Roles of T cells in disease cures and causes

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Yisong Wan, PhD

T cells aren't as simple as you might think. Some attack infections and keep us healthy. Others allow tumors to grow. Understanding how these cells – the soldiers of our immune systems – develop and function is the goal of Yisong Wan, an immunologist in the UNC School of Medicine.

For his work, he earned a Jefferson-Pilot Fellowship from the UNC School of Medicine. We sat down with Dr. Wan to discuss the role of T cells in cancer and autoimmunity and what his research has revealed.

Why did you decide to become a scientist and why did you decide to study biochemistry and then microbiology and immunology at the University of Colorado?

I'm a curious person. When I was a child, I liked to tinker with complicated systems. Well, the human body is a complicated system. I decided to go into biological science so I could see how the human body works, while at the same time trying to potentially help people in need.

When I was an undergraduate, we compared gene expression in tumor cells to gene expression in healthy cells. This led me to study something called signaling transduction pathways – how cells communicate and respond to each other and the environment. My philosophy is that we have to understand signaling transduction and gene regulation under normal circumstances so we can understand what goes wrong in diseases.

For graduate school, I came to the United States from China because there's no doubt this is the best place to get PhD training, especially for biological research. That was the driving force to come here. And the more I learned in grad school about T cells the more fascinated I became, because any kind of disease has an immune implication.

What is the overarching goal of your research?

My overarching goal is to figure out precisely how T cell function is regulated. Equipped with that knowledge, we could identify targets for therapies against inflammatory diseases and tumors. Until we can really manipulate T cell function or immune cell-function, we cannot sufficiently tip the balance against diseases.

Recently, immune-function-based therapy for tumors has gotten a lot of

attention. That's when we enhance the natural immune response to eliminate cancerous cells – or even precancerous cells – before they cause damage. Two drugs that could be on the market soon are really effective at targeting T cells, which is important because certain T cells play a major role in the onset and development of diseases. And we really need to understand how T cell function is regulated during different stages if we want to target those pathways to create better therapies.

What sorts of roles do T cells play in the development of disease?

Basically, there are subsets of T cells. One subset is conventional T cells – they promote immune function; they help us fight infection. But another subset is called suppressor or regulator T cells. These suppress the immune function; they can prevent autoimmunity and inflammation. We're interested in this because these suppressor T cells are also enriched in tumor tissue. That is, they prevent immune surveillance against a tumor.

Our lab identified a kind of protein that's important for the regulation of FOXp3, a bio-molecule involved in the function of suppressor T cells.

We also study TGF-beta – or transforming growth factor beta – that can be produced by tumor cells. TGF-beta has two functions: it suppresses the activation of the immune response from conventional T cells. At the same time, TGF-beta promotes the function of suppressor T cells. So you can imagine that tumors make a lot of this TGF-beta, which means that tumors can suppress whatever conventional T cells might try to kill it.

Therefore, we're trying to study the TGF-beta signaling pathway with the

overall goal of shutting it down in suppressor T cells to treat disease. If we can block this suppressor T cell-function in tumor tissue, then we would enhance an immune response against the tumor.

You also study the role of specific enzymes called MAPKs. Why are they important?

We found that a MAP kinase is important for the generation, activation, and proliferation of T cells. We need to learn about how it works so we can manipulate it to dampen the function of T cells. And that could be beneficial for autoimmune diseases and inflammation.

This molecule is so important for T cell survival and proliferation. Right now, we and others are studying how this molecule might be important in leukemia. In normal T cells, MAPKs are tightly regulated. In T cell leukemia, something goes wrong with them.

We're thinking that this MAP kinase might be a good drug target to help restore normal T cell-function in leukemia patients.

What's the most rewarding part of your work?

Translating our findings into the clinic would be the most rewarding thing, although our studies haven't reached that stage yet. But for now, the most rewarding part is to have unexpected findings. We perform research based on certain hypotheses and we're happy when our hypotheses are correct. But we often find things that are unexpected. For me, that is the most rewarding part in basic research, because these findings will correct, direct, and further our understanding of how nature works.