“Regulatory T cells play a key role in the immune system to limit excessive immune reactions and prevent autoimmune diseases. Research in my lab is focused on the underlying molecular mechanisms that are involved in regulatory T cell differentiation and their immune suppression function.”

The immune system is a powerful double-edged sword. On one hand, it is armed to fight a wide range of invading foreign pathogens. On the other hand, if left unchecked, it can also attack an organism’s own tissues and cause autoimmune diseases, such as type 1 diabetes, multiple sclerosis and rheumatoid arthritis. There are multiple safeguard mechanisms built into our immune system to prevent an autoimmune reaction. A subset of T cells, named regulatory T cells (Tregs), plays a key role in maintaining immune homeostasis.

Abnormal Treg function has been linked to a number of autoimmune diseases. Recent studies showed that a protein known as Foxp3 is a pivotal regulator for Treg differentiation and function. Mutations of Foxp3 in humans and mice lead to a deficiency of regulatory T cells and fatal autoimmune disease. Zheng’s lab is interested in mapping both the up-stream pathways that turn on Foxp3 expression and the downstream genes that Foxp3 regulates. Zheng and his colleagues identified several genes in the area of DNA that codes for Foxp3 and are found in a number of mammalian species. These genes appear to be involved in controlling and maintaining Foxp3 activity and in regulating the development and stability of regulatory T cell lineage.

Using genomic approaches, the researchers were able to map all Foxp3 downstream target genes. They showed that among all Foxp3 targets, a small group of proteins is implicated in Treg-mediated suppression of different subtypes of autoimmune responses.

Zheng and his team are now further exploring the Foxp3 transcriptional network in regulatory T cells and searching for key molecules involved in the Treg suppression function. Since manipulations of Tregs can either weaken or strengthen the immune response, their findings can potentially open new avenues in the treatment of autoimmune diseases, improve organ transplant survival and enhance anti-tumor immunity.

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

From left to right: Lauren Mack, Sagar Bapat, Christina Chang, Albert Cheng, Ye Zheng, Carmen Zhou, Xudoing Li, Yuqiong Liang, Yang Zhang