PhD thesis (F/M) offer

36 month from 01/09/2022, funded by ICPAR/CEFIPRA (Campus France) 1,500€ net salary/month

Title Bivalent pharmacophores for simultaneous targeting of the N- and C-terminal domains of the SARS-CoV-2 spike protein

Socio-economic and scientific context

The emergence of the novel pathogenic Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV-2) which has rapidly led to a pandemic, points out the urgent need for the development of novel therapeutic and prophylactic agents. The spike glycoprotein of the SARS-CoV-2 is an attractive target for both medicinal and vaccine approaches since it is responsible for the virus entry into the host cells and is surface-exposed to the immune system. Along this line, recently launched RNA-based vaccines proved successful but require repetitive boosts because induced protection wanes fast and might become ineffective if major mutations occur. On the other hand, drug repositioning is the most reliable option to design an efficient therapy for infected patients without delay. Efforts aim at blocking interactions between the Recognition Binding Domain (RBD) of the spike glycoprotein and the human Angiotensin-Converting Enzyme 2 (ACE2) which mediate the infection. However, these efforts has not yet met with success because SARS-CoV-2 RBD differs from RBDs of previously known related coronavirae.

Objectives

There is evidence that the spike glycoprotein can interact through its N-terminal domain with sialic acid-containing glycoproteins and/or gangliosides/heparin sulfates expressed at the host cell surface as an alternative receptor to ACE2. In this proposal we will develop constructs able to inhibit interactions between the spike protein and both ACE2 and sialic acid-based receptors.
As an outcome, very strong inhibition of SARS-Cov-2 entry is expected thanks to dual targeting and multiple presentation of the inhibitors, even if the inhibitory effect of the molecules considered individually is moderate.

Keywords: Antiviral agents – Nanotechnology – Carbohydrate chemistry – Nanoparticles – Molecular interactions

Profile & Skills

Master 2 in Organic Chemistry awarded by an Indian University
Know-how in carbohydrate chemistry or bioconjugaison or nanotechnology would be a plus.
Skills in analytical chemistry/biomolecular interaction measurements.
Strong interest for medicinal chemistry and health.

Work context

The work will be carried out within the "Molecular Engineering & Glycocobiology" team of the Unit of Biological Sciences and Biotechnologies (US2B), UMR CNRS 6286 located on the Lombarderie campus of the Nantes Faculty of Science and Technology (https://us2b.univ-nantes.fr/). The team is specialized in glyco-enzymology and glyco-technology applied to the development of antimicrobial agents, vaccines or drugs. It is an interdisciplinary team developing expertise in chemistry, biochemistry, molecular biology as well as in immunology and in the study of sugar / protein interactions. The work is part of collaborative research project funded by IFCPAR/CEFIPRA (Indo-French Centre for the Promotion of Advanced Research), involving an Indian research team headed by Dr Kapil Kumar, Associate Professor at Apeejay Stya University, Haryana, India. A short internship in this laboratory at the end of the first year thesis is scheduled within the program framework.

Additional information

Interested candidates are invited to send a motivation letter + a CV comprising detailed professional experiences, to
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