the body, helper T cells, would be activated in lymph nodes and then accumulate in the liver, a

non-lymphoid organ, after exposure to the bacteria. Activating helper T cells initiates a cascade of events that leads to the most potent and effective immune response possible. However, when they studied mice that lacked all lymphoid tissues, they made a surprising discovery: only half of the mice exhibited a helper T cell response to the bacterial infection in the liver after infection.

“The difference was so stark that we presumed we had accidentally infected only half of the mice,” McLachlan said. “When we examined every distinctive parameter, only one stood out: the biological sex of the mice. Female mice that lacked lymphoid organs responded well to infection — they activated helper T cells that accumulated in the liver — while male mice did not. Our serendipitous finding suggests that females may have evolved an immune system that allows them to respond in extra-lymphoid tissues while males cannot.”

The Keck Foundation grant will allow the team to delve deeper into these initial findings where they will explore what cells of the adaptive immune system are activated in non-lymphoid tissues in male and female mice when lymphoid tissues are absent. Specifically, they will study helper T cells, B cells, which make antibodies, and cytotoxic T cells, which attack and kill viruses and cancers in a multitude of non-lymphoid tissues in response to a variety of challenges including infection and autoimmunity.

“The immune system affects nearly everything in our daily lives, from combatting infections or tumors, causing pain in our joints and healing cuts when we fall to changing the way that our bodies respond to drugs,” McLachlan said. “We have yet to fully comprehend how these things are regulated differently between males and females. Our study goes beyond the current thinking and actually invokes a new immune system in females – the non-lymphoid immune system. The impact of determining a major mechanism that regulates sex-based immunity has the potential to transform what we understand about basic biology, how we approach human health and potentially change the way men and women are treated for immune-mediated diseases.”

Based in Los Angeles, the W. M. Keck Foundation was established in 1954 by the late W. M. Keck, founder of the Superior Oil Company. The Foundation’s grant making is focused primarily on pioneering efforts in the areas of medical, science and engineering research.

The grant is part of Only the Audacious: The campaign for an ever bolder Tulane. Through the collective power of donors, alumni and supporters, the campaign fuels pioneering research, transformative teaching, increased opportunity and diversity, and building an environment for excellence. For more information, visit https://audacious.tulane.edu.

James McLachlan, PhD, (center) will lead the project with researchers John McLachlan, PhD, (left) and Dr. Franck Mauvais-Jarvis (right). The team will study how sex differences shape disparate immune responses in men and women. Photo by Paula Burch-Celentano.