

July 22, 2010

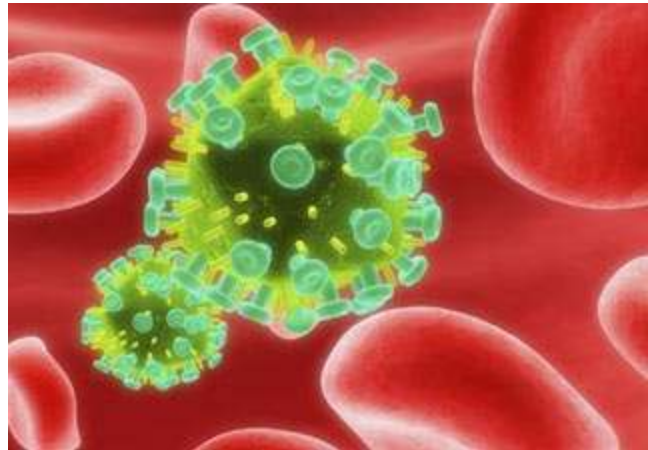
IAC: HIV Cure No Longer a 'Taboo'

Michael Smith, North American Correspondent, MedPage Today

VIENNA -- For years, HIV researchers have shied away from the whole notion of a cure largely because evidence showed the virus can persist even under intensive treatment.

But now, they are -- tentatively -- expressing a renewed interest in the idea.

That interest is sparked by clinical data showing [an apparent cure in a single case](#) and some technical advances that make it easier to track very low levels of HIV infection, experts said here at the International AIDS Conference.



But progress is hampered by lack of money for research in the field and by what one prominent researcher called "fundamental gaps" in the understanding of how HIV and the human body interact.

Nonetheless, researchers gathered here last week -- before the start of the AIDS conference -- for a two-day workshop called "Towards a Cure." Led by Nobel laureate Françoise Barré-Sinoussi, PhD, the workshop considered a host of questions, including:

- What are the clinical implications of HIV persistence under treatment?
- Where and how does HIV hide from the immune system and anti-HIV drugs?
- How does HIV persist?
- What are potential therapeutic interventions and how can they be evaluated?

There has been some study of those issues "but we can certainly do better," according to Barré-Sinoussi, who was one of the researchers involved in identifying the human immunodeficiency virus.

She noted that vaccine research -- which has been much in [the news here](#) -- is supported by international groups that coordinate the science and lobby for money. "There is no equivalent for research into remission or functional cure," Barré-Sinoussi said.

One thing that is clear is that current therapies can only control the virus, not eradicate it, according to Maureen Goodenow, PhD, of the University of Florida. That's because the virus persists -- even when it is undetectable in plasma -- in "diverse" cells and physical locations.

These so-called "reservoirs" consist of cells that harbor the virus, but in which it is not actively replicating. One important question is whether it is even possible for current therapies to eradicate any of the reservoirs, Goodenow said.

So far, the evidence is weighted against that possibility, according to Frank Maldarelli, MD, PhD, of the National Cancer Institute. "All the drugs we have now available only affect active replication," he told reporters.

Controlling replication is enough to keep a patient alive and well, but won't have any effect on cells in which the virus is lying dormant, he said. So it's critical to know if the virus can piggyback on cells without replication, he said, since there's evidence that simple growth of such cells is enough to allow the virus to spread, even when it is not actively replicating.

Researchers have tried to "intensify" therapy -- adding drugs to a successful treatment regimen in an attempt to completely eliminate all traces of HIV -- but without success, Maldarelli said. He told attendees at the workshop that even in such circumstances, low levels of HIV viremia persist.

One piece of data that has galvanized researchers is the recent case of a bone marrow transplant that appears to have cured a man of HIV.

The lead researcher in that case, Gero Hütter, MD, of Berlin's Charité-Medical University, reported at the workshop that the patient remains well and off antiretroviral drugs two years after the transplant, Maldarelli said.

The apparent cure was possible because the man's HIV was CCR5-tropic -- it preferentially used the CCR5 receptor to enter target cells -- and the donor had a mutation that left his immune cells without that receptor.

The patient's virus may still be present, Maldarelli said, but it is apparently not replicating.

Researchers are now trying to see if the apparent cure can be duplicated therapeutically, perhaps through [gene transfer technology](#).

That's one of the "breakthroughs and changes in the science" that have renewed interest in searching for a cure, according to Carl Dieffenbach, PhD, who directs the AIDS division at the National Institute of Allergy and Infectious Diseases.

Among others, Dieffenbach said, are the invention of highly sensitive tests that can detect single copies of HIV RNA, making it possible for the first time to address the question of how the virus persists, and the development of safe vectors for gene transfer.

He and others would also like to see the development of small molecules that would target HIV-infected cells, he said.

Because of those breakthroughs, the idea of curing HIV infection is "less of a taboo" than it once was, Dieffenbach said.

But Dieffenbach conceded that even at the NIAID, which has perhaps the most money of any HIV research program in the world, the search for a cure is not getting a huge share of available resources. He and the leaders of two major European research organizations said their total budget for such research is no more than about \$100 million.

More than half of that is from the NIAID, Dieffenbach said.

But that's a tiny fraction of the \$1.54 billion the institute spent on HIV and AIDS research in 2009, according to activist Kate Krauss, of the San Francisco-based AIDS Policy Project. She said cure research amounts to about 3% of the budget for HIV and AIDS.

Cure research "is astonishingly underfunded," Krauss said