Gold Drug Shows HIV Eradication Potential

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Using a compound containing gold to treat six monkeys infected with an HIV-like virus, a team of researchers has been able to shrink the reservoir of virus-infected CD4 cells impervious to modern-day antiretroviral (ARV) drugs. These early stage results, to be published in a forthcoming issue of AIDS, contribute to a growing body of research exploring the possibility of curing HIV, this time using a drug already approved for the treatment of rheumatoid arthritis: Ridaura (auranofin).

Current antiretroviral (ARV) therapy is quite potent. When it works well, it completely shuts down HIV reproduction. Unfortunately, a small reservoir of long-lived HIV-infected cells remains in the body, and when people stop taking their HIV medication, the virus quickly reseeds newly produced CD4 cells and resumes replication.

Traditional ARVs can't target HIV genetic material (HIV DNA) inside this reservoir of infected cells, notably long-lived "memory" CD4 cells. This is because the cells are inactive; most ARVs only work in cells that are actively reproducing. Researchers are now exploring compounds that wake up these resting cells to help purge their HIV DNA payload or, more controversially, that kill the cells harboring dormant virus.

The rheumatoid arthritis drug Ridaura falls into the second category. According to the paper published by Andrea Savarino, MD, of the Istituto Superiore di Sanità in Rome and his colleagues, Ridaura works by killing off memory CD4 cells while also shortening the lifespan of new CD4 cells produced by the immune system. In effect, Ridaura shows HIV eradication potential on two levels: It can help wipe out the existing reservoir while at the same time prevent new long-lived reservoirs from developing.

To explore Ridaura's potential, Savarino's group conducted a study involving six macaques infected with simian immunodeficiency virus (SIV), HIV's primate equivalent. After maintaining undetectable SIV levels in the macaques for at least eight weeks using a typical ARV regimen, the researchers added twice-daily Ridaura treatment.

According to the researchers' report, the addition of Ridaura significantly shorted both the lifespan and size of the long-lived CD4 cells. What's more, there was no significant effect on the size of the new CD4 cell population and the monkeys' CD4 counts remained stable throughout treatment. Marked reductions in SIV DNA levels were also documented.

When ARV therapy was stopped in the six monkeys, SIV viral loads rebounded, but to levels that were significantly lower than those seen before ARV treatment was initiated. Conversely, in six

monkeys who underwent therapy with ARVs alone, viral loads rebounded to pre-treatment levels in less than two weeks.

“Our [Ridaura-treated] monkeys showed, upon suspension of all therapies, an improved capacity to keep the infection under control; one of them maintained a low viral load and high CD4 counts for one year,” Savarino is quoted as saying in a press release.

The researchers have decided to wait before moving Ridaura into trials involving people living with HIV. “We prefer not to involve people in a trial of the drug immediately,” said Enrico Garaci, MD, president of the Italian Institute of Health, and coauthor of the study. “That’s because in this phase the trial could only be a proof-of-concept study, and we have already this proof in monkeys. We prefer to put all our effort in the intensification of the attack on the virus reservoir in monkeys by using a combined approach.

“This will also allow,” he added, “a more thorough evaluation of the safety of the approach.”

The authors also caution against using Ridaura outside of clinical trial settings. “[T]he side effects of this approach in the presence of HIV are as yet largely unexplored,” Savarino notes. “I strongly recommend that people living with HIV/AIDS do not buy the drug from uncontrolled sources such as eBay and start self-treatment outside highly medicalized settings.”

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