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Neuroinvasion of SARS-CoV-2 in human and mouse brain

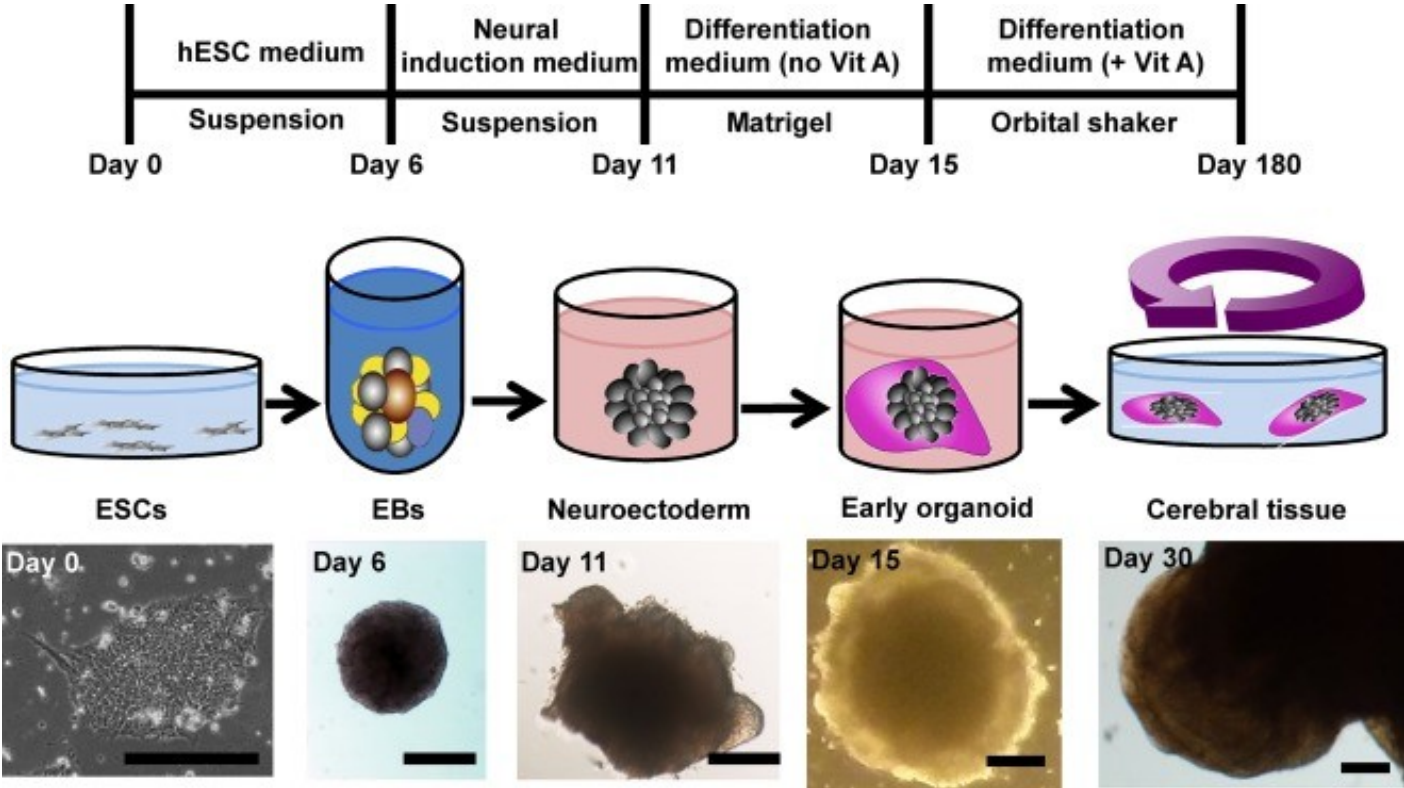
[Eric Song](#)^{1,#} [Ce Zhang](#)^{2,3,#} [Benjamin Israelow](#)^{1,4} [Alice Lu-Culligan](#)¹ [Alba Vieites Prado](#)⁵ [Sophie Skriabine](#)⁵ [Peiwen Lu](#)¹ [Orr-El Weizman](#)¹ [Feimei Liu](#)^{1,6} [Yile Dai](#)¹ [Klara Szigeti-Buck](#)^{3,6} [Yuki Yasumoto](#)^{3,7} [Guilin Wang](#)⁸ [Christopher Castaldi](#)⁸ [Jaime Heltke](#)⁸ [Evelyn Ng](#)⁸ [John Wheeler](#)⁸ [Mia Madel Alfajaro](#)^{1,9} [Etienne Levavasseur](#)⁵ [Benjamin Fontes](#)¹⁰ [Neal G. Ravindra](#)^{11,12} [David Van Dijk](#)^{11,12} [Shrikant Mane](#)^{2,8} [Murat Gunel](#)^{2,3,13} [Aaron Ring](#)¹ [Syed A. Jaffar Kazmi](#)¹⁴ [Kai Zhang](#)¹⁴ [Craig B Wilen](#)^{1,9} [Tamas L. Horvath](#)^{6,15,16} [Isabelle Plu](#)^{5,17} [Stephane Haik](#)^{5,17,18,10} [Jean-Leon Thomas](#)^{5,19} [Angeliki Louvi](#)^{3,13} [Shelli F. Farhadian](#)^{4,19} [Anita Huttner](#)²⁰ [Danielle Seilhean](#)^{5,17} [Nicolas Renier](#)⁵ [Kaya Bilguvar](#)^{2,8,*} and [Akiko Iwasaki](#)^{1,16,21,22,*}

by Michael Springer

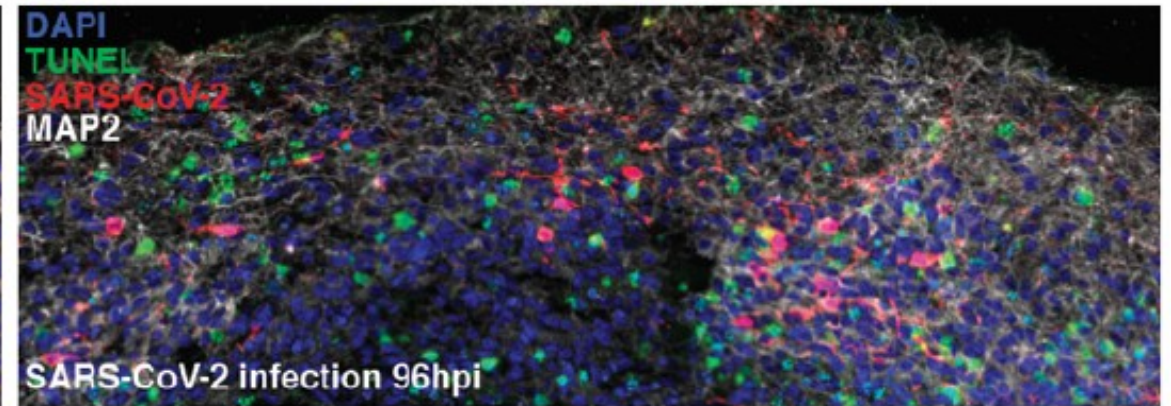
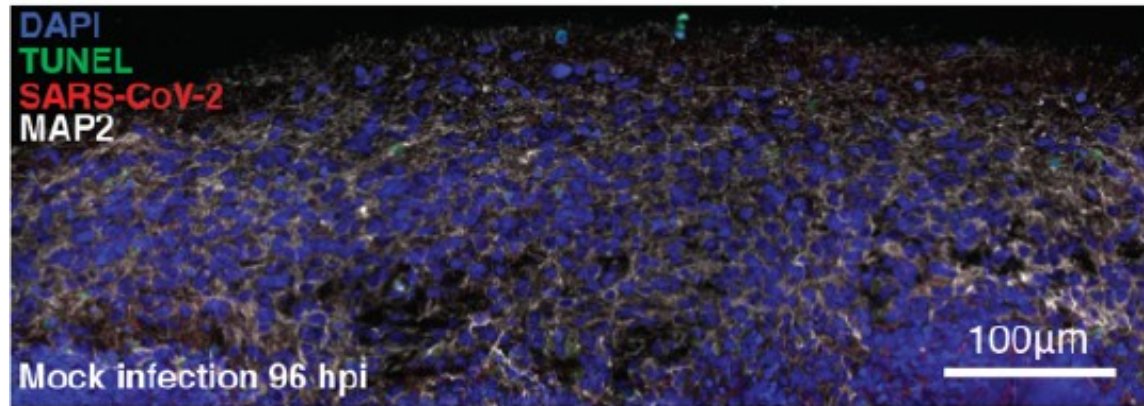
Contents

- Human brain organoids
 - Spread and route of infection
 - Cellular responses to infection
- Mouse model
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- Human brain autopsies
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Brain organoid

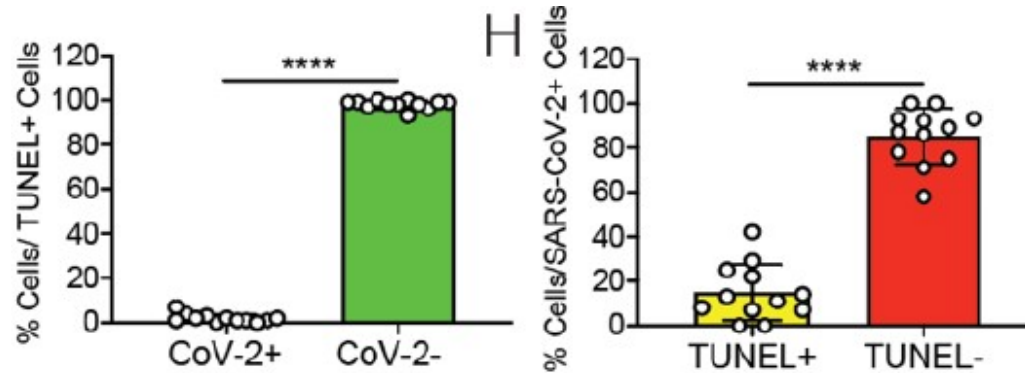
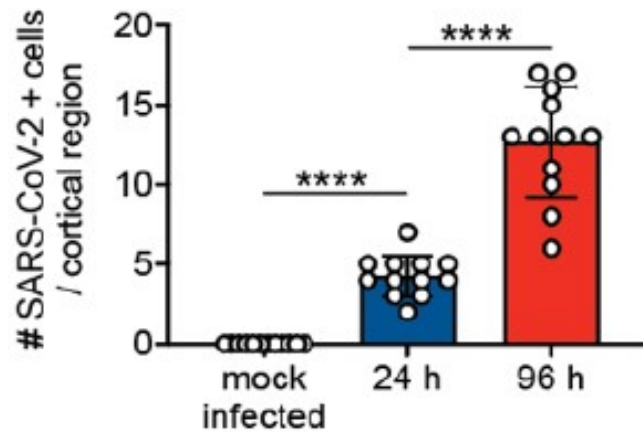


Infection and induced cell death



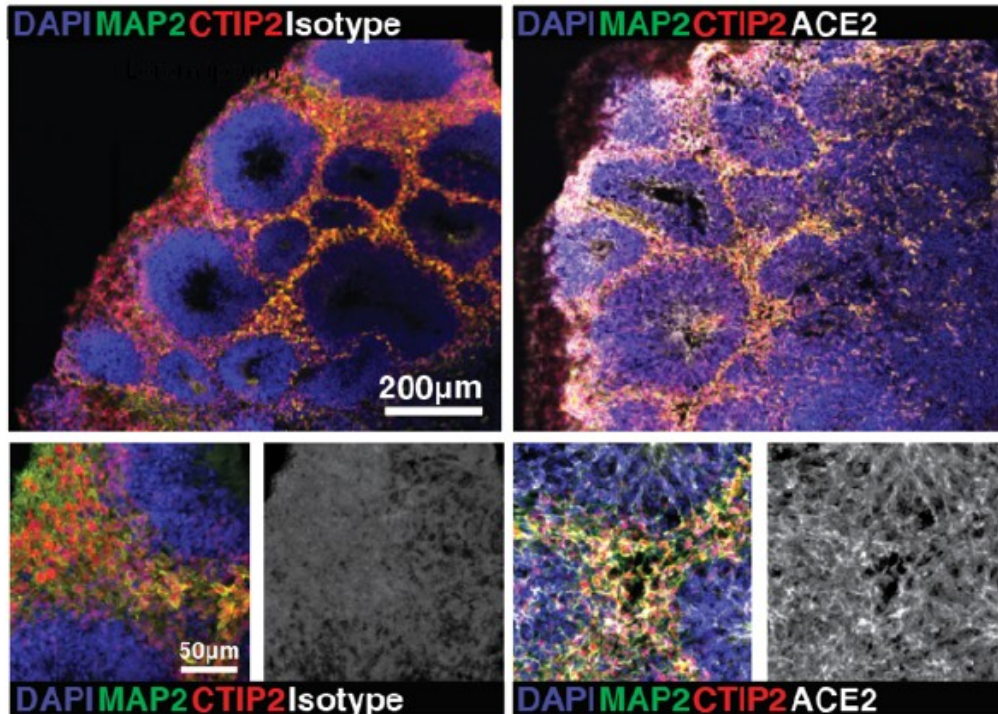
- TUNEL: double-strand DNA breaks (apoptosis)
- MAP2: marker of dendrites and perikarya (neurons)

Infection and induced cell death



- SARS-CoV-2 infects human brain organoids
- Infected cells induce cell death in its surroundings

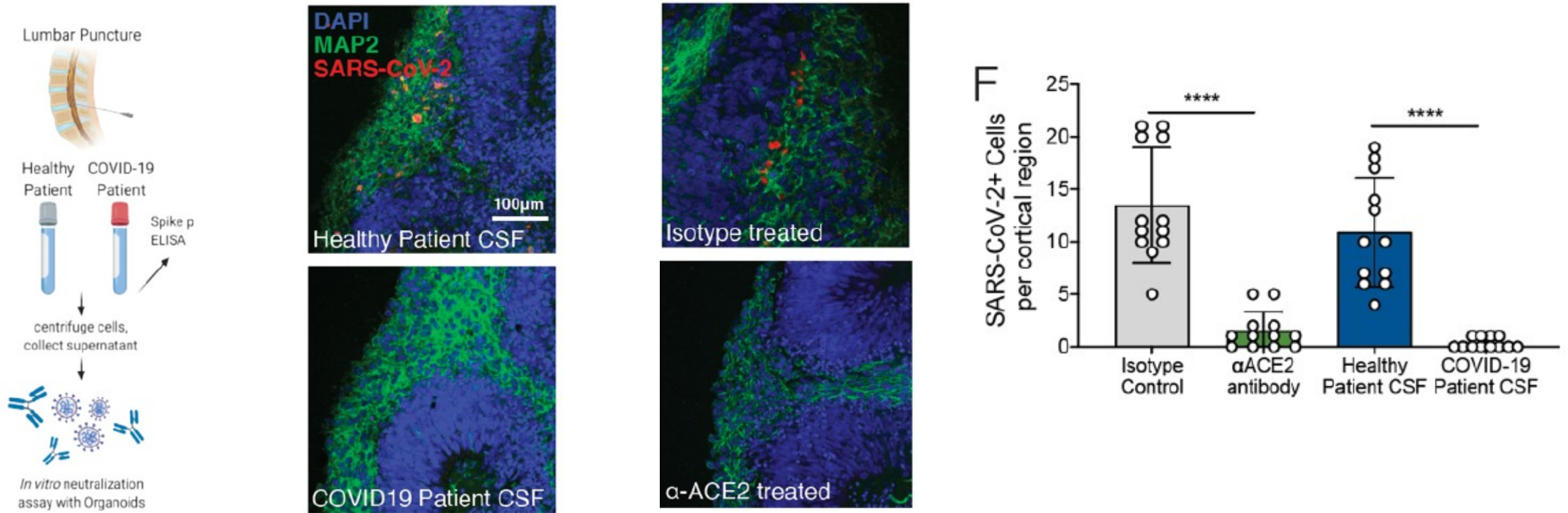
Route of infection



- MAP2: marker of dendrites and perikarya (neurons)
- CTIP2: indicates 'immune regulation'
- ACE2: ACE2, transmembrane protein

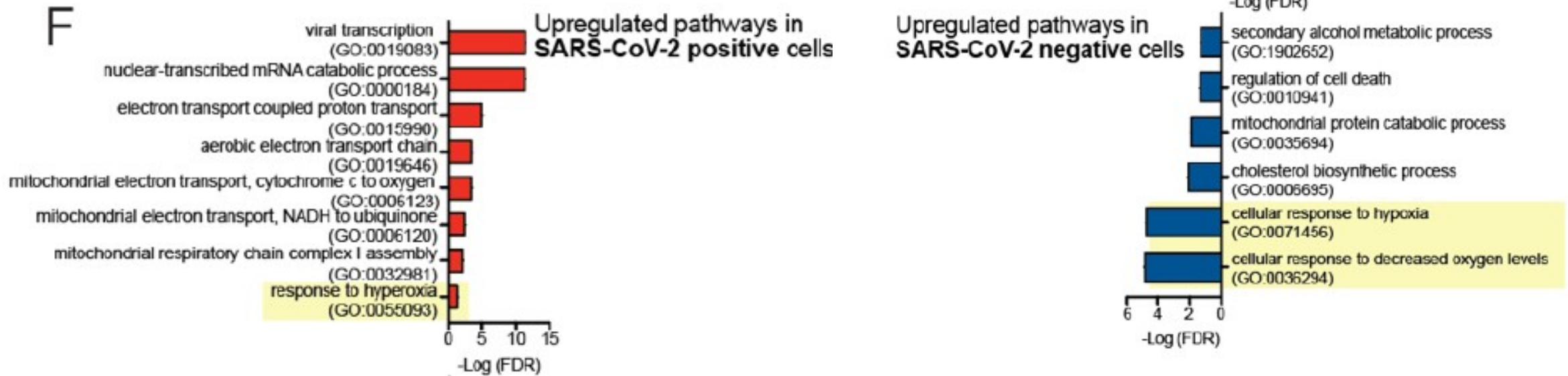
→ ACE2 is present

Route of infection – verification by blocking



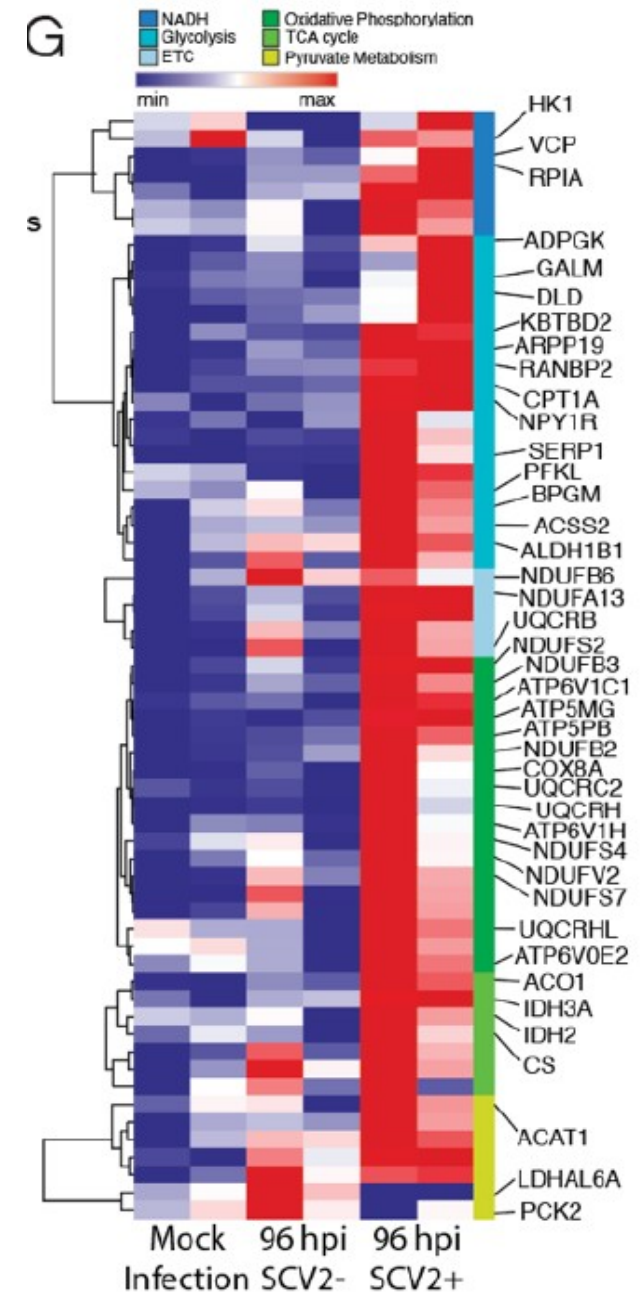
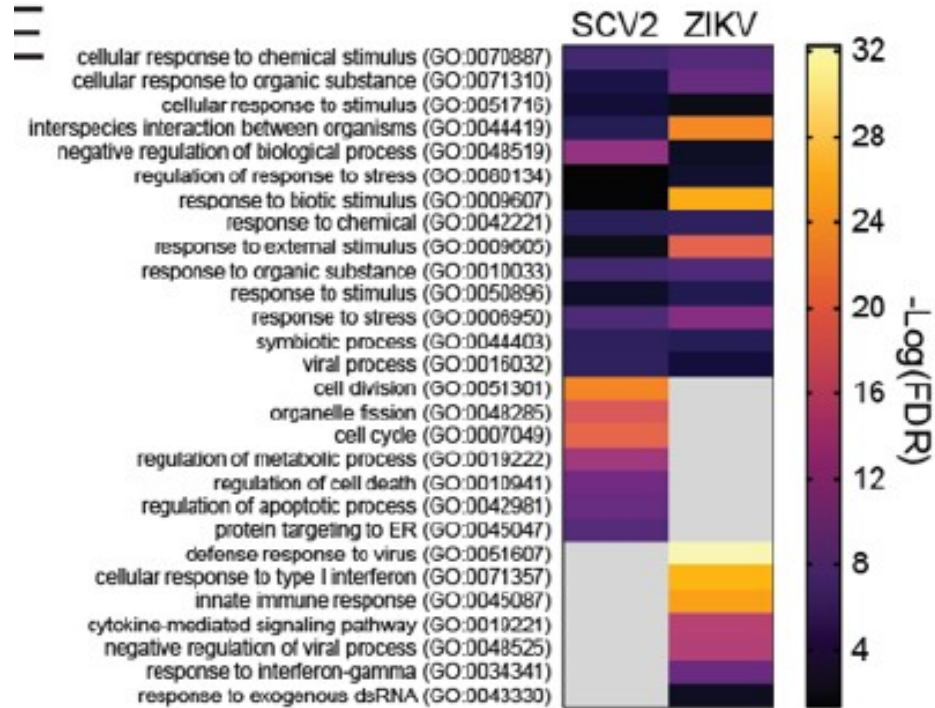
- MAP2: marker of dendrites and perikarya (neurons)
 - Infection depends on ACE2
 - Infection can be blocked by CSF of COVID-19 patients

Up-regulation of metabolism

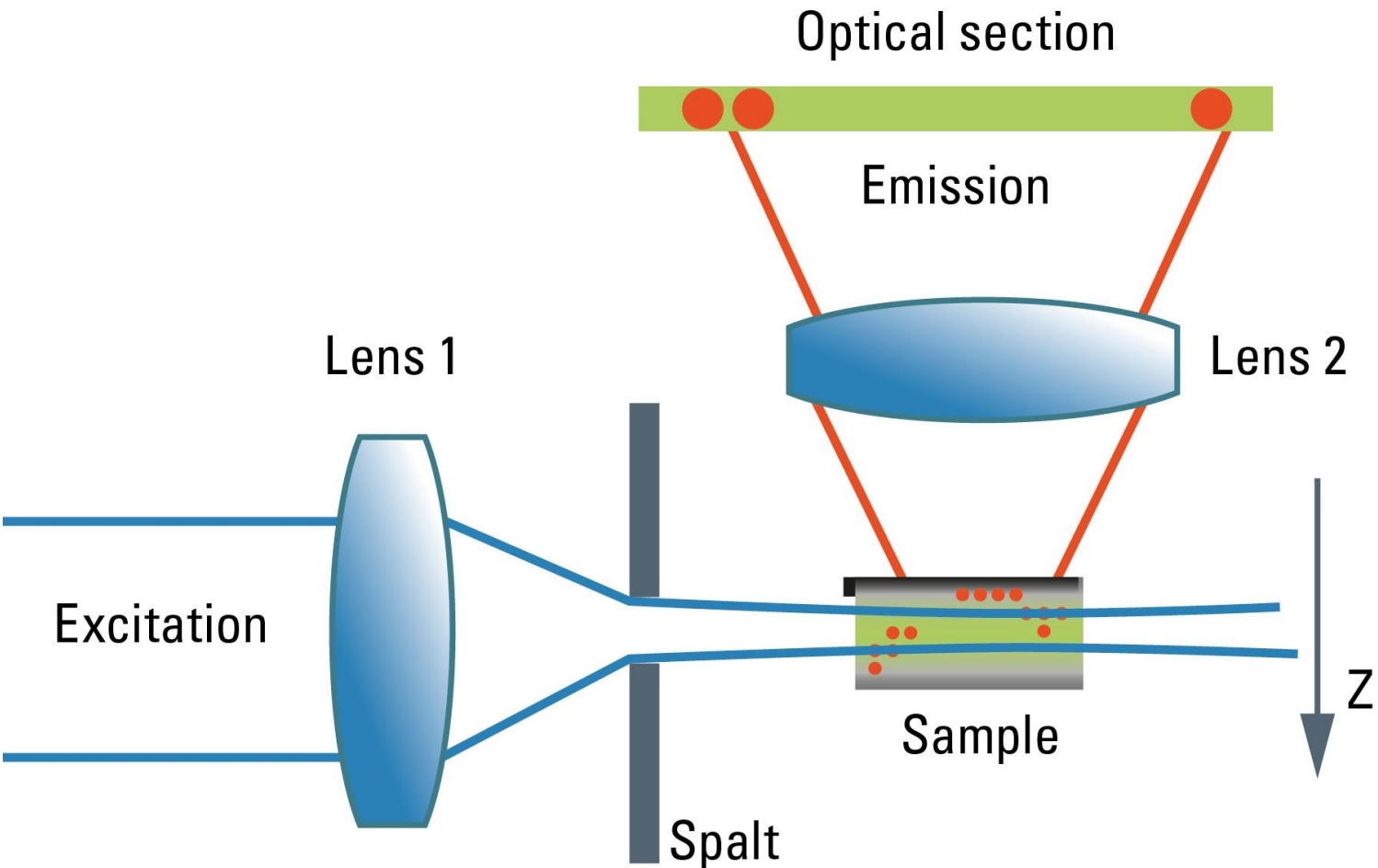


→ High metabolism induces hypoxia in surroundings

Up-regulation of metabolism

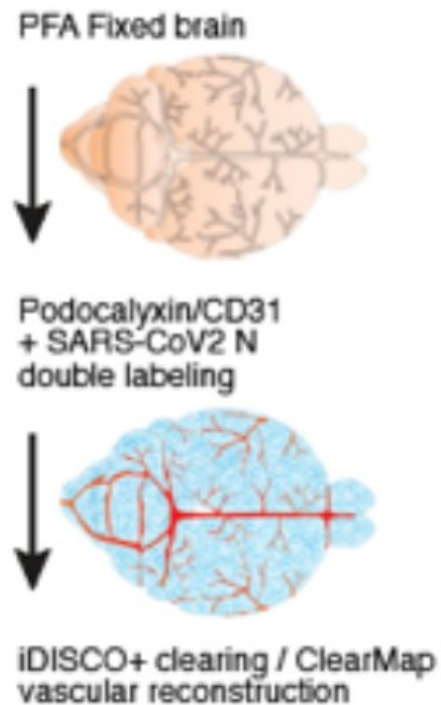


Light sheet microscopy



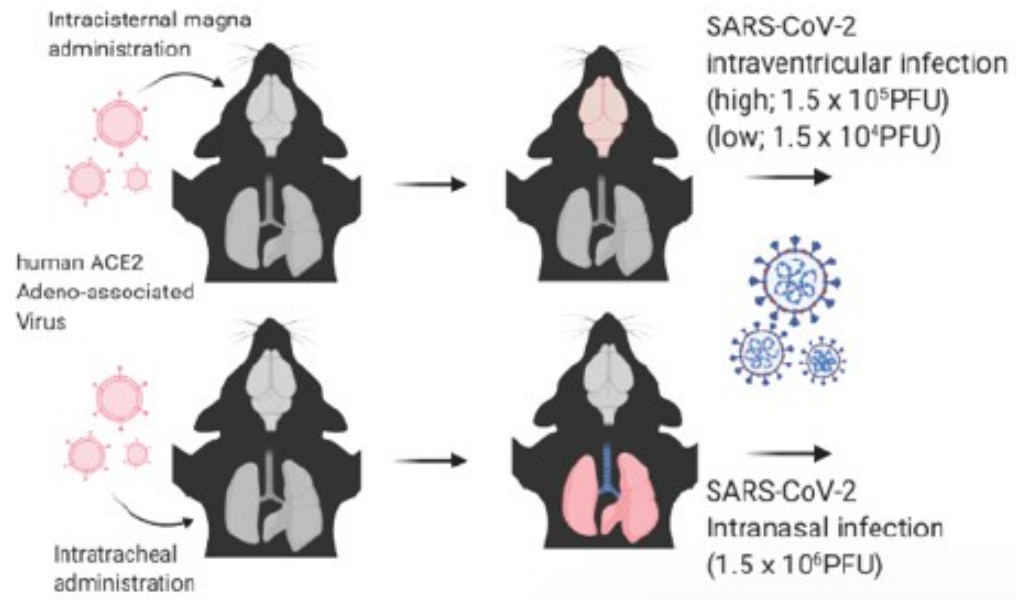
iDISCO

3DISCO = 3D imaging of solvent-cleared organs

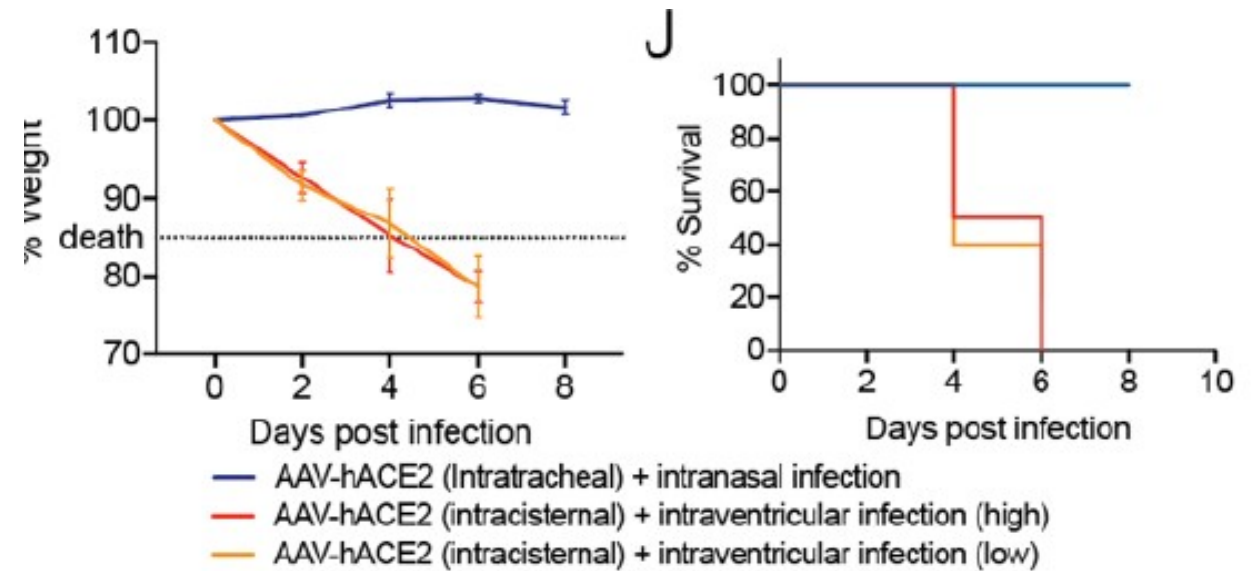
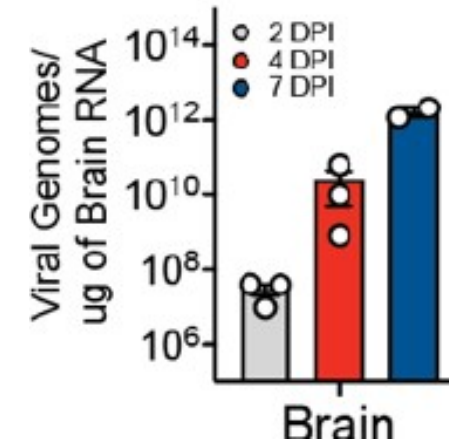


Solvent based matching of refractive index of tissue

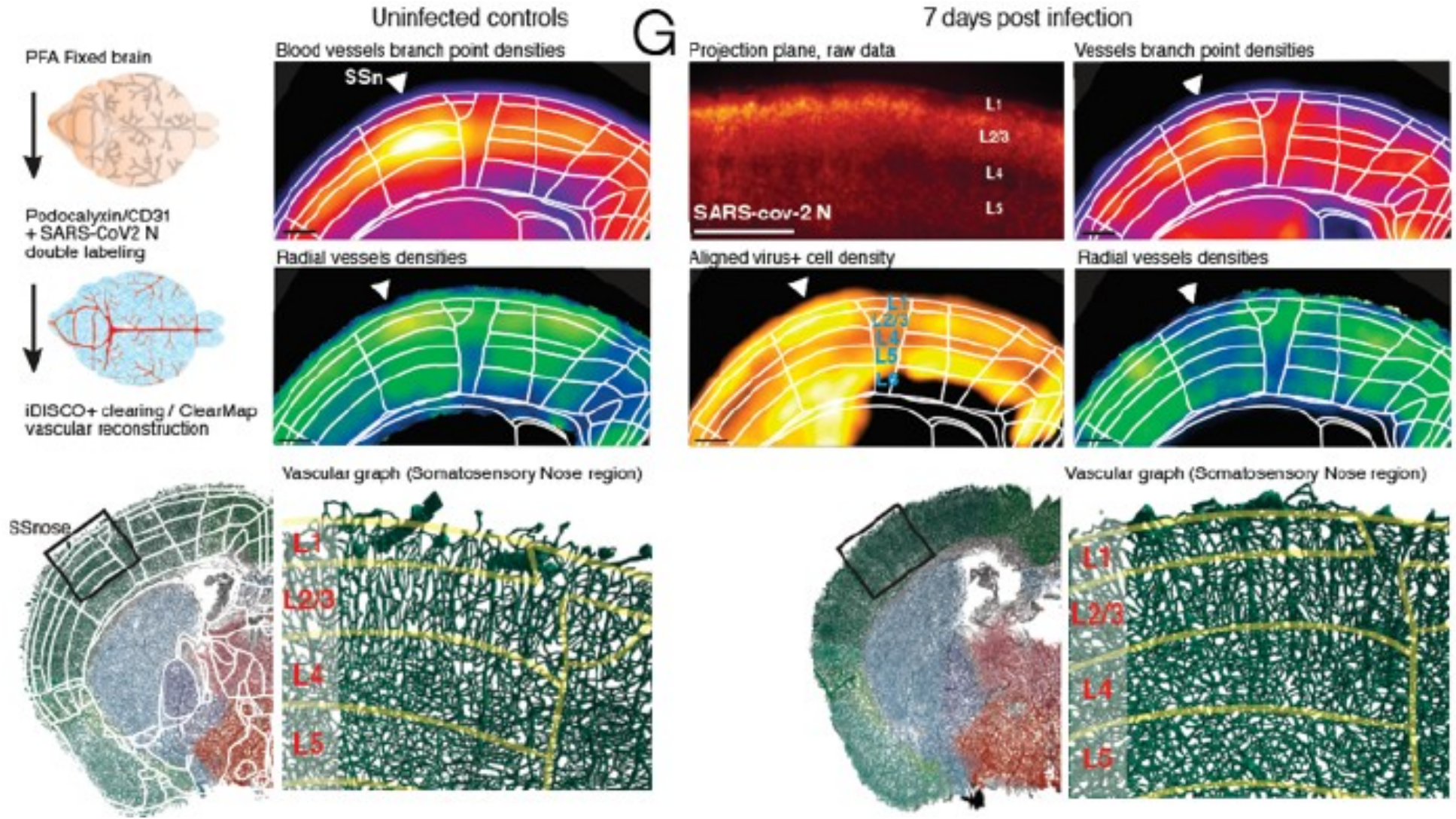
Expressing hACE2 in mice



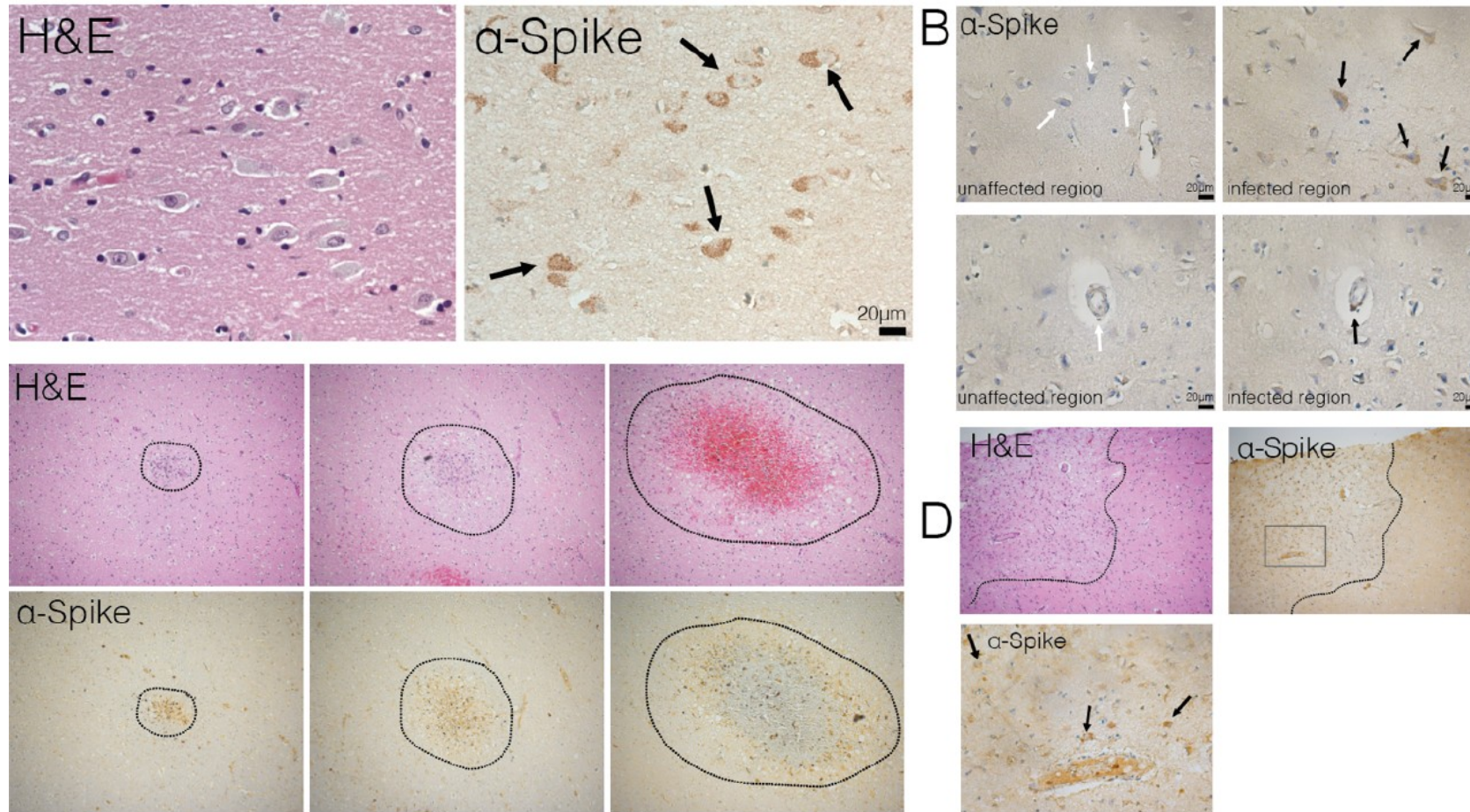
- Virus is cultivated in brain
- Sham operation is missing



Expression of N viral protein



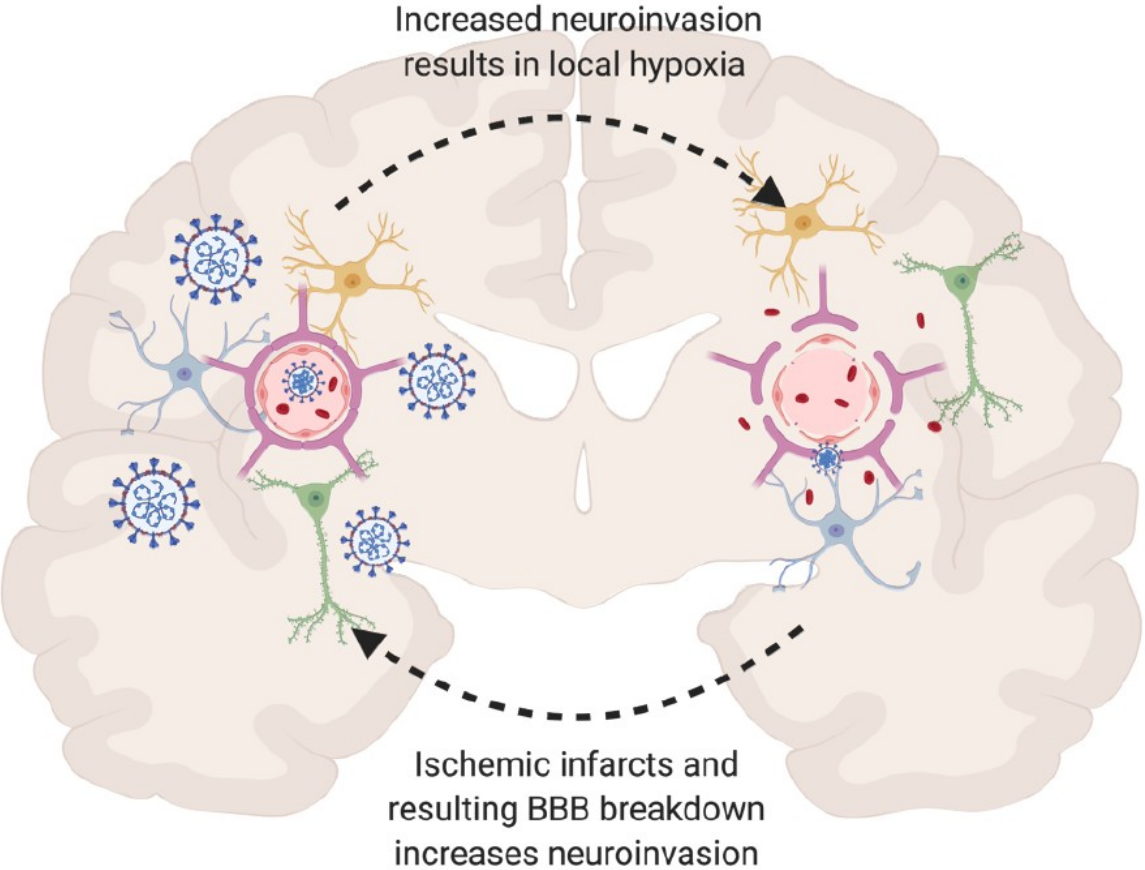
Human brain autopsies



→ Neuroinvasion

→ Positive staining focused around ischemic infarct

Schematic



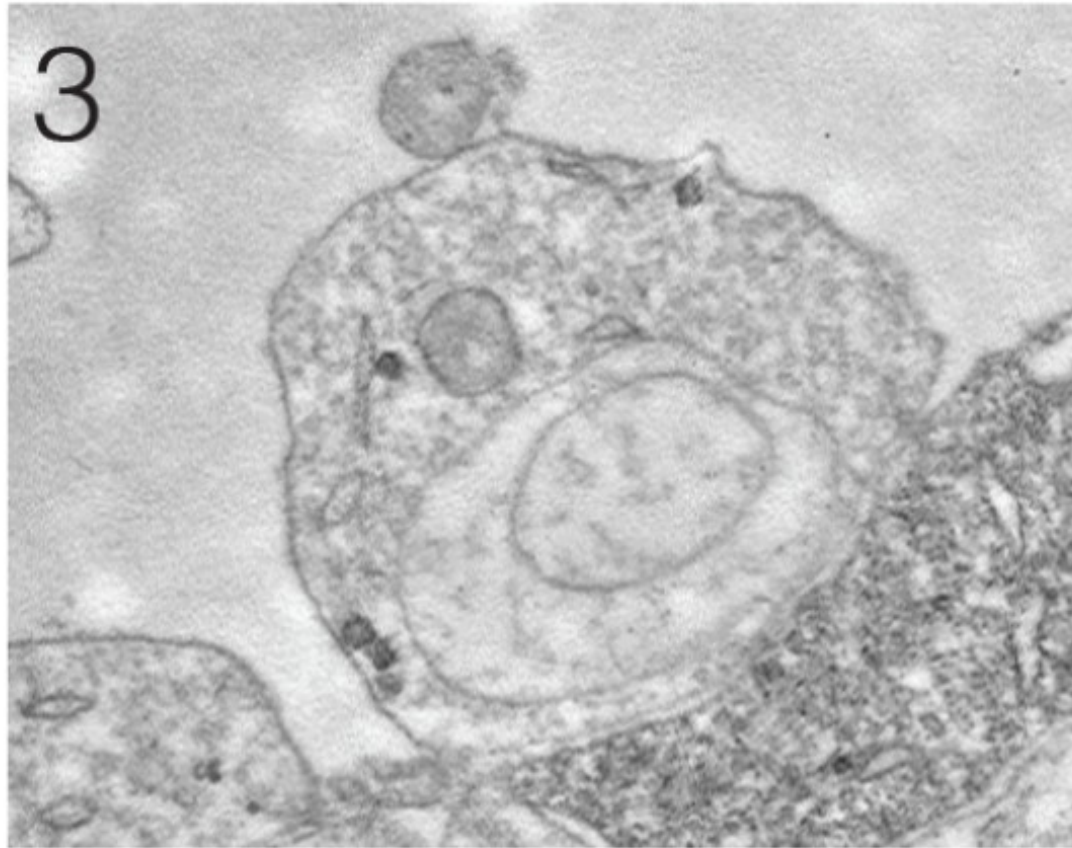
Schmematic

Summary

- SARS-CoV-2 can infect the brain and cause significant damage
- Increased metabolism causes local ischaemia
- SARS-CoV-2 causes unique infection pattern in the brain

Discussion

AMT CAMERA SYSTEM



OR-COVI-7-3.tif

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