Session 1
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Molecular determinants of the SARS-CoV-2 fusion peptide activity

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The COVID-19 pandemic, caused by the SARS-CoV-2 virus, emerged in late 2019 and quickly spread worldwide, resulting in over 125 million infections and 2.7 million deaths as of March 2021 accordingly to the World Health Organization. Despite the great advances achieved by the scientific community in providing crucial information about this virus, we are still far from completely understanding it.

SARS-CoV-2 is an enveloped virus, meaning that it is encapsulated by a lipid membrane, which needs to be fused to the host membrane to begin the infection process. Fusion between viral and host membrane is catalyzed by the spike (S) glycoprotein. The S-protein is composed of essential elements for the infection mechanism, namely the receptor-binding domain known to bind to angiotensin-converting enzyme 2 during the viral entry pathway. Another important region, known as the fusion peptide (FP), plays an essential part in the fusion mechanism, by inserting into and disturbing the host membrane. There is still not a consensus among scientists in terms of the fusion peptide location on the S-protein sequence, with two major candidate regions having been proposed.

We recently used a machine learning-based tool developed by us to identify viral FPs with accuracies over 85%. With this tool a putative FP, previously suggested in the literature, has been identified, as well as other proposals including the requirement of more than one FP. To further address this question, we are performing a systematic analysis of the SARS-CoV-2 putative FPs, using Molecular Dynamics (MD) simulations, which provide a detailed perspective of how these peptides insert and interact with the membrane. In parallel, we are characterizing these systems experimentally. Additionally we are exploring therapeutic strategies targeting these regions. Given the major role of the FP in the virus infection process, this work provides relevant insights and contributes to the fight against COVID-19.