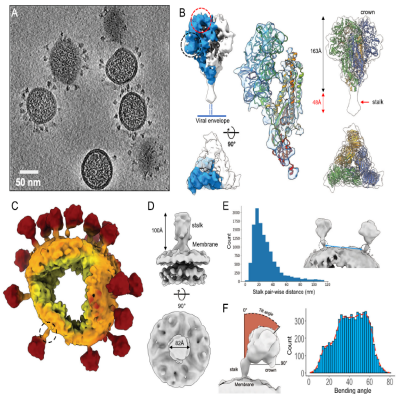
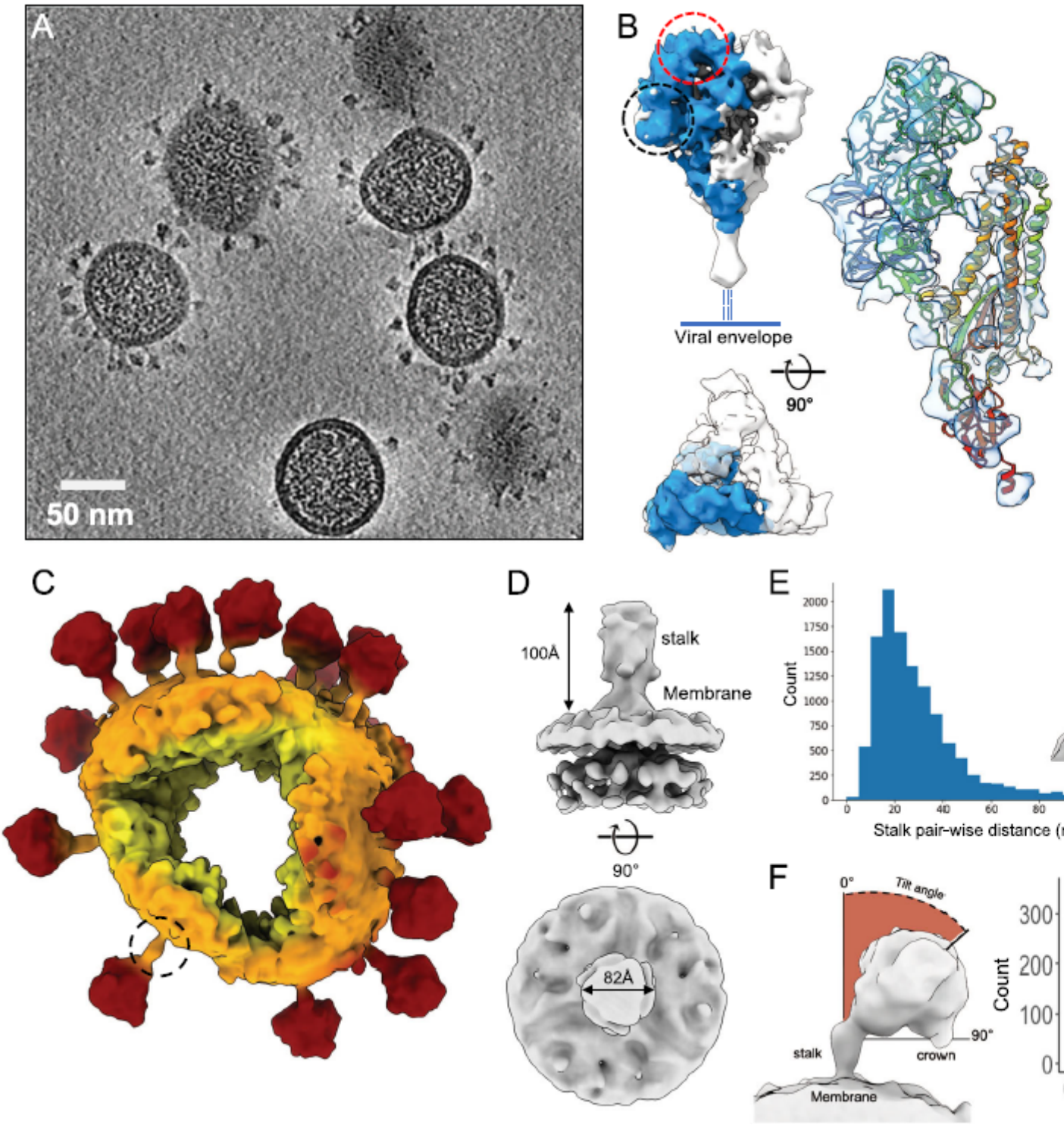


Structural Insights into the Modulation of Coronavirus Spike Tilting and Infectivity by Hinge Glycans

Description

Coronavirus spike glycoproteins presented on the virion surface mediate receptor binding and membrane fusion during virus entry and are the primary target for vaccine and drug development.How the structural dynamics of the full-length spikes incorporated into the viral lipid envelope correlate with virus infectivity remains poorly understood. The authors present structures and distributions of native spike conformations on vitrified human coronavirus NL63 (HCoV-NL63) virions without chemical fixation by cryogenic electron tomography (cryoET) and subtomogram averaging, together with site-specific glycan composition and occupancy determined by mass spectrometry.



CryoET of HCoV-NL63 intact virions.

The higher oligomannose glycan shield on HCoV-NL63 spikes than on SARS-CoV-2 spikes correlates with stronger immune evasion of HCoV-NL63. Incorporating cryoET-derived native spike conformations into all-atom molecular dynamics simulations elucidates the glycosylated spike's

conformational landscape, revealing hinge glycans’ role in modulating spike bending.

Glycosylation at N1242 on the upper part of the stem is responsible for the extensive freedom of orientation of the spike crown. Subsequent infectivity assays implicated the N1242 glycan in virus entry. These results suggest a potential therapeutic target for HCoV-NL63.

Category

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