

Fake News: Rectifying Published Ultrastructural Misidentifications of Coronavirus

S.E. Miller¹, H.A. Bullock², D.F. Ferreira¹

¹ Department of Pathology, Duke University Medical Center, Durham, NC 27710 USA; ² Centers for Disease Control and Prevention, Infectious Diseases Pathology Branch, Atlanta GA 30329 USA.

Abstract

During and following the COVID-19 pandemic, many researchers strove to elucidate the mechanisms of infection and organ damage by SARS-CoV-2. Ultrastructural research looked for it in various organ systems to determine whether pathology is caused by direct virus destruction of infected cells, toxin and debris release by infected upstream organs, or systemic response of downstream organs. To this end, close to 70 publications declared observance of coronavirus particles that were, in reality, only normal organelles, e.g., clathrin-coated vesicles, multivesicular bodies, and circular membrane structures. For correct identification, attention must be directed not only to particle shape and size, but to viral morphogenesis (how and where they are produced). Coronaviruses receive their external membranes as the nucleocapsids bud into cytoplasmic vacuoles; the vacuoles then fuse with the plasma membrane, which opens to the extracellular space so that the virus particles inside the vacuole are dumped to the extracellular space. They may also remain attached to the inside-out membrane but do not appear to bud through the plasma membrane, like some other viruses. It is wise to be well versed, not only in virus appearance, but especially in other pathognomonic features of infection and in normal cell structures; this will ensure correct identification.

References

1. Goldsmith CS, Miller SE, Martines RB, Bullock HA, Zaki SR. Electron microscopy of SARS-CoV-2: a challenging task. *Lancet*. 2020 May 30;395(10238):e99. doi: 10.1016/S0140-6736(20)31188-0.
2. Miller SE, Goldsmith CS. Caution in Identifying Coronaviruses by Electron Microscopy. *J Am Soc Nephrol*. 2020 Sep;31(9):2223-2224. doi: 10.1681/ASN.2020050755.
3. Miller SE, Brealey JK. Visualization of putative coronavirus in kidney. *Kidney Int*. 2020 Jul; 98(1): 231–232. doi: 10.1016/j.kint.2020.05.004.
4. Bullock HA, Goldsmith CS, Miller SE. Best practices for correctly identifying coronavirus by transmission electron microscopy. *Kidney Int*. 2021 Apr;99(4):824-827. doi: 10.1016/j.kint.2021.01.004.
5. Hopfer H, Herzig MC, Gosert R, Menter T, Hench J, Tzankov A, Hirsch HH, Miller SE. Hunting coronavirus by transmission electron microscopy - a guide to SARS-CoV-2-associated ultrastructural pathology in COVID-19 tissues. *Histopathology*. 2021 Feb;78(3):358-370. doi: 10.1111/his.14264.