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“The immune system must keep a delicate balance between effectively fighting foreign pathogens while minimizing collateral damage. Research in my lab is focused on generating and maintaining regulatory T cells, which prevent biological ‘friendly fire’ by ensuring that the immune system does not overly attack the body’s own tissues.”

The immune system is often described as a kind of military unit, a defense network that guards the body from intruders. Seen in this way, a group of white blood cells called T cells are the frontline soldiers of immune defense. The majority of T cells engage invading pathogens head on, while a smaller subset, called regulatory T cells, limit excessive immune reactions. Autoimmune diseases such as type 1 diabetes, Crohn’s disease, lupus, and rheumatoid arthritis occur when the balance of power between the two breaks down.

Regulatory T cells are controlled by a pivotal gene regulator called Foxp3. In fact, when Foxp3 stops functioning, the body can no longer produce working regulatory T cells. Until now, however, scientists had barely understood what signals lead to Foxp3 expression and how Foxp3 in turn controls regulatory T cells because they knew very little about the actual genes under Foxp3’s purview. Zheng identified several DNA elements in the Foxp3 locus that are directly involved in inducing and maintaining Foxp3 expression and that regulate the development and stability of regulatory T cell lineage. He then focused

on the downstream targets of Foxp3. Using a genome-wide screen, Zheng mapped all genes directly regulated by Foxp3 and identified a small group of transcription factors—proteins that control the expression or “transcription” of genes—that drive the expression of genes involved in regulatory T cell function. One of them, IRF4, stood out as the key player in regulatory T cells’ ability to control type-2 T helper cells, which, if uncontrolled, can activate other immune cells and lead to allergy and asthma.

In the future, Zheng will expand his current studies to determine how regulatory T cells are generated and maintained. His experiments not only will provide a better understanding of regulatory T cells but will suggest new therapeutic approaches for treating a wide range of autoimmune diseases, improving organ transplant survival, and boosting the immune system’s response to tumors.

For more information, please visit salk.edu/faculty/zheng.html



Left to right:
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