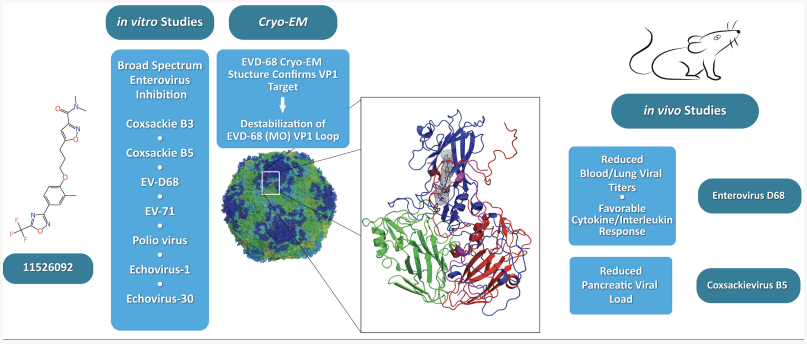
Collaborations Pharmaceuticals Announces Publication of New Enterovirus-D68 and Coxsackie B5 inhibitor

A new paper published in Antiviral Research describes a new inhibitor of Enterovirus-D68 and Coxsackie B5.

RALEIGH, NC, USA, June 15, 2023 /EINPresswire.com/ -- Dr. Thomas Lane and Dr. Sean Ekins from Collaborations Pharmaceuticals, Inc. (CPI) with Dr. Vadim Makarov and collaborators at the Research Center of Biotechnology RAS, Moscow; and collaborators at Purdue University, North Carolina State University, Utah State University, University of Colorado Anschutz Medical Campus and Saint Petersburg Pasteur Institute are pleased to announce their new publication in Antiviral Research "Efficacy of an isoxazole-3-carboxamide analog of pleconaril in mouse models of Enterovirus-D68 and Coxsackie B5".

Collaborations Pharmaceuticals logo



Enteroviruses (EV) and coxsackieviruses (CVs) cause a wide range of acute and chronic diseases, such as aseptic meningitis, encephalitis, hand-foot-and-mouth disease, conjunctivitis, diarrhea, herpetic angina, acute and chronic myocarditis, etc. These viruses represent the main cause of death in low-income countries and the third largest cause of death worldwide. EV-D68 is known to cause respiratory illness in children that can lead to acute flaccid myelitis, a polio like illness, while Coxsackievirus B5 (CVB5) is commonly associated with hand-foot-mouth disease. There is no antiviral treatment available for either. The most promising results against EVs to date have been obtained with the capsid-binding inhibitors.

“We have previously developed several new pleconaril-based molecules which displayed potent in vitro activity against a panel of CVs and rhinoviruses. We have now discovered that one of these compounds, 3-(3-methyl-4-(3-(3-N,N-dimethylcarbamoyl-isoxazol-5-yl)propoxy)phenyl)-5-trifluoromethyl-1,2,4-oxadiazole (11526092) displays potent in vitro inhibition across various EVs. This molecule demonstrated promising antiviral activity against EV-D68 in a mouse respiratory model of EV-D68 infection. Cryo-electron microscopy (cryo-EM) was used to demonstrate that 11526092 binds to the EV-D68 VP1 from the MO strain. We have additionally determined that 11526092 inhibits CVB5 in vitro and in vivo, and therefore may represent a promising new lead compound” said CPI CEO Dr. Sean Ekins.

Dr. Thomas Lane, Associate Director at CPI remarked “The CDC has recognized the reemergence of EV-D68 infections causing hospitalization of children and adolescents in the US based on a report published in November 2022. As these only capture instances that required hospitalization, this likely represents a small fraction of the total cases of EV-D68 in the US, reemphasizing the need for antivirals for EV-D68 and related viruses following the 2014 EV-D68 outbreak. This new compound has improved properties over its analog pleconaril, where it shows higher activity against multiple viruses, including some pleconaril-resistant strains, as well as reduced CYP3A4 upregulation, both of which likely contributed to pleconaril’s clinical failure. Our compound shows significant in vivo efficacy in an EV-D68 respiratory model, including viral reduction and a favorable cytokine response. This compound also showed in vivo antiviral activity against CVB5, one of the most common causes of hand-foot-and-mouth disease worldwide, expanding its potential use as a broad spectrum therapeutic.”

“11526092 is a new antiviral compound for EVs which we have studied in detail. It binds to EV-D68 in a similar manner to pleconaril, and we have now described the unique mechanism of action for compounds binding to different strains of the EV-D68 virus. 11526092 is well-tolerated in mice and demonstrates promising antiviral efficacy in in vivo mouse models. Based on this study and in the absence of any suitable antiviral treatments for these viruses, further testing of 11526092 may be warranted against these and other related EV’s We look forward to partnering with other companies to further develop this molecule.”

Publication information:
Efficacy of an isoxazole-3-carboxamide analog of pleconaril in mouse models of Enterovirus-D68 and Coxsackie B5.
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