Discovery of building blocks for new drug classes to prevent and treat HIV

Burnet Institute researchers have made a major advance in developing drugs that can be used to prevent the 2.1 million new HIV infections each year and treat the 35 million people living with HIV globally.

The new research, published in the prestigious international journal, The Proceedings of the National Academy of Sciences of the United States of America, reveals the discovery of new drug building blocks that target a critical HIV molecule in ways that are distinct to drugs currently used for HIV treatment and prevention.

Head of Burnet’s Retroviral Biology and Antivirals Laboratory, Associate Professor Gilda Tachedjian, said the discovery of new chemical building blocks that inhibit a proven HIV drug target in new ways is critical for developing more potent drugs able to combat virus that are resistant to currently available HIV inhibitors.

The use of antiretroviral drugs in Pre-exposure prophylaxis (PrEP) is gaining momentum as a key tool in a variety of settings to protect high-risk individuals from HIV infection. This proven prevention tool urgently needs to be made accessible to those individuals who need it to prevent the 2.1 million new infections globally. However, the drugs that are being used for PrEP are the same antiretroviral drugs that are used for HIV treatment.

“Our long-term concern is that, in a real-world setting, PrEP could lead to the generation and transmission of drug-resistant strains of HIV that could compromise first line drug regimens, particularly in individuals from resource-poor settings,” Associate Professor Tachedjian said.

“To address this concern, a relatively new paradigm in drug discovery (fragment based drug design) was used to identify very small chemicals called “fragments” that are half the size of conventional drugs that are efficient at binding to new drug sites on the viral target.

“Despite their small size, these fragments were found to bind and block the functioning of the critical HIV molecule. Notably, three of these fragments inhibited the function of this molecule in ways that are distinct to licensed drugs that target this protein and would be expected to block virus resistant to these licensed drugs.

“Using these building blocks we can now start to grow these molecules into larger and more potent inhibitors to develop new drugs that are effective against drug-resistant HIV that can be used in the future for HIV treatment and prevention.”
Burnet collaborated with researchers from Monash Institute for Pharmaceutical Sciences and the University of Pittsburgh School of Medicine.

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