



## Methods of Reducing HIV Transmission/Infection and Compositions Effective for Reducing HIV Transmission and Infection

*A researcher at Howard University has identified the presence of multiple drug targets (ABC drug efflux transporters) on the primary human CD4+ T-cells freshly isolated from human donor blood and found that modulation/inhibition of the drug targets is leading to significant increases in the HIV drug (Tenofovir) absorption by T-cells and increased intracellular concentrations.*

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### Inventors

Pradeep K. Karla, PhD.

### Benefits / Features

- Novel therapeutic target.
- Increasing therapeutic efficacy of HIV drugs avoiding the extensive side effect profile of these drugs.
- Pre-exposure/post-exposure prophylaxis.

### Potential Commercial Applications

- Vaginal Mucosal Microbiocidal gel.

### Stage of Development

Patent application filed

### Status

Seeking research collaboration & licensing partners

### Background

The HIV virus can be transmitted to uninfected human subjects via unprotected sex, pregnancy, childbirth, breast milk, IV drug use, occupational risk, blood transfusions, and organ transplant. However, it is widely acknowledged that sexual transmission accounts for  $\geq 90\%$  of new HIV infections. Further, it is widely accepted by the scientific community that human CD4+ T-cells are the initial sites of HIV attachment and infection in healthy humans. As the virus enters the host; the gp120 viral envelope protein binds to the CD4+ receptor site of the T-cells and injects a combination of viral genetic material and enzymes into the T-cells. After reverse transcription of the viral genetic material (RNA) into viral DNA, the viral DNA integrates with the host T-cell genetic material. Current HIV drugs target the key components of HIV infection, such as: 1. attachment of the HIV virus to T-cells 2. reverse transcription of HIV genetic material 3. cleaving of polyproteins by HIV protease and 4. integration of viral genetic material into host cell DNA by HIV integrase. Except for the class of HIV drugs preventing the attachment of the HIV virus to T-cells, which act at an extracellular level, **all other major classes of HIV drugs exert the therapeutic action at an intracellular level.** Dr. Karla discovered the presence of multiple potent ABC drug efflux transporters on the primary human CD4+ T-cells. He observed that the transporters are leading to significant decreases in intracellular HIV drug concentrations of T-cells, contributing to the possible failure of HIV prophylactic therapy. Further, surprisingly, Dr. Karla observed a  $\geq 2$  fold increase in intracellular HIV drug (tenofovir) accumulation in the CD4+ T-cells isolated from fresh human blood of donors. The discovery of these new barriers may explain the prime reason for contradictory success/failure profiles of recent clinical trials with vaginal gels containing HIV drug (tenofovir). Further, the presence of new drug barriers on prime targets of HIV infection (**CD4+ T-cells**) and substantial improvement in HIV drug delivery with modulation of the barriers can have a significant impact towards the development of a successful HIV prophylactic therapy (a vaginal gel, etc.), for achieving a significant reduction (or) a total prevention of sexual transmission of HIV.

### Description of Technology

Never before has anyone identified ABC drug efflux transporters on the surface of human CD4+ T-cells. Through the use of fresh blood human cell isolate from human donors, Dr. Karla has identified these transporters to be a novel therapeutic target for the discovery of a new HIV drug class. This new drug class would consist of a drug efflux transporter inhibitor along with a NRTI, NNRTI, or PI. The clinical indication of this new class would

be in HIV pre/post-exposure prophylaxis, treatment of HIV, prevention or decreasing HIV transmission and/or infection. These drug efflux transporters are responsible for decreasing the intracellular concentration of the HIV drug. Through the use of drug efflux transporter inhibitors, intracellular HIV drug concentrations increased significantly. Eleven different drug efflux transporters have been identified. Drug efflux transporter inhibitors specific for the transporters are used at different concentrations with the use of tenofovir, a NRTI, and via functional drug screening analysis, Dr. Karla has shown a  $\geq$  two-fold increase in intracellular drug concentrations as compared to tenofovir administered alone. The application of this technology can be used in a vaginal (mucosal) microbiocidal gel form. Dr. Karla has shown that he can increase the bioavailability of a drug by modulating the efflux of the drug in the primary human CD4+ T-cells that are freshly isolated from the blood of a human donor. Furthermore, Dr. Karla has also identified the presence of the drug targets on vaginal epithelial cells. Dr. Karla aims to develop a potent vaginal microbicide drug delivery strategy by employing “ABC Drug Efflux Transporter Inhibition” to significantly increase the HIV drug absorption by human CD4+ T-cells and prevent the sexual transmission of HIV. Uninfected, high risk individuals along with HIV patients will be asked to apply the drug efflux transporter inhibitor chemically altered tenofovir vaginal gel, as a pre-exposure prophylaxis strategy. Dr. Karla aims to further explore “ABC Drug Efflux Transporter Inhibition” as an oral HIV drug delivery strategy for increasing the effectiveness of current post exposure prophylaxis therapies.

### **Opportunity**

Howard University and Dr. Karla are seeking partners to continue further development of the technology. These novel therapeutic targets and methods of using them for decreasing HIV transmission/infection are available under a license or research collaboration with Howard University. **Dr. Karla is available for further discussions about technical details and project status under an NDA.**