The challenges of developing a vaccine

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Research Promotion

Nearly everyone on the planet will, at some point, have a run in with a species of Chlamydia, an obligate intracellular bacterium that mainly infects epithelial cells.

There is no vaccine against the two common species that cause human disease, but Xi Yang, Canada Research Chair in Infection and Immunology, has recently made some profound discoveries that will impact the development of one.

About 150 million people worldwide suffer from Chlamydiya trachomatis. It breeds under eyelids and causes so much inflammation and scarring that eyelashes turn inwards and begin scratching the cornea; blindness usually results. It is also a sexually transmitted disease that can cause pelvic inflammatory diseases and infertility. C. muridarum is a species of this bacterium used to study the pathogenesis of C. trachomatis infection in animal models.

The second species infecting humans is C. pneumoniae, which causes mild pneumonia and appears to be linked to cardiovascular and neurological diseases. Half of all people in their 20s have been exposed to it. By the time you’re a senior, you’ve likely hosted it at least once.

Yang wants to know how and when a body defends itself from Chlamydia. He uses gene knockout mice to study the cellular and molecular basis of immune responses to the different strains with the goal of developing a vaccine. He’s paying particular attention to the correlation that certain cells have with protection and pathology.

Antibodies, Yang has found, offer little protection. But cell-mediated responses seem to provide better protection. This immune-response uses T cells, which develop in the thymus and come in a variety of types, with each impacting health in different ways—sometimes good, sometimes bad.

“When we talk about immune response, we mostly think of it as having positive effects, but certain immune responses to Chlamydia can be harmful,” Yang said.

What has become of particular interest to him is Natural Killer T cells (NKT). These cells job description straddles innate immunity and adaptive immunity.

When NKT-free knockout mice were infected with C. muridarum they fared better than the normal mice. Conversely, NKT-free knockout mice developed serious symptoms (compared to normal mice) when infected with C. pneumoniae.

This discrepancy happens because NKT cells modulate T cell responses. Different Chlamydia strains cause NKT cells to signal T cells in different ways. The pneumonia strain makes NKT cells activate Th1 cells—a particular type of T cell. The more Th1 a host produces, the better it will battle the bacterium. So here NKT cells are vital.

C. muridarum strain, however, causes the NKT cells to activate cells called Th2. Compared to Th1, they are inferior opponents to Chlamydia. But since NKT cells are being told to produce it, they do, which undermines both Th1 production and the host’s health. But when NKT cells are absent, the Th1 response gets elevated.

“It was surprising to find this,” Yang said. “And it shows that universally activating NKT cells is not always the best way to go about designing drug therapies because you may actually be doing harm in some instances.”