“Shock and Kill” HIV Cure Method May Be Too Anemic to Work

A recent study found that agents used to wake up resting HIV-infected cells probably work only on 5 percent of such cells.

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The method known as shock and kill that has been a major avenue in the HIV cure research field may be far too inefficient to yield significant success in eradicating the virus from the body.

Standard antiretroviral (ARV) treatment for HIV does not cure the virus at least in part because of the stubborn presence of the latent reservoir, an amorphous collection of immune cells infected with the virus that are in a resting state, meaning they are not replicating and producing new copies of the virus. Because ARV treatment works only on active HIV-infected cells, latent cells stay under its radar.

Seeking to drain the viral reservoir, researchers have been experimenting with various latency reversal agents (LRAs) to prompt latent cells to wake up again (shock) so that they can be identified as infected and ultimately destroyed (kill). Thus far, LRAs have shown little success.

Publishing their findings in the journal eLife, researchers developed a virus called HIVGKO that encoded two different types of fluorescent proteins, known as GFP and mKO2, into the genomes of cells. These proteins allowed the researchers to determine 1) whether a cell is infected; and 2) whether an HIV-infected cell is in a latent or active state.

The investigators drew CD4 cells from HIV-positive individuals and tested three LRAs on those cells: the HDAC inhibitor panobinostat, the BRD4 inhibitor JQ1, and the PCK activator bryostatin-1. Thanks to the encoding of the fluorescent proteins in such cells, the researchers were able to see that the LRAs prompted less than 5 percent of the latent HIV-infected cells to begin replicating.

Next, the study authors conducted genetic sequencing analyses of the cells and determined that the virus integrates its genetic material into different points in the cell genome among those cells that responded to the LRAs compared with the cells that did not respond to those agents.

“Together, these results indicate that while shock and kill might be helpful in reactivating and possibly eliminating a small subset of highly reactivatable latent HIV genomes, other approaches will be necessary to control or eliminate the less readily reactivatable population identified both

here and in patients," the study's senior author, Eric Verdin, MD, president and CEO of the Buck Institute for Research on Aging in Northern California, said in a press release.

Verdin suggested that perhaps a more effective strategy to yield at least a functional cure for HIV would be to "block and lock" HIV by promoting infected cells to fall into a protracted state of latency.

To read a press release about the study, click here.

To read the study abstract, click here.

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