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Discovery of HIV-1 Protease Inhibitors Using Imatinib/Nilotinib Templates for HIV/AIDS Treatment

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Category
Pharmaceuticals/Drug Discovery & Development

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Sustainable, 100× yield improvement over wild type for amino acid biomanufacturing.

Researchers at Purdue have developed a novel series of compounds using structure-based design that show significant inhibition of HIV-1 protease. Current anti-retroviral drugs are contending with new drug-resistant strains of HIV-AIDS and have several major side effects associated with the cardiovascular and central nervous system. In order to provide new treatment options, researchers have developed a series of novel compounds by maximizing hydrogen bonding interactions with the active site protease backbone atoms.

The series of compounds made by researchers at Purdue incorporated derivatives of nilotinib-like pyridyl pyrimidinyl groups and thiazole heterocycles in combination with the hydroxyethylamine sulfonamide isostere group of the HIV-1 protease inhibitor darunavir. The researchers tested the enzyme inhibitory ability and the IC50 of each molecule and found that several had inhibitory activity at the nanomolar and sub-nanomolar level as well as antiviral activity at the low nanomolar level.

Technology Validation:

- Enzyme inhibitory activity of molecules verified through an enzyme-inhibitory assay with HIV protease.

- Antiviral activity of molecules validated with MT-2 human-T-lymphoid cells model with HIVLAI.

Advantages:

- Select compounds among series have better and/or comparable antiviral and enzyme inhibitory activity of HIV and HIV-1 protease.

- Distinct chemical structure from other commercial HIV protease inhibitors, potentially more difficult for new strains to develop resistance to new series of compounds.

Applications:

- HIV/AIDS treatment: New series of compounds could be developed into anti-retroviral drugs against multi-drug resistant strains of HIV.

- HIV/AIDS diagnostics: Fluorophores could be bound to compounds and be used to visualize distribution of HIV-1 protease within cells.

TRL: Pharmaceuticals

Intellectual Property:

NATL-Patent, N/A, United States

NATL-Patent, N/A, Europe

Provisional-Gov. Funding, 2023-03-24, United States

PCT-Patent, 2024-03-22, WO

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