

Research infrastructure for infection-associated chronic disease biomarker discovery

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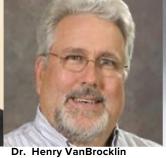


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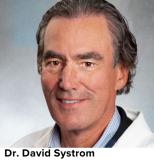
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We must embrace open science



Long COVID or Post-acute Sequelae of COVID-19 (PASC): An Overview of Biological Factors That May Contribute to Persistent Symptoms

Amy D. Proal¹ and Michael B. VanElzakker^{1,2,*}

We must study tissue in addition to body fluids such as blood

Autopsy studies

Tissue biopsy studies

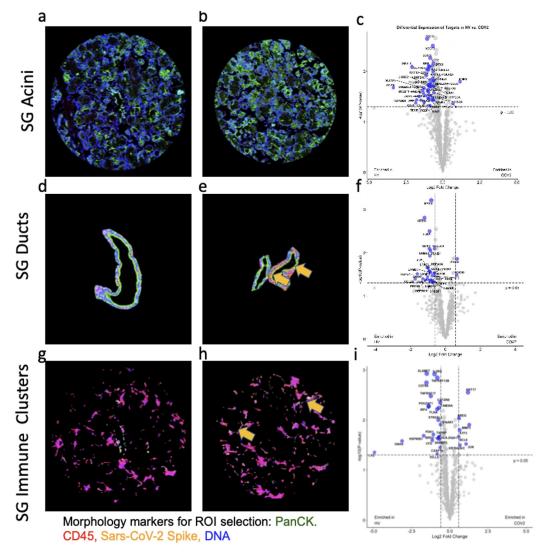
Imaging studies

Fluid biomarker studies

Organoid/animal studies

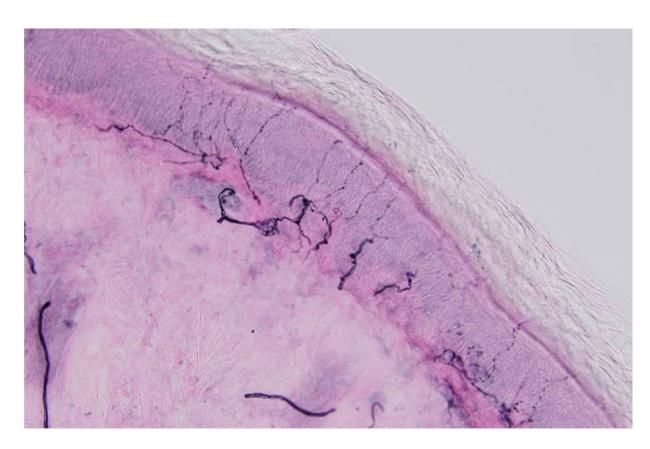
We must determine the *activity* of pathogens and the immune response

- Sequencing technologies like spatial transcriptomics that allow for a detailed understanding of immune and host genome activity near identified pathogens.
- Single nuclei RNA sequencing to identify the detailed landscape of tissue, blood vessel and nervous system changes.
- Microbiome-based technologies that can characterize the collective activity of microbial ecosystems in body tissues.
- Technologies (TCR seq, BCR seq) that capture the activity of individual immune cells responding to pathogen or microbiome activity.



Salivary gland tissue examined via spatial transcriptomics technology. Yellow arrows indicate regions positive for the SARS-CoV-2 spike protein (Image courtesy of Marcelo Freire, JCVI)

We should perform similar forms of analysis on patients with different infection-associated chronic conditions



Long COVID

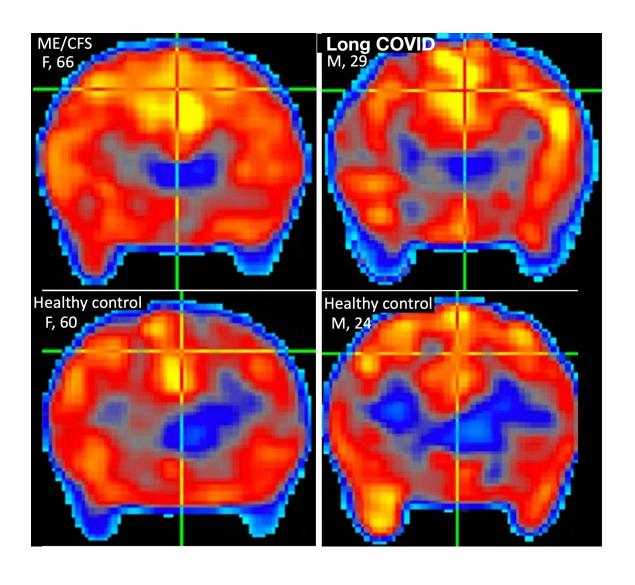
ME/CFS

LongLyme

Ehlers-Danlos Syndrome

A skin punch biopsy sample used in the diagnosis of small fiber neuropathy Source: Therapath

We should perform many different forms of analysis on the same well-characterized study participants



- Fibrin-amyloid microclots
- Platelet activation
- Neutrophil motility
- Neutrophil extracellular traps (NETs)
- Pathogen proteins
- Gut permeability biomarkers
- Microbiome
- Viral neutralization/IgG glycosylation