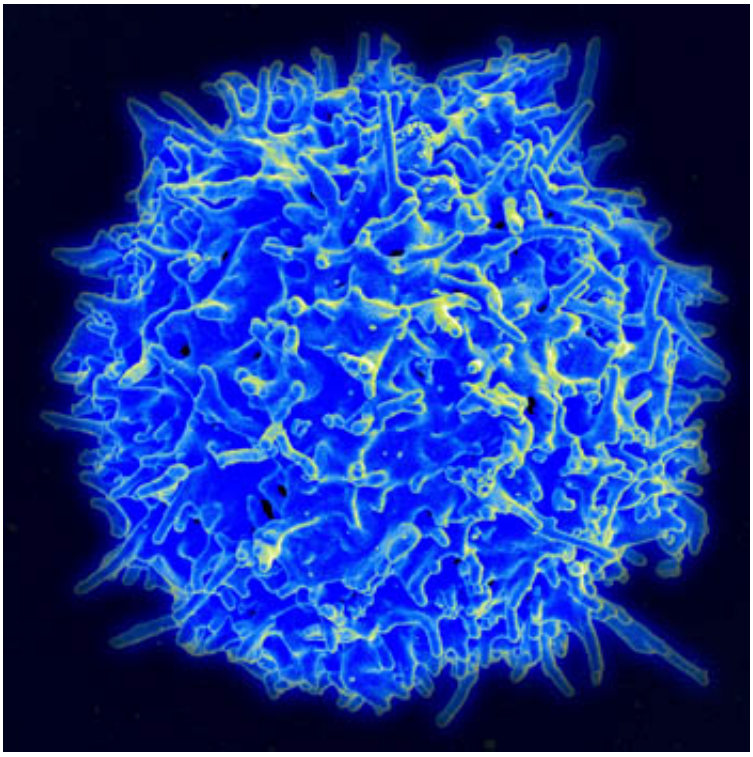
MedicalXpress

A possible way to reenergize T cells exhausted from fighting a tumor

January 28 2019, by Bob Yirka



Scanning electron micrograph of human T lymphocyte or T cell. Credit: NIAID/NIH

An international team of researchers has found a possible way to reenergize T cells exhausted from fighting a cancerous tumor. In their paper published in the journal *Science Immunology*, the group describes their study of the impact of a decrease in enolase 1 on T cells and how bypassing it allowed them to recharge immune cells.

Prior research has shown that one of the reasons the immune system is sometimes unable to fight off a cancerous tumor is because tumor-infiltrating lymphocytes (TILs) lose energy as they attack a tumor. The tired T cells become incapable of putting up a strong fight and the tumor grows bigger. Prior research has also suggested that the reason such cells become tired is because they are outcompeted for glucose by hungry tumor cells. In this new effort, the researchers sought to find a way to overcome this problem so that TILs could continue to fight.

The researchers began by studying T cells, (CD8+ TILs) both in their dormant state and when active. They found that the cells did become exhausted after battling cancer cells for a time. More specifically, they found that T cell exhaustion was caused by a lowered amount of enolase 1, an enzyme found in the glucose metabolic pathway, due to consumption by tumor cells. The end result was a reduction in glucose metabolism and a 10-fold decrease in oxidative phosphorylation

To reenergize the T cells, the researchers chose to bypass enolase 1 altogether and instead fed the T cells pyruvates, which are end products of enzyme activity. The researchers report that doing so resulted in increased glucose metabolism and oxidative phosphorylation, which in turn resulted in improved energy levels in the T cells. Pleased with their findings, the researchers tested a variety of checkpoint inhibitors in live animals (pyruvate was not a viable option for use in test animals). They report a combined cocktail of such inhibitors caused an increase in active T cells and slowed tumor growth.

The next step for the team will be to find suitable inhibitors for use in humans, to test them and if they are successful, to enter clinical trials.

More information: Lelisa F. Gemta et al. Impaired enolase 1 glycolytic activity restrains effector functions of tumor-infiltrating CD8+ T cells, *Science Immunology* (2019). DOI:

10.1126/sciimmunol.aap9520