Process controlling T cell growth and production identified

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Identifying one of the processes that plays a role in naďve and memory T-cells' growth and production could one day lead to better vaccines and possibly more effective cancer immunotherapy, said researchers at Baylor College of Medicine and Texas Children's Hospital in a report that appears in the current edition of *Nature Immunology*.

In previous work, Dr. Daniel Lacorazza, assistant professor of pathology at BCM, along with his research team, identified a transcription factor, ELF4, which regulates blood stem cells. A transcription factor is a protein that regulates how genes are translated into a form that leads to the making of the proteins associated with them.

"We knew ELF4 played a role in maintaining T cells," said Lacorazza, who is the principal investigator of the current study. "What we discovered was that ELF4 activates an inhibitor that leads to cell arrest, stopping naive T cells from proliferation."

A population of naďve CD8 T-cell is always circulating in the body and maintained at a constant level. Memory T cells are created when naďve CD8 T cells are activated to fight intracellular pathogens such as viruses or bacteria. The fight against infections prompts creation of memory T cells that then "remember" antigens or proteins found on cells infected with viruses or bacteria. In the future when same infections arise, memory T-cell enhances the body's ability to fight them.

Lacorazza and his research team focused on how ELF4 affected the

process of inhibiting proliferation of CD8 T cells. Using mice generated to lack ELF4, researchers found that CD8 T-cells grew over time and acquired a "memory phenotype" without being exposed to any type of infections. At the same time, they determined that expression of the tumor suppressor gene called KLF4 was reduced in these mice.

"We discovered that ELF4 directly activates the tumor suppressor KLF4, which signals cell cycle arrest in naďve CD8 T cells," Lacorazza said. "This inhibitory process is important to T cells because it stops them from proliferating out of control." Cell cycle arrest means the cells do not go through the normal events of their life cycles: growth, replication and division. The description of cell intrinsic regulation of quiescence in normal T cells will provide insights on the pathobiology of lymphoid malignancies.

The researchers then immunized mice deficient for ELF4 to test their immune response. These mice had a larger memory T cell response, indicating that the absence of ELF4 eliminated control over the proliferation of CD8 T cells.

"If we can control ELF4 activation during vaccination, we can enhance long-term immune response, making a vaccine more effective," Lacorazza said.

"We could enhance in vitro T cell activation of T cells extracted from patients to heighten immune response", said Lacorazza. "In addition, a future line of study is to determine whether deletion of KLF4 expands pre-leukemic clones leading to overt leukemia in pediatric patients".

Lacorazza said these are still hypotheses, but understanding the process that controls T cell proliferation will help in future research.

Source: Baylor College of Medicine (news : web)