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# RETROPATH 2022

## 32<sup>nd</sup> International Workshop on Retroviral Pathogenesis

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SARS-CoV-2 induces expression of a proinflammatory  
human endogenous retrovirus envelope protein in COVID-19 patients

Hervé Perron, PhD

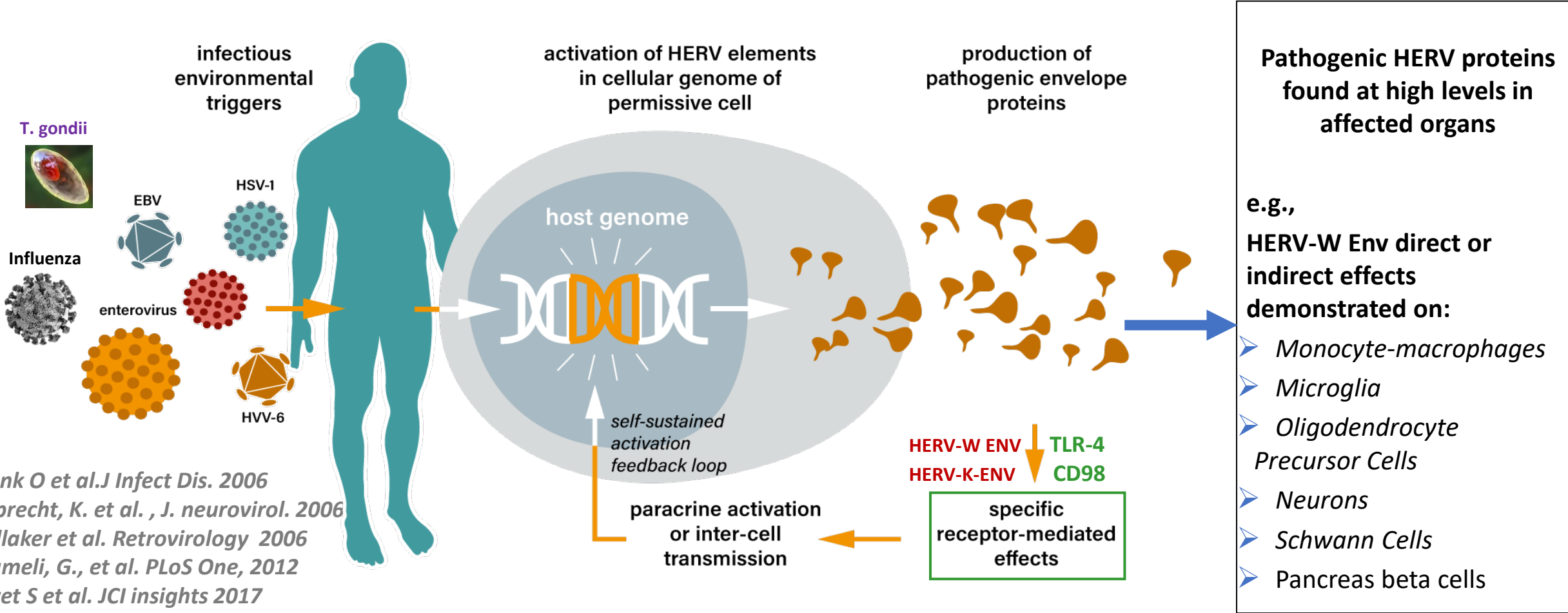
*GeNeuro Switzerland & Geneuro-Innovation France*

*University of Lyon, France.*

**Declared conflict of interest:** Hervé Perron is presently CSO of Geneuro.

# Environmental infectious factors can activate HERV elements

*HERVs may be a key missing link between viral infections and poorly understood autoimmune / neurodegenerative diseases*

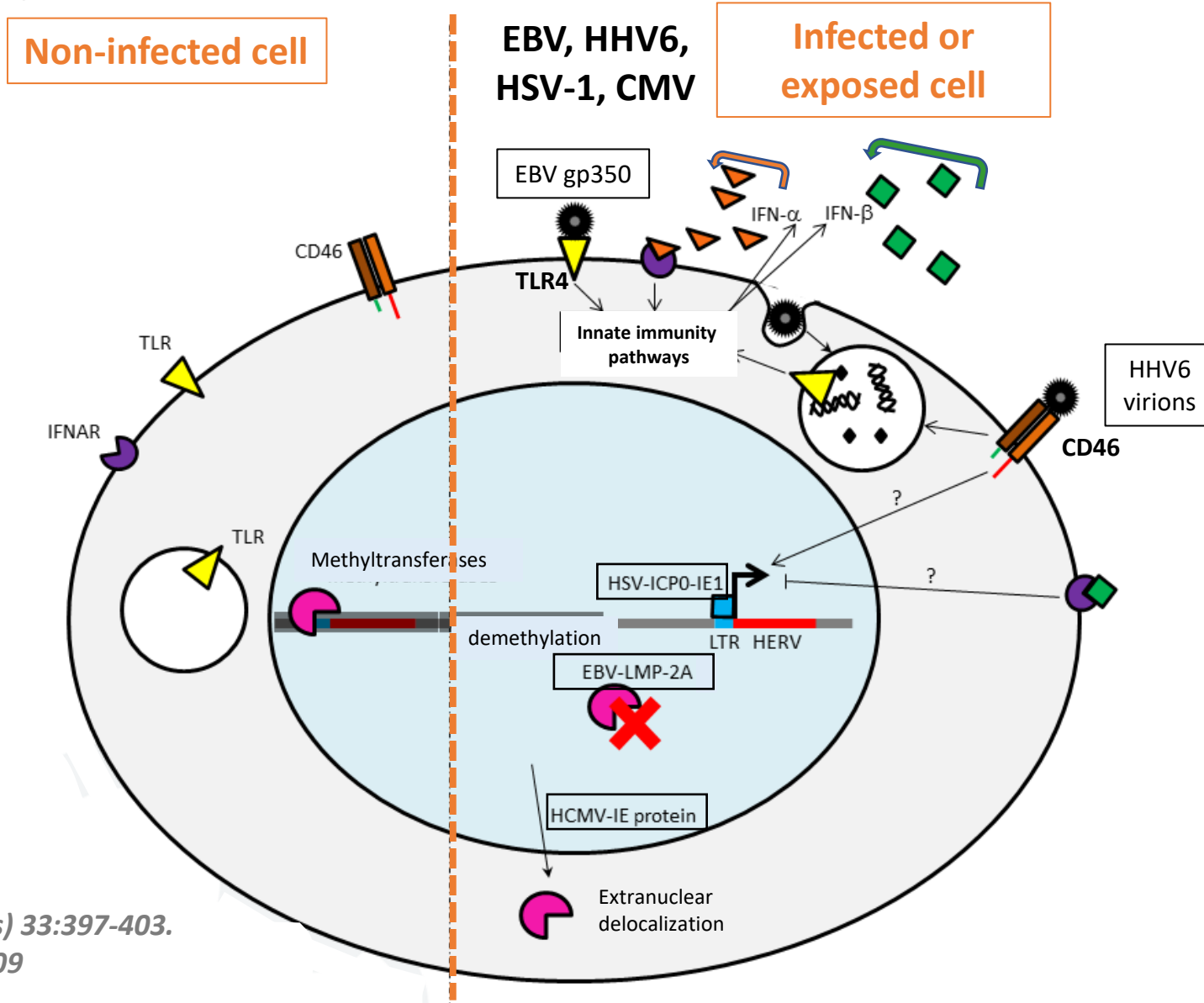


Frank O et al. *J Infect Dis.* 2006  
Ruprecht, K. et al. , *J. neurovirol.* 2006  
Nellaker et al. *Retrovirology* 2006  
Mameli, G., et al. *PLoS One*, 2012  
Levet S et al. *JCI insights* 2017  
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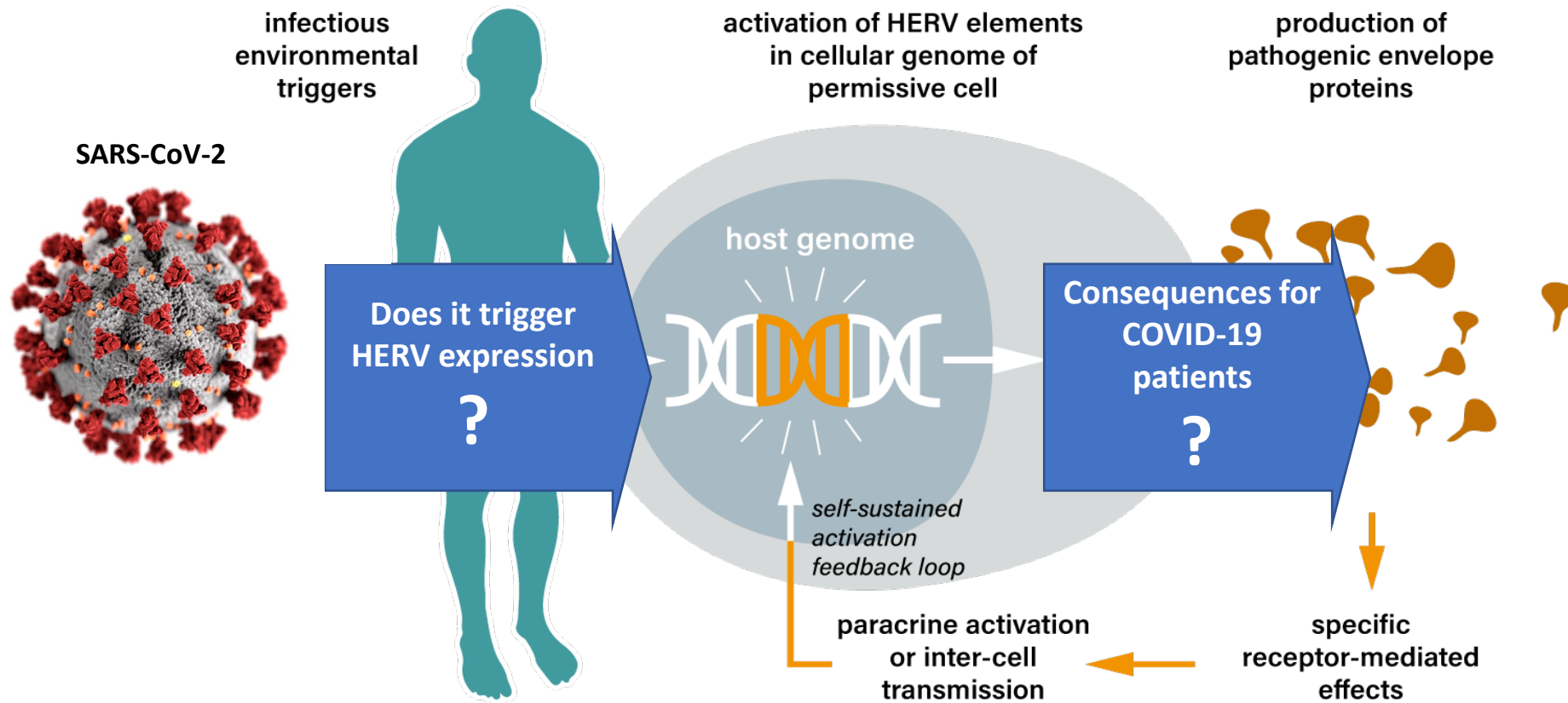
Rolland et al. *J. immunol.* 2006; Kremer et al. *Ann. Neurol.* 2013; Levet et al. *JCI Insights* 2016  
Kremer et al. *PNAS* 2019 ; Johansson et al. *Sci. Adv.* 2020

# HERV epigenetic dysregulation and gene activation by Herpesviridae

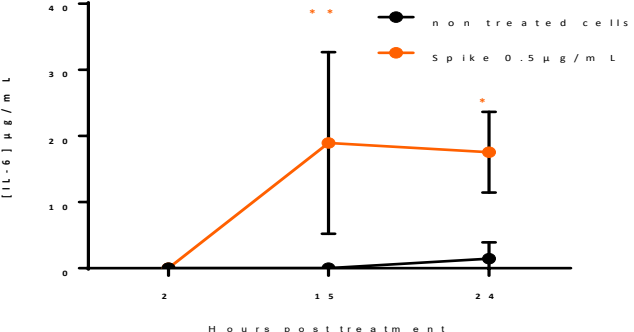
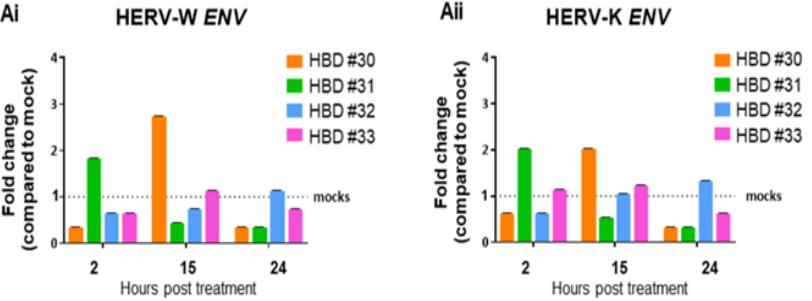
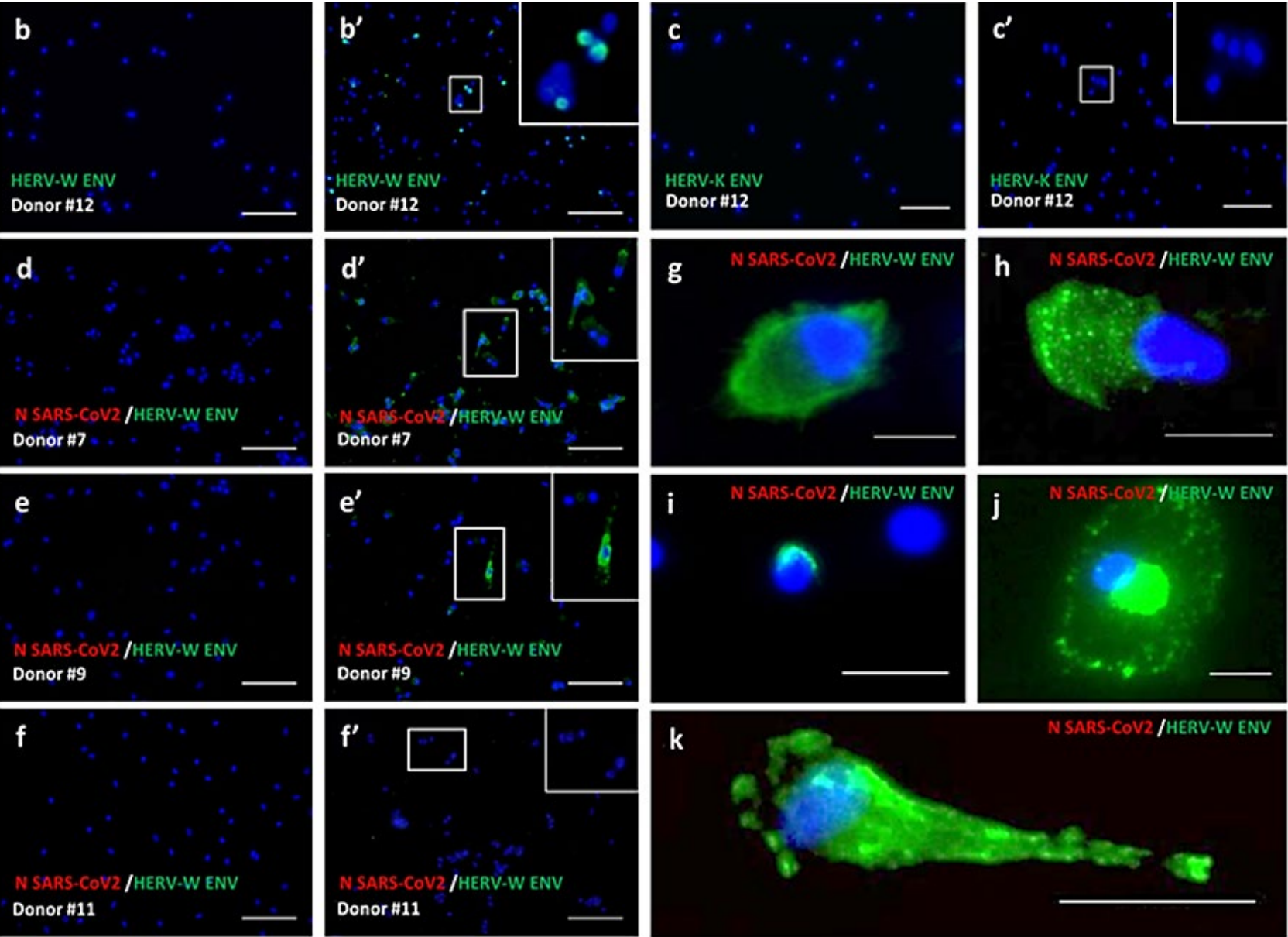
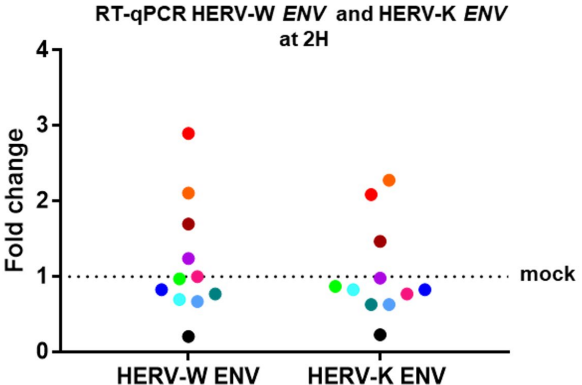
## mechanisms and pathways



# Environmental infectious factors can activate HERV elements playing a critical role at the Gene/environment interface



# SARS-CoV2 is a potent activator of HERV elements –*in vitro*

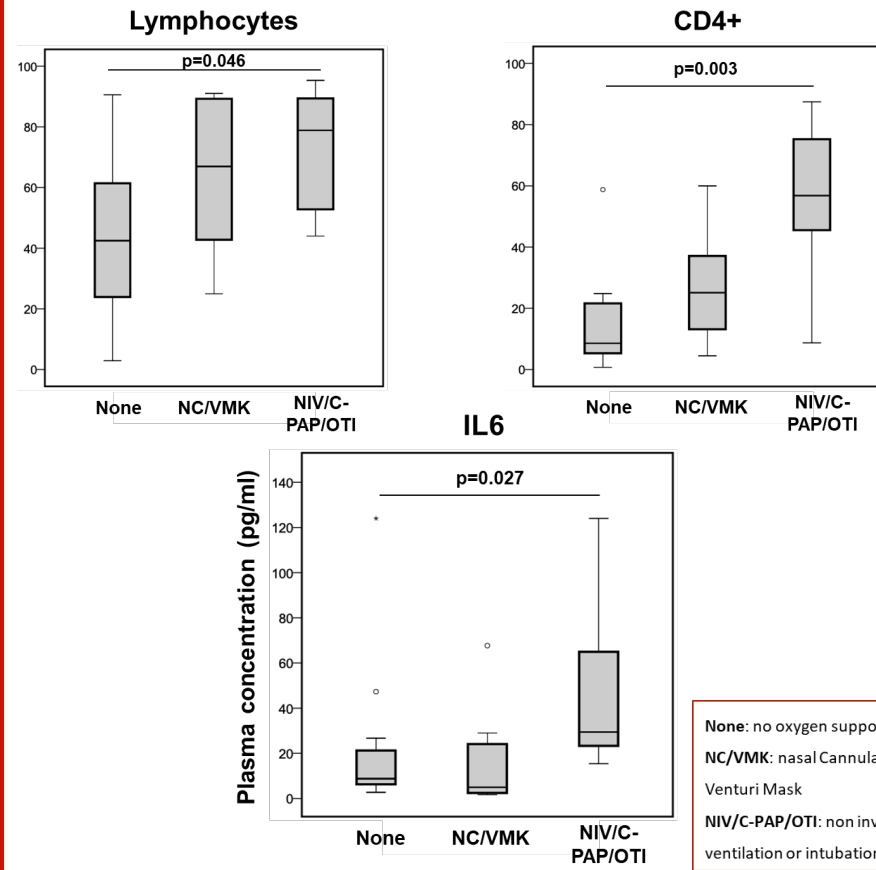


# HERV-W Env in COVID-19 patients

Detection of ENV surface antigen on lymphocytes and of soluble antigen in plasma

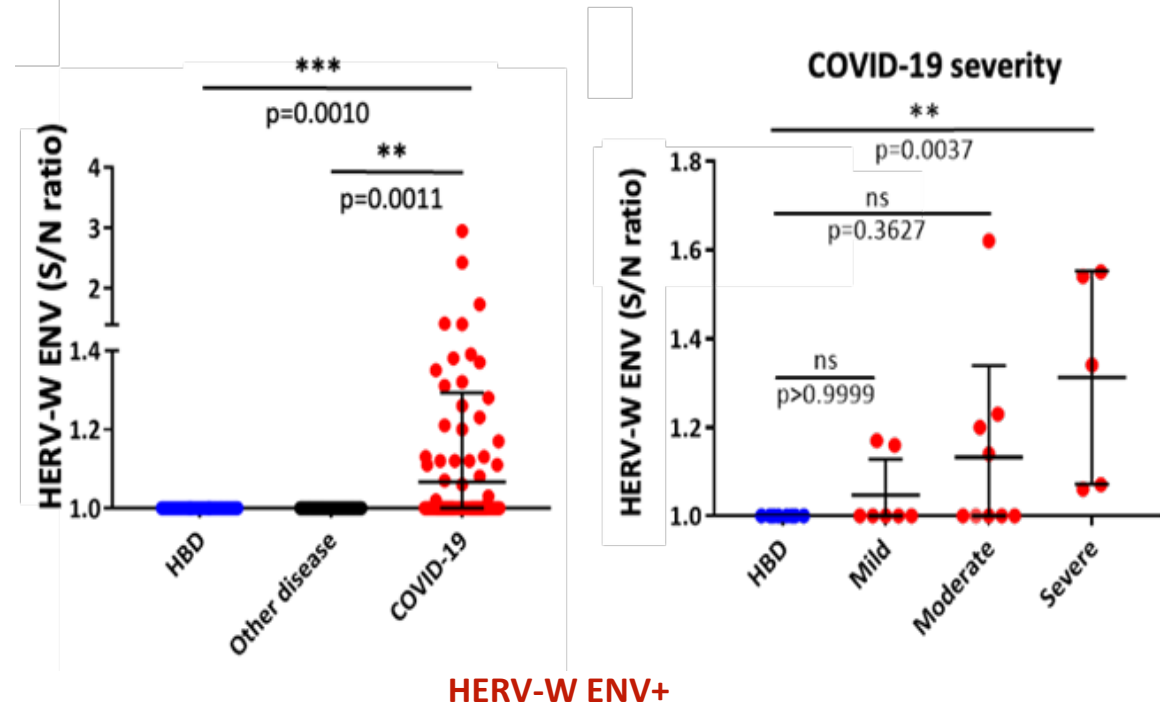
## HERV-W ENV membrane antigen

### Cytofluorometry on Leukocytes



## HERV-W ENV soluble antigen

### Immunocapillary WB (Wes) in serum

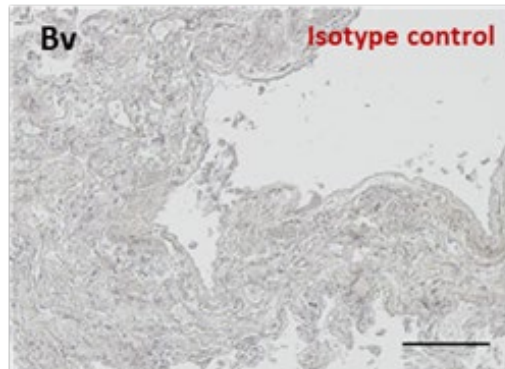
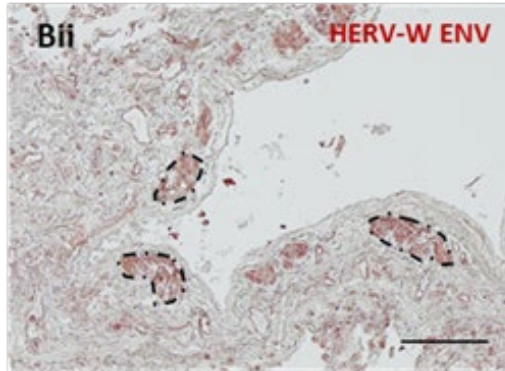
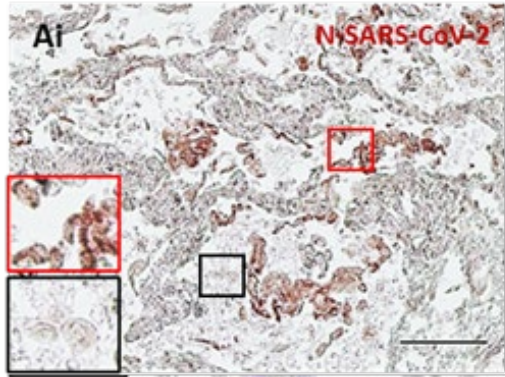


COVID-19 at diagnosis (PCR+): n=143 / 21%  
 COVID-19 at Hosp: n=57 / mild 30% / mod 45% / severe 100%  
 Other Dis: n=43 & HBD: n=44 / 0%

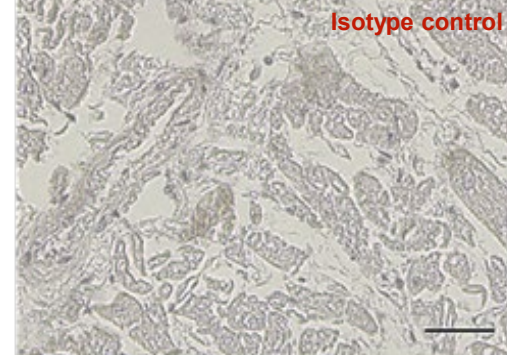
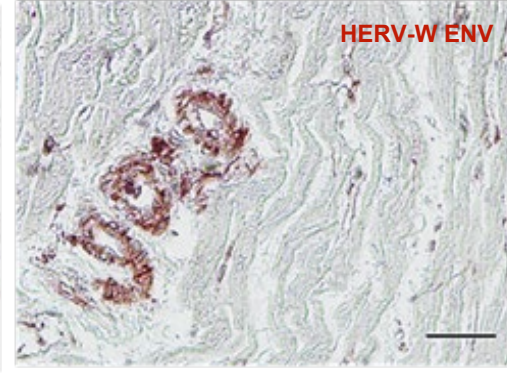
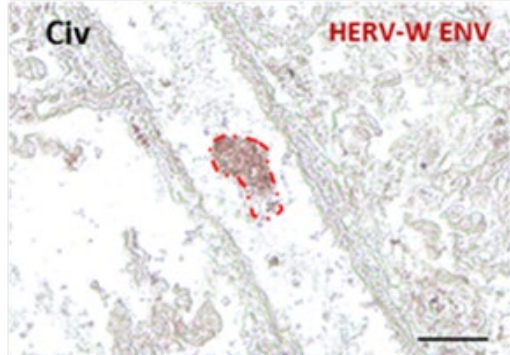
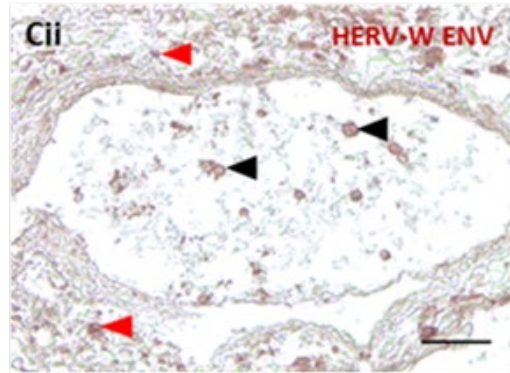
# HERV-W Env in COVID-19 tissues

SARS-CoV-2 detection in different cells than HERV-W ENV

## Lung

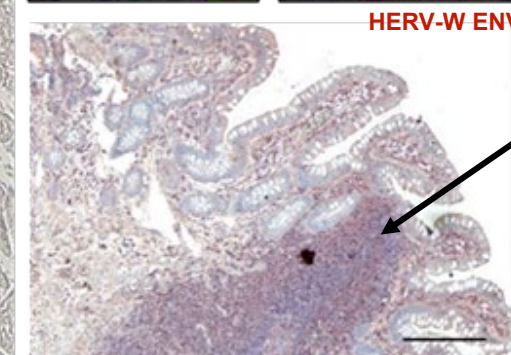
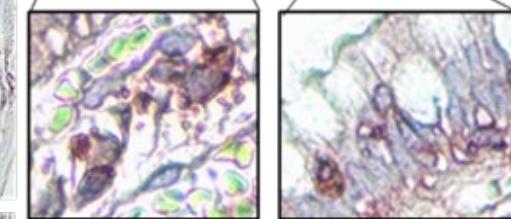
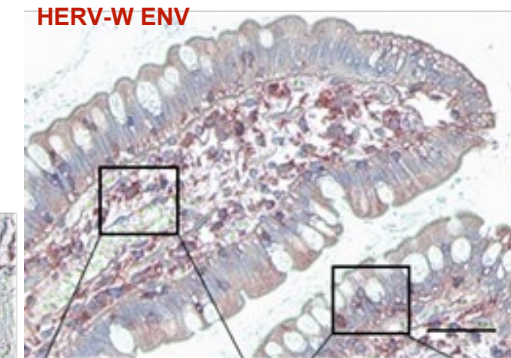
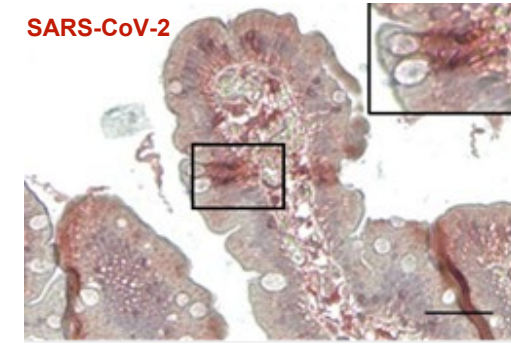


## Lung



## Heart muscle

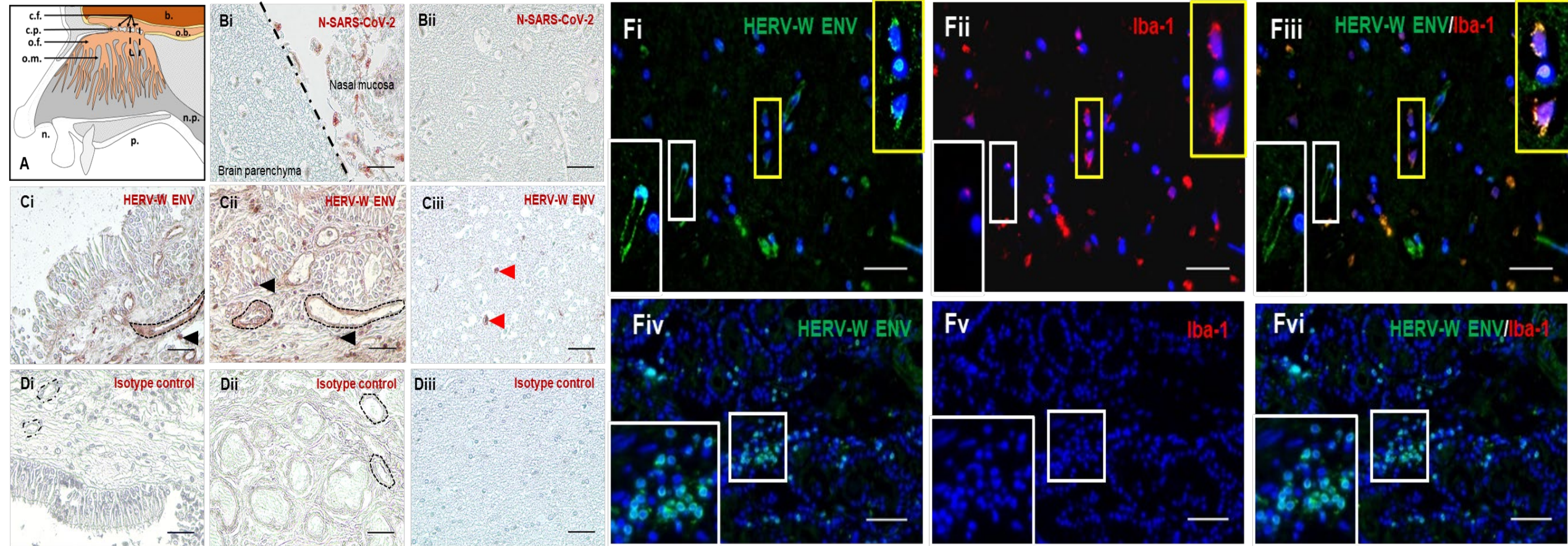
## Terminal Ileum



Mucosa Associated Lymphoid Tissue (MALT)

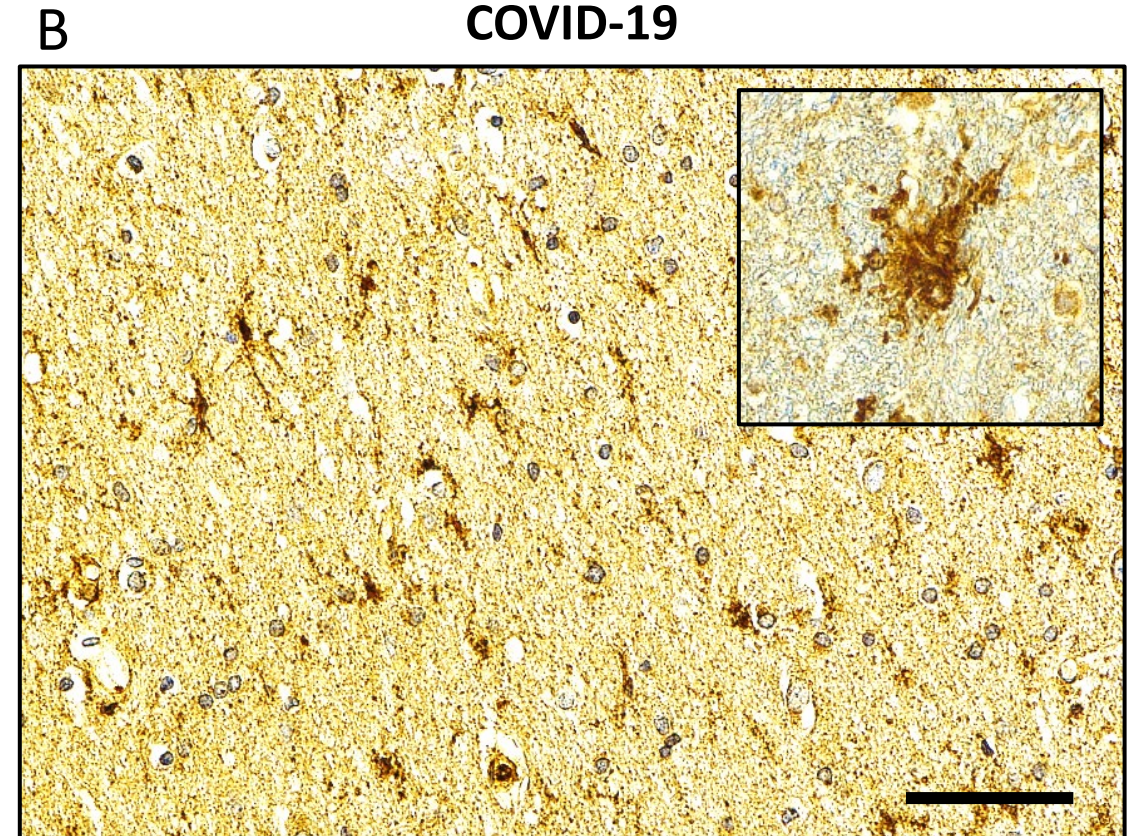
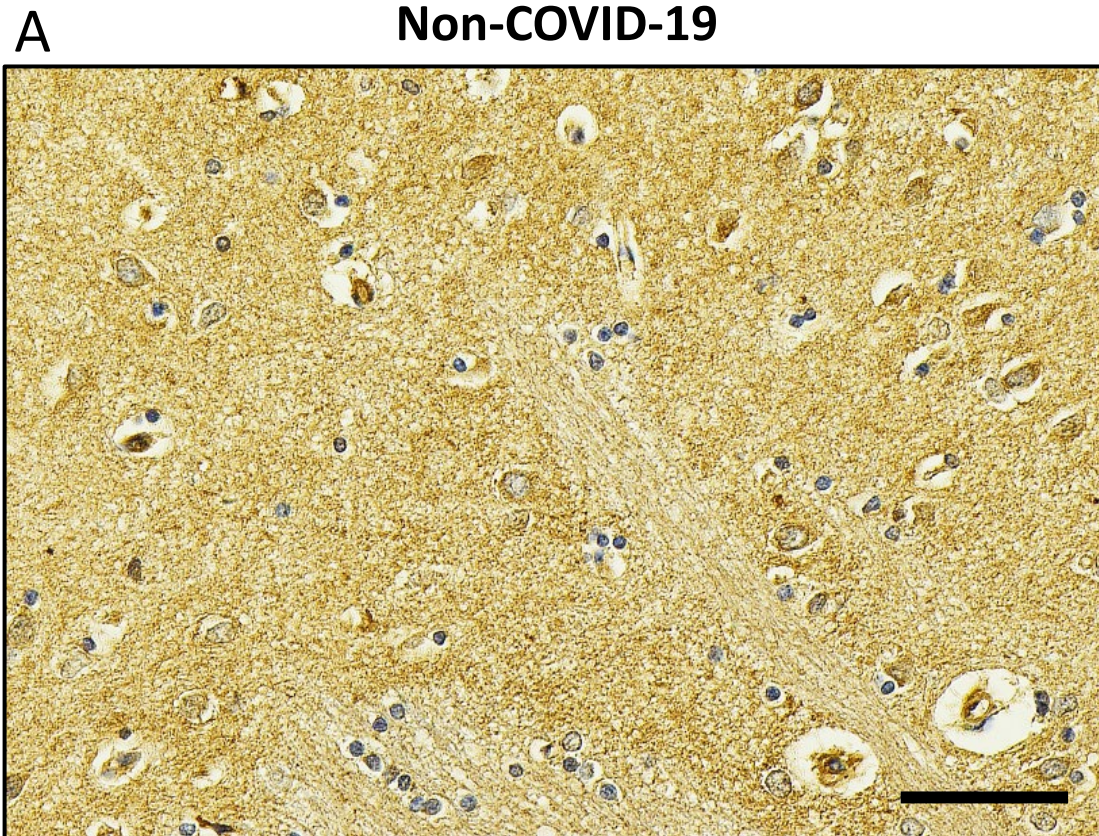
# HERV-W Env in COVID-19 tissues

Detection in brain microglia in the absence of SARS-CoV-2 detection





# Activated HERV-W in the brain of patients with COVID-19



# Case	Age/ Sex	PMI (hours)	Medical History
Control 6	54/M	15	Hypertension, Heart disease with prior myocardial infarction and coronary stent placement, Colorectal tumor resection

# Case	Age/ Sex	PMI (hours)	Medical History	Recent History	Days from symptom onset to death
Case 1	73/M	38	Hypertension Obesity	Pneumonia, Renal failure, Pericardial effusion, Arrythmia, Hospitalized for 8 days, Intubated for 3 days	16 days

# HERV-W Env in Post-COVID patients

Pilot series from Northwestern Hospital, USA

Detection of ENV soluble antigen in serum versus IL-6 and SARS-CoV-2 serology

**HERV-W ENV+**

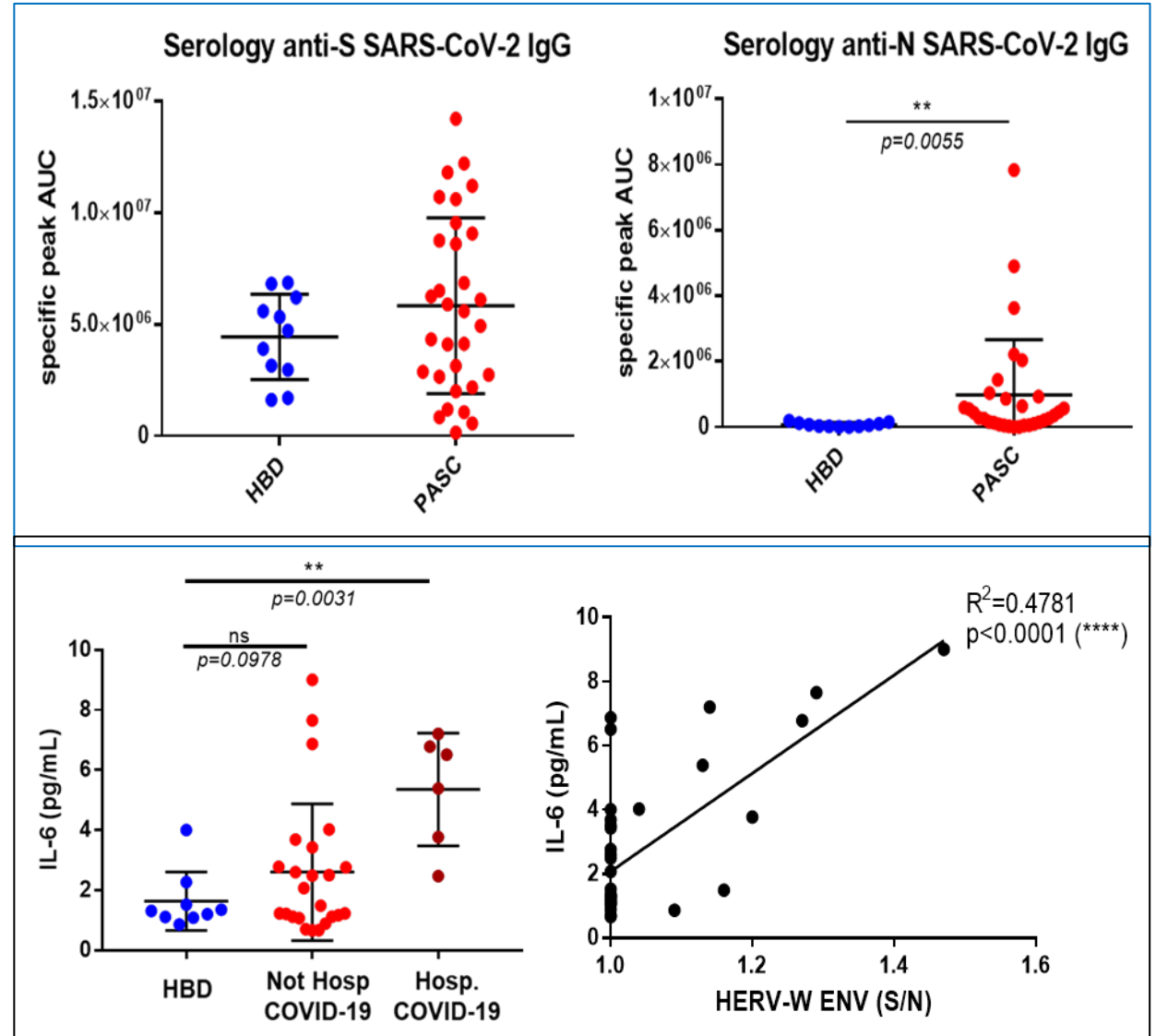
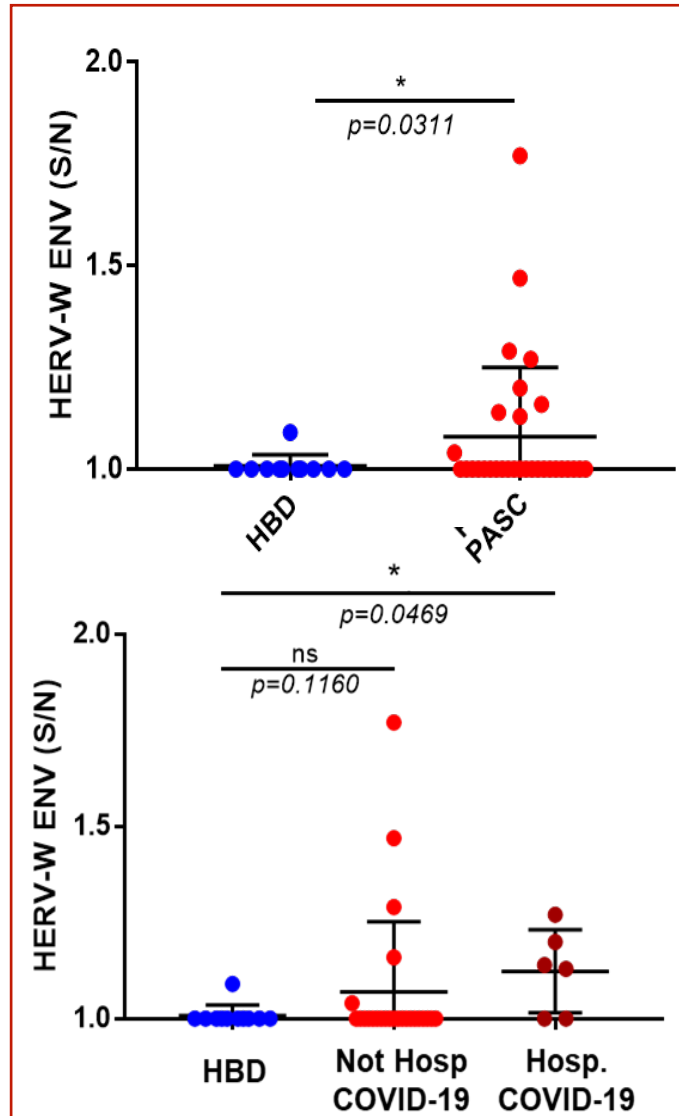
PASC: 28%

Hosp: 67%

N.Hosp: 19%

HBD: 1\*/12

\* No clin. record



# HERV-W Env is present in a sub-group of patients with Post-COVID

Post/Long COVID patients represent a heterogeneous nosological entity that can be stratified by biomarkers:

Different pathogenic drivers and subtypes of Post-COVID syndrome ?

## Main groups defined by biomarkers:

### A. Ig anti-SARS-CoV-2 N+

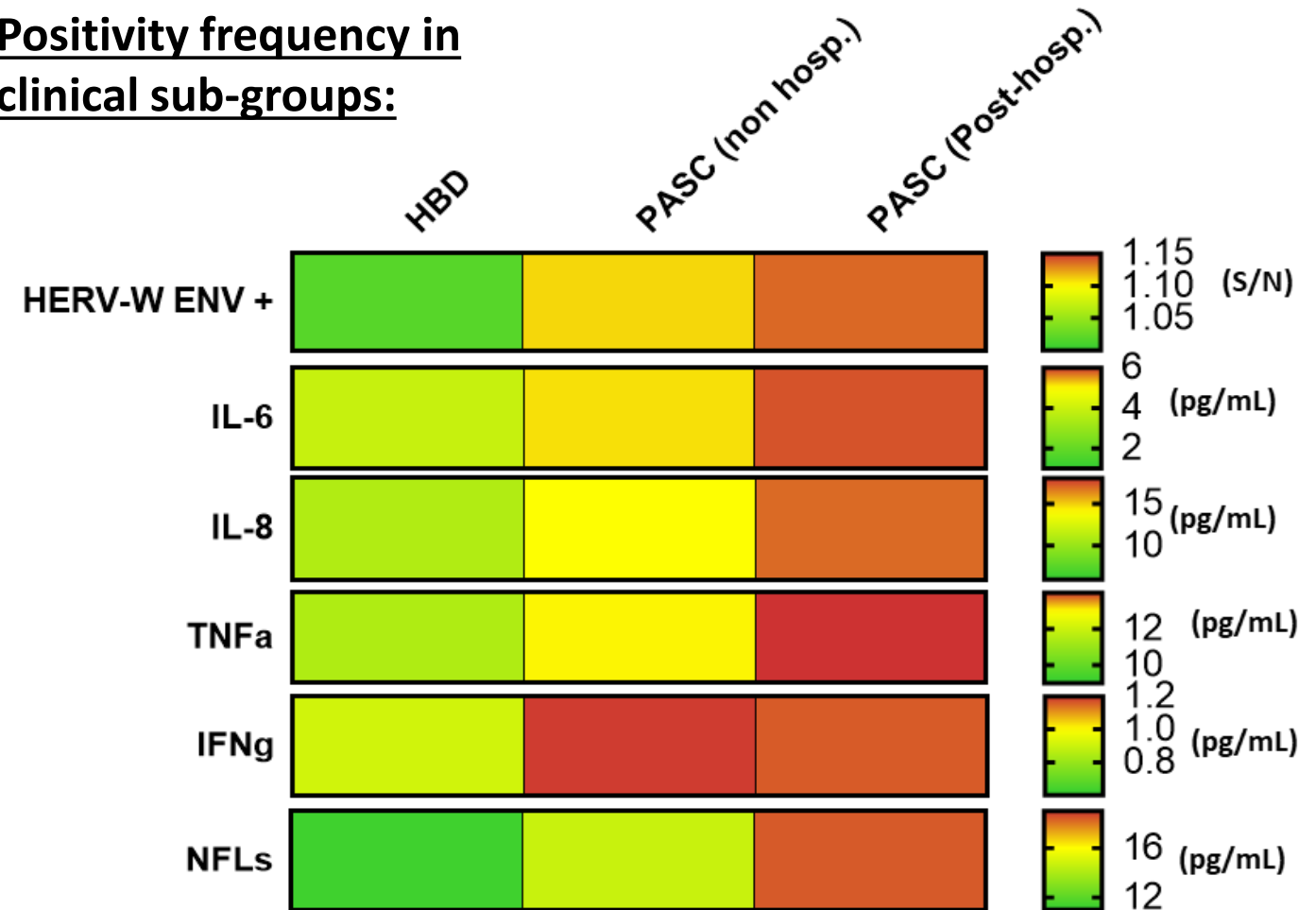
1. Ig anti-SARS-CoV-2 N+ / HERV-W ENV+ / IL6+ / TNF- $\alpha$ + / NfL+

2. Ig anti-SARS-CoV-2 N+ / HERV-W ENV- / TNF- $\alpha$ - / NfL-

### B. Ig anti-SARS-CoV-2 N-

Ig anti-SARS-CoV-2 N- / HERV-W ENV- / all biomarkers low or negative.

## Positivity frequency in clinical sub-groups:





Funded by the European Union

# HERVCOV

“SARS-CoV-2-induced activation of pathogenic endogenous retrovirus envelope HERV-W: towards personalized treatment of COVID-19 patients”



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## The PARTNERS



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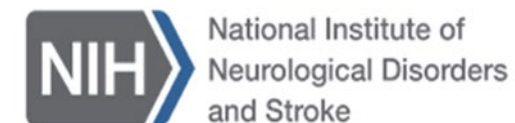
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