Space station experiment will probe failure of immune system in space

April 1 2010

(PhysOrg.com) -- In April 2010, personnel aboard the International Space Station plan to carry out an experiment designed by a San Francisco VA Medical Center researcher that will investigate why the immune system's T cells stop working in the absence of gravity. The experiment has implications for understanding the body's ability to mount an immune response on earth, as well.

On earth, T cells - white blood cells that are essential for proper immune function - stop functioning in people with untreated HIV/AIDS, as well as in some elderly people, leading to the development of potentially fatal opportunistic infections.

The experiment aboard the ISS is meant to shed light on the genetic mechanisms behind T cell shutdown, according to principal investigator Millie Hughes-Fulford, PhD, director of the Laboratory for Cell Growth at SFVAMC and an astronaut who flew aboard the space shuttle in 1991.

"From the beginning of the U.S. Apollo moon program, we've known that about half of our astronauts develop suppressed immune systems, either during flight or shortly afterwards, and we have since learned that non-functioning T cells are at least partly responsible," says Hughes-Fulford, who is also a professor of medicine at the University of California, San Francisco.

"If we can get to the root cause, we can potentially help older people, people with HIV/AIDS, and anyone else who is immunocompromised

here on earth," she says. "We will also overcome a serious obstacle to long-term space exploration. A runaway infection among the crew due to compromised immune systems would mean disaster for a multi-year Mars mission, for example."

Normally, Hughes-Fulford explains, the immune system responds within four hours of exposure to an infectious agent by expressing certain genes. This gene expression, in turn, initiates a series of molecular and cellular reactions that ultimately result in the activation of T cells and other white blood cells, which then migrate to the site of the infection.

In previous experiments with human cell cultures aboard the ISS, Hughes-Fulford found that a group of 47 genes associated with T-cell activation are not expressed in the absence of gravity. "Now we're taking this research one step further by investigating this phenomenon in live mice on the space station, outside of earth's gravity field," she says. "We hope this will allow us to pare down our list of non-expressing genes to a much smaller number of genes, and give us a better handle on what's happening in humans."

Hughes-Fulford notes that even though mice have far fewer genes in total than humans, mouse genetics and human genetics have proven to be "very much the same" in terms of immune response.

Shuttle flight STS-131, currently scheduled for lift off on April 5, 2010, will deliver two self-contained experimental rodent habitats called Animal Enclosure Modules to the space station. Each module will contain one half of Hughes-Fulford's two-part experiment.

In part one, mice with so-called nad′ve T cells - cells that have not previously been exposed to an infectious agent - will live aboard the ISS without gravity, while a matched group of control mice live on earth under normal gravity. After the experimental mice return to earth aboard

the shuttle, both groups of mice will be exposed to OVA, a protein found in egg white that functions as a model of infection. The expectation is that the T cells in the experimental mice will not activate, while the T cells in the control mice will. Hughes-Fulford and the rest of her team will compare gene scans for the two groups of mice to see which genes do not express in the experimental animals.

Part two of the experiment will use orbital experimental mice and earth-bound control mice to compare the reactions of memory T cells, which are T cells that have already been exposed to a disease agent - or, in this case, OVA - when they are exposed to OVA a second time. As in part one, the expectation is that the memory T cells in the orbital mice will not activate. Comparative gene scans will reveal which genes do not express in those mice.

Hughes-Fulford explains that memory T cells react much more quickly and effectively than nad′ve T cells in the presence of the disease agent to which they have been exposed, which is what gives vaccinations their protective effect. “We’re doing this experiment because there is evidence that memory T cells don’t work in microgravity,” she says. “Apparently, some astronauts are not protected against diseases they have been inoculated for. And we want to find out why.”

Hughes-Fulford, who was a payload specialist aboard shuttle flight STS-40 in 1991, says the ultimate goal of her experiment is to point the way toward gene therapy for people with non-functioning immune systems. “If we can find which molecules are regulating the expression of these key genes, we could theoretically take those molecules, put them into cells, and turn on genes that are not expressing.”

She cautions that such therapy is “many, many years away.” At this stage, “We’re just laying the groundwork. At the same, time, we’re uncovering fundamental mechanisms that control the immune system,

and what happens to those mechanisms when you remove them from the gravity field in which they evolved."

Provided by University of California, San Francisco