Monitoring how T cells respond to HIV

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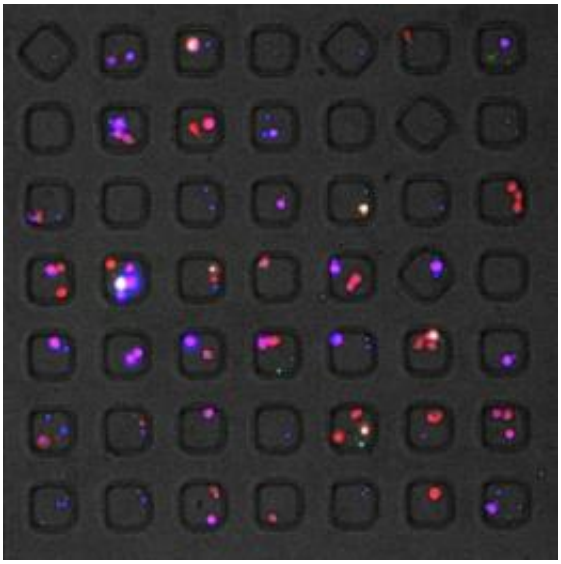

Inside these squares, single T cells taken from HIV-infected patients interact with infected cells. This technology, developed by MIT chemical engineers, offers the first way to study how effectively individual T cells respond to HIV-infected cells. Image: Navin Varadarajan

One of the obstacles to developing an effective AIDS vaccine is the difficulty in measuring how well a potential vaccine primes the body to defend itself against HIV.

Ideally, scientists would like their vaccines to provoke T cells, a critical component of the immune response, to recognize and kill HIV-infected cells. Unfortunately, there is no fast and easy way to monitor whether T cells are actually doing that. Instead, researchers measure the amount of

a protein called interferon gamma that T cells secrete when they encounter an infected cell. Studies have shown, however, that this "surrogate" measurement doesn't necessarily predict a T cell's ability to kill HIV-infected cells.

In an advance that could overcome that obstacle, a team of researchers at MIT has developed a new technology that can measure multiple aspects of individual T cells' responses to HIV-infected cells, including their ability to kill them. The technology could make it easier to monitor and design vaccines against HIV, says J. Christopher Love, the Latham Family Career Development Associate Professor of Chemical Engineering and leader of the research team.

The technology, described in a paper published in the Oct. 3 online edition of the Journal of Clinical Investigation, involves two steps. First, the researchers place single T cells taken from HIV-infected patients into tiny wells on a plate, where they are exposed to HIV-infected cells. The researchers can detect whether the T cells kill the infected cells with probes that glow when the dying cells' nuclei become compromised.

Watch T cells attack HIV-infected cells:

Next, the researchers measure interferon gamma production with a microengraving technique they developed in 2008. Secretions from each cell are imprinted on a glass slide, which can then be tested for the presence of specific proteins. Because each cell has its own "address" on the slide, the secretions can be traced back to individual cells, and their interferon gamma production can be correlated directly to their cell-killing ability.

The same technology could be adapted to measure cells' output of any other immune system protein.

In this study, the researchers found that while the percentage of T cells that secrete interferon gamma is similar to the percentage of those that kill infected cells, the populations are not identical. In future studies, the researchers hope to find markers that do correlate with cell-killing ability, making it easier to evaluate a potential vaccine's effectiveness.

"Now that we have a tool to look directly at a variety of different functional activities, you can go in and start to evaluate other markers that may be better predictors of killing. Those then become what you would want to monitor in vaccine trials," says Love, who is also a member of the Ragon Institute of MGH, MIT and Harvard and the David H. Koch Institute for Integrative Cancer Research at MIT.

"The appeal of this technology is that it can help us understand more about what's going on in single cells," says Alan Landay, professor of immunology and microbiology at Rush Medical College. "It helps us rethink what we understand about immunology and immune function."

More research will be needed to develop the technology to the point where it can be used routinely in vaccine trials for large-scale studies of patient samples.

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