



# Mitochondrial dysfunction, herpesviruses and autoimmunity in ME/CFS and long COVID

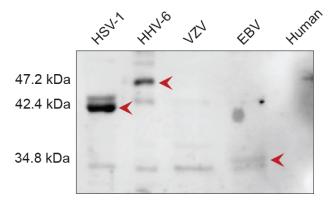
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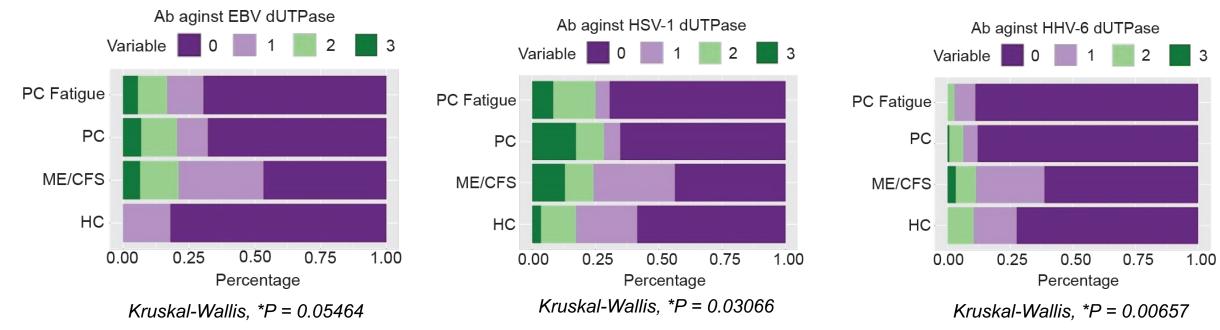




#### Herpesvirus signature in ME/CFS and long COVID



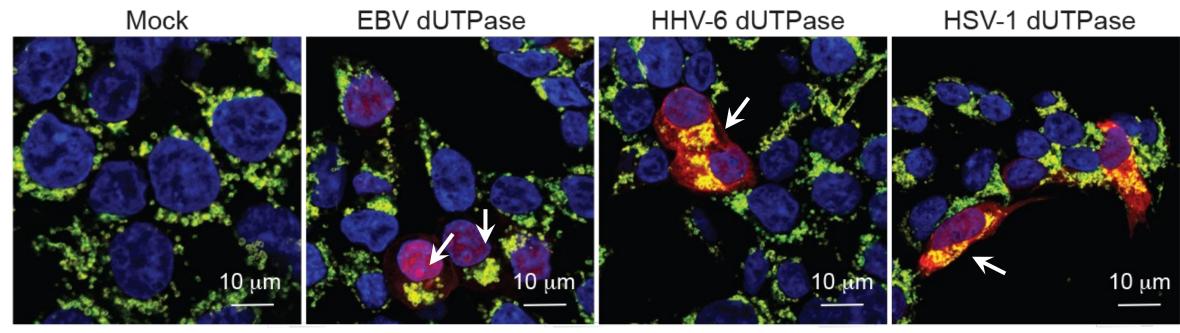
IgG detection in patient serum using recombinant proteins against specific herpesvirus dUTPase proteins



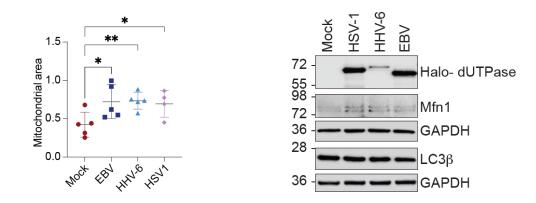
Likert chart with percentage of IgG antibody levels against EBV, HSV-1 and HHV-6 dUTPase



#### Functional significance of herpesvirus dUTPase proteins



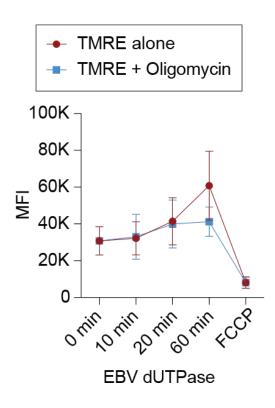
Tom20 Halo-dUTPase Mitofilin DAPI



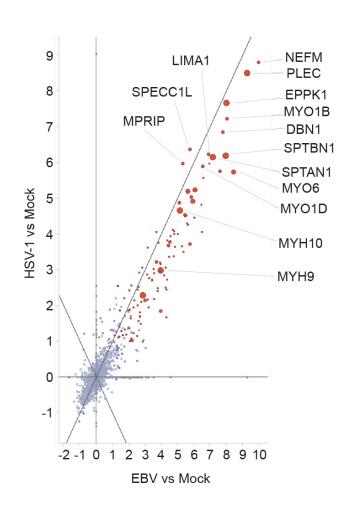
Mitochondrial hyperpolarization by herpesvirus dUTPases



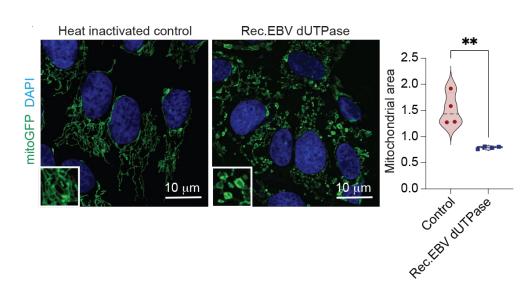
#### Functional significance of herpesvirus dUTPase proteins



EBV dUTPase damages mitochondrial energetics



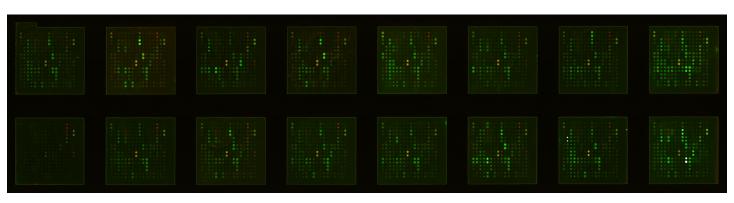
HSV-1, HHV-6 and EBV dUTPase target cellular cytoskeleton that leads to mitochondrial alterations



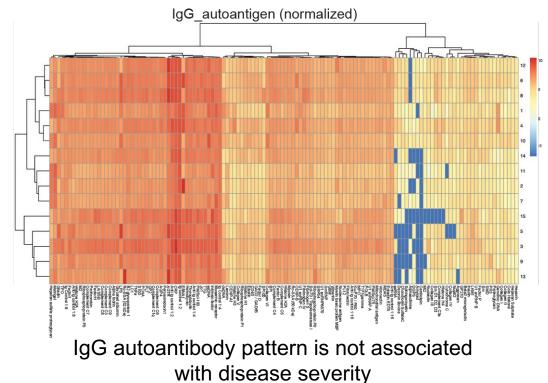
Extracellular herpesvirus dUTPases also hyperpolarize mitochondria but differently



# ME/CFS and autoimmunity



Protein microarray to detect IgG and IgM against 120 different autoantigens and pathogenic antigens



ME/CFS patients have overlapping autoantibodies with SLE and MS

Healthy controls

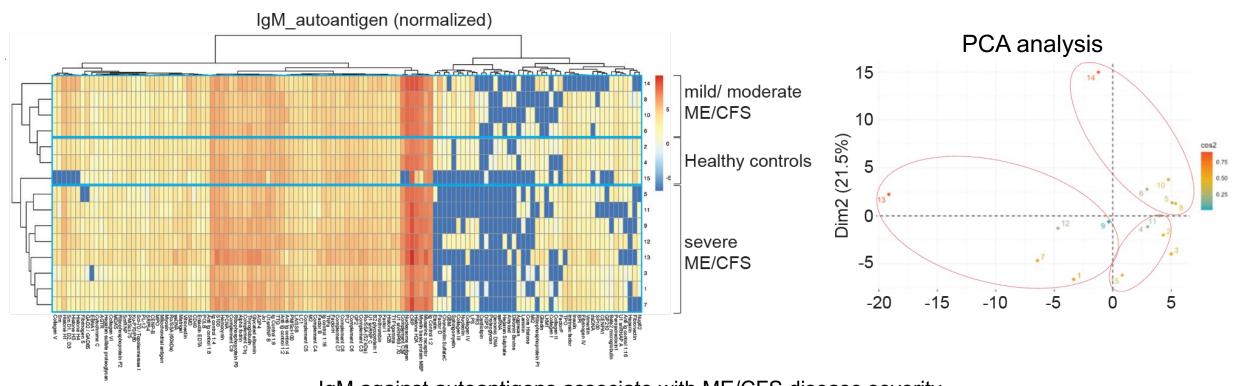
Collagen V
DGPS
Nucleosome
Histone H1
Complement C3a

Sm GP210 dsDNA Collagen VI ssDNA 1.5

ME/CFS patients



# ME/CFS and autoimmunity

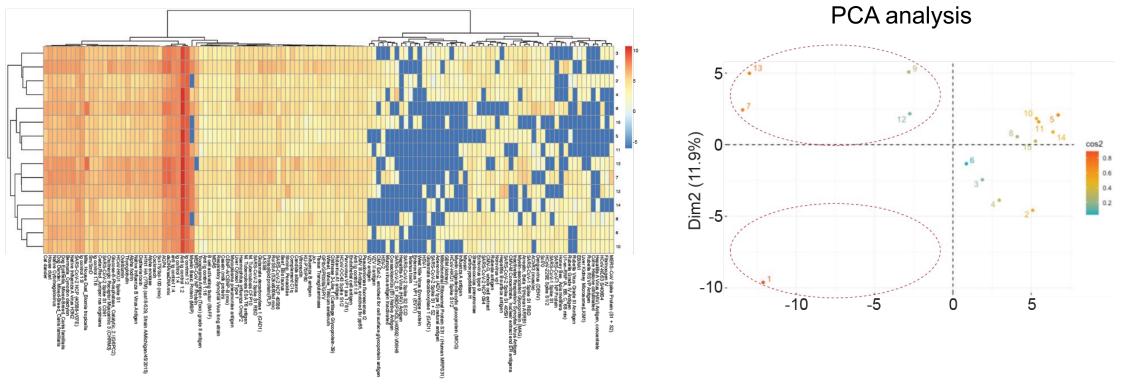


IgM against autoantigens associate with ME/CFS disease severity

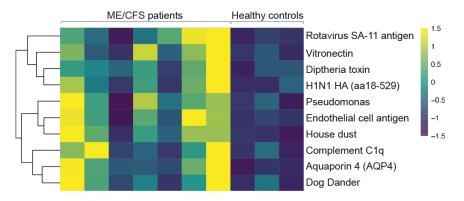


### ME/CFS and autoimmunity

IgM\_pathogenic antigen (normalized)

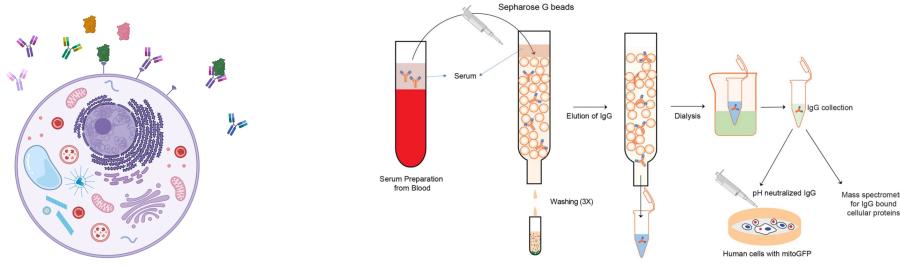


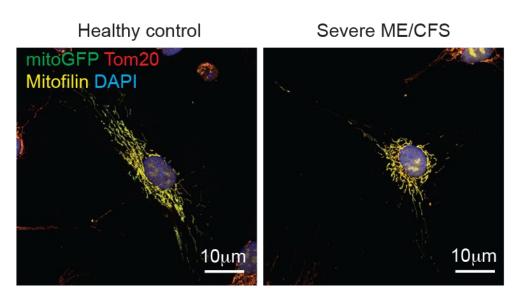
Increased IgM response against common pathogenic antigens in ME/CFS patients



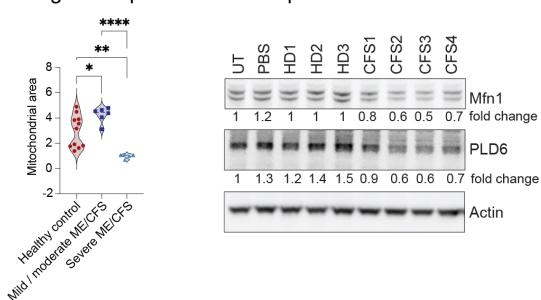


#### Circulating immunoglobulins and mitochondrial health





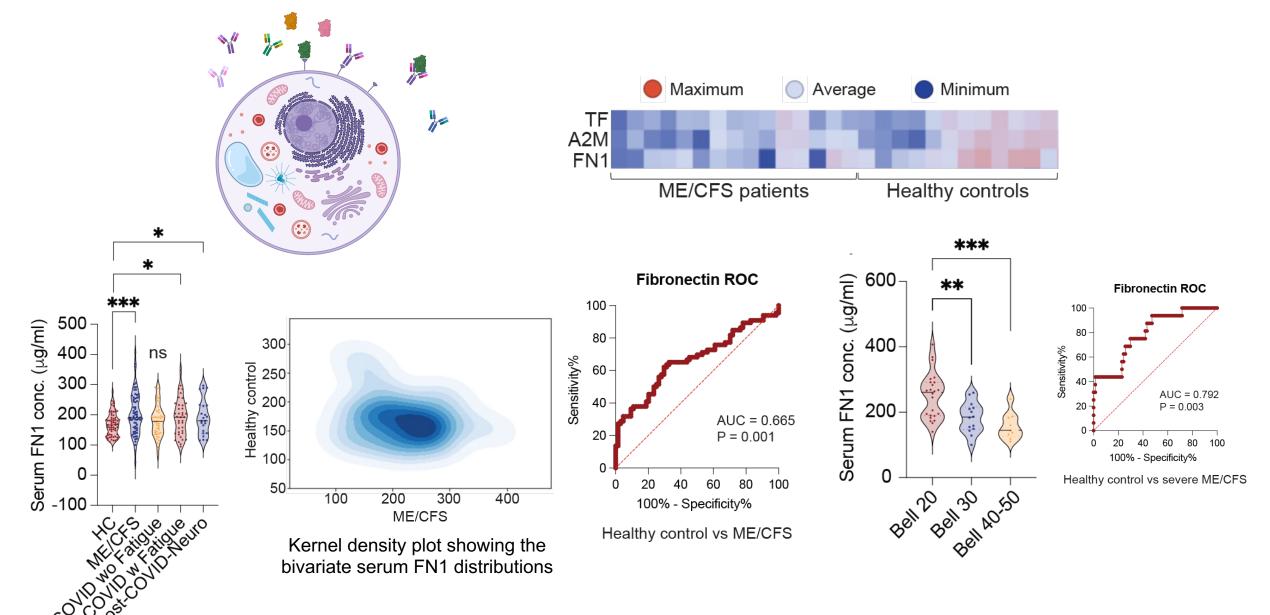




Immunoglobulins from severe ME/CFS patients can induce mitochondrial fragmentation in primary human endothelial cells



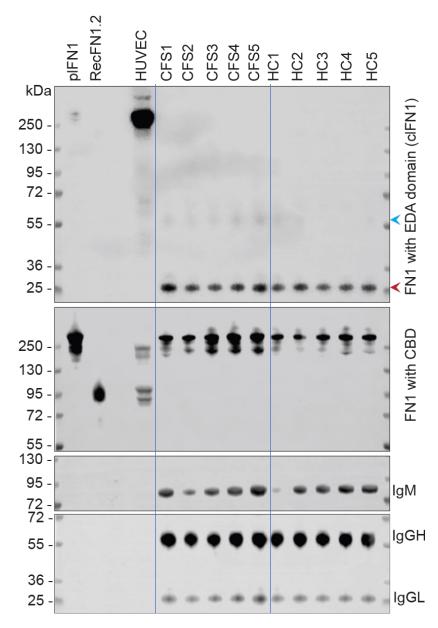
#### Circulating immune complex alterations in ME/CFS



Circulating fibronectin levels are increased significantly in ME/CFS patients



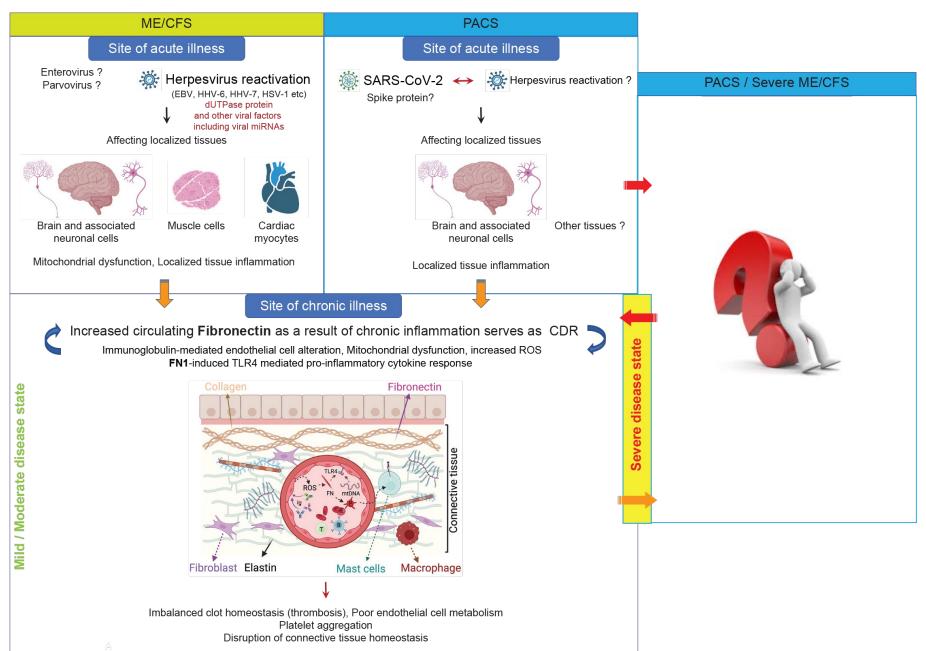
#### Circulating fibronectin in ME/CFS and long COVID



Both plasma fibronectin as well as cellular fibronectin is increased in ME/CFS



# ME/CFS shares only a few features with long COVID



#### Collaborative Partners and Funders

Prof. Carmen Scheibenbogen, Charite, Berlin

Prof. Uta Behrends, Helmholtz Zentrum, Munich

Dr. Franziska Sotzny, Charite, Berlin

Prof. Robert K Naviaux, UCSD, USA

Prof. Marshall V. Williams, Ohio State University, USA

Prof. Maria Ariza, Ohio State University, USA









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The ME/CFS Patient Community