**Unconventional idea for antiviral contraceptive gel wins Gates Foundation grant**

November 9 2010

A vaginal gel that affords both contraception and HIV protection using nanoparticles that carry bee venom is one of the bold, unconventional ideas that won a 2010 Grand Challenges Explorations grant from the Bill & Melinda Gates Foundation.

Grand Challenges Explorations is a Gates Foundation initiative to foster innovative projects in areas where unorthodox thinking is most urgently needed. Recipients receive grants to explore creative solutions to global health issues.

Sam Wickline, MD, professor of medicine, of cell biology and physiology, of physics and of biomedical engineering at Washington University School of Medicine in St. Louis is one of 65 scientists selected in November to participate in the grant program.

Wickline proposes to develop a contraceptive, antiviral gel containing trillions of nanoparticles that will target both HIV and sperm and deliver a bee venom toxin that will incapacitate them.

"Sperm and HIV (the human immunodeficiency virus that can lead to acquired immune deficiency syndrome, or AIDS) are remarkably similar in their natural mechanism of genetic transmission," Wickline says. "Both need to fuse with their target cell in order to deliver their genetic payloads - DNA in the case of sperm, and RNA in the case of HIV."
Wickline's plan is to use the very means by which sperm and HIV operate to destroy them.

"The idea is to trick each to fuse with a synthetic Trojan Horse - a nanoparticle that will overwhelm sperm and HIV in numbers and in destructive power."

It is an unconventional and creative plan for sure, but it is grounded in proven technologies and research-based knowledge. If the idea shows promise, the initial seed money grant can lead to additional funding.

The Trojan Horse or decoy that will be used to attract the sperm and HIV is a lipid nanoparticle created by Wickline and colleague Gregory Lanza, MD, PhD, professor of medicine, that has already been proven safe for clinical use. Given the size of nanoparticles - spheres of around six millionths of an inch in diameter - "Trojan Pony" may be a better metaphor.

A toxin derived from the substance bees insert into their victims when they sting is the agent that will destroy the sperm and HIV. The toxin, called melittin, comprises more than half of the dry weight of the venom of the honeybee Apis mellifera.

The nanoparticles will carry a synthetic version of the toxin melittin to the targets.

"Cells readily take in melittin," Wickline says. "But once it gets in, it pokes holes in cell membranes destroy the cells."

A local biotech startup company, Kereos Inc., is testing melittin as an anti-cancer agent.

Since melittin can annihilate almost any cell, the trick is to target the
melittin to the specific cells intended for destruction (cancer, sperm, HIV) without causing collateral damage to other cells in the body.

Wickline and colleague Paul Schlesinger, MD, PhD, associate professor of cell biology and physiology, attacked that problem two years ago when they developed "nanobees," the name coined for nanoparticles that sequester melittin so that it neither harms healthy tissue nor is degraded before it reaches the intended target.

Wickline and his colleagues have also developed the ability to add agents to the nanobees to cause them to home in on specific target cells. Although nanoparticles are a few thousand times smaller than the dot above an "i," each can carry hundreds of thousands of molecules on its surface.

"We have the ability to attach and swap in various specific targeting molecules to nanoparticles that will bind with receptors on the surface of selected cells," Wickline says. "This gives the particles the ability to home in on specific target cells."

To get the nanobees to hook up with sperm and offload their lethal cargo, Wickline intends to target a well-known "docking site" on the sperm cap. Sperm cells, which are roughly 160 times bigger than the 250-nanometer particles, will be swarmed with nanobees.

HIV virions (individual HIV particles), which are less than half the size of the nanoparticle, will be captured and destroyed with special molecules attached to the nanobees that bind to complementary molecules on the virion that play a role in initiating HIV fusion to cells.

Although these nanoparticles have been proven safe in the body, they are too large to move outside the vaginal vault, and will remain on site in surveillance for sperm and HIV until washed out by the body's natural
fluids.

"We believe this can succeed because both sperm and HIV are built to target, fuse and discharge their cargo," Wickline says. "Our nanoparticles are similarly built to target, fuse and deliver their cargo. These attributes will enable a process of mutual assured destruction in a sequestered biological environment."

If successful, Wickline's idea could have enormous benefits for women, particularly in sub-Saharan Africa, a region that accounted for 68 percent of new HIV infections among adults in 2008. Women and girls in this area continue to be affected disproportionately - in some countries up to four times higher than males.

Sub-Saharan Africa also has the world's highest fertility rate -- 5.6 children per woman and twice the world average. The region's population is expected to increase to 1.6 billion people by 2050 unless women are empowered to prevent unwanted pregnancies.

A contributing factor to the vulnerability of women to both HIV and unintended pregnancy in sub-Saharan Africa is fear of violence from male partners if condom use is suggested. This technology could enable women to protect themselves without the need to seek approval from male partners.

While bringing the technology forward for clinical use by women would require many months of testing, the concept is supported by a recent trial of vaginal gel-based anti-HIV drugs in South African women. That study found that gel based delivery systems can substantially decrease the spread of AIDS with no harmful side effects.

Wickline has assembled a multidisciplinary team of collaborators to carry out the proof of concept activities that the grant funds. Kelle
Moley, MD, professor of obstetrics and gynecology, will contribute expertise in reproductive biology; Lee Ratner, MD, PhD, professor of medicine, of molecular microbiology and of pathology and immunology, will serve as the authority on HIV and human retrovirus infections; Schlesinger will provide expertise in membrane biophysics; and Josh Hood, MD, PhD, instructor in medicine, providing expertise in immunological targeting.

Provided by Washington University in St. Louis

Citation: Unconventional idea for antiviral contraceptive gel wins Gates Foundation grant (2010, November 9) retrieved 7 October 2023 from https://medicalxpress.com/news/2010-11-unconventional-idea-antiviral-contraceptive-gel.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.