

FPU2025 - Salicylamide derivatives of niclosamide for use as broad-spectrum antiviral agent

PROJECT DESCRIPTION

There is an urgent need to develop new families of broad-spectrum antiviral drugs able to block virus infection and dissemination by targeting host factors, which would increase their spectrum of clinical utility while reducing the chances of viral resistance. In addition, the repurposing of drugs is gaining increasing interest as a more efficient, cheaper, and faster alternative to the generation of new antiviral therapies. An example of this is niclosamide, an anthelmintic drug approved by the health authorities that has been shown to have significant antiviral activity in vitro against a wide variety of viruses including SARS-CoV-2, IV, CHIKV, WNV, DENV, VACV, CMV, and HAdV, which also support a potential host target. However, the poor aqueous solubility of niclosamide, as well as its low oral bioavailability and moderate cytotoxicity, pose important limitations that must be addressed before it can be used in clinic as a broad-spectrum antiviral agent.

Toward this end, two years ago we began a collaboration with the group of Prof. Jia Zhou from the Department of Pharmacology and Toxicology at the University of Texas Medical Branch, TX, USA, to identify novel niclosamide derivatives with improved broad-spectrum antiviral activity and enhanced pharmacokinetics. After evaluating the antiviral activity against HAdV of a series of newly designed and synthesized salicylamide niclosamide derivatives, we have identified several druglike molecules that showed potent antiviral effects at submicromolar concentrations and different mechanisms of action.

The present project will be oriented to optimize the anti-viral activity of these derivatives.

TASK TO DEVELOP BY THE STUDENT:

The student will participate in the implement of the cellular and molecular techniques required to achieve the proposed research objectives. She/he will be in charge of the maintenance of the cell lines used in this project along the duration of her/his stay. She/he will carry out the purification, propagation, production and storage of viral particles stocks of the virus to be evaluated. The student will use techniques of molecular and cell biology such as, viral plaque assays to evaluate de antiviral activity of the selected compounds, or RT-PCR and others to determine the potential mechanism of action of those molecules with antiviral activity. The student will implement infection protocols with adenovirus and other respiratory viruses, such as influenza virus, respiratory syncytial virus or rhinovirus.
