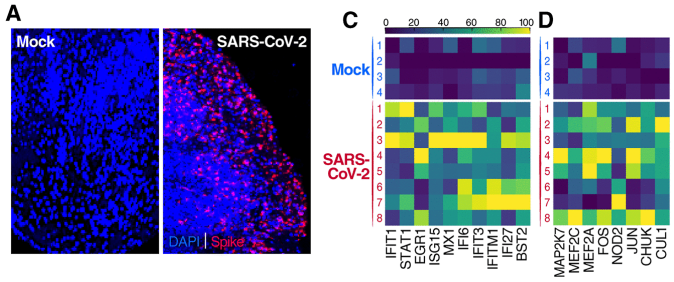
GeoMx® DSP enables characterization of SARs-CoV-2 infection of astrocytes in a brain organoid model

Background

- Central nervous system (CNS) symptoms of COVID-19 include loss of smell and taste, headache, delirium, acute psychosis, seizures, and stroke, yet it's unclear what causes the neurological effects of COVID-19
- Loss of gray matter occurs but it is unknown if it's due to infection, inflammation, or a bystander effect

Research Questions

1. What receptor(s) mediates the entry of SARS-CoV-2 into astrocytes that poorly express ACE2?
2. Do different variants of SARS-CoV-2 display different abilities to infect astrocytes?
3. How does SARS-CoV-2 infection alter astrocyte gene expression?
4. How do these transcriptomic changes impact neuronal function and survival?



Experimental Setup

Instrument	GeoMx® DSP
Sample Type	FFPE
Tissue Type	Human Brain Organoids
Assay	Human Whole Transcriptome Atlas
Analyte	RNA
Readout	NGS

Why GeoMx?

Spatial profiling allows for precise transcriptional characterization of virally infected cells within the brain organoids which could not be done with scRNA-seq or bulk expression profiling.

-Kong et al.

12 Regions of Interest (ROIs) were selected on each slide based on the number of cells in each ROI and positive staining for the spike protein. Figures reproduced with permission from Kong et al. mBio. 2022 Nov-Dec; 13(6): e02308-22. under the ***Creative Commons license.***

Results & Conclusions

- Astrocytes are the primary target for SARs-CoV-2, and it likely enters the cells via NRP1 and TPCN2.
- Infection leads to an increase in expression of genes associated with the Type 1 interferon response, chromatic remodeling, and apoptosis.
- Expression of genes involved in cell communication, cell junction organization, solute membrane transporters, and synapse function are also downregulated upon infection.
- SARS-CoV-2 triggers a potentially pathological interferon response that combines with an inflammatory response to create an environment that promotes neuronal dysfunction.

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For more information, please visit nanostring.com/geomx

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