Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: A NEW ANTIVIRAL STRATEGY FOR PANDEMIC AND SEASONAL INFLUENZA

Synopsis: Over the past century, several influenza pandemics have occurred. The H1N1 pandemic of 1918 still stands as the deadliest event in human history. Recently, COVID-19 pandemic has evidenced the lack of effective antiviral drugs and the gap between the rapid spread of diseases and the discovery of new drugs. Thus, it seems clear that there is an urgent need for the development of new and safe antivirals. This project aims to test the use of a new family of small molecules as inhibitors of viral infection, targeting a viral entry-related process common to several enveloped viruses, including influenza viruses. Exploiting the ability of those molecules to block the entry of the viral genome into the cytosol, this proposal seeks to develop new antiviral agents against influenza viruses. To do so, new small molecules synthesized by our collaborators will be characterized and tested to assess their antiviral activity against influenza viruses *in vitro*. Pharmaceutical nanoformulations of the selected lead compounds will be explored to optimize their solubility and toxicity, as well as to enhance a pulmonary delivery route, aiming at increasing the selectivity of the treatment avoiding unwanted side effects. This project will explore the potential of a new family of small molecules as antiviral agents against influenza viruses, and probably against other viruses with replication cycles dependent on the same mechanisms. This will possibly contribute to the preparation of a global and effective response in future pandemic outbreaks**.**

The specific objectives of this project are:

- To characterize and screen novel libraries of small molecules in order to discover hit compounds suitable to block the entry of the viral genome into the cytosol with potential antiviral activity against influenza viruses.
- To assess the *in vitro* antiviral activity and cytotoxicity of those compounds, and optimized formulated products.
- To explore optimal pharmaceutical nanoformulations for the candidates to improve their solubility and reduce toxicity, aiming at a pulmonary delivery route.

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Bibliography:

Tomás AL, Reichel A, Silva PM, et al. UV-C irradiation-based inactivation of SARS-CoV-2 in contaminated porous and non-porous surfaces. J Photochem Photobiol B 234 (2022), 112531. DOI: 10.1016/j.jphotobiol.2022.112531.