Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Host proteases as determinants of coronaviral neurotropism and virulence

To the Editor:

Recently, the study by Wu et al. (2020) presented a concise report on the epidemiological and molecular underpinnings of coronaviral neurotropism, and their potential implications for COVID-19 disease phenotypes. The report presented by the authors covers an important aspect of coronaviral infections, that may be increasingly recognized as COVID-19′s clinical phenotypes expand. An equally important parameter of coronaviral nervous system involvement that was not covered in this paper, despite being directly implied by its aim, was the interaction between host and virus at protease cleavage sites, as a determinant of neurotropism and virulence.

Spike protein cleavage at specific residues by host proteases is considered a priming step during SARS coronaviral infection, subsequently determining adsorption, tissue tropism and host compatibility (Millet and Whittaker, 2015). Despite the genomic similarities with other betacoronaviruses, including SARS-CoV, SARS-CoV-2 was recently shown to contain a unique furin-like cleavage site in its spike protein (Coutard et al., 2020). Interactions between host furin-like proteases and furin-like cleavage sites have been previously shown to be important determinants of neurotropism in other coronaviridae, with cleavage status determining disease phenotype (Cheng et al., 2019;11(10).). Interestingly, in a murine model examining the neurotropic potential of the human coronavirus strain O43 (HCoV-O43), a furin-protease gain-of-function mutation did not impact neuroinvasion, but did affect viral egress, producing a more indolent and correspondingly persistent pathogen within the CNS (Le coupanec et al., 2015).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbi.2020.04.010.

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