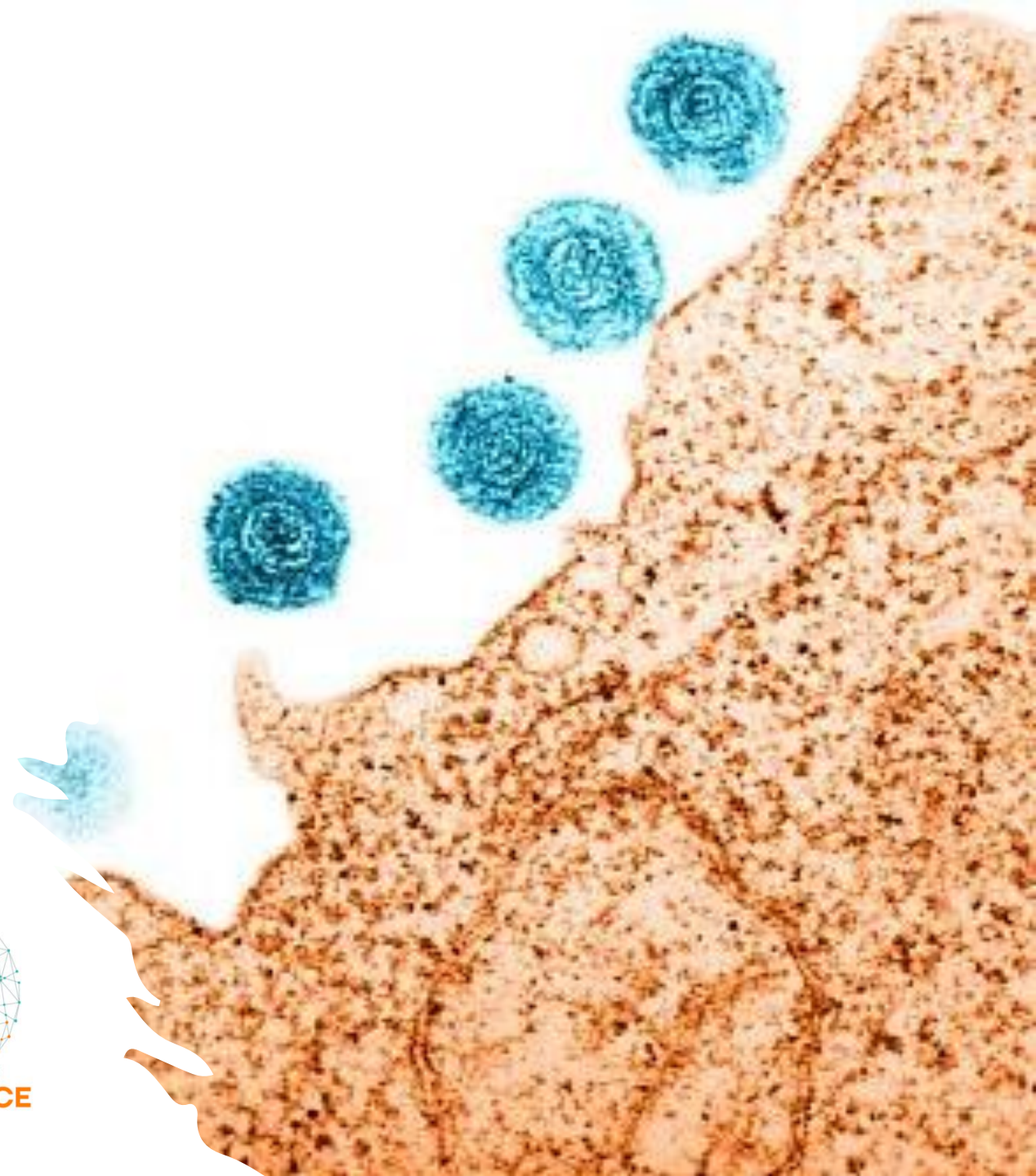


Association Between HHV-6 Reactivation Signatures and Monocyte Dysregulation in Long-COVID

27-08-2026

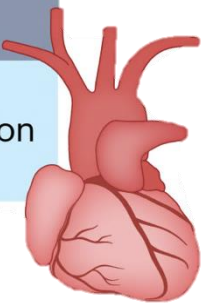
Laszlo Groh, Abstract 73



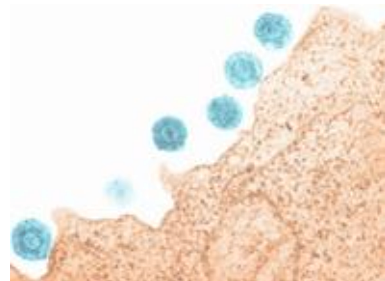
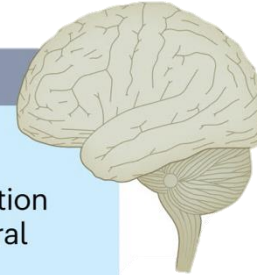
Long-COVID: clinical features and epidemiology

- ‘Post-COVID-19 condition’ (WHO):
unexplained symptoms > 3 months after infection, lasting > 2 months
- Multi-organ disease, many different symptoms
> Extreme fatigue, ‘Brain fog’, POTS
- Diverse estimates of prevalence: 3-10% of population(s)¹

Heart	
• Chest pain • Palpitations	• Cardiac impairment • Myocardial inflammation • POTS



Neurological system	
• Cognitive impairment • Fatigue • Disordered sleep • Memory loss • Tinnitus	• Dysautonomia • ME/CFS • Neuroinflammation • Reduced cerebral blood flow • Small fibre neuropathy

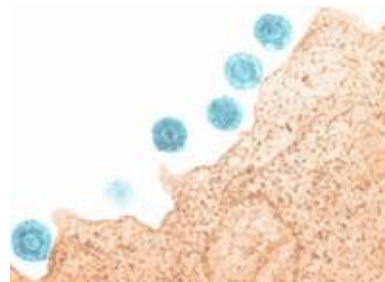


1) Peluso & Deeks. Cell, 2024

2) Fig. adapted from Davis et al. Nature Reviews Microbiology, 2023

Immune profiling in patients reporting severe post-COVID symptoms (**IMPACO**): Study aim

- We have seen signs of elevated inflammation 2 years post COVID infection [LMC Jacobs et al. Front Immunol 2023]
 - Are immune cells responsible for this systemic inflammation?
- What are the cellular underpinnings of this inflammation?



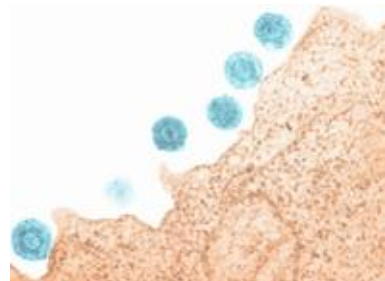
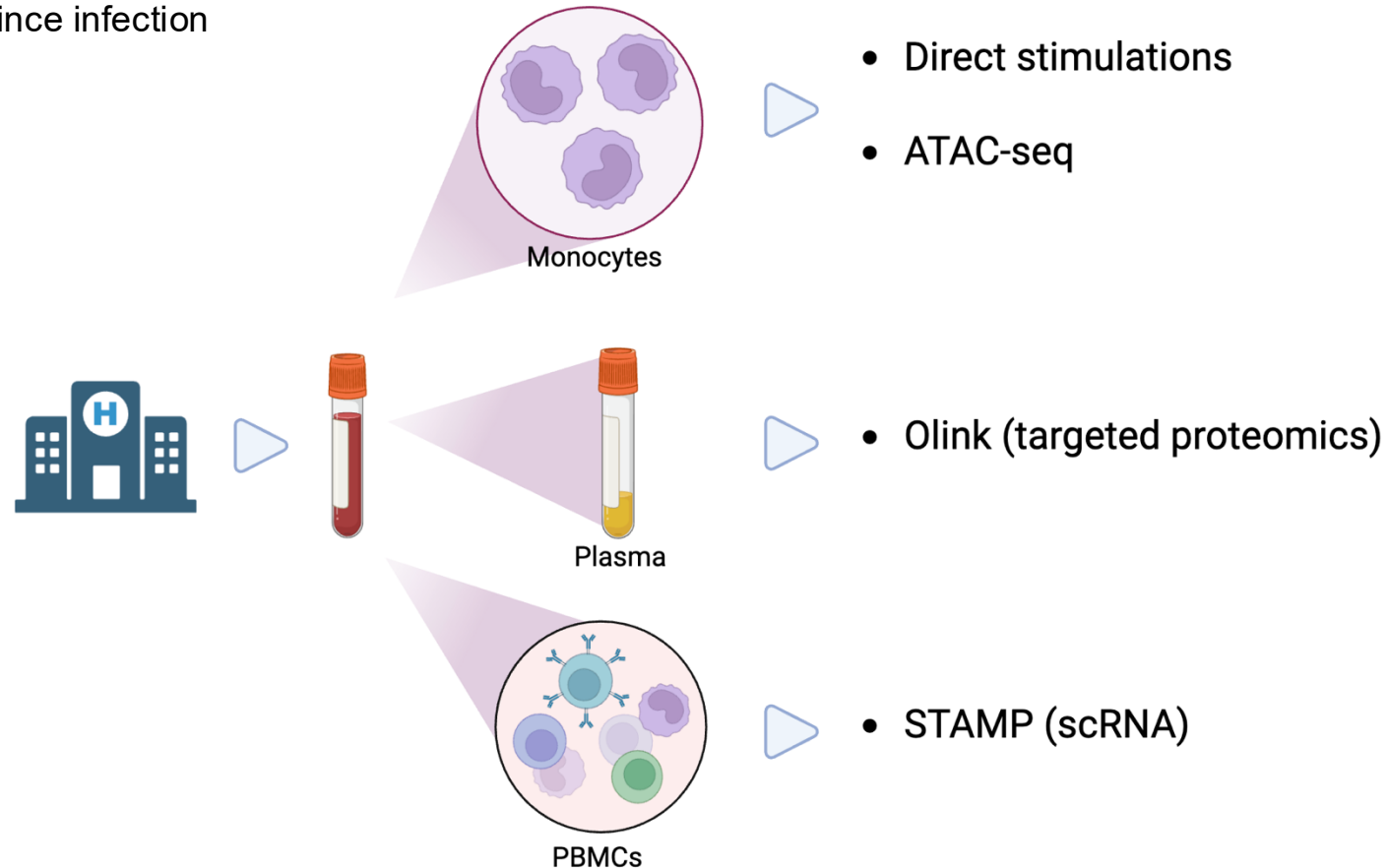
Study cohorts

COVAS

- ~20 donors without symptoms
- ~20 donors with (mild) symptoms
- ~ 4 years since infection

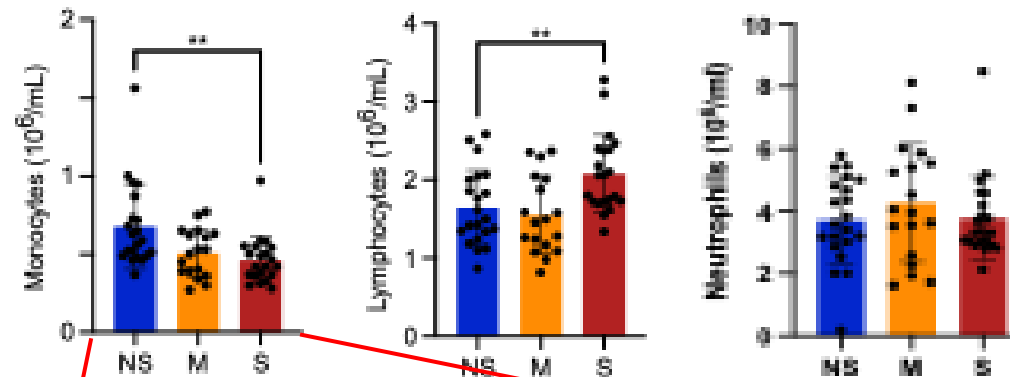
DECI-LOCO

- ~20 donors with severe symptoms
- >1 year since diagnosis



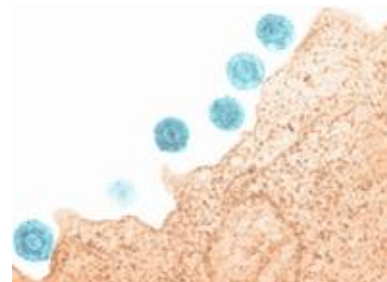
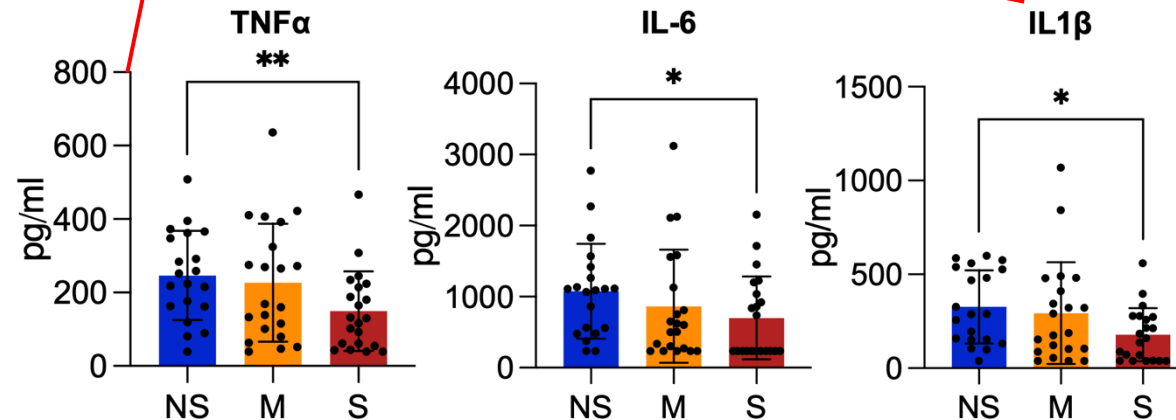
Severe Long-COVID: immune cell composition changes and reduced monocytes responsiveness

Drop in monocyte counts

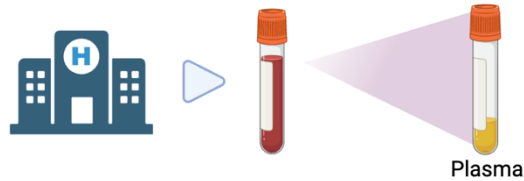


NS - Nonsymptomatic
M - Mild
S - Severe

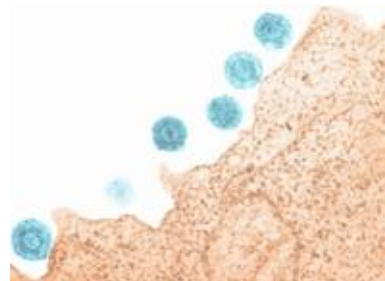
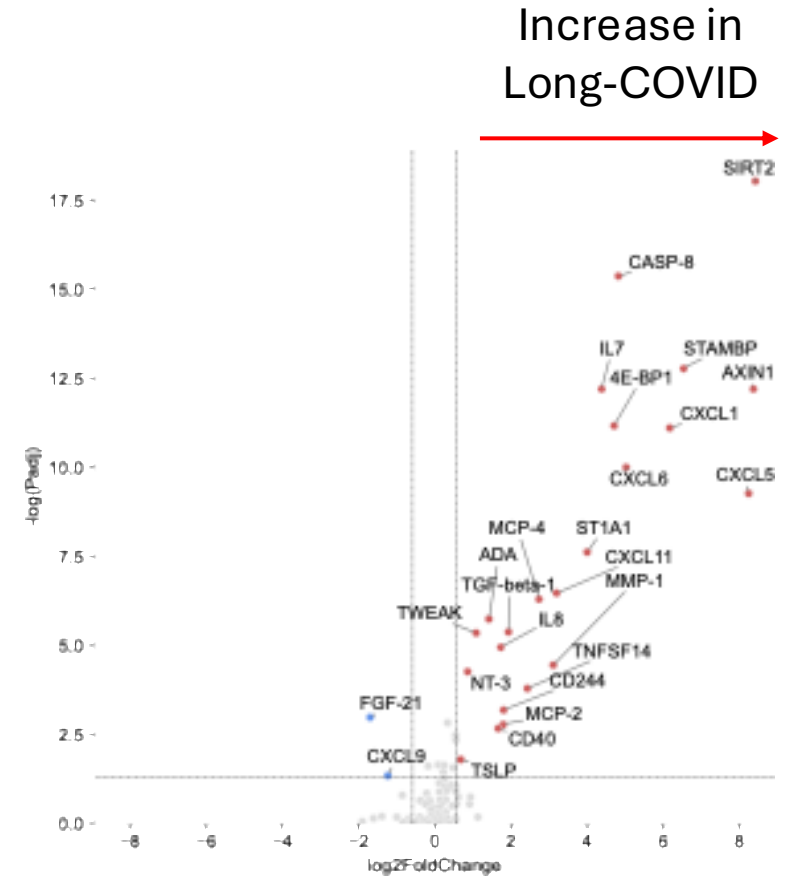
Monocytes lose responsiveness



Elevated inflammatory proteins in severe Long-COVID plasma



- Olink (targeted proteomics)



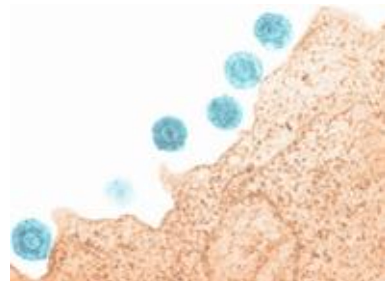
Interim summary

↓ Monocytes responsiveness

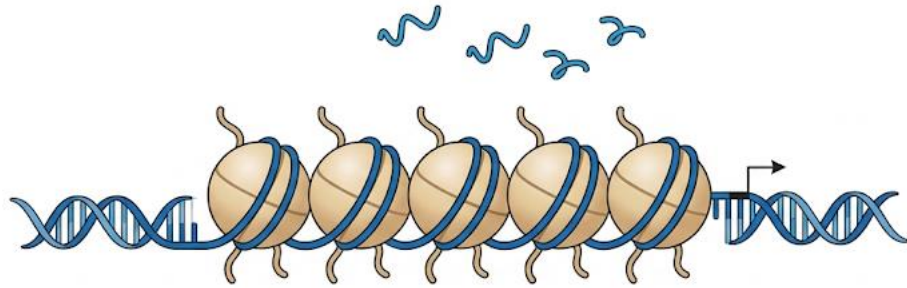
↑ Systemic inflammation

Could this be due to a change in the state of the cells?

Look into the epigenetic status of the cells → ATAC-seq

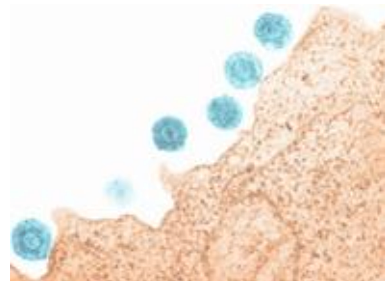


Could this be due to epigenetics?

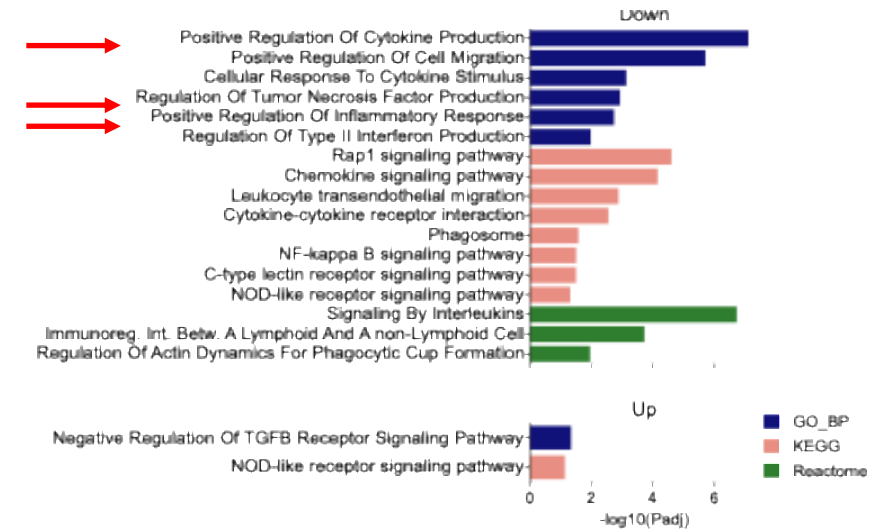
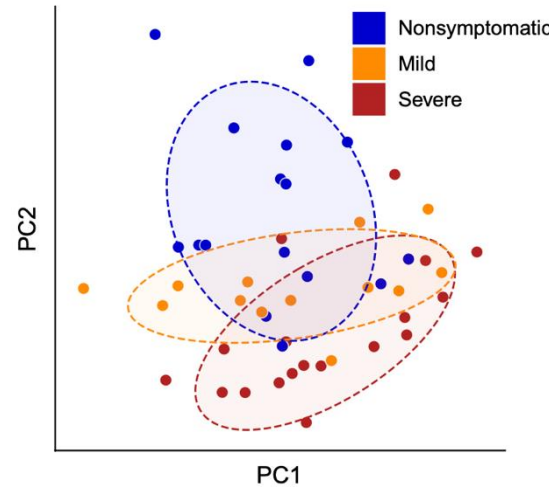
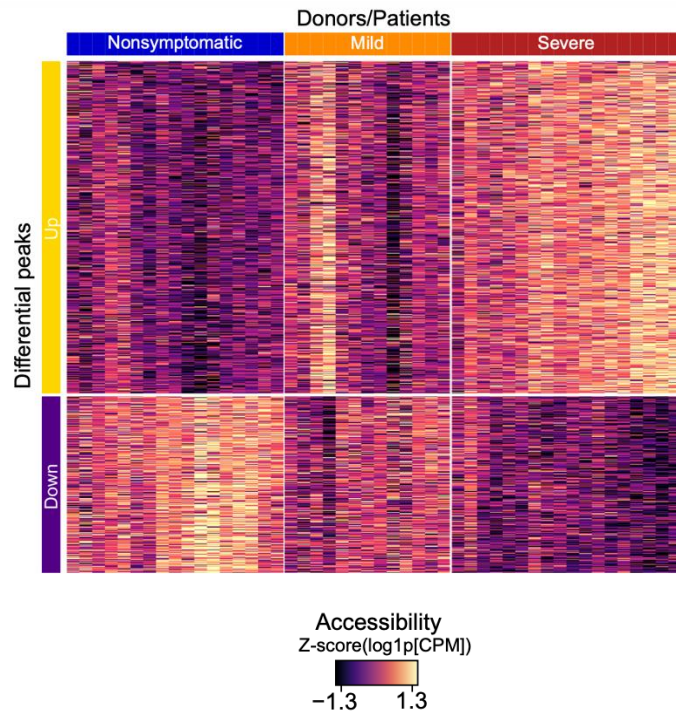


Closed region minimal
expression

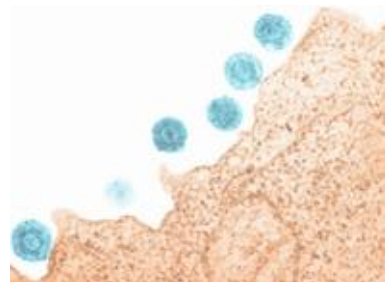
Open region enhanced
expression



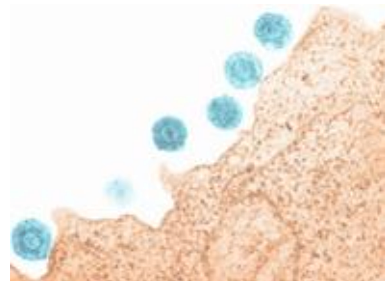
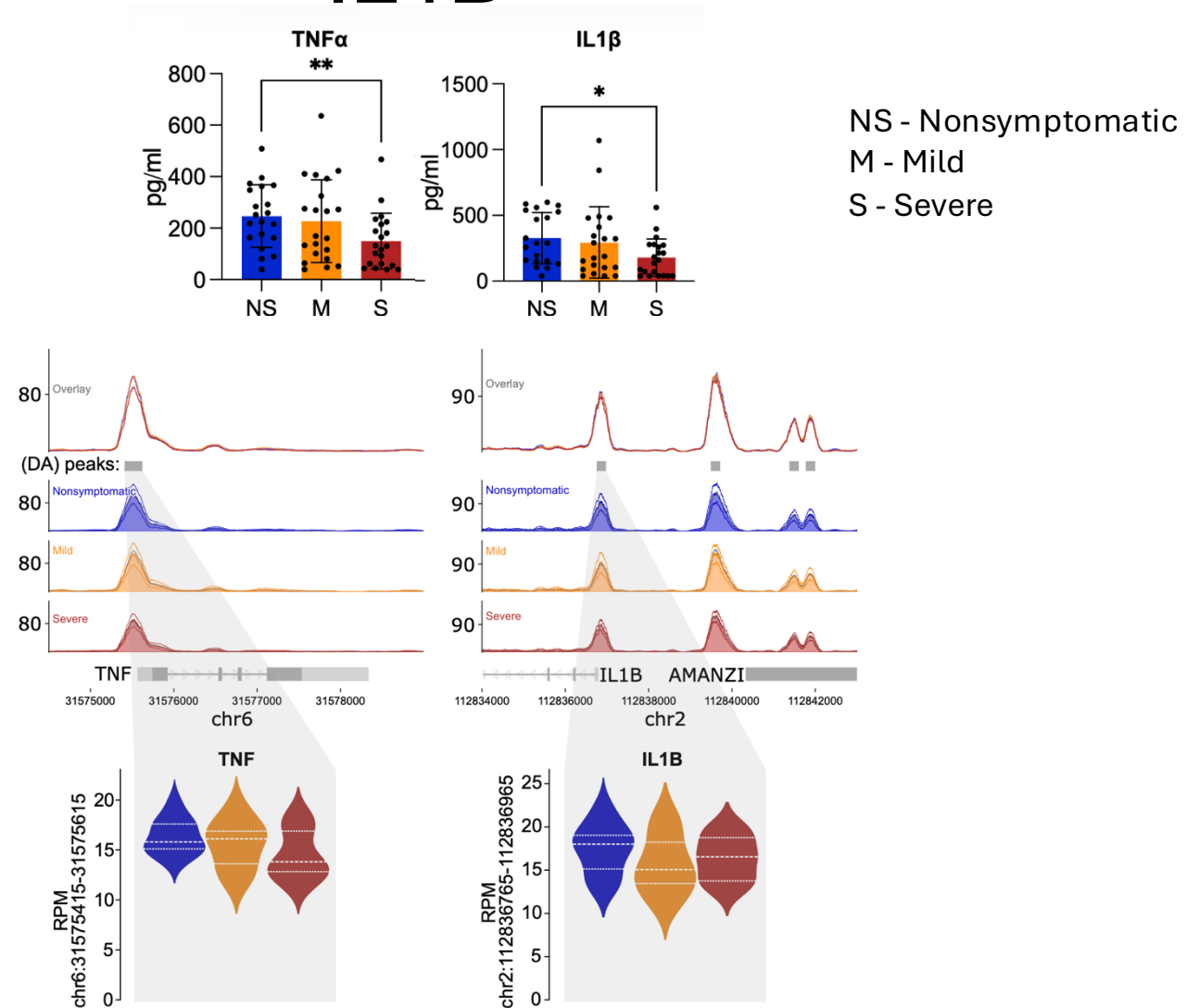
Monocytes lose accessibility on inflammation/cytokine related genes



Aligns with reduced response to stimulation

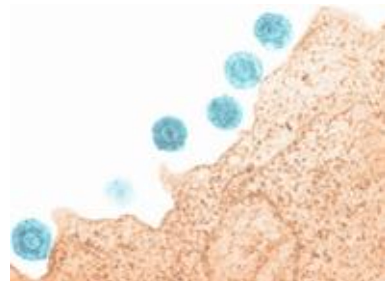
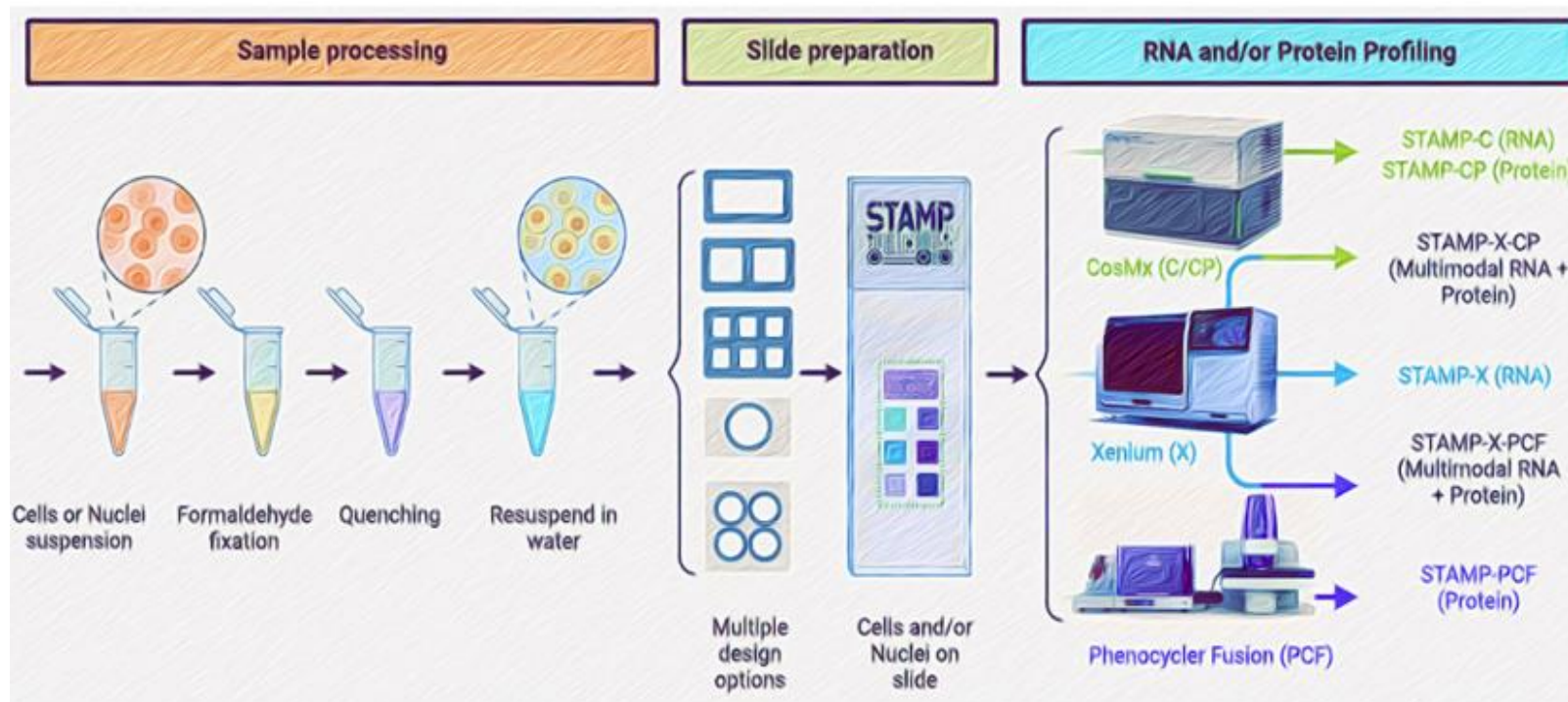


Discrete loss of epigenetic accessibility on TNF and IL1B

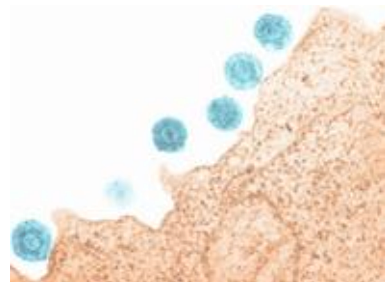
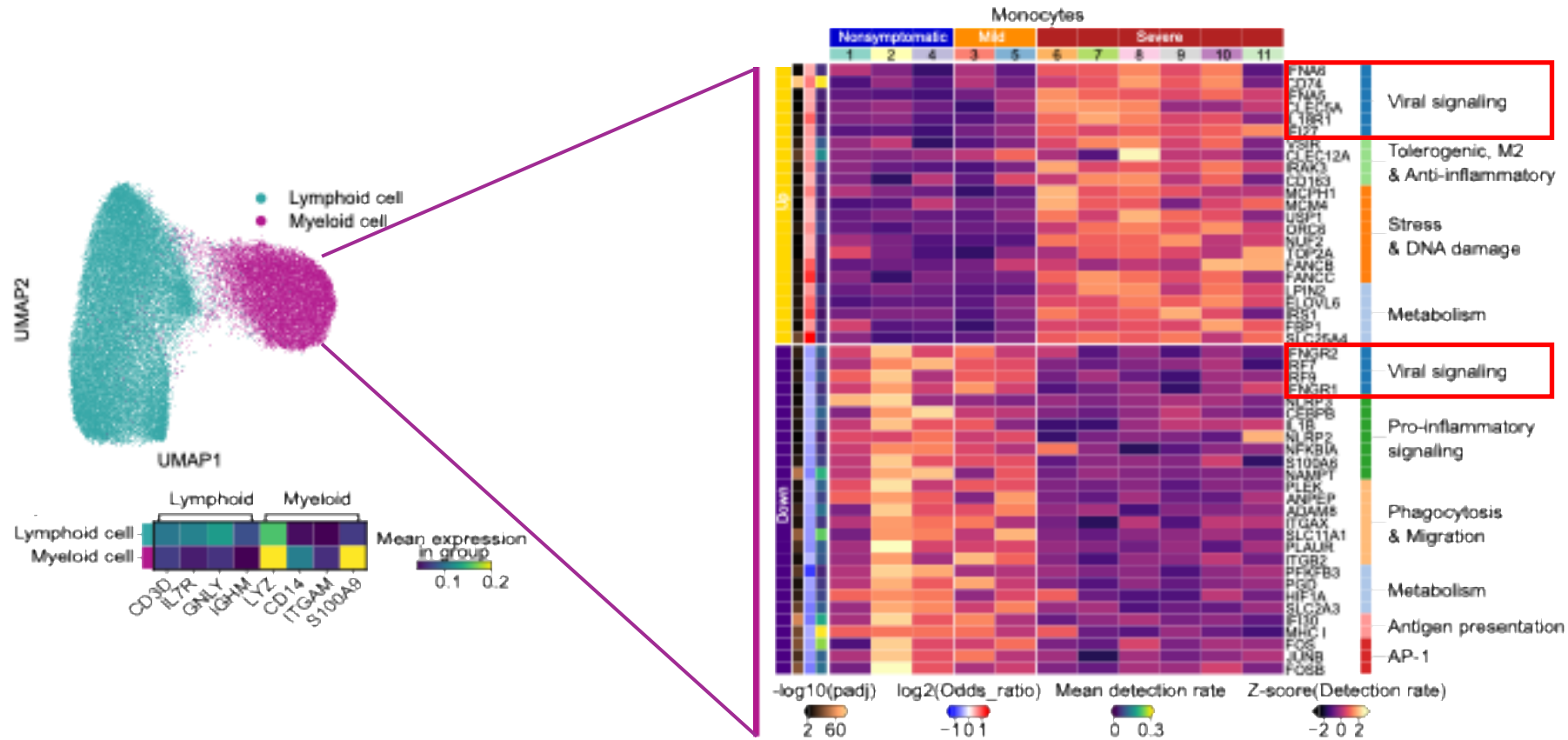


Single-Cell Transcriptomics Analysis and Multimodal Profiling through Imaging (STAMP)

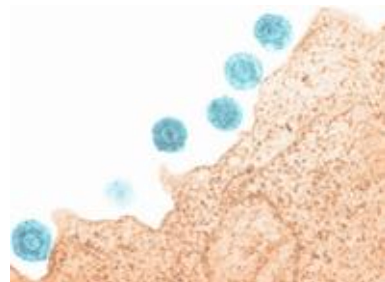
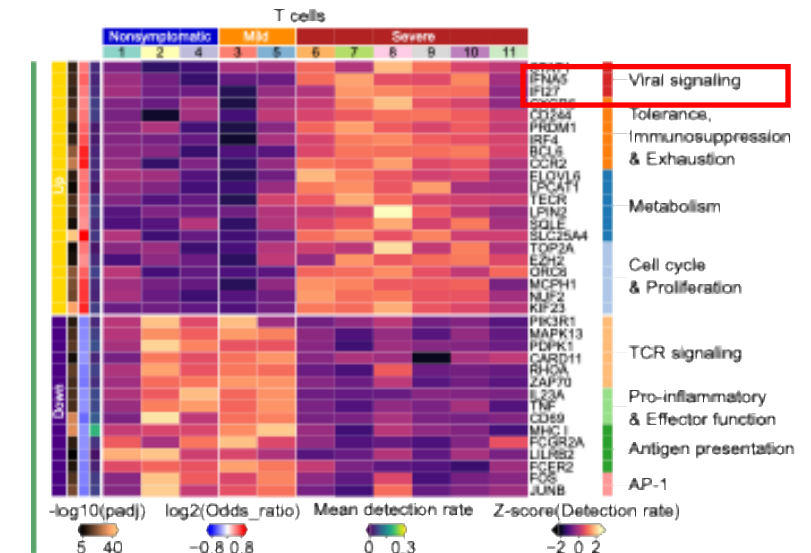
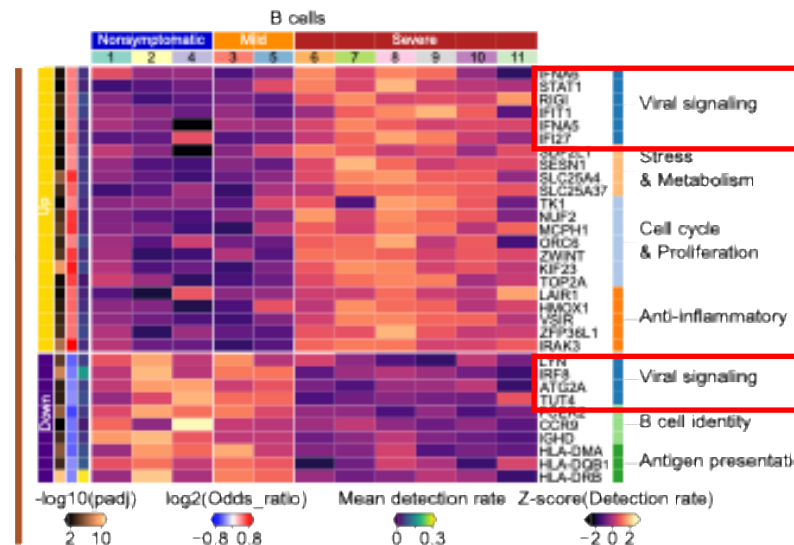
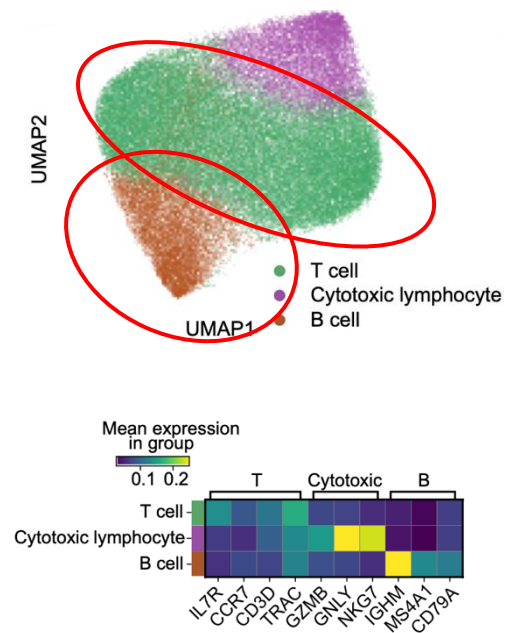
Using imaging-based spatial transcriptomics platforms to generate scRNA data



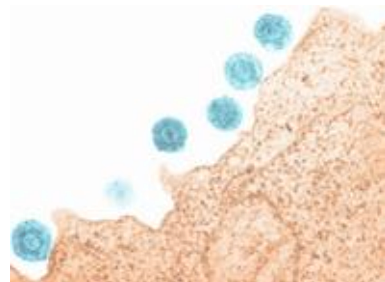
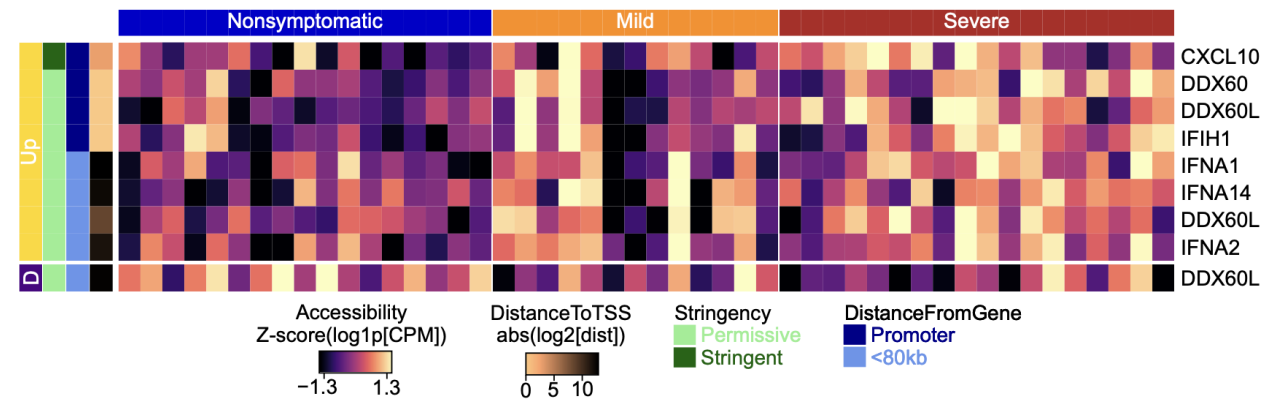
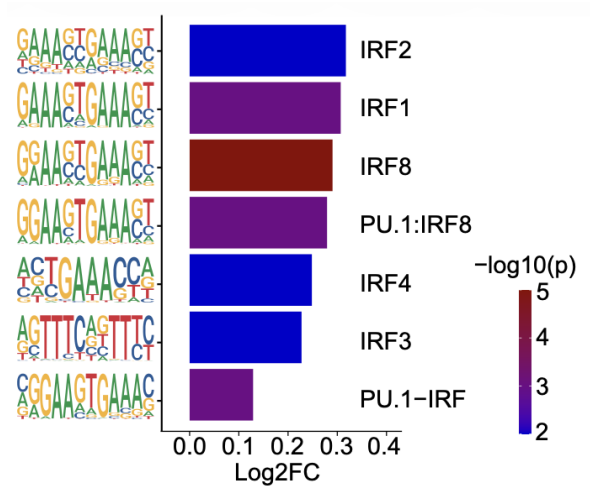
Monocytes display dysregulated interferon signaling



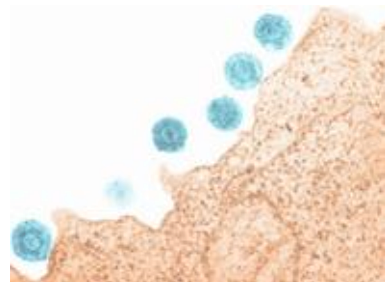
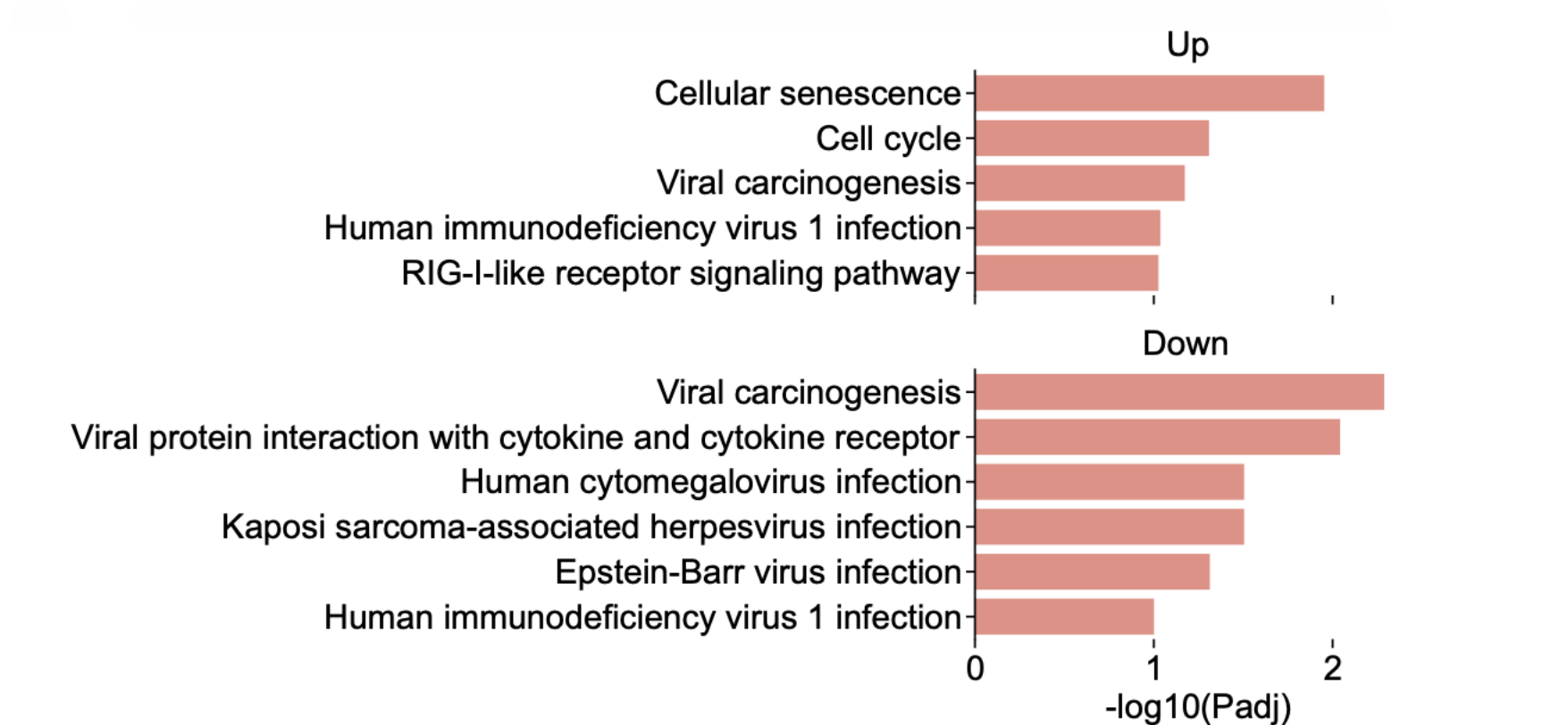
B and T cells share this interferon dysregulation



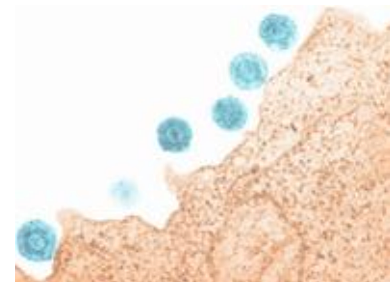
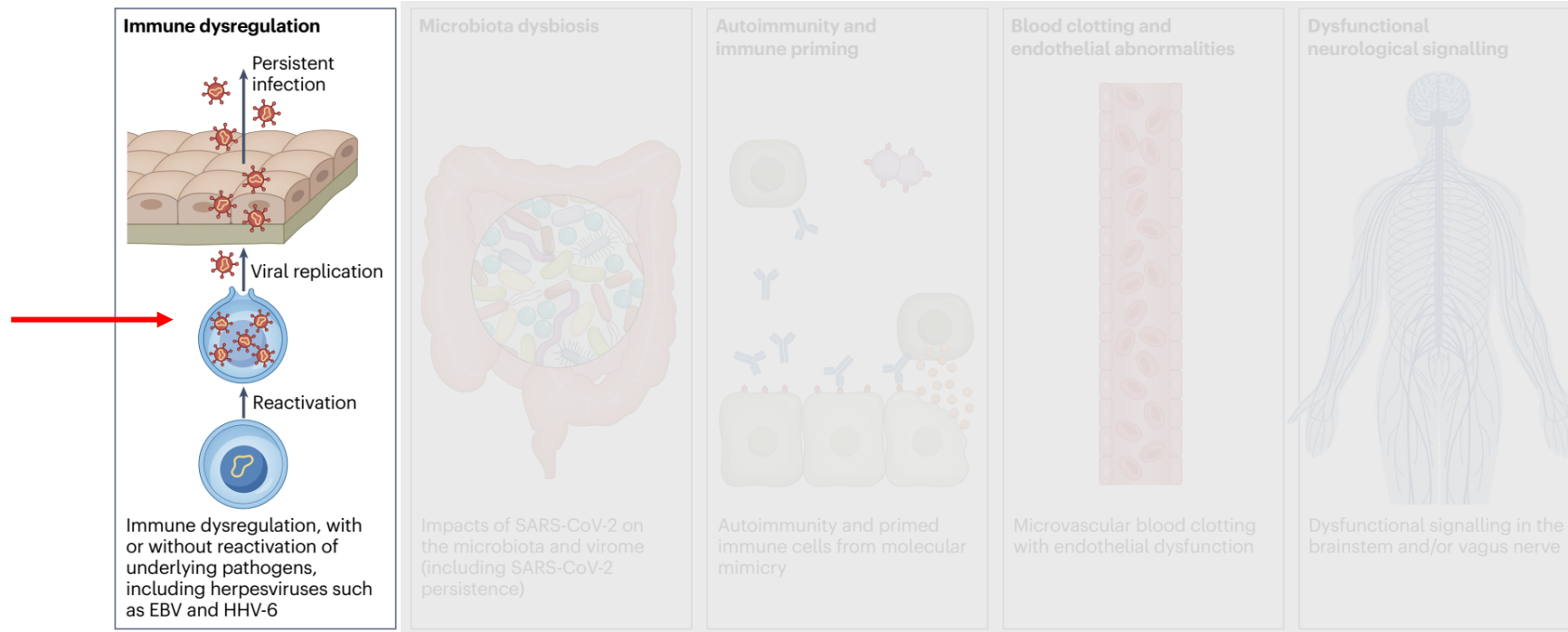
Viral Interferon regulatory factor (IRF) motifs are more epigenetically accessible in Severe Long-COVID monocytes



Epigenetic accessibility suggest persistent viral signaling

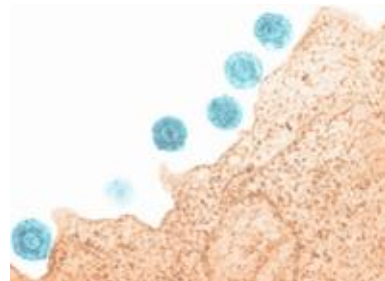
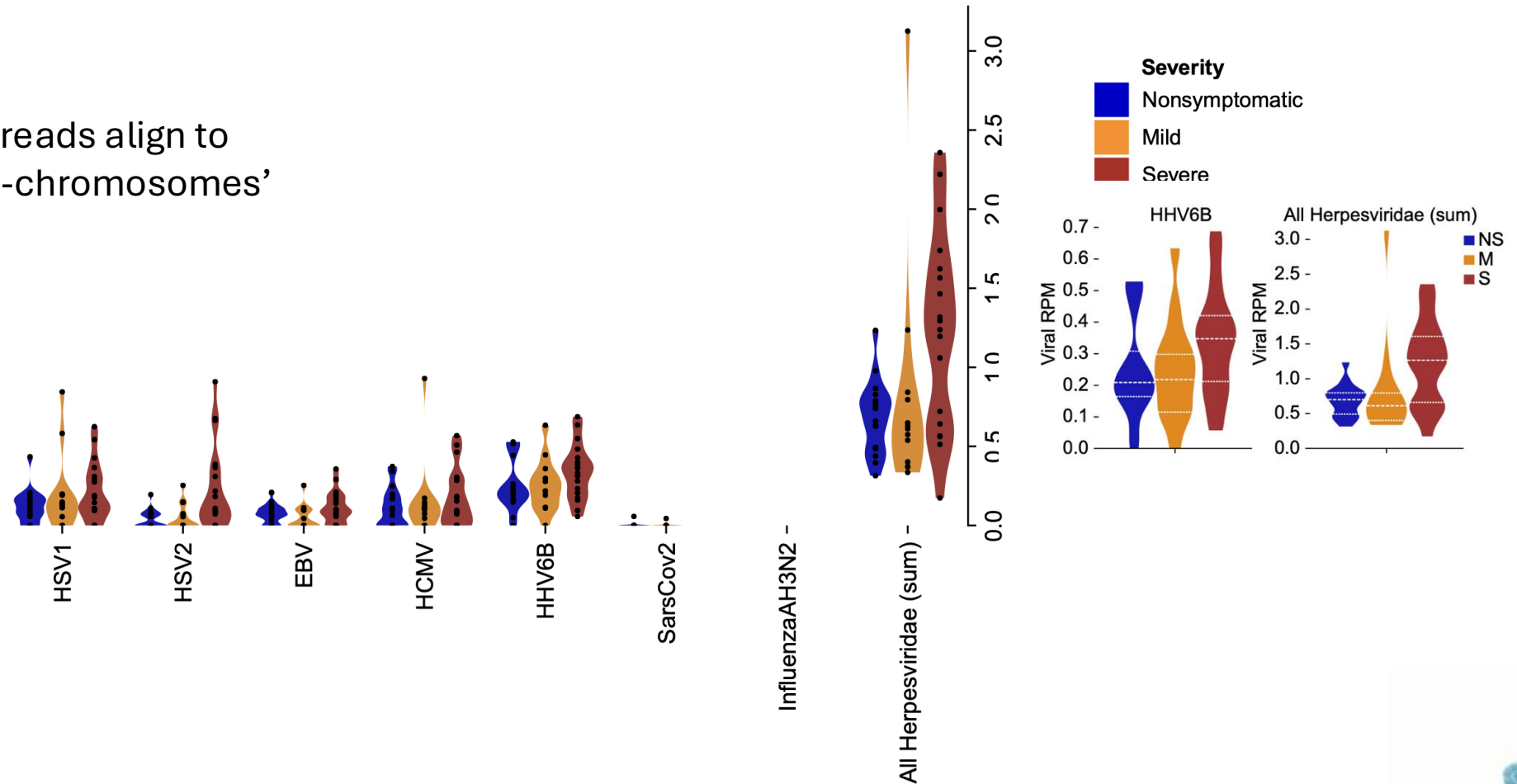


What could be behind this continued viral signaling?

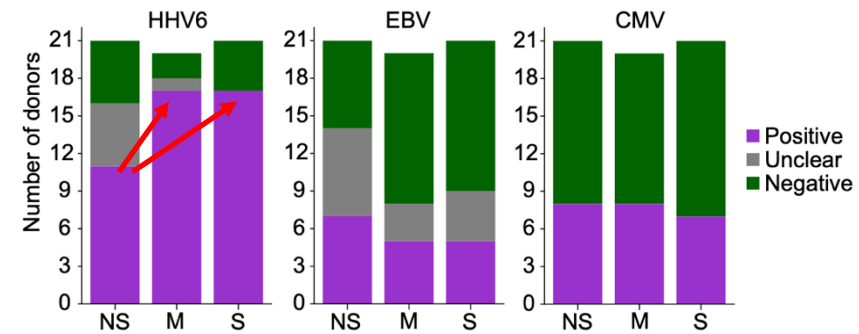
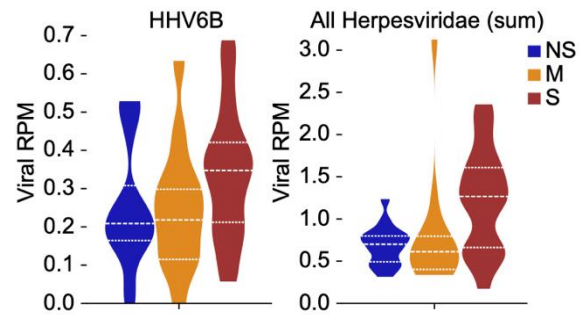


Herpes viruses and not RNA viruses relate to severity

ATAC-seq reads align to viral 'pseudo-chromosomes'

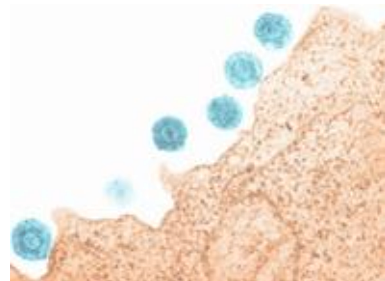


Herpes viruses and not RNA viruses relate to severity

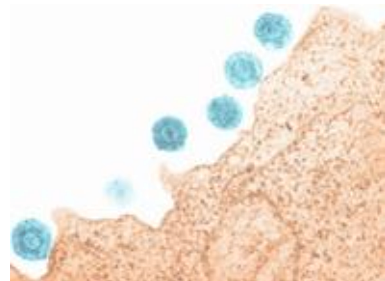
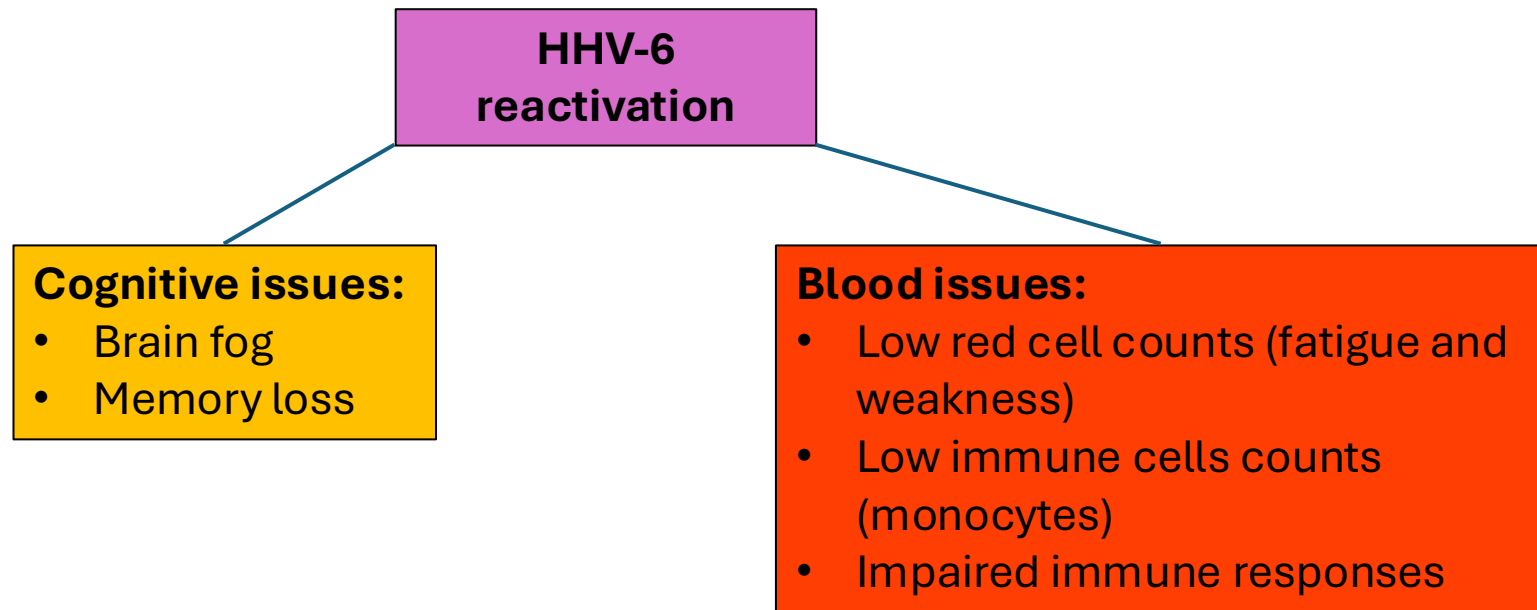


Antibody levels in plasma are uniquely elevated for HHV-6

Unchanged for EBV and CMV

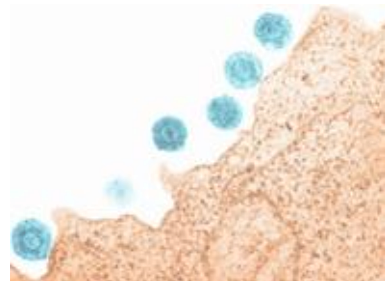


HHV-6 reactivation as a driver of Long-COVID symptoms?



Future directions

- Verifying that HHV-6 is reactivation in Severe Long-COVID
 - Does this contribute to symptoms?
 - Does this contribute to immune phenotype?
- Can HHV6 be a target for treatment?
- Check out Poster # 77 (Berend Röring) for more!



Acknowledgements

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- Niels Velthuijs
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Radboudumc

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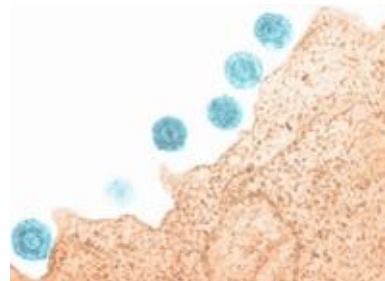
- Research Bureau
- André van Petersen



bernhoven

**All the wonderful participants
that contributed to this trial!**

STICHTING
longcovid



Moving forward

Investigating Neuroinflammation and its effects in post-COVID syndrome: an imaging study

