Instituto de Medicina Molecular João Lobo Antunes

PhD Project Proposal
"Doctorates 4 COVID-19"

Title: Development and testing of SARS-CoV-2 fusion inhibitors

Brief description:

SARS-CoV-2 is an enveloped virus, which entry into target cells is mediated by the envelope spike (S) glycoprotein. This protein belongs to the class I of viral fusion proteins and has two domains, S1 and S2. S1 (N-terminal region) is responsible for binding to ACE2 cell receptor and S2 (C-terminal) mediates membrane fusion. S2 contains two heptads repeat regions, HRC and HRN. Our previous results with broad-spectrum or virus-specific fusion inhibitor peptides against different enveloped viruses, including SARS-CoV (now SARS-CoV-1), and the work of other groups, have shown that HRC-derived peptides can interact with HRN region and block the six-helix bundle formation, a key step for the fusion of the viral and cell membranes and the entry of the viral content into the cytoplasm of a target cell. With this project, we aim to develop lipid-conjugated and dimerized fusion inhibitor peptides based on the HRC domain as membrane fusion inhibitors of SARS-CoV-2. Initial studies will be performed in order to optimize peptides sequence/lipid tagging. Afterwards, fluorescence spectroscopy and molecular virology techniques will be used to evaluate their bioavailability at the membrane level and their antiviral activity on infected cells.

Supervisor: Nuno C. Santos, Biomembranes & Nanomedicine Unit / NSantos Lab, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa; nsantos@medicina.ulisboa.pt; https://scholar.google.pt/citations?user=hmISCFoAAAAJ&hl=en