Beitrag ID: **114** Typ: **Poster**

Timescales of Cell Membrane Fusion Mediated by SARS-CoV2 Spike Protein and influence of an antiviral drug candidate

Dienstag, 17. September 2024 22:40 (20 Minuten)

We investigated the SARS-CoV2 membrane fusion timescale by means of small-angle neutron scattering (SANS) using hydrogen/deuterium contrast variation. After the successful production of virus-like vesicles and human- host-cell-like vesicles we were able to follow the fusion of the respective vesicles in real-time. This was done using deuterated and protonated phospholipids in the vesicles in a neutron-contrast matched solvent. The vesicles were identical apart from either the presence or absence of the SARS-CoV2 spike protein. The human host-cell-like vesicles were carrying an ACE2 receptor protein in all cases. In case of the absence of the spike protein a fusion over several hours was observed in agreement with literature, with a time constant of 4.5 h. In comparison, there was not time evolution, but immediate fusion of the vesicles when the spike protein was present. Those two figures, fusion over several hours and fusion below 10 s corresponding to the absence or presence of the spike protein allow an upper-limit estimate for the fusion times of virus-like vesicles with the SARS-CoV2 spike protein of 10 s. This very fast fusion, when compared to the case without spike protein it is a factor of 2500, can also help to explain why infection with SARS-CoV2 can be so effective and fast. In order to access very short timescales we also performed continuous flow experiments, which support the stopped flow and static experiments. This fusion process could be strongly influenced by a promising drug candidate, which inhibited the fusion process.

In addition to the time-resolved contrast matching SANS experiments we also performed neutron-spin echo experiments to investigate the dynamics of the membrane during the fusion process.

Studying spike protein variants using our method may explain differences in transmissibility between SARS-CoV2 strains. In addition, the model developed here can potentially be applied to any enveloped virus.

References

Hayward, D., Dubey, P. S., Appavou, M. S., Holderer, O., Frielinghaus, H., Prevost, S., … & Jaksch, S. (2023). Timescales of Cell Membrane Fusion Mediated by SARS-CoV2 Spike Protein and its Receptor ACE2. arXiv preprint arXiv:2303.10746.

Hauptautor: JAKSCH, Sebastian (European Spallation Source ERIC)

Co-Autoren: FRIELINGHAUS, Henrich (Jülich Centre for Neutron Science at MLZ, Forschungszentrum Jülich GmbH, Garching, Germany); HOLDERER, Olaf (JCNS); DUBEY, Purushottam (Forshungszentrum Jülich am MLZ); Dr. EHMANN, Rosina (Institut für Mikrobiologie der Bundeswehr)

Sitzung Einordnung: Mounting Posters, Beer and light Dinner

Track Klassifizierung: Health & Life