Rapid Electron Microscopy Protocols for the Examination of High-Consequence Viral Pathogens, Lessons Learned from Two Pandemics

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Abstract

Background

As novel and emerging viruses continue to pose significant threats to public health, it is imperative that we continually advance detection and characterisation methodologies, to complement clinical and public health responses. A critical element during the initial stages of an emerging viral pandemic situation is the morphological confirmation of the agent in question, via gold-standard techniques. Historically, this morphological confirmation has occurred via the use of transmission electron microscopy to observe characteristic virus features, using negative staining, and ultrastructural changes in infected cells using thin-sectioning protocols. However, traditional methods for preparing thin sections can be time-consuming and labour-intensive, resulting in delays during the critical initial public health response period. Drawing on the lessons from the COVID-19 and Mpox pandemics within our facility, we prioritised the development and implementation of rapid protocols for identifying and characterizing high-consequence pathogens.

Discussion

We successfully integrated two new rapid microwave-based thin-section sample preparation protocols into our routine laboratory workflows. By integrating advanced imaging and computational tools like deep learning with these methods, we can rapidly extract complex information, including high-definition 3D ultrastructural data, from samples in one day, using tomographic reconstructions and AI-assisted segmentation.