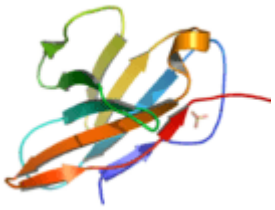
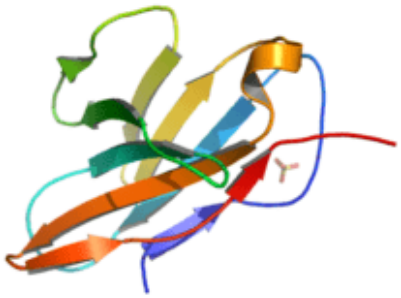
Changes in CD8 T cells during viral infection





Crystal structure of human CD8 molecule (DJ.Leahy, R.Axel, and WA.Hendrickson, Wikimedia Commons)

Researchers from the La Jolla Institute for Allergy and Immunonolgy have found mechanisms that determine the fate of CD8 T cells and how these cells respond differently to acute and chronic viral infections.

Viral infection leads to the immune activation of naïve CD8 T cells. Once the naïve T cells have been activated, they proliferate into effector T cells. The role of these effector cells is to kill the virus-infected cells. They also have a role in killing cancerous cells. Once the virus has been controlled, most of the effector T cells die but some of them remain as memory T cells which can help protect against future

exposure to the same pathogen.

In chronic infections such as HIV and hepatitis, the T cells fail to eliminate the virus and instead begin expressing inhibitory receptors on their surfaces that establish a negative feedback loop. This results in the dampening of the immune response and is known as T cell exhaustion.

Researchers, led by Renata Pereira, wanted to determine the factors which contribute to the different states CD8 T cells can take. The researchers mapped out regulatory elements in naïve, effector, memory as well as exhausted CD8 T cells from mice who either had acute or chronic lymphocytic choriomeningitis virus (LCMV). They did this by using a method known as ATAC-seq which identifies accessible regions of chromatin.

They found that between the different subsets of CD8 T cells there were differences in chromatin accessibility. There were some regions which had shared chromatic accessibility between the different types of cells too. In general, when naïve CD8 T cells were activated and turned into effector cells, there were big changes in certain regions of chromatin. However, effector, memory and exhausted T cells had similar chromatin structure.

The researchers found that the nuclear factor of activated T cells (NFAT) protein was involved in CD8 T cell exhaustion as previously shown and found a novel NFAT-induced transcription factor that is also implicated in CD8 T cell exhaustion.

This study has extensively looked at the differences between the different CD8 T cells subsets and what mechanisms lead to CD8 T cell exhaustion. Knowledge of how T cells get exhausted may aid in the understanding of how to reverse or prevent the process in chronic diseases.

Journal article: Scott-Browne et al., 2016. Dynamic Changes in Chromatin Accessibility Occur in CD8+ T Cells Responding to

Viral Infection. *Immunity*

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