GLADSTONE INSTITUTES

TIPs: Therapeutic Interfering Particles

A New Paradigm for HIV Treatment and Prevention

SCIENCE OVERCOMING DISEASE

Therapeutic Interfering Particles, or TIPs, could represent a fundamentally new approach to stopping HIV and other infectious diseases. The theory behind TIPs is this: Since viruses are dynamic—that is, they mutate and spread—our approach to controlling them must also be dynamic. But until now our approach has been static—we develop drugs that do not mutate or spread. As a result, HIV continues to evolve and outwit us, rendering our treatment strategies limited at best—and, at worst, ineffective.

TIPS, however, are designed to both spread and evolve alongside the viruses they attack, including HIV. As a result, TIPs have the potential to dramatically reduce the lethality of HIV and slow its spread, or stop it completely, on a global scale. There is more research to be done, but the promise of TIPs is being diligently pursed as a part of Gladstone's broader goals to better prevent and treat—and ultimately cure—HIV/AIDS.

What are TIPs?

TIPs are genetically engineered HIV particles that have been stripped of all their harmful material. What's left is an empty "outer envelope" that has no infectious qualities but is able to piggyback onto HIV, allowing it evolve to and spread with HIV. This empty envelope (or therapeutic particle) interferes with HIV by disrupting the way the virus replicates, thereby eliminating its power to destroy cells.

How do TIPs work?

To understand TIPs, we must understand what makes HIV so effective and so lethal. And that is, HIV inserts itself into the very DNA of our cells—specifically, the white blood cells in our immune system. In doing so, it turns these cells into mini "HIV factories" that busily produce more and more HIV particles. Eventually, the cells die, releasing HIV into the bloodstream where the virus infects and kills yet more cells. This process repeats millions of times, eventually destroying our immune system.

TIPs beat HIV at its own strategy by hijacking the virus. In other words, once inside a cell, TIPs piggyback onto HIV and transform the cell from an "HIV factory" into a "TIPs factory." Instead of producing HIV, the cell produces more and more interfering particles. Like HIV, these TIPs then spread into other HIV-infected cells, hijacking those factories.

And because TIPs are essentially empty envelopes, they reproduce and spread more quickly than HIV, which is laden with genetic material. Think of a race car zipping alongside an overloaded 18-wheeler truck. Eventually, the roadster (TIPs) overtakes the more sizable HIV and speeds ahead, producing more and more TIPs—and causing HIV production to plummet.

How do TIPs help someone who already has HIV?

Because TIPs interrupt the way HIV reproduces, the amount of HIV virus in an individual person—that is, their viral load—drops considerably. This allows the immune system to remain robust, helping the person stay strong and healthy. This also makes it much more difficult for the virus to spread from person to person, because lower viral loads mean lower transmission rates.

So TIPs serve two absolutely essential functions: they reduce the amount of HIV in an infected individual and make it harder transmit the virus to others.

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How could TIPs stop HIV on a global scale?

Remember, TIPs piggyback onto HIV and spread with it. So if an HIV-infected person with TIPs spreads the virus, he or she is also spreading a treatment. In this way, TIPs can spread throughout a population and gradually reduce both the prevalence and virulence of HIV.

Gladstone researchers expect that this approach can reduce the global spread of HIV—including the world's hardest hit areas, such as sub-Saharan Africa, where HIV infection rates range from 15–30% of the population. For any strategy to work on this scale, it must overcome what epidemiologists call the "universal barriers" to stopping infectious diseases:

- **Access**—getting the drugs and vaccines to the target populations;
- **Adherence**—getting people to stick to the regimen and take their meds;
- **Resistance**—treating viruses that mutate and can become treatment-resistant; and
- **"Superspreaders"**—reaching small groups of individuals who engage in behaviors that are likely to transmit the virus and have a disproportionate impact on the spread of the disease.

Unlike current treatment-and-prevention strategies—including lifesaving antiretroviral medications—TIPs leap over each of these barriers:

- **Access**—TIPs are a single-dose treatment that spread the same way HIV spreads.
- **Adherence**—TIPs' one-time exposure eliminates the need to adhere to lifelong drug-treatment regimens.
- **Resistance**—TIPs piggyback onto HIV and evolve with it, undermining HIV's ability to become treatment-resistant.
- **"Superspreaders"**—Because TIPs spread alongside HIV (i.e., by those sharing needles and/or having unprotected sex with someone who has HIV), they will reach this otherwise difficult-to-identify and treat population, thereby dramatically reducing HIV prevalence.

What is the potential impact of TIPs?

Gladstone scientists project that if just 1% of the population in sub-Saharan Africa were to receive TIPs, the prevalence of HIV in 10 years would drop to less than 10% of the population. In 50 years, the prevalence rate would drop to less than 2% of the population. In short, these game-changing results are vast improvements over even the most optimistic projections for reducing HIV prevalence through antiretroviral medications or an effective vaccine.

What is next for TIPs at Gladstone?

Our researchers are poised to take TIPs from the petri dish, where it so successfully interrupts HIV, into lab animals, the essential next-step in researching both its safety and efficacy. Gladstone investigators are actively seeking funding to advance this research as quickly as possible.

We invite you to get in touch with Gladstone to discuss how you can help support our TIPs research, as part of our goal to improve HIV/AIDS treatment and prevention—and to ultimately cure this disease.

Contact Leor Weinberger, PhD, Director and Bowes Distinguished Professor, at leor.weinberger@gladstone.ucsf.edu.

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