ABSTRACT:
We use molecular dynamics (MD) simulations to study key molecular processes of the SARS-CoV-2 virus. We concentrate on the structure of the spike (S) protein at the viral surface, its interactions with the host cell, and on viral modulation of the host immune response. In molecular dynamics (MD) simulations of full-length S with a palmitoylated transmembrane domain and a fully glycosylated ectodomain, we identified three hinges in the stalk connecting the S head to the viral membrane. Hinge flexibility and glycosylation have been confirmed by high-resolution cry-electron tomography (Turonova, Sikora, Schürmann et al., Science 2020). We are now using the detailed structural and dynamic models for a computational antibody epitope scan (Sikora et al., biorxiv). In addition, we study the interactions of S with the host-cell receptor ACE2 (Mehdipour, Hummer, biorxiv). In MD simulations of the SARS-CoV-2 papain-like protease PLpro, MD simulations provided detailed insight in its function as immunomodulator by suppressing the host interferon (IFN) and NF-κB pathways through preferential cleavage of ISG15 (Shin et al., Nature 2020). Overall, MD simulations help us to uncover some remarkable biology associated with viral infection and, as we hope, guide our fight against COVID-19.

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