PURDUE INNOVATES | Office of Technology Commercialization

Discovery of highly potent HIV-1 protease inhibitors with polycyclic-THF ligands

Novel HIV-1 protease inhibitors with high yield synthesis and promising pharmacokinetic properties show 100-fold increased antiviral activity against drug-resistant HIV strains compared to darunavir.

NCS: Researchers at Purdue University have designed and developed a new class of highly potent HIV-1 protease inhibitors with polycyclic-THF ligands for treatment of human immunodeficiency virus type 1 (HIV-1). Improvement of current HIV protease inhibitors is needed to combat drug-resistant HIV strains. Although antiretroviral therapies (ART) have had a major impact on the AIDS epidemic, they have not eradicated HIV-1 in part due to the viral reservoirs remaining in blood and infected tissues. Purdue researchers developed novel protease inhibitors with improved properties over darunavir. In testing in vitro, the new inhibitors showed 100-fold increased antiviral activity against drug resistant strains of HIV-1 relative to darunavir. The high yielding synthetic schemes (79-90%) of these inhibitors and derivatives offer an encouraging potential for reaction scale-up. Moreover, structurally, these compounds are expected to have good pharmacokinetic properties for drug development.

Technology Validation: High resolution crystal structures of inhibitor bound wild-type HIV-1 protease have shown increased binding properties compared to darunavir. The new protease inhibitors have also been tested in vitro wherein they exhibit improved treatment of HIV-1 over darunavir by 100-fold.

Advantages:

- High antiviral activity against resistant HIV-1

- Structurally promising pharmacokinetic properties

- High yield synthesis

Applications:

Technology ID
2020-GHOS-68891

Category
Pharmaceuticals/Small Molecule Therapeutics
Pharmaceuticals/Pharmaceutical Manufacturing & Methods

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- HIV-1 therapeutics

- Drug discovery

Related Publications:

"Design and Development of Highly Potent HIV-1 Protease Inhibitors with a Crown-Like Oxotricyclic Core as the P2-Ligand to Combat Multidrug-Resistant HIV Variants"

Journal of Medicinal Chemistry

DOI: 10.1021/acs.jmed.chem.7b00172

"Design of Highly Potent, Dual Acting and Central Nervous System Penetrating HIV-1 Protease Inhibitors with Excellent Potency against Multidrug-Resistant HIV-1 Variants"

ChemMedChem

DOI: 10.1002/cmdc.201700824

TRL: 3

Intellectual Property:

Provisional-Gov. Funding, 2020-03-18, United States | NATL-Patent, 2021-01-18, Canada | NATL-Patent, 2021-01-18, Europe | NATL-Patent, 2021-01-18, Japan | PCT-Gov. Funding, 2021-01-18, WO | NATL-Patent, 2022-09-16, United States

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