PURDUE INNOVATES | Office of Technology Commercialization

Analogs of Diphyllin

A developed bacterial strain enhances cancer immunotherapy for solid tumors by activating host immune responses, disrupting the suppressive microenvironment, and causing rapid tumor destruction.

There are many hundreds of viruses that can cause human diseases, but currently, there are only ten approved antiviral treatments. Antiviral design generally targets multiple components of the virus to enhance preparedness and ability to counteract the virus by lowering the likelihood of resistance mutations, but sometimes viruses take advantage of host factors to proliferate, which makes this design strategy flawed. For example, Vacuolar H+-ATPase (V-ATPase) is an ATP-driven proton pump that regulates the acidity of endosomes and lysosomes in cells, but viruses can co-opt this machinery to initiate infection. Current treatments for this are antibiotics like Baf A1 and ConcA, but they lack therapeutic selectivity and drug-like properties to be used as viable drug leads for further drug development. Diphyllin, a naturally occurring compound, has shown significant potency and selectivity as a V-ATPase inhibitor, but it suffers from in vivo toxicity and poor metabolic stability and oral bioavailability. However, diphyllin can be used as a drug lead to design new therapeutic analogs for inhibiting V-ATPase. Researchers at Purdue University have designed a library of diphyllin analogs with improved in vivo toxicity, metabolic stability, and oral bioavailability compared to diphyllin itself. This technology provides a robust foundation for the development of diphyllin-based V-ATPase inhibitors with potential therapeutic applications for variety of conditions including viral infections, parasitic infections, cancer, obesity, and osteoporosis.

Technology Validation:

-Proton Nuclear Magnetic Resonance (H-NMR) to validate structures of compounds

-High-Performance Liquid Chromatography (HPLC) purified to isolate products

-Antiviral activity tested with Ebola Virus, Chikungunya Virus, and Venezuelan Equine Encephalitis Virus showed potent activity and potential use as broad-spectrum antiviral

Technology ID

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Category

Agriculture, Nutrition, & AgTech/Crop Genetics & Breeding
Agriculture, Nutrition, & AgTech/Regenerative Ag & Soil Health
Pharmaceuticals/Drug Delivery & Formulations
Pharmaceuticals/Other

Authors

Vincent Davisson
Amr Elkabbany
Naoaki Fujii
Laura Sanford

Further information

Joe Kasper
JRKasper@prf.org

Nathan Smith
nesmith@prf.org

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-In vivo pharmacokinetics and maximum tolerated dose assays to assess toxicity of compounds at EC90 blood level required for oral dosing showed good potency and negligible toxicity

Advantages

-First selective antiviral for V-ATPase inhibition with improved in vivo toxicity, metabolic stability, and oral bioavailability

Related Publications

Sanford et al., Evaluation of potency and metabolic stability of diphyllin-derived Vacuolar-ATPase inhibitors. European Journal of Medicinal Chemistry, Volume 275, 2024, https://doi.org/10.1016/j.ejmech.2024.116537.

TRL: 3

Intellectual Property:

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Keywords: Diphyllin analogs, V-ATPase inhibitors, broad-spectrum antiviral, host factor targeting, viral infections, parasitic infections, cancer, obesity, osteoporosis, metabolic stability