A ROOT-CAUSE APPROACH TO LONG COVID IN THE POST-PANDEMIC ERA

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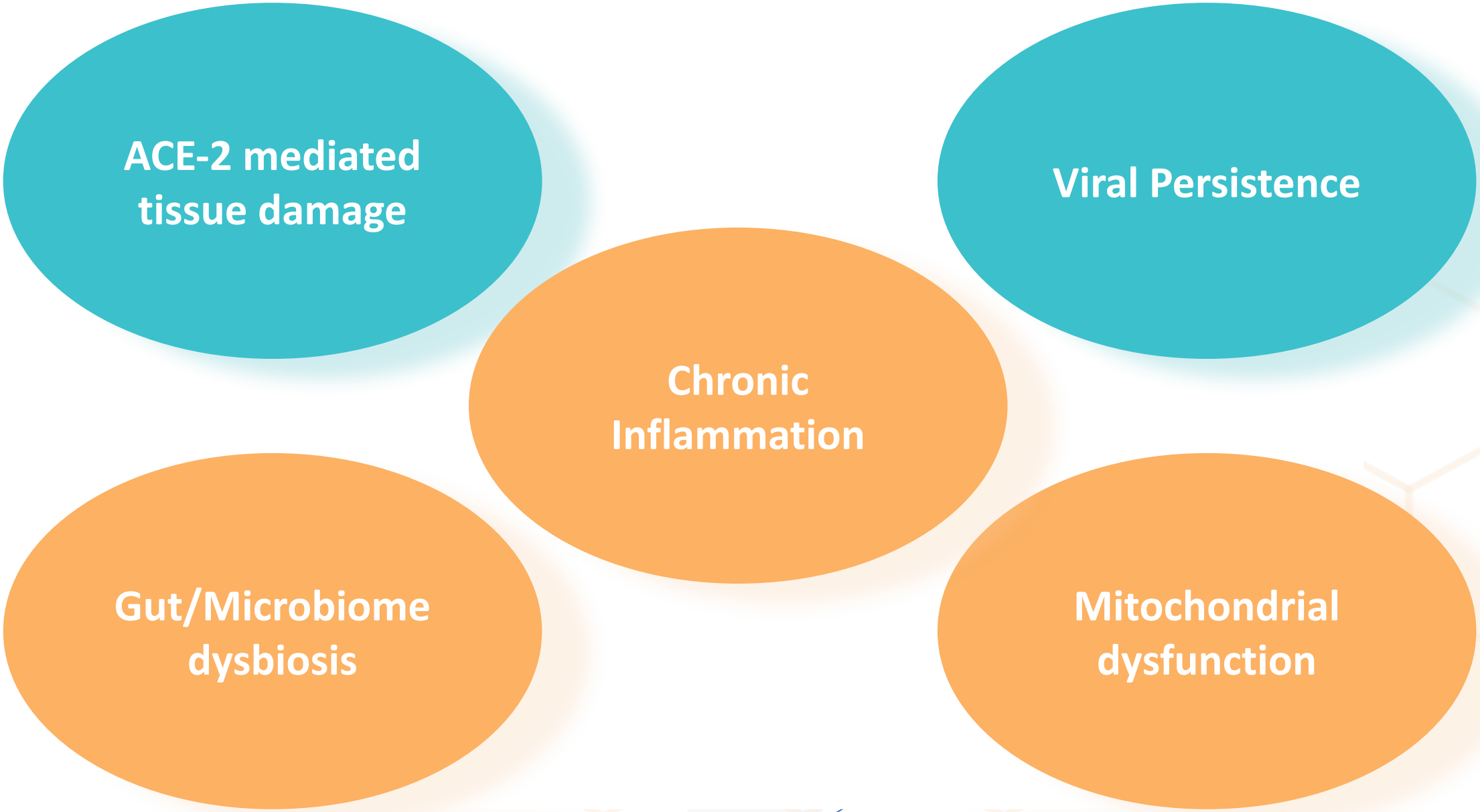
Long COVID does not appear to be self-resolving, in the sense of spontaneous recovery or recovery in the absence of a cure or a treatment that has been validated. It further raises the importance of finding treatment because this is not going to go away.

STAT Health Tech, 9/20/2023
https://www.statnews.com/2023/09/20/do-long-covid-odds-increase-with-second-infection/?utm_campaign=breaking_news&utm_medium=email&_hsmi=275130536&_hsenc=p2ANqtz-_Fz5sQzp45OzS1UyaREko82SfD8HXId2tVTahbKLPYeT_IzbsU0EZCjEYEIU-qBJptPUPhyCM_6OqMlbAfcKQeCUgpWQ&utm_content=275130536&utm_source=hs_email


ACE-2 mediated tissue damage
Viral Persistence
Chronic Inflammation
Gut/Microbiome dysbiosis
Mitochondrial dysfunction

Long COVID: major findings, mechanisms and recommendations

Davis, HE, McCorkell, L, Vogel, JM et al. Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol 21, 133–146 (2023). https://doi.org/10.1038/s41579-022-00846-2

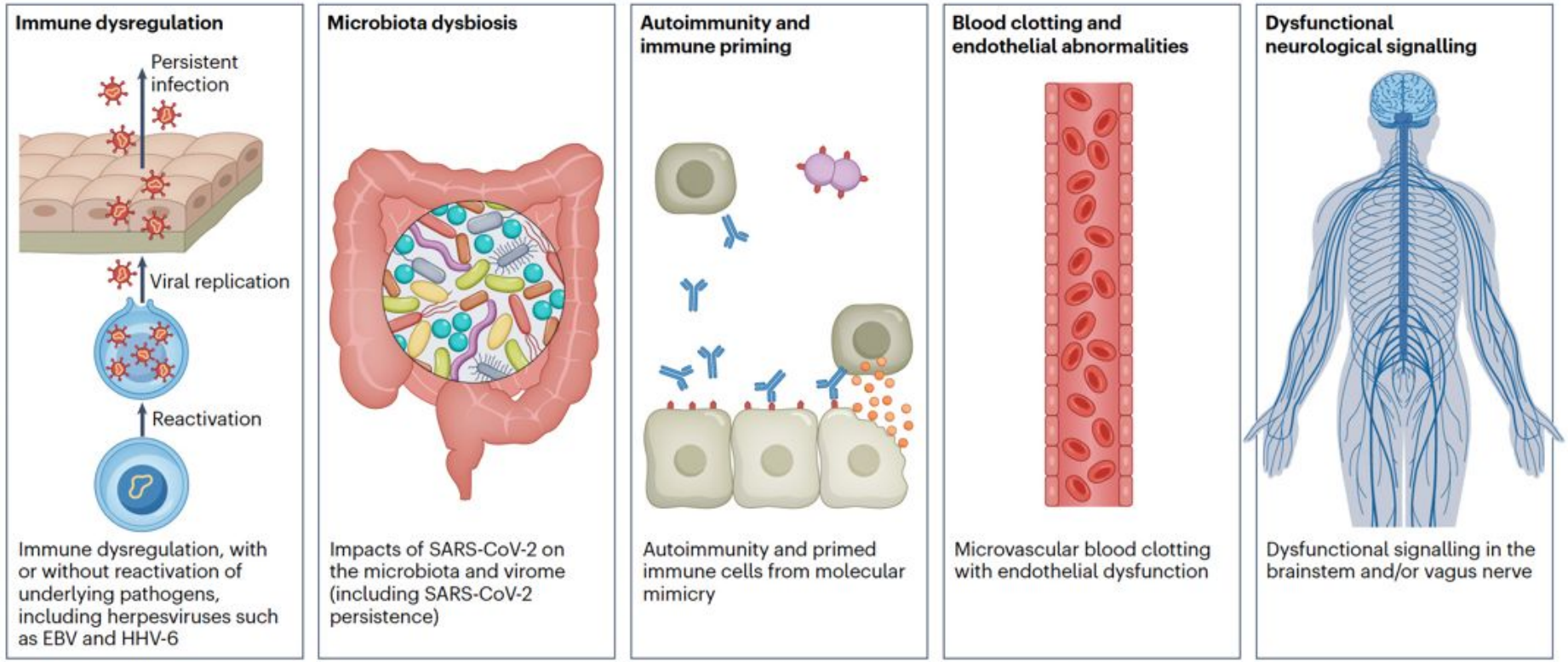
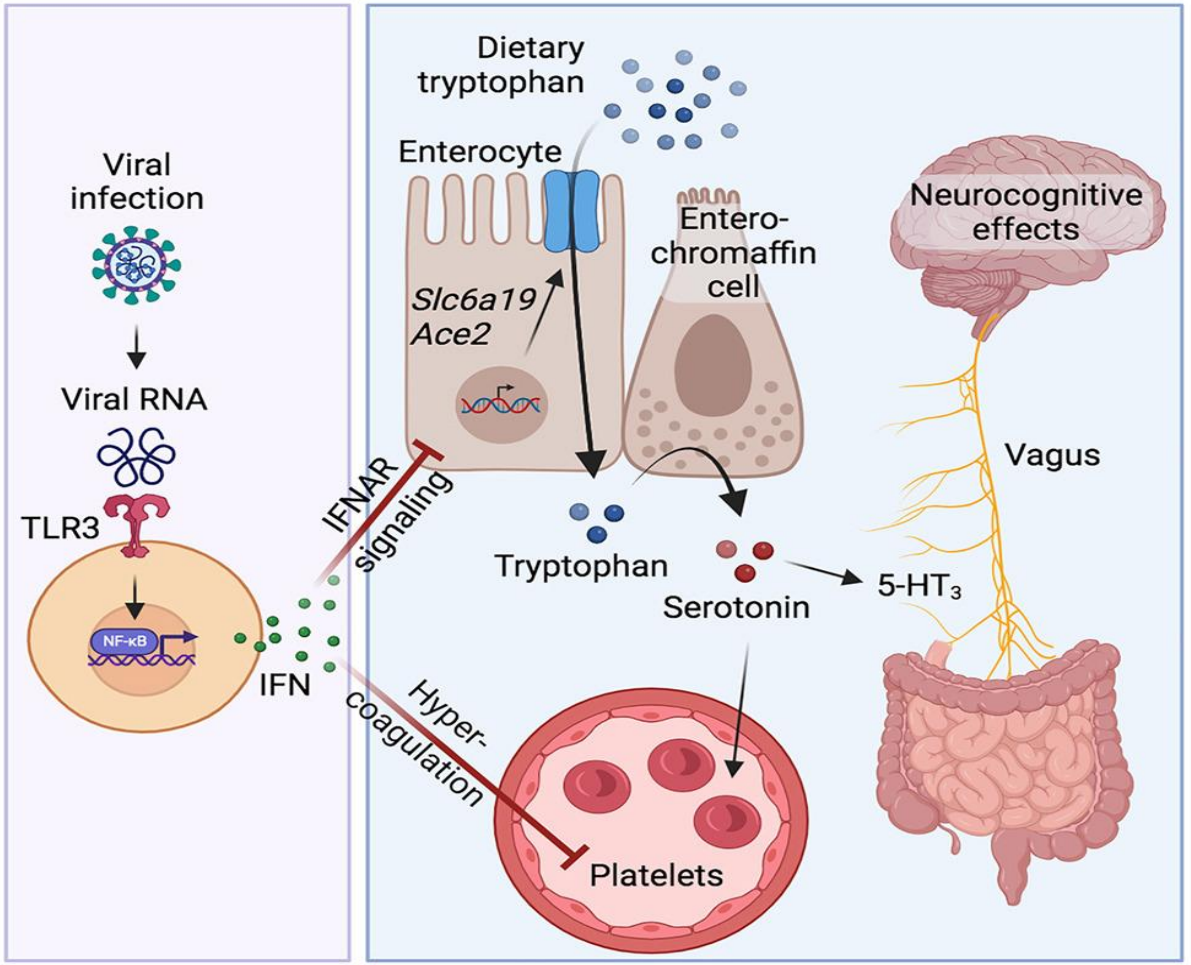


Fig. 3 | Hypothesized mechanisms of long COVID pathogenesis. There are several hypothesized mechanisms for long COVID pathogenesis, including immune dysregulation, microbiota disruption, autoimmunity, clotting and endothelial abnormality, and dysfunctional neurological signalling. EBV, Epstein–Barr virus; HHV-6, human herpesvirus 6; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

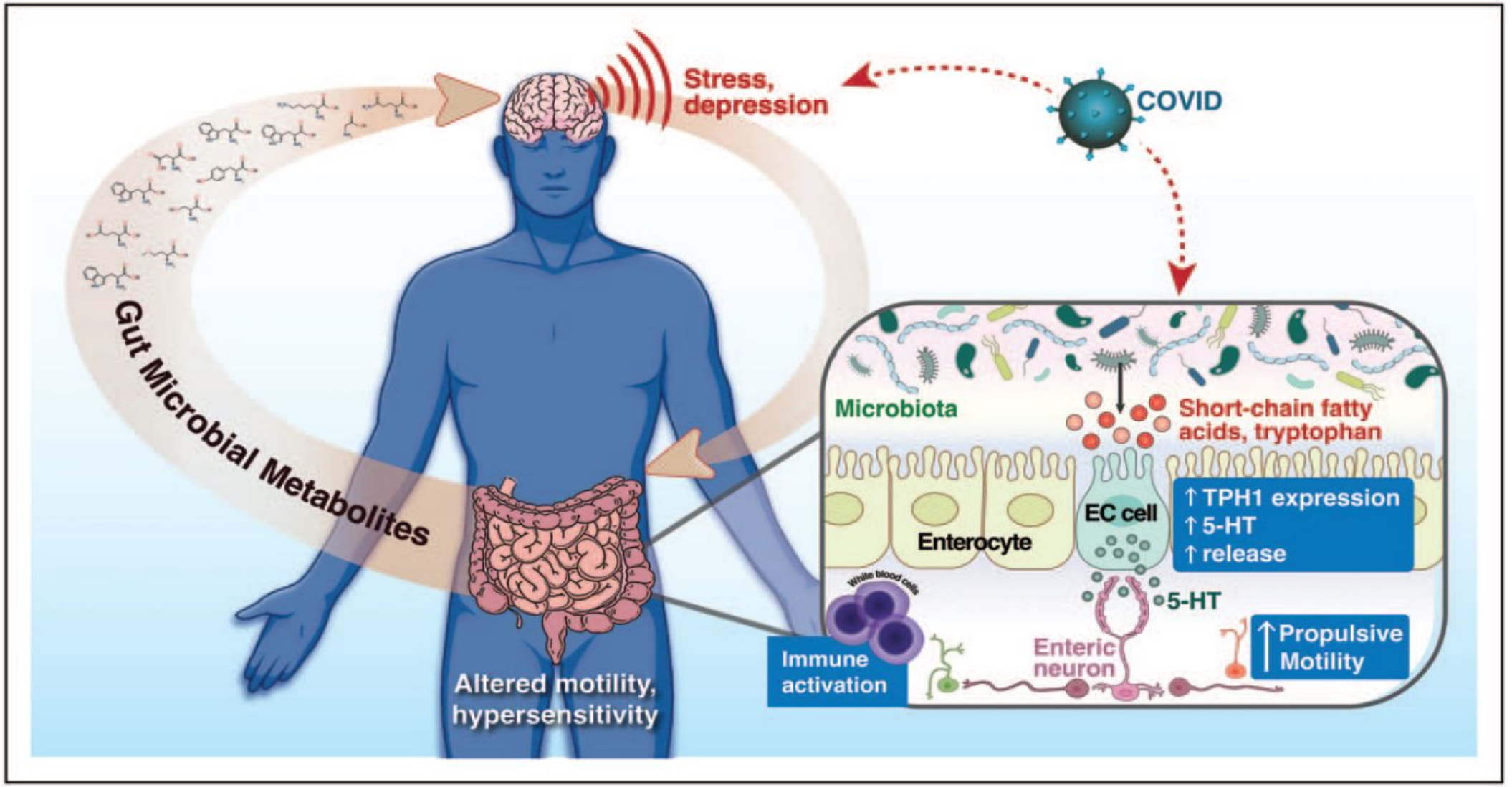
Serotonin reduction in post-acute sequelae of viral infection



Highlights

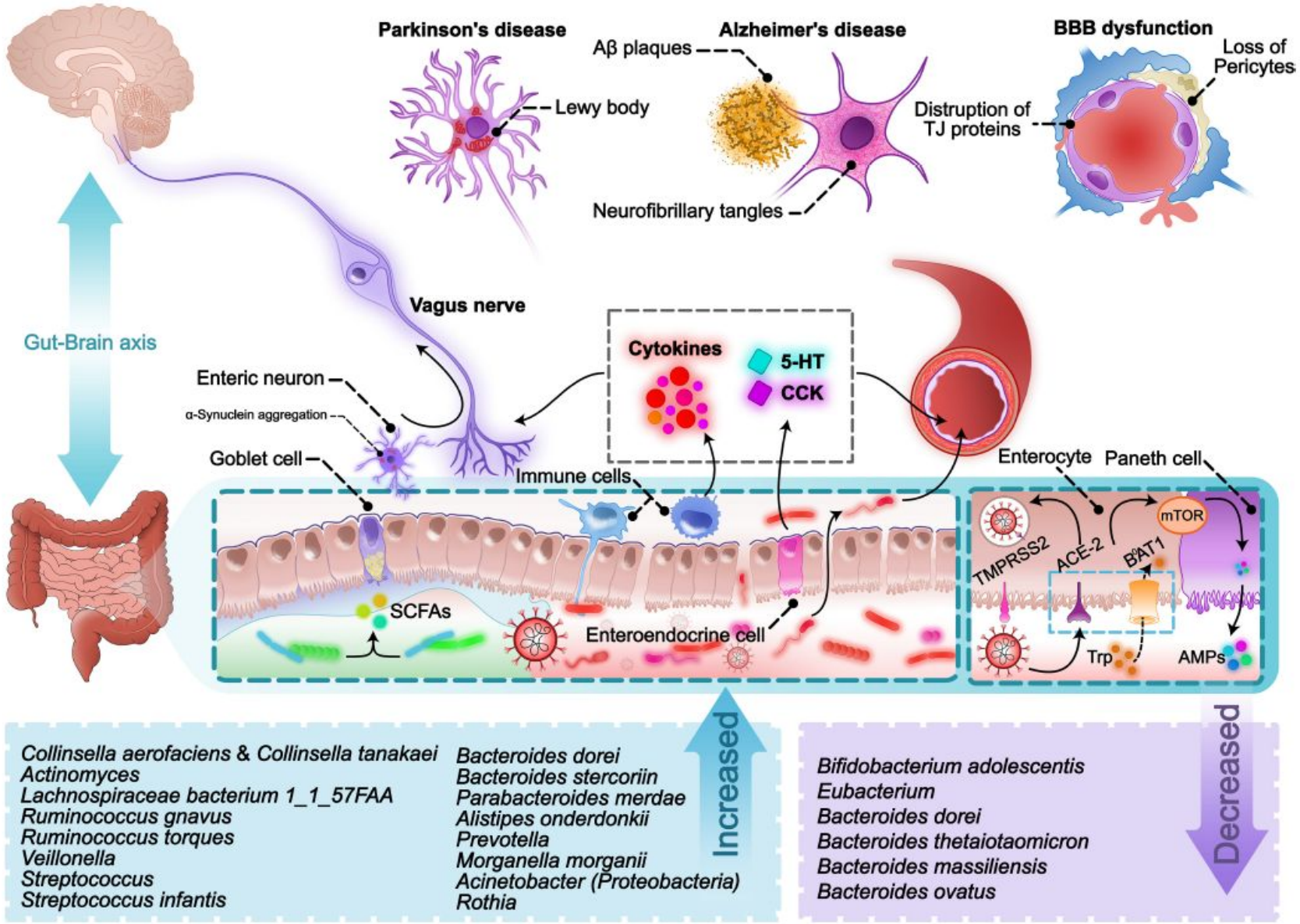
- Long COVID is associated with reduced circulating serotonin levels
- Serotonin depletion is driven by viral RNA-induced type I interferons (IFNs)
- IFNs reduce serotonin through diminished tryptophan uptake and hypercoagulability
- Peripheral serotonin deficiency impairs cognition via reduced vagal signaling

Wong, AC, et al (2023). Serotonin reduction in post-acute sequelae of viral infection. Cell. https://doi.org/10.1016/j.cell.2023.09.013



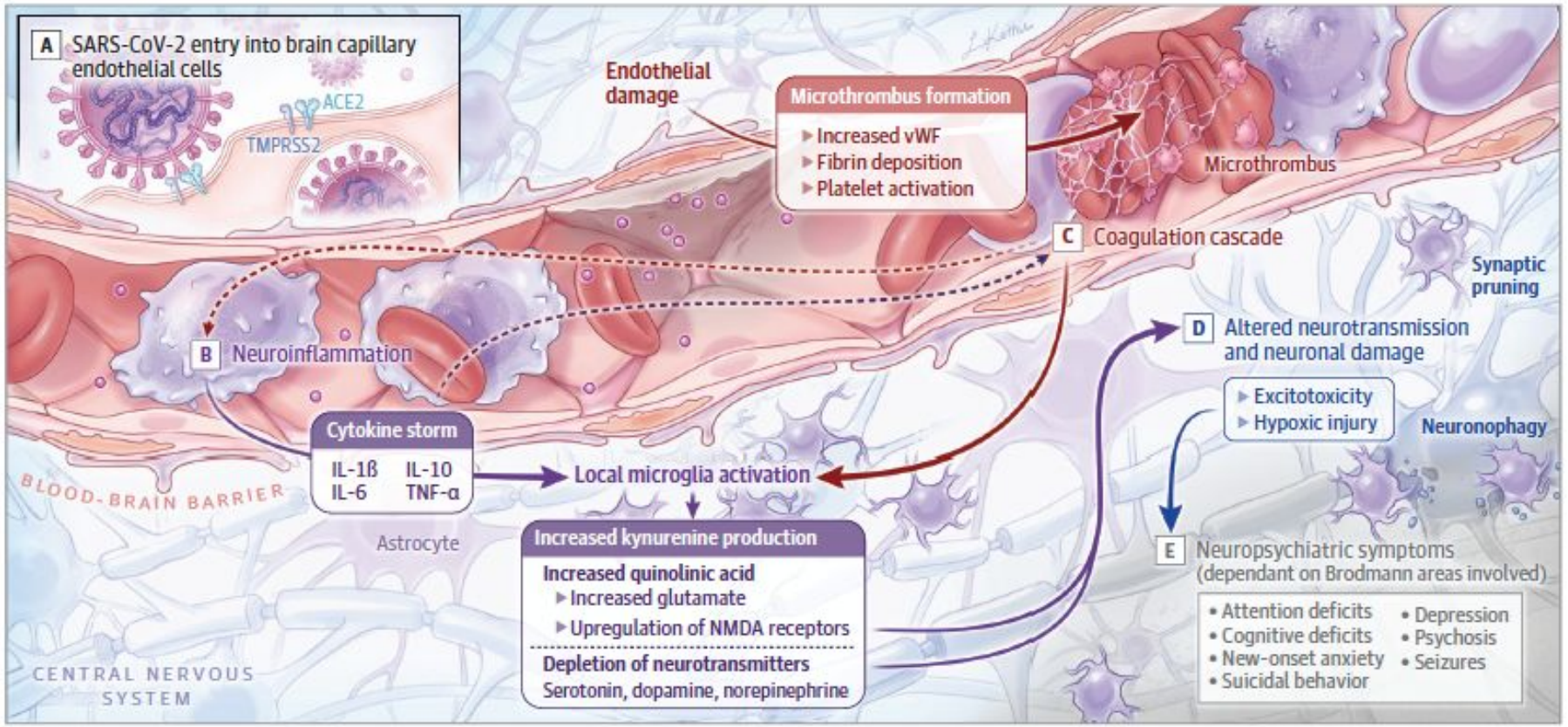
Freedberg, DE, & Chang, L. (2022). Gastrointestinal symptoms in COVID-19: the long and the short of it. Current Opinion in Gastroenterology, 38(6), 555–561. https://doi.org/10.1097/mog.0000000000000876

Vakili K, et al. The contribution of gut-brain axis to development of neurological symptoms in COVID-19 recovered patients: A hypothesis and review of literature. Front Cell Infect Microbiol. 2022 Dec 22;12:983089. doi: 10.3389/fcimb.2022.983089. PMID: 36619768; PMCID: PMC9815719.



Boldrini M, Canoll PD, Klein RS. How COVID-19 Affects the Brain. JAMA Psychiatry. 2021 Jun 1;78(6):682-683. doi: 10.1001/jamapsychiatry.2021.0500. PMID: 33769431; PMCID: PMC9894299.

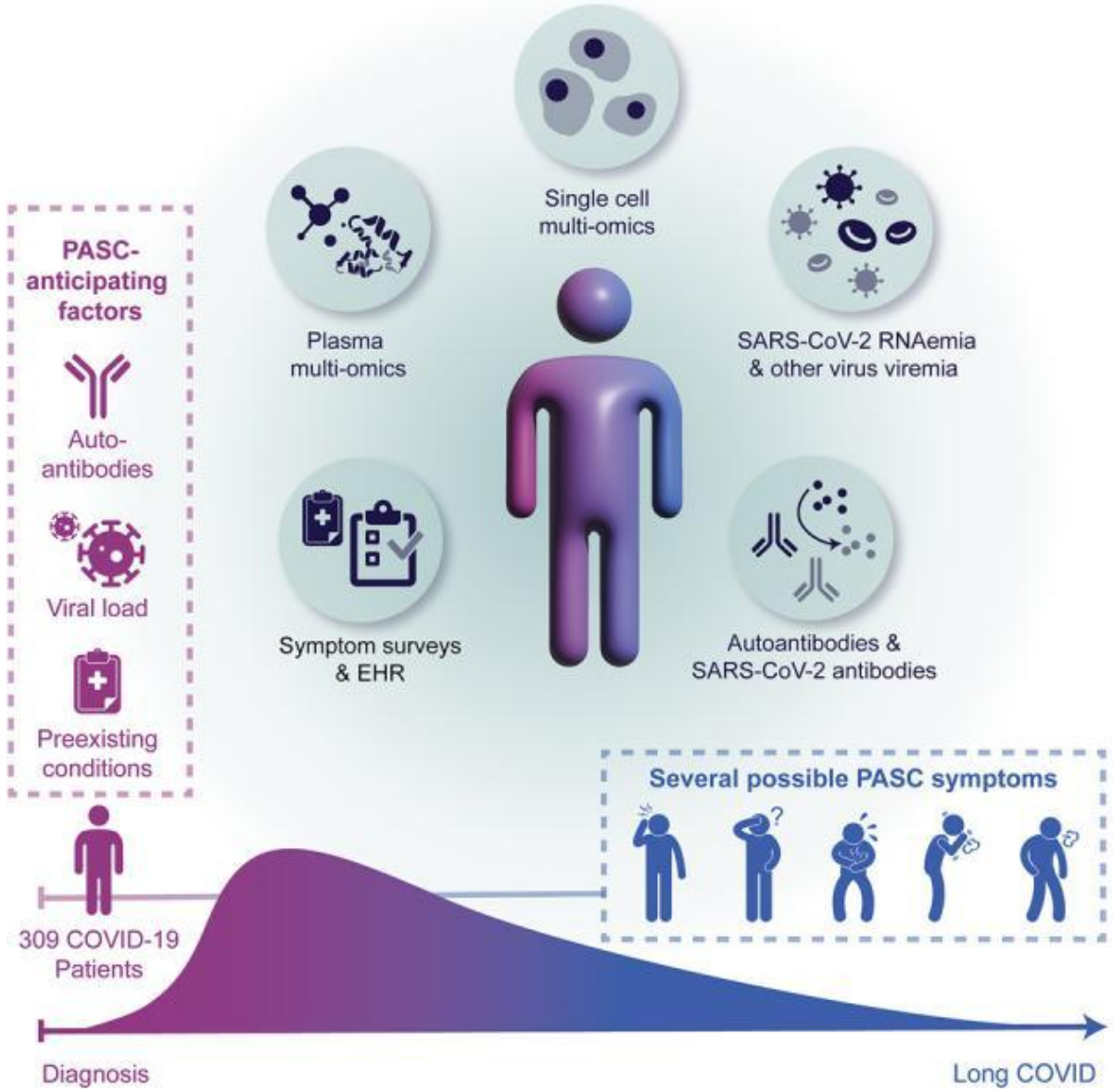
Figure. Brain Vascular Injury, Neurotransmitter System Dysfunction, Thrombotic Events, Neuronal Damage, and Neuropsychiatric Symptoms

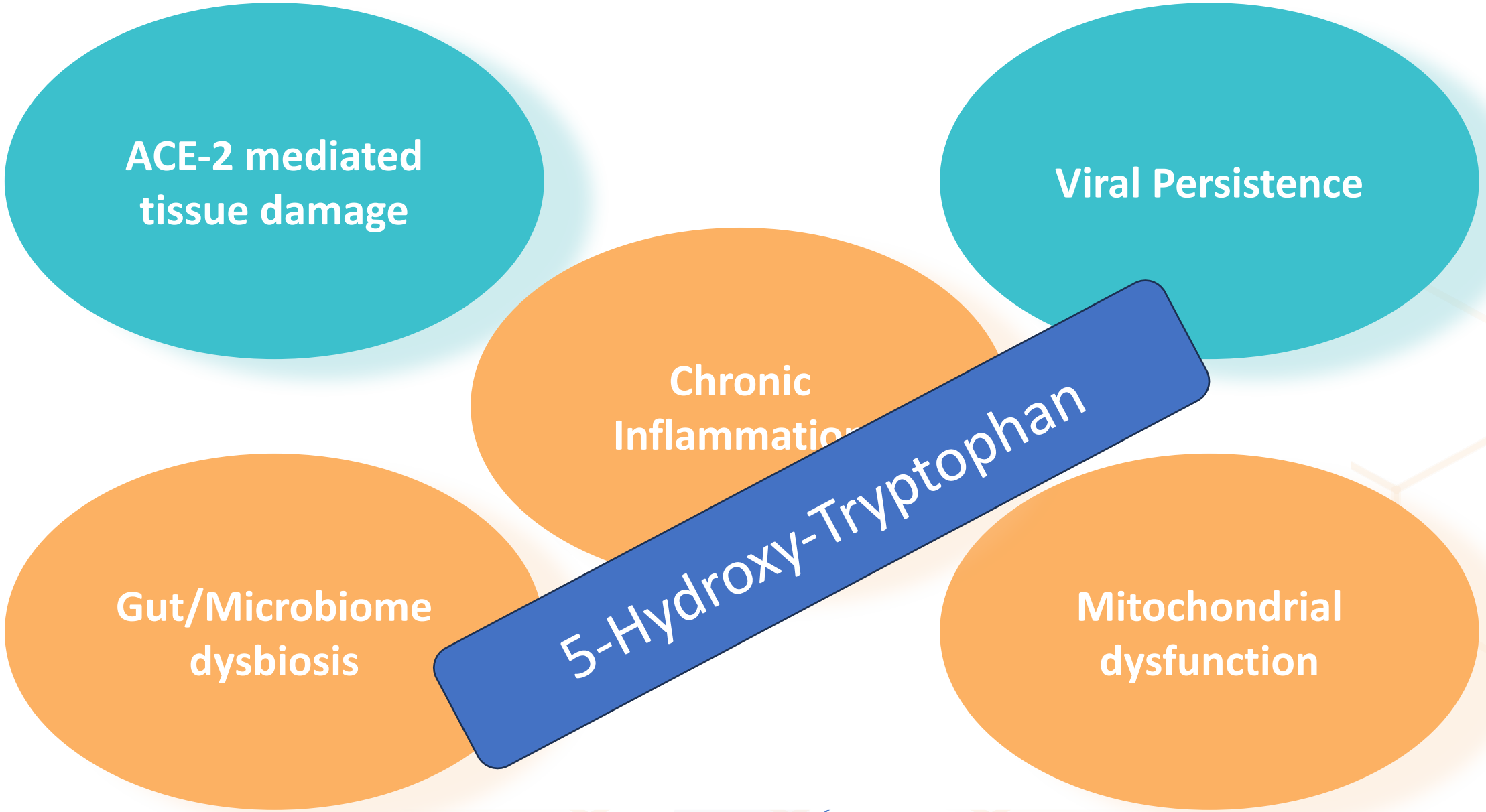


A, SARS-CoV-2 invades endothelial cells via transmembrane angiotensin-converting enzyme 2 (ACE2) receptor, enabled by transmembrane protease, serine 2 (TMPRSS2). B, Cytokine elevation and microglia activation result in increased kynurenine, quinolinic acid, and glutamate, and neurotransmitter depletion. C, Coagulation cascade and elevation of von Willebrand factor (vWF) lead to thrombotic events. D, Altered neurotransmission, excitotoxicity by increased glutamate, and hypoxic injury contribute to neuronal dysfunction and loss. E, Neuropsychiatric symptoms differ depending on the Brodmann area involved. IL indicates interleukin; NMDA, *N*-methyl-D-aspartate; TNF, tumor necrosis factor.

Multiple early factors anticipate post-acute COVID-19 sequelae

Su, Y, Yuan, D, et. al. (2022). Multiple early factors anticipate post-acute COVID-19 sequelae. Cell, 185(5). https://doi.org/10.1016/j.cell.2022.01.014

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