GARP makes the difference

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Scientists from the Helmholtz Center for Infection Research in Braunschweig, Germany and the Medical School Hannover, Germany have succeeded in treating immune cells in a way that enables them to inhibit unwanted immune reactions such as organ rejection. Their results have now been published in the current issue of the scientific journal *Journal of Cellular and Molecular Medicine*.

The immune system keeps us healthy: day and night it protects us against invading and harmful pathogens. But this fulltime surveillance can also turn into a problem, for example after an organ transplant. The immune system recognizes the new organ as "foreign" and starts fighting it. In the end, the life-saving transplant will be rejected. Until now, only special drugs have managed to keep the immune system silent and thus inhibit organ rejection.

Theoretically, these drugs are not necessary because the immune system has its own unique "peace makers": regulatory T cells (Tregs), a special group of helper T cells, an important cell type of the immune system. Tregs inhibit immune reactions and are thus of special medical interest. Until now, distinguishing between Tregs and helper T cells has represented a problem for scientists. Now, in co-operation with the Medical School Hannover, researchers from the Helmholtz Centre for Infection Research in Braunschweig have identified a molecular factor that plays an essential role in Treg function. This protein constitutes the key difference between Tregs and helper T cells. Furthermore, the scientists have also generated Tregs from helper T cells that permanently maintained their characteristics.

The key to Tregs is called "GARP". Michael Probst-Kepper is a researcher in a junior research group that is financed by the German Volkswagen foundation, he works at both HZI and MHH. He has now deciphered the special role of the GARP protein. Until now, scientists had only little distinguishing features to aid them in separating T cells that trigger a transplant rejection from those that inhibit such a reaction: they mainly looked at molecular features that both cell types have - the one more, the other less. "It's like looking at two cars that appear to be the same. Except that one is capable of driving while the other doesn't drive anymore. But you cannot see that from the outside," says Michael Probst-Kepper. He deciphered the role of GARP: this new-found factor only exists in Tregs and initiates a complex network of various molecules. "If you don't want a car to drive anymore, you pull the key out and cut the petrol pipe. GARP does the same: it prevents Tregs from stepping on the gas."

The scientist artificially inserted GARP into those T cells that start an immune reaction against transplants. The result was a substantial advance for medicine: the transplant-rejecting T cells developed permanently into Tregs - those cells that inhibit the activation of aggressive T cells and thus prevent organ rejection. Furthermore, the researchers also furnished the counter evidence: Michael Probst-Kepper muted the GARP gene in Tregs. As a result, the Tregs lost their "peace making" characteristics. "The cells could start driving again," he says. "With this study we were able to show the complexity of the Treg system for the first time, developing a powerful tool for medicine to develop new therapies and drugs."

Source: Helmholtz Association of German Research Centres (news : web)