

Séminaire de Chimie Autour des Nanosciences

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Molecular modelling, homo-oligomerisation and membrane interactions of hepatitis E virus pORF1 replication polyprotein

Hepatitis E virus (HEV) is one of the main causative agents of acute hepatitis and jaundice, affecting both developed and developing countries. At least 20 million people are infected each year worldwide. HEV usually causes a minor and asymptomatic infection that resolves on its own but around 70,000 people die per year after HEV infection. HEV is particularly problematic in immunocompromised patients such as tranplant recipients, where infection progresses in most cases to a chronic and highly liver-damaging disease, for which antivirals are needed. However, despite its severity, its prevalence and its impact in health systems, HEV is poorly characterized and many questions remain unanswered about its functioning, especially at the structural level.

In recent years, the subject of structural biology has witnessed major revolutions. The most recent of these is the capacity of the software AlphaFold to properly predict protein 3D structures from their sequences alone. We used AlphaFold modeling to study I) the full-length pORF1 and ii) oligomers of a pORF1 subdomain (MetY)1. It turns out that MetY is highly similar to nsP1 of Chikungunya virus, for which the structure was published of a dodecamer putatively topping the membrane spherule harbouring the replication complex 2. We modelled a similar MetY dodecamer and used coarse-grained3 molecular dynamic simulations (MD) to investigate its interaction with membranes. To mimic a membrane spherule system, we used a torus (or donut-like) membrane system to mimic the membrane curvature at a spherule exit.

We will discuss the conclusions we can draw from these models, specifically I) the breakdown of pORF1 into a limited number of domains and possible alternate conformations, ii) the possible organization, oligomerization, and membrane association of the pORF1 MetY.

LE VENDREDI 3 AVRIL À 11h00

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