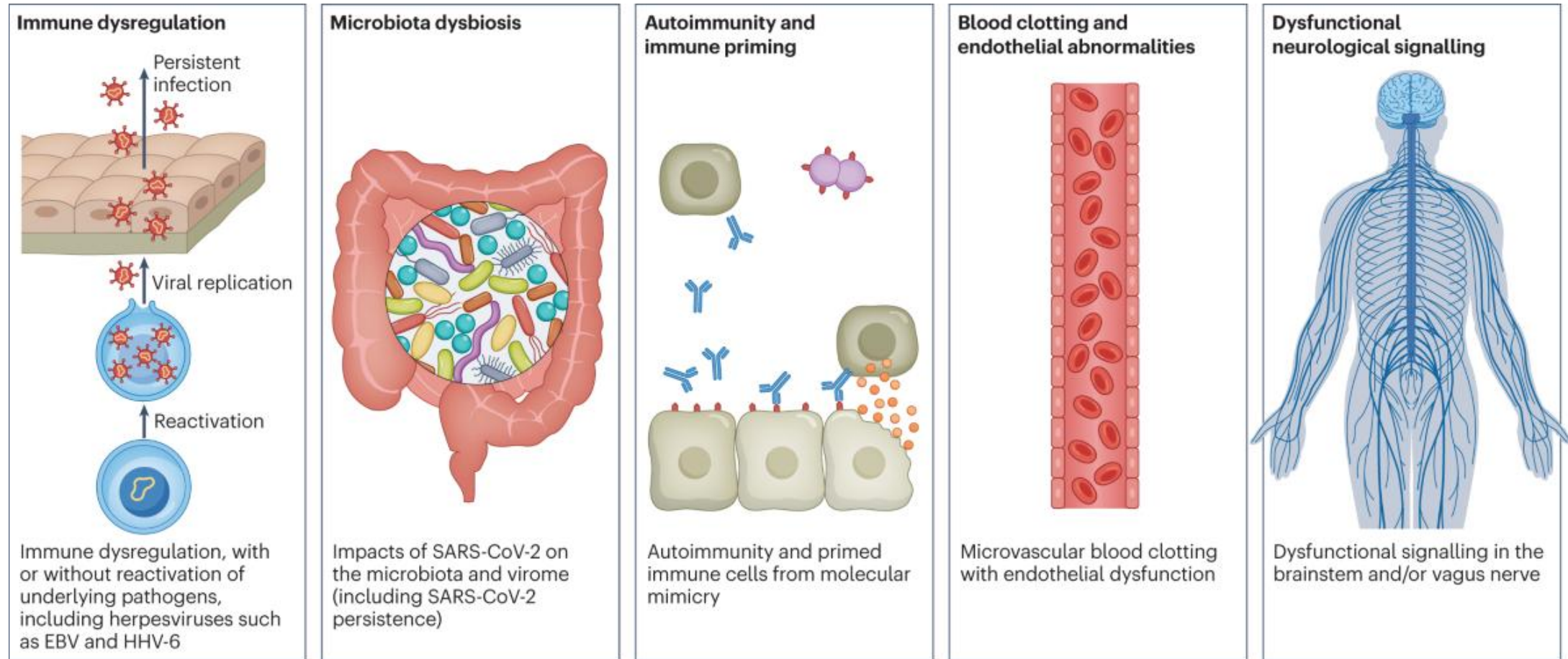
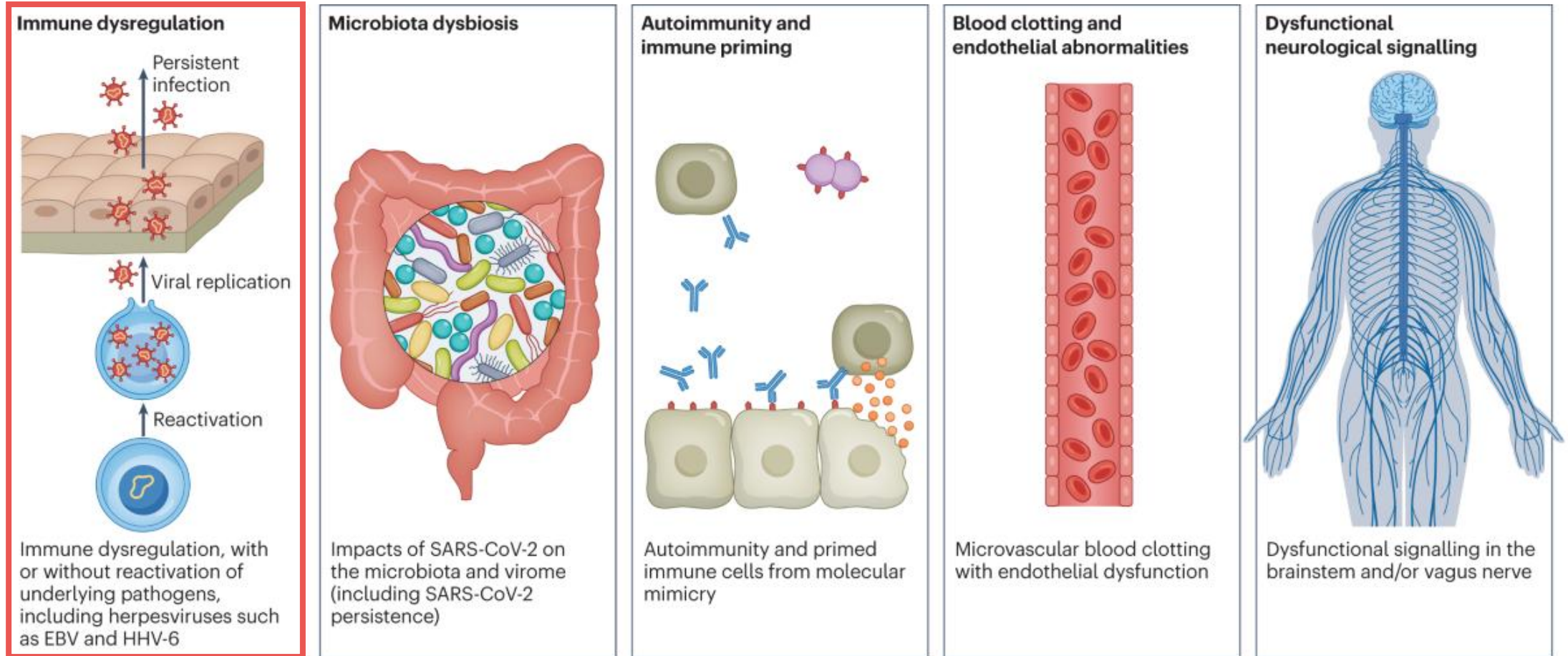


Multi-layered immune profiling reveals treatment-relevant endotypes in Long Covid-ME/CFS

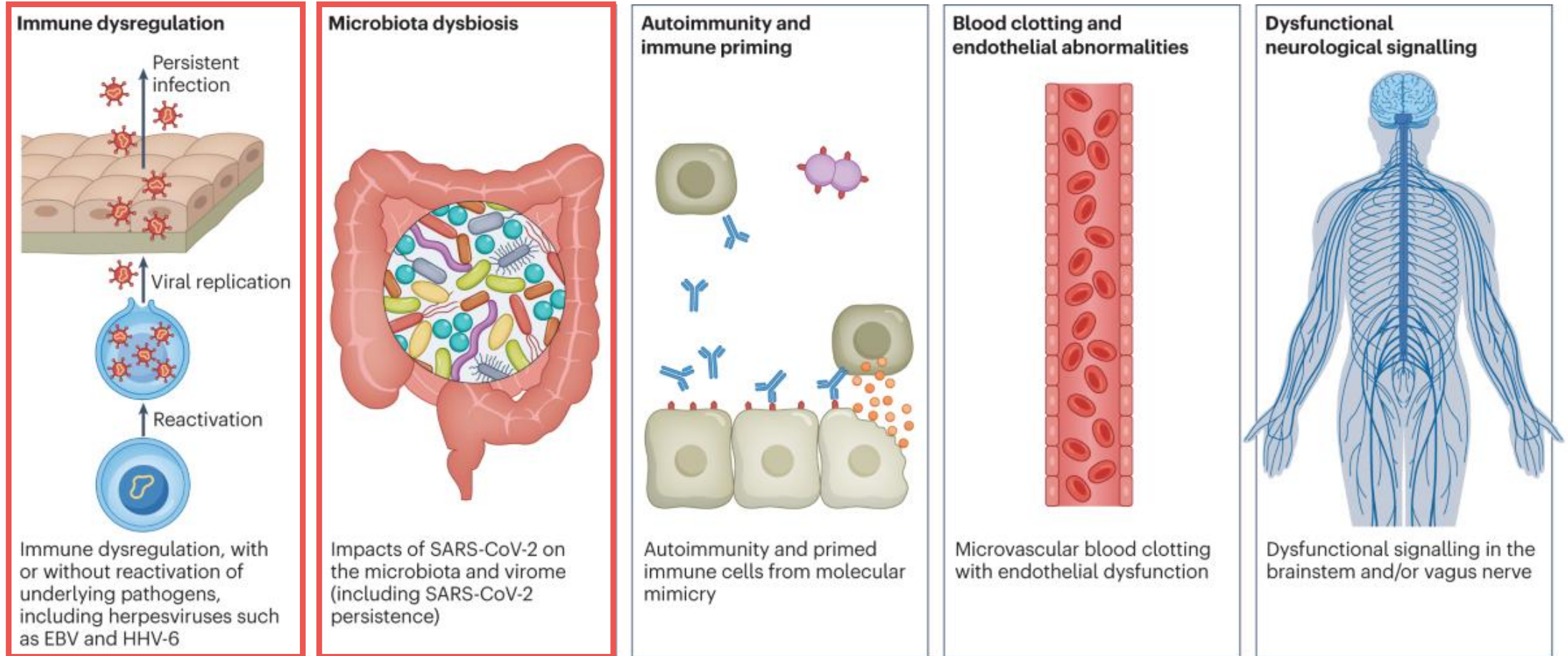
Potential drivers of PAIS involve immune processes



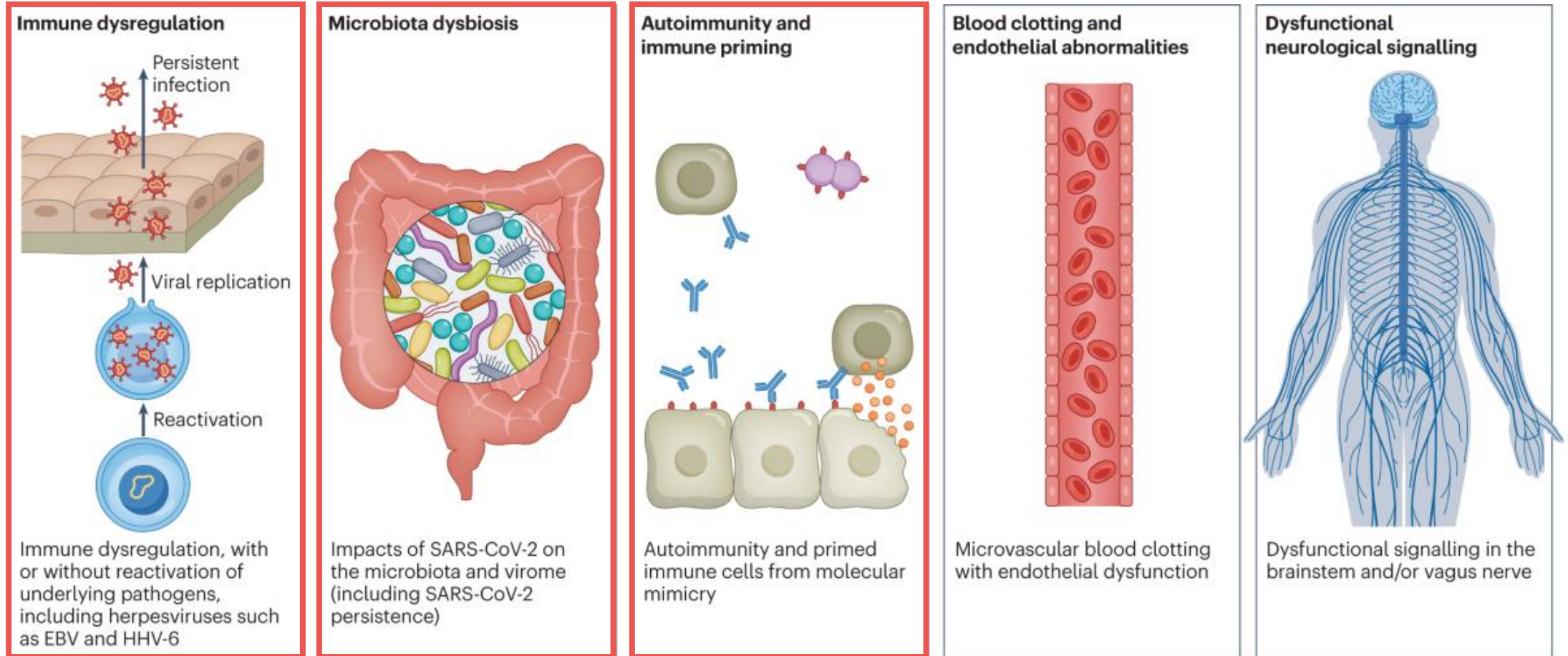
Potential drivers of PAIS involve immune processes



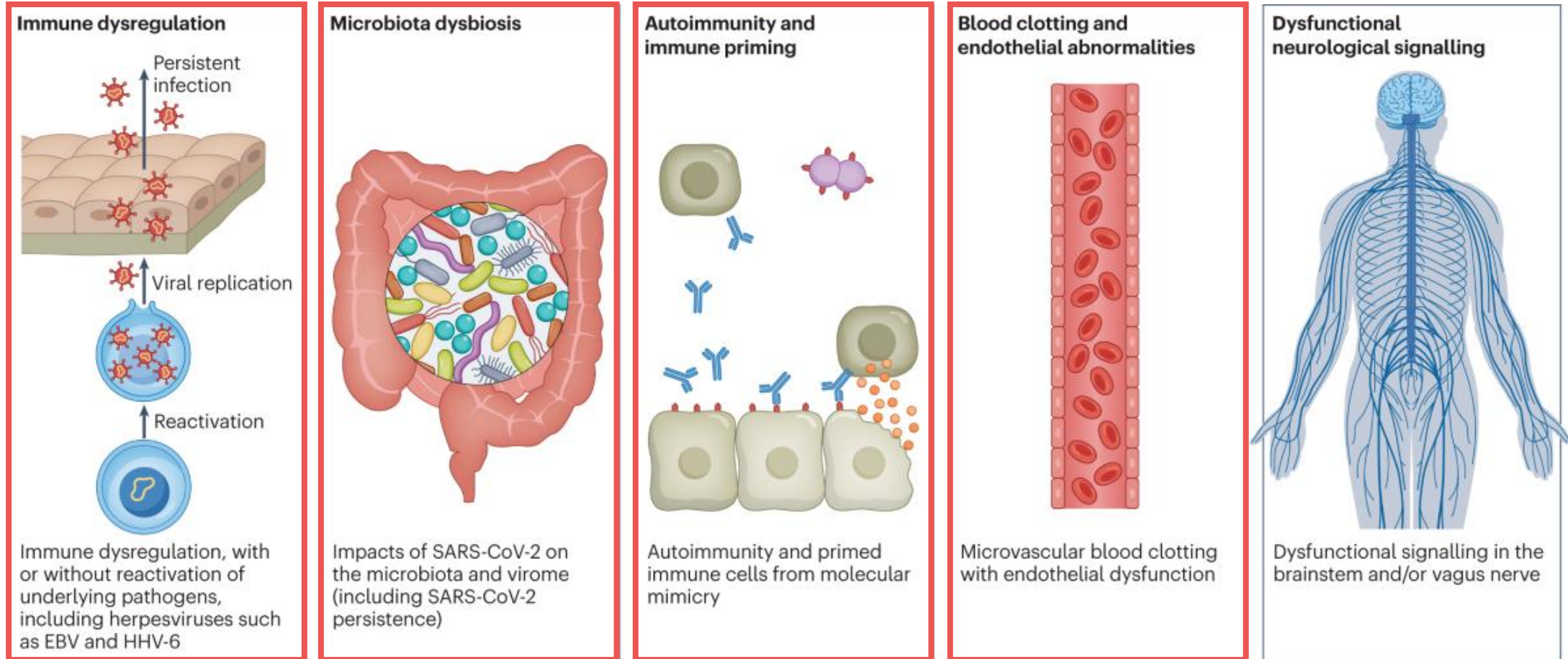
Potential drivers of PAIS involve immune processes



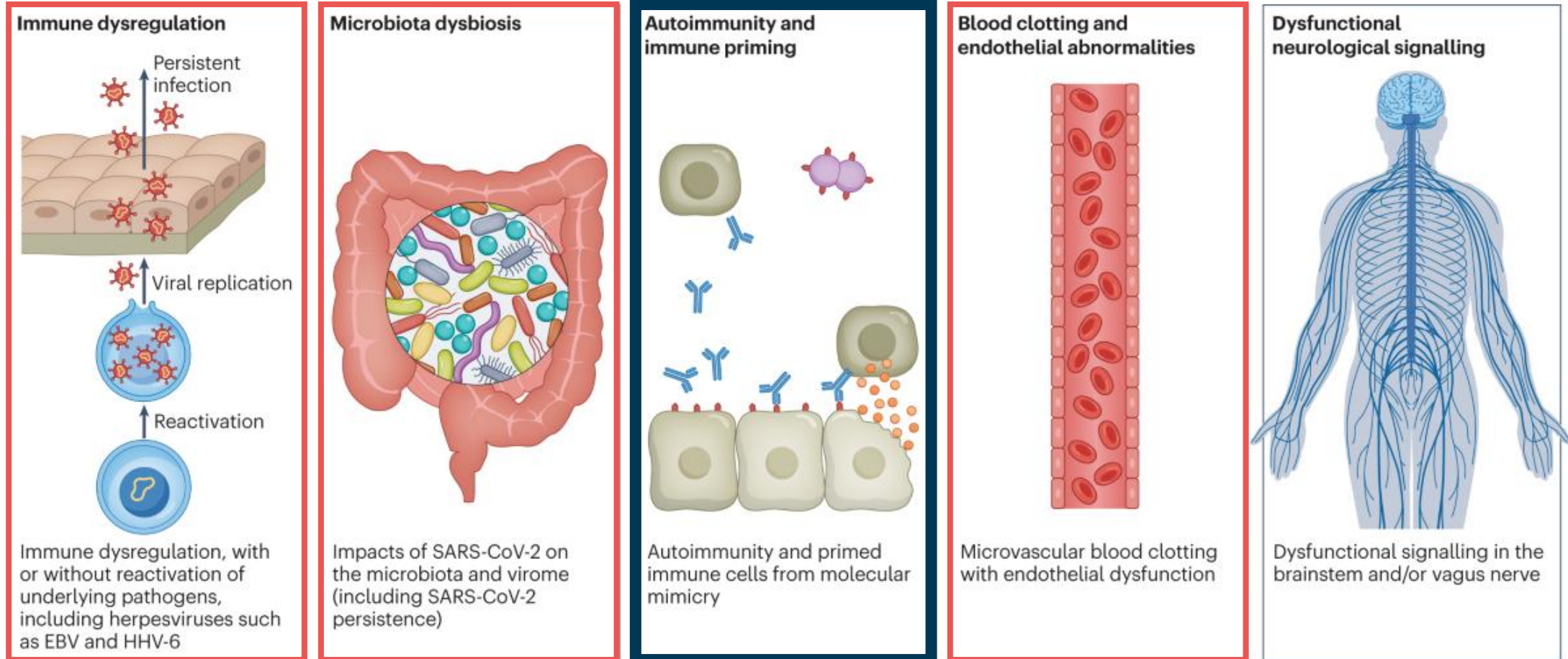
Potential drivers of PAIS involve immune processes



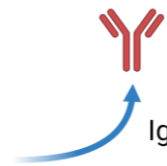
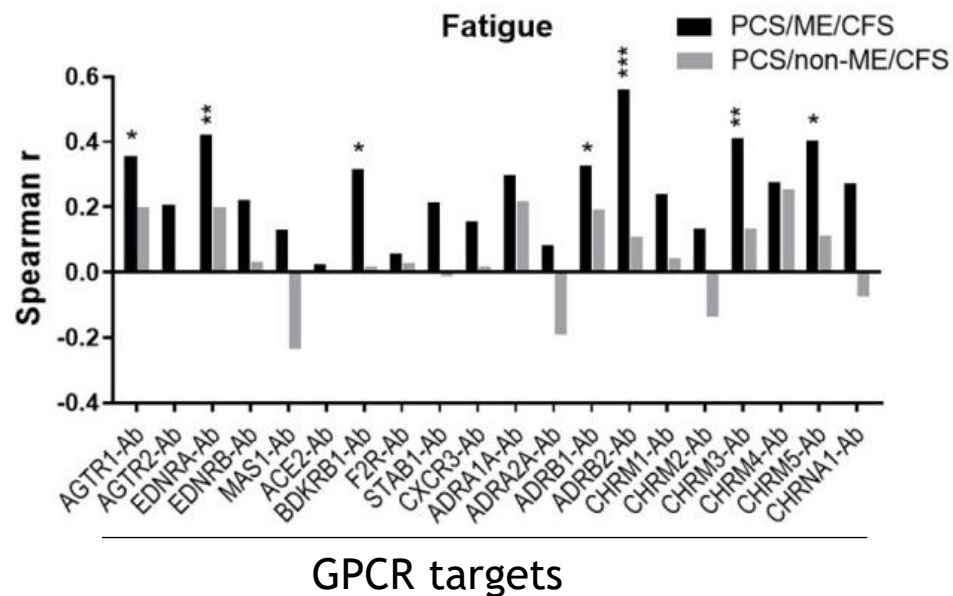
Potential drivers of PAIS involve immune processes



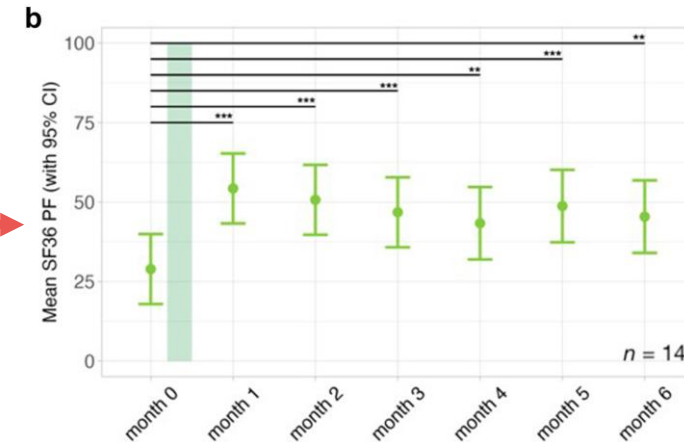
Potential drivers of PAIS involve immune processes



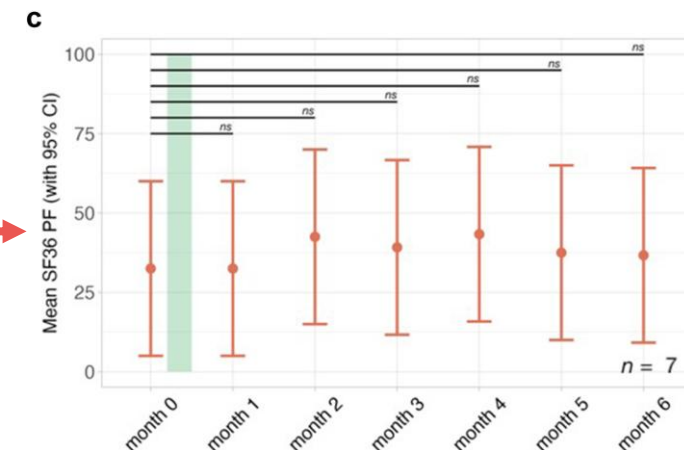
AABs against GPCRs correlate with ME/CFS symptoms and removal benefits a subgroup of patients



Immunoadsorption



Responder

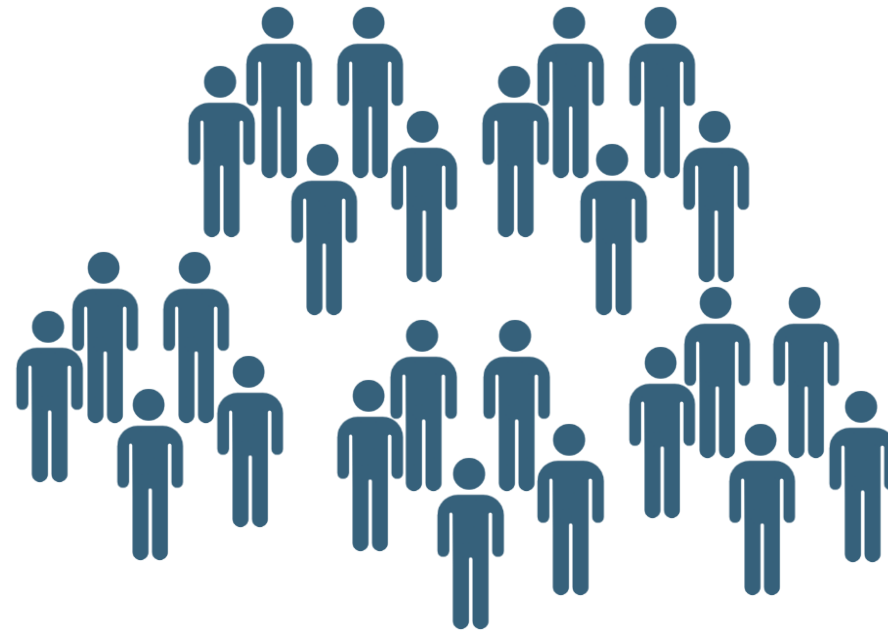


Non-responder

Sotzny et al., 2022

Stein et al., 2022

A „cohort of ME/CFS patients“ doesn't look like this...



... but much rather like this.



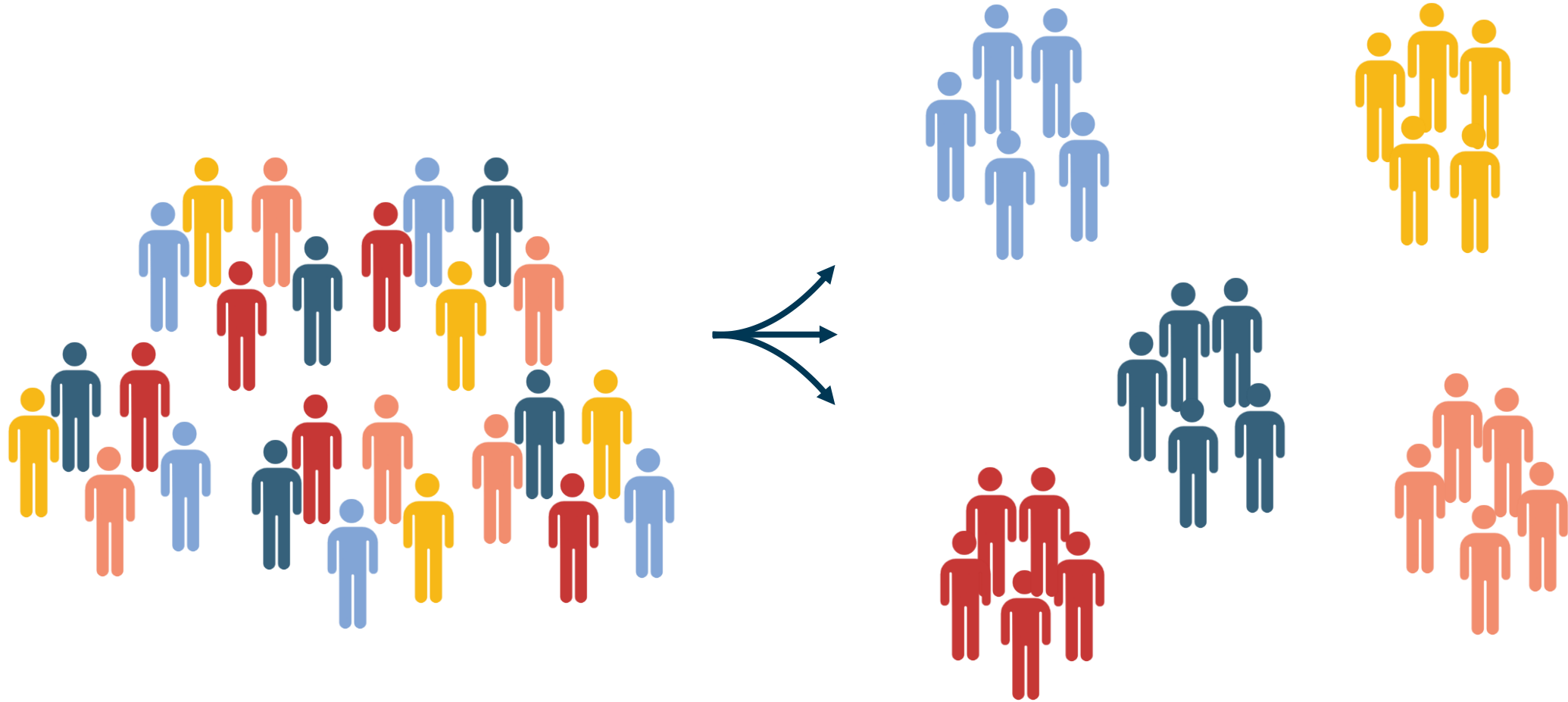
So naturally, a one-drug-fits-all solution...



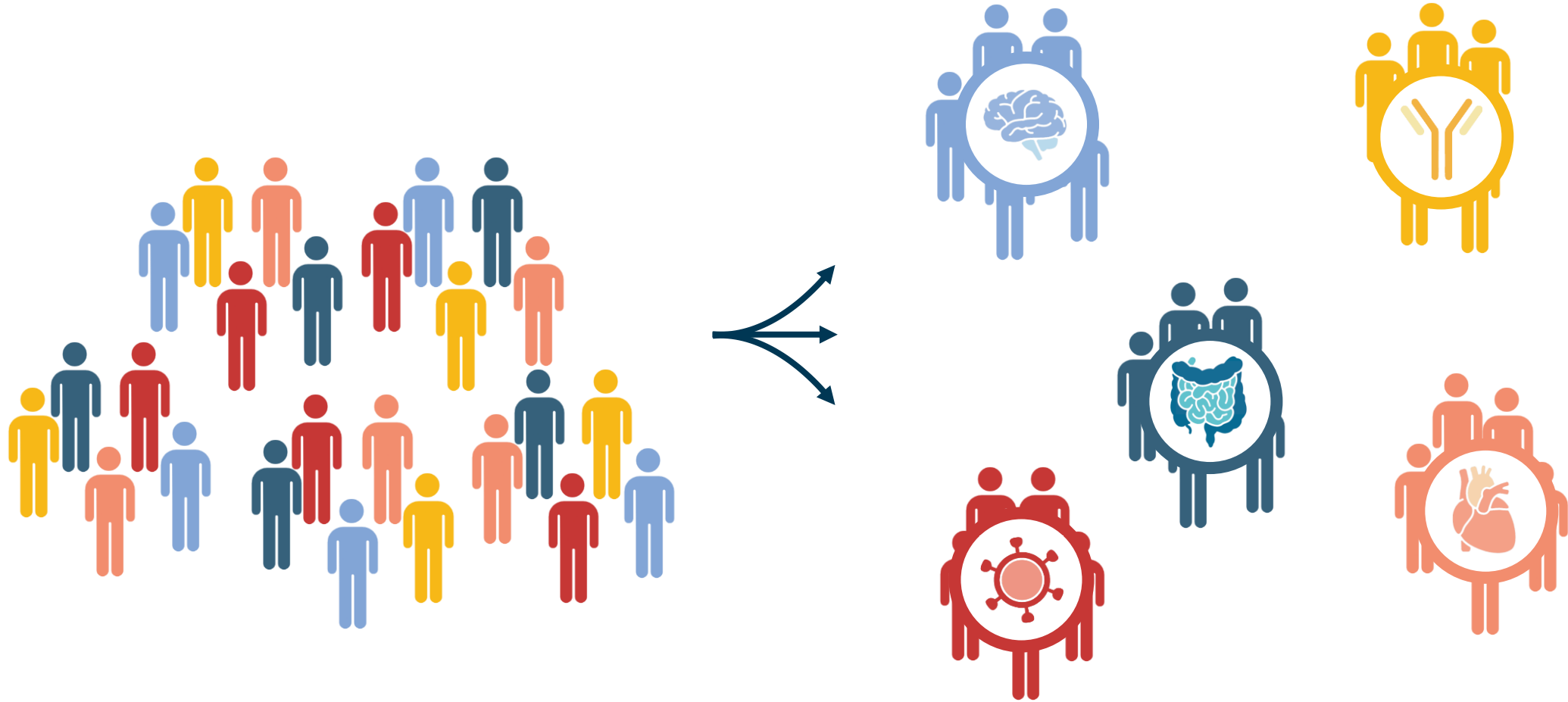
... is not realistic.



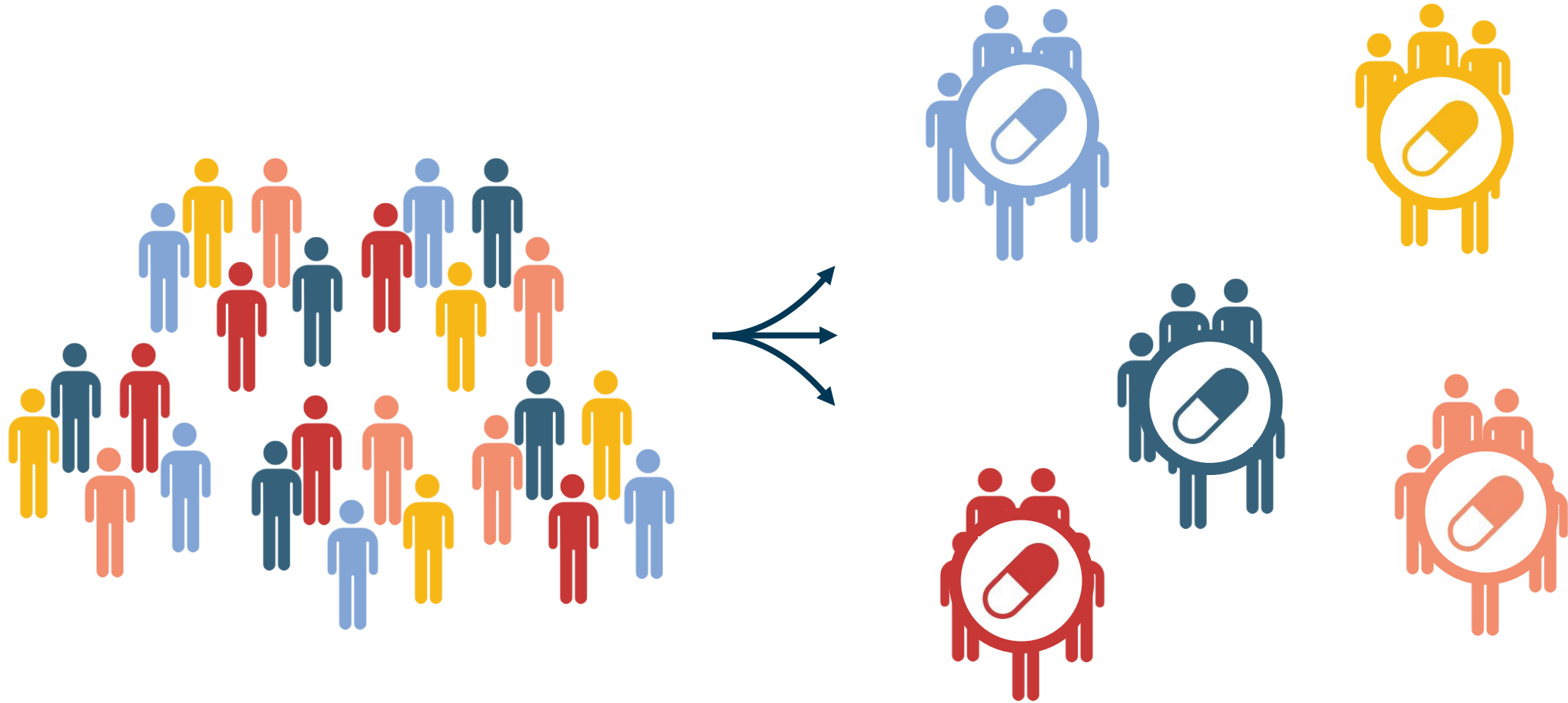
Aim 1: Identify patient subgroups using multi-layered immune profiling.



Aim 2: Link subgroups to molecular drivers of PAIS.



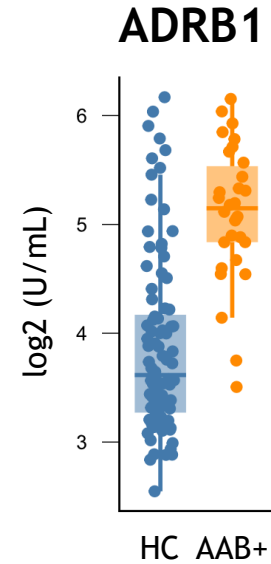
Aim 3: Assign treatments, tailored to subgroup.



Test cohorts

AAB+ cohort (n = 30)

- increased GPCR AABs
- autoimmune endotype



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Test cohorts

AAB+ cohort (n = 30)

- increased GPCR AABs
- autoimmune endotype



Broad cohort (n = 57)

- ~ 30 % AAB+
- all endotypes



Healthy controls (n = 80)

- age-and sex matched

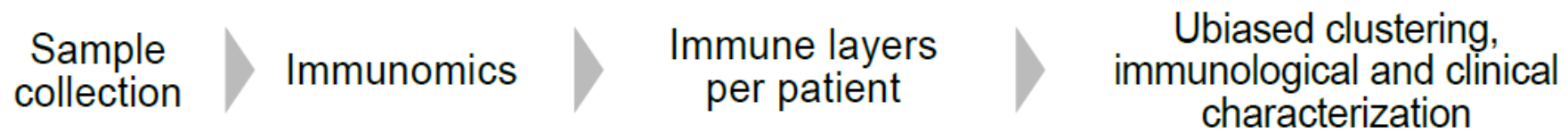


Validation cohort (n = 60)

- ~ 30 % AAB+
- all endotypes



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Plasma

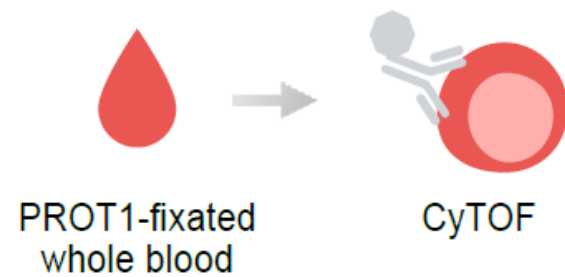
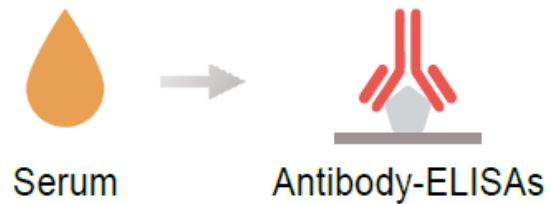
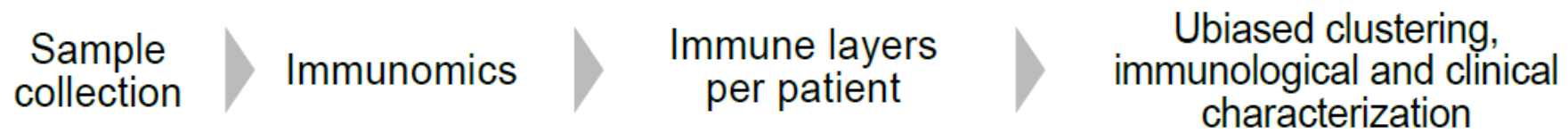


Serum

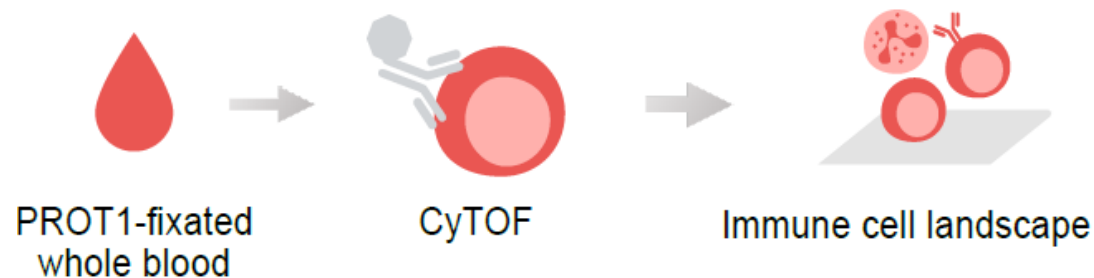
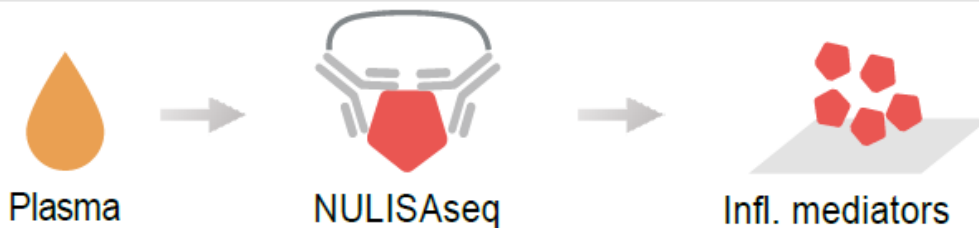
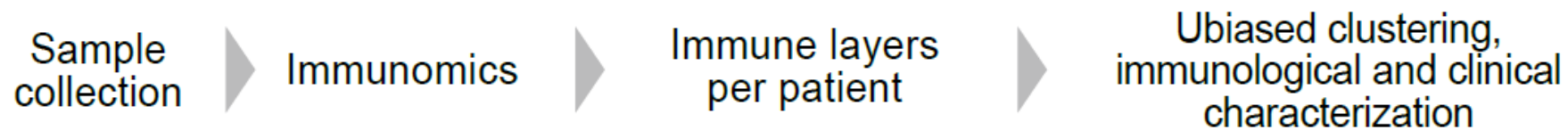


PROT1-fixated
whole blood

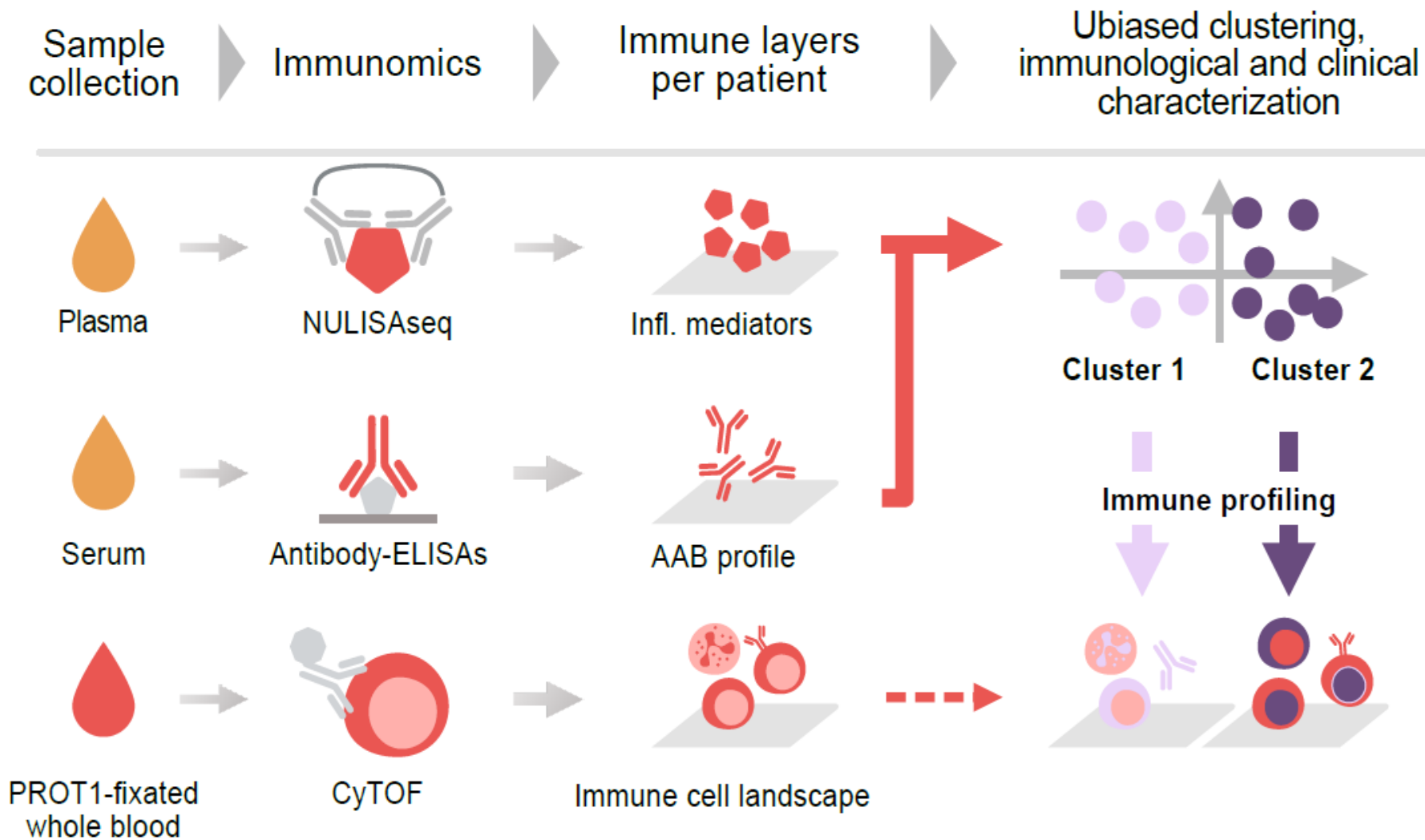
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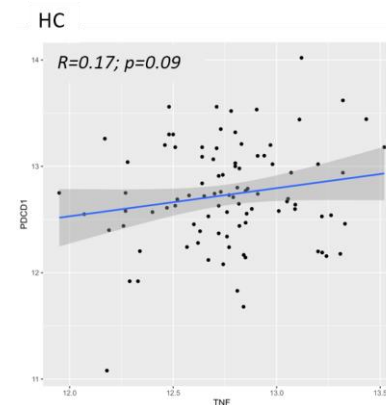
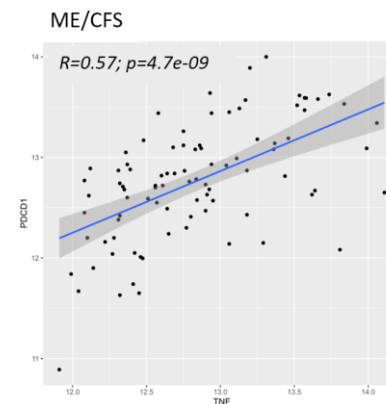
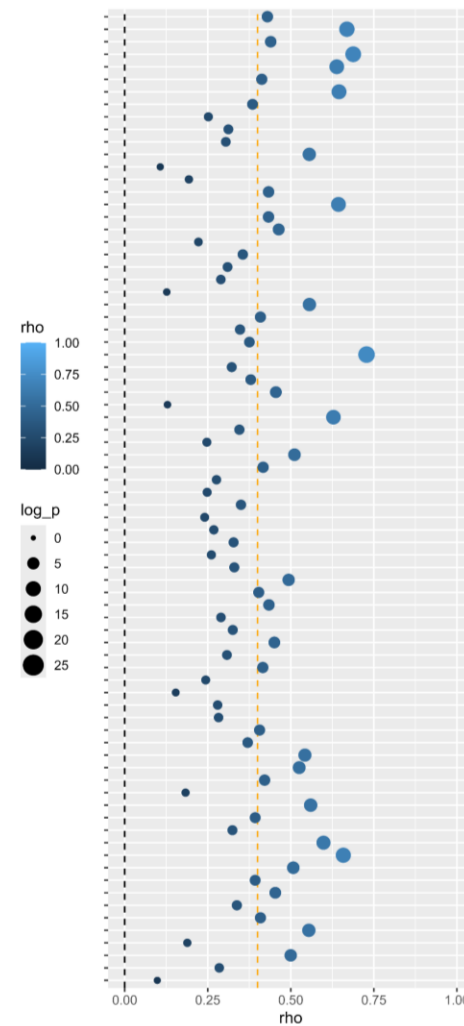
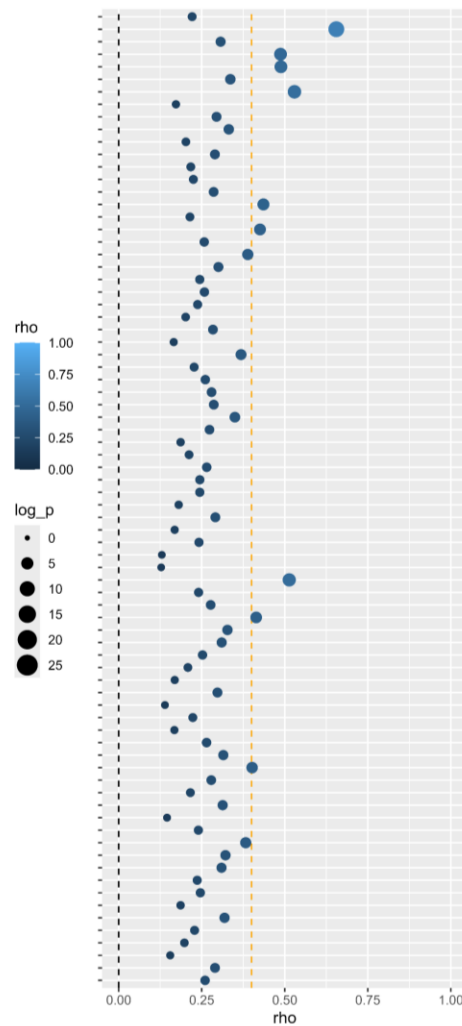
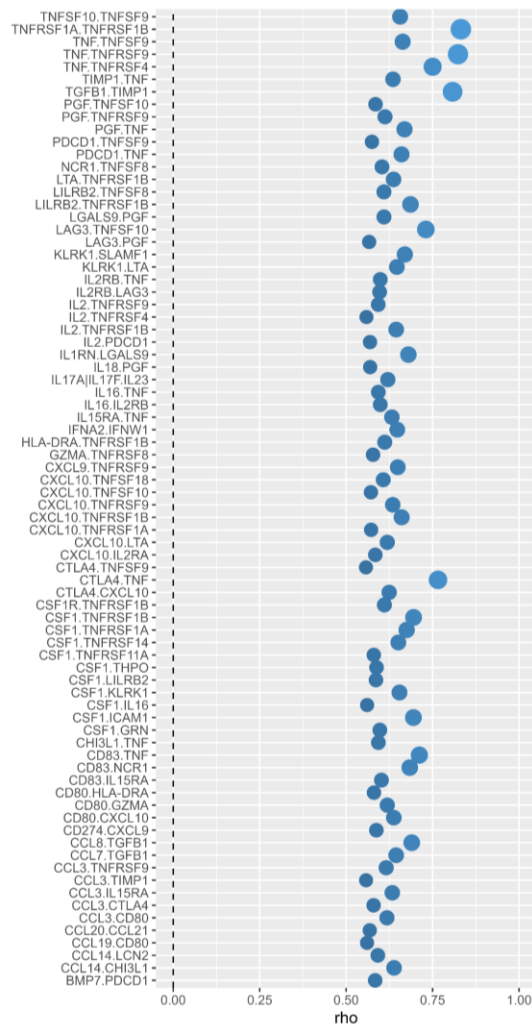
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Correlation (-network) analysis of NULISaseq 250 inflammatory mediators

correlate in test cohorts

but not in HC

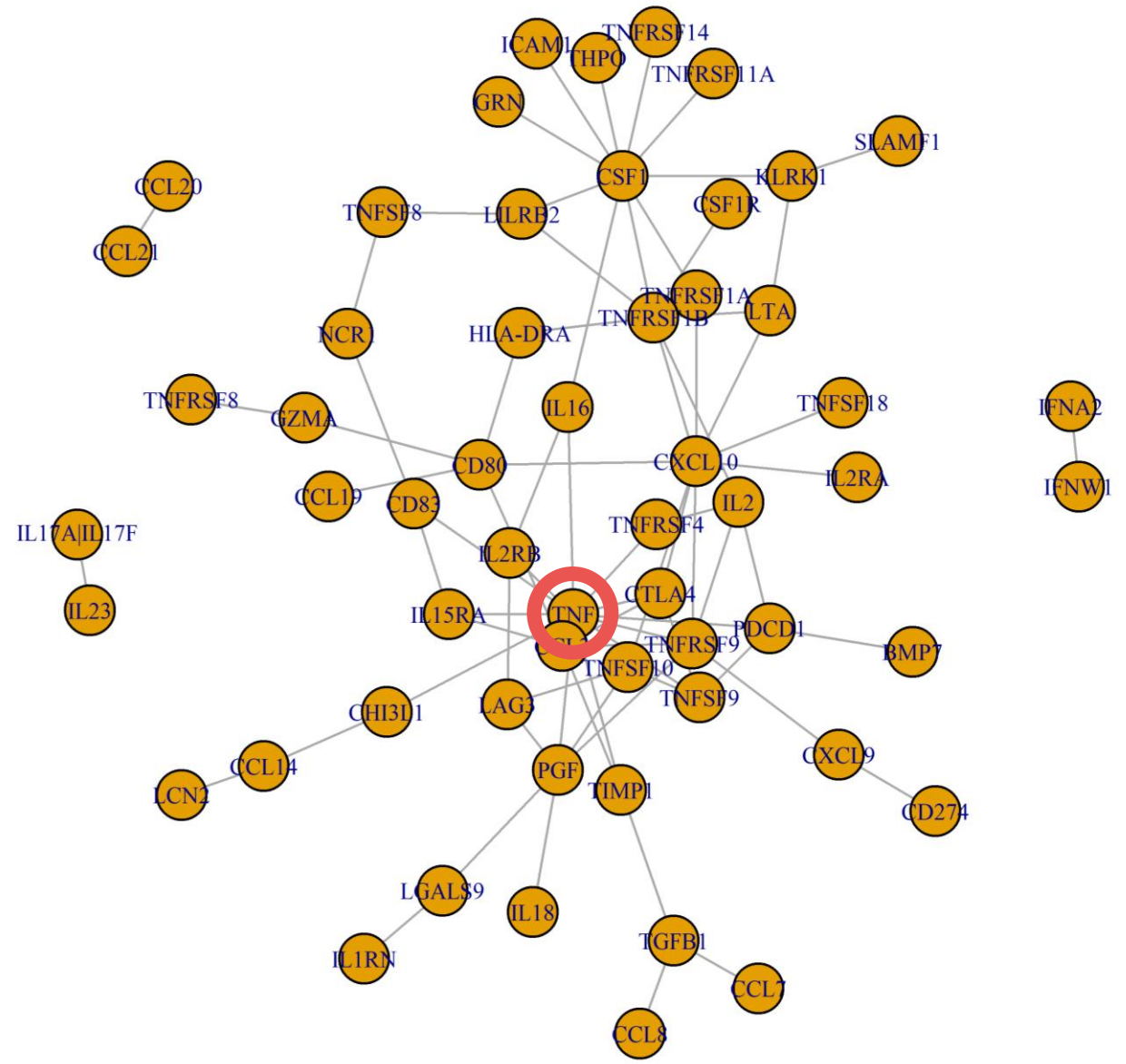
validate



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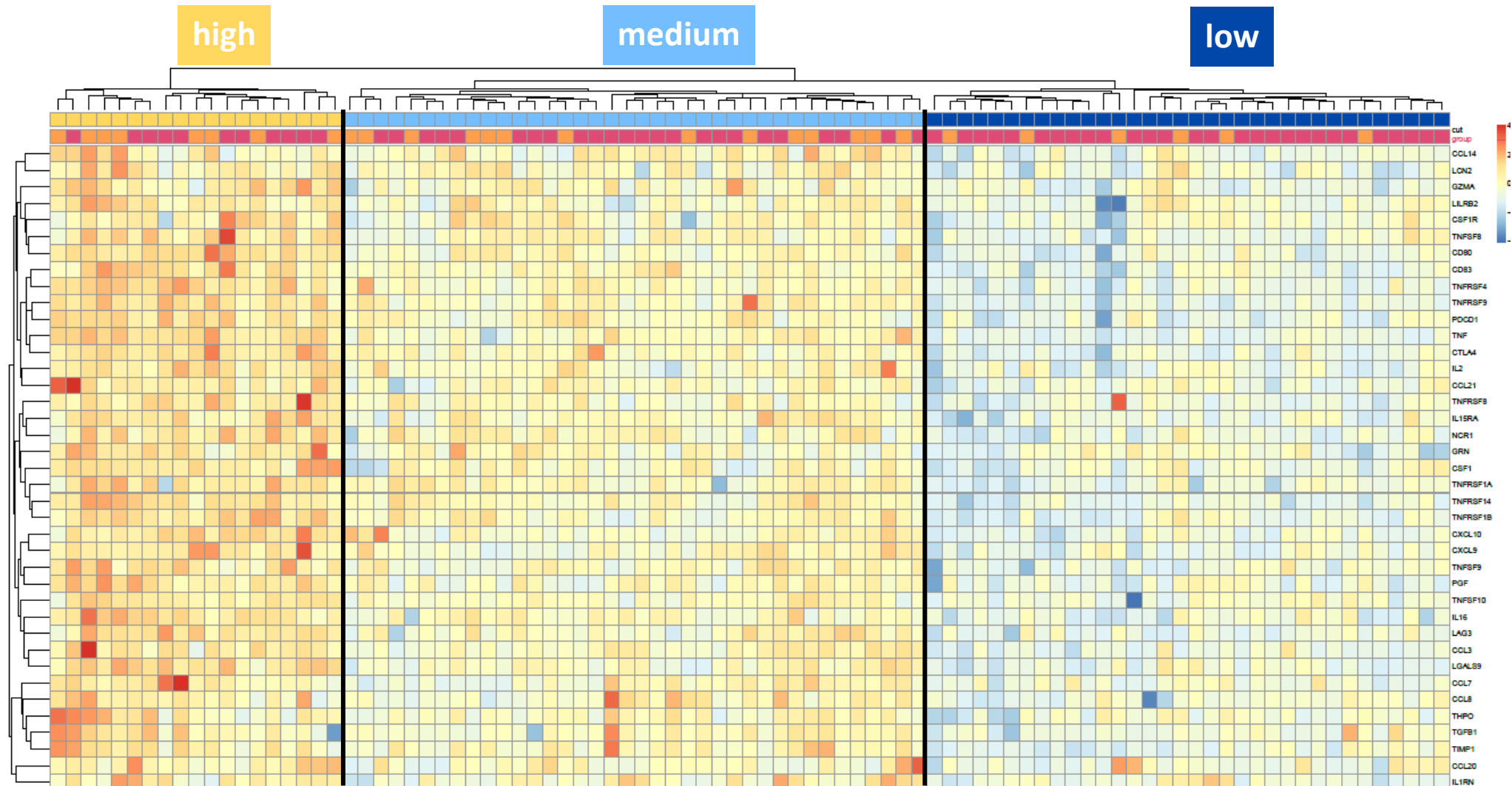
Constructing a network of the correlating mediators:

seems to be centered
around TNF and TNFR-
superfamily members



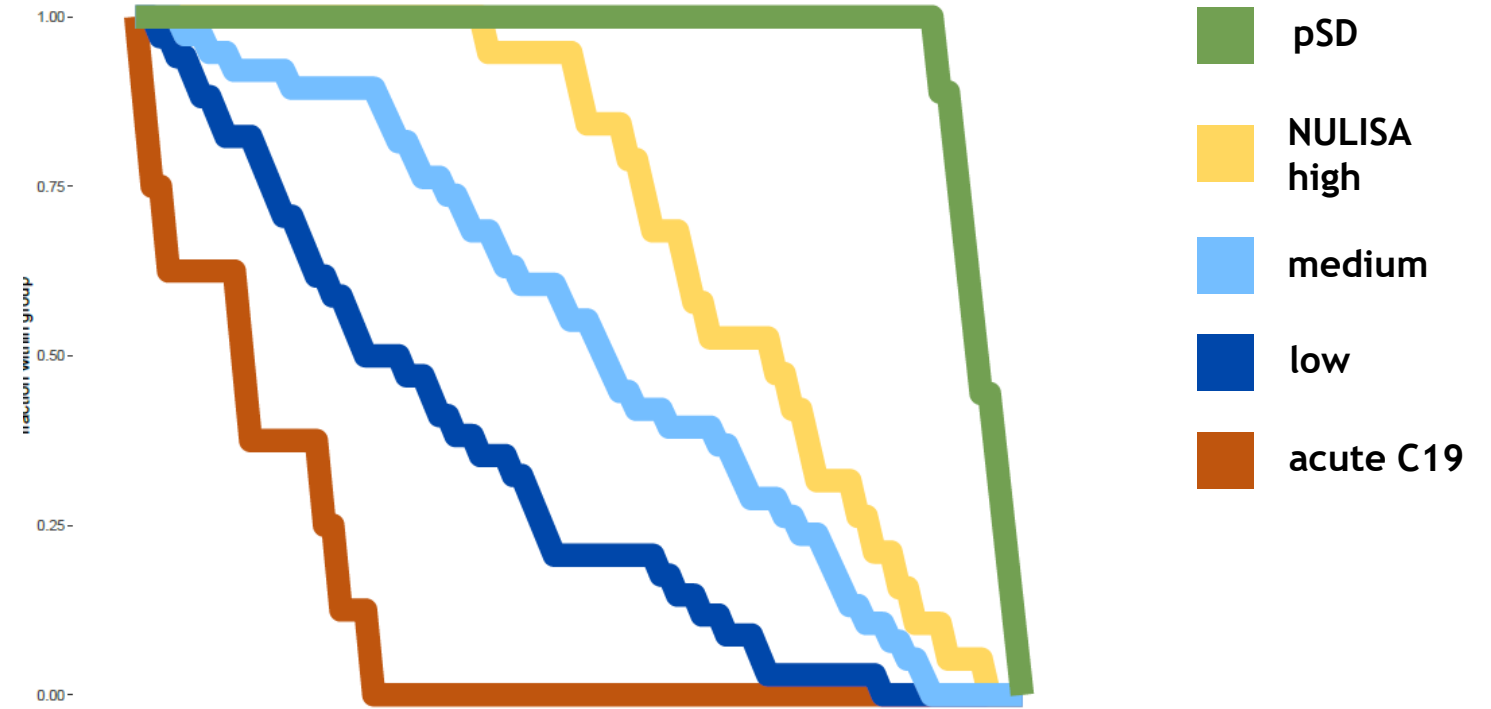
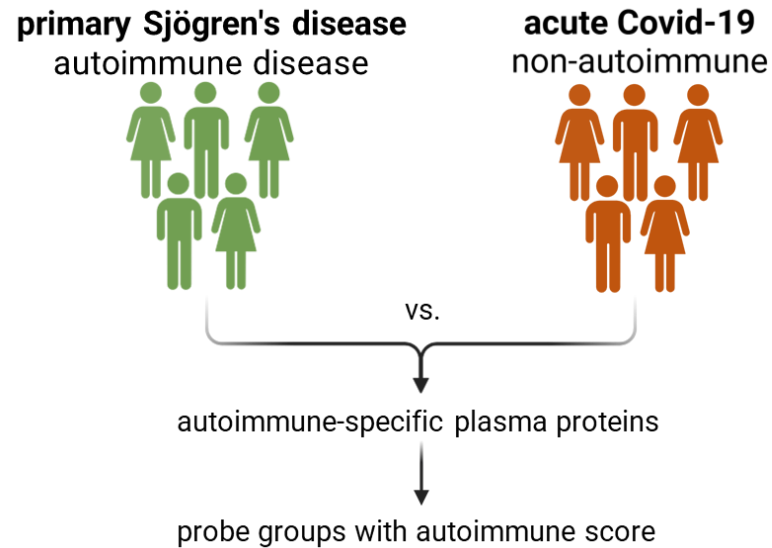
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Selected mediator network yields 3 clusters



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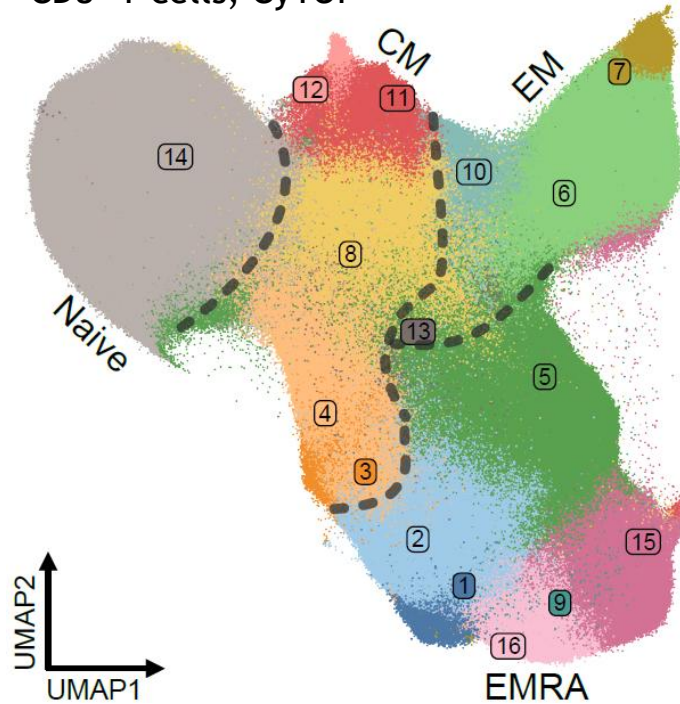
NULISA-High cluster shows autoimmune features



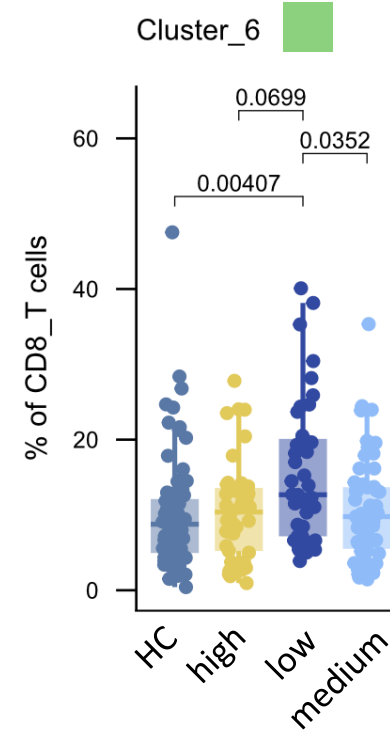
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NULISA clusters differ in T cell response

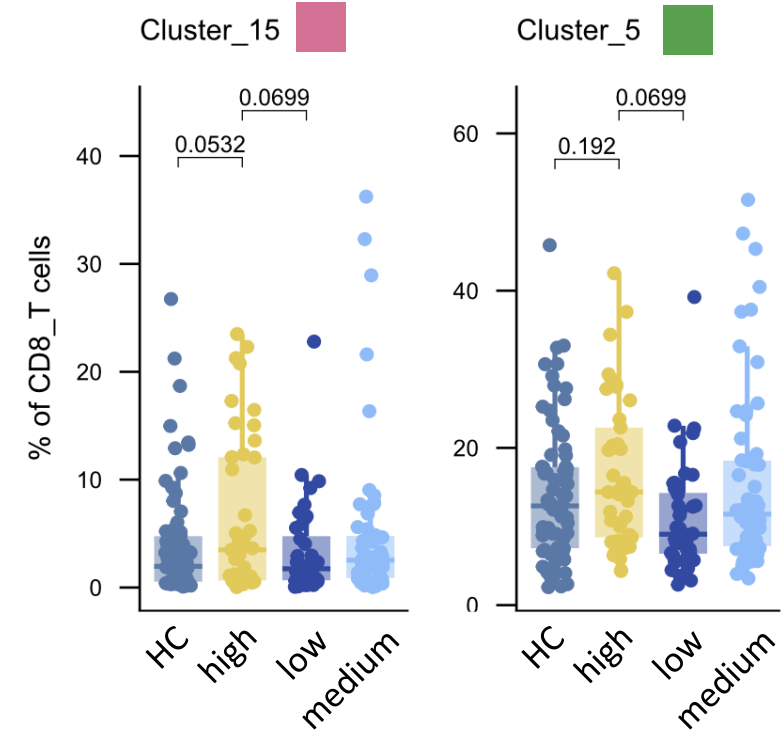
CD8⁺ T cells, CyTOF



Low cluster:
CD127⁺CD161⁺
"MAIT"-like cells

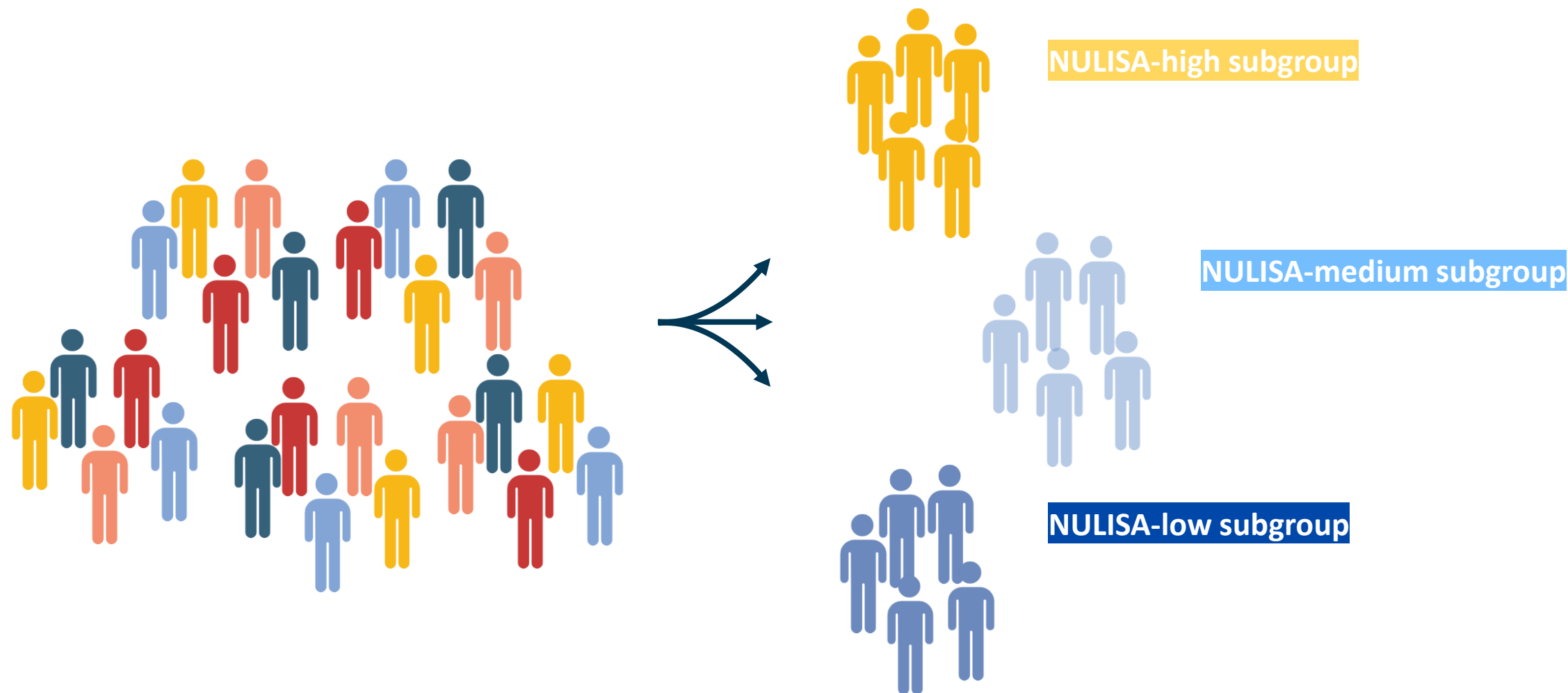


High cluster:
CD27⁻CD28⁻
chronically activated T cells



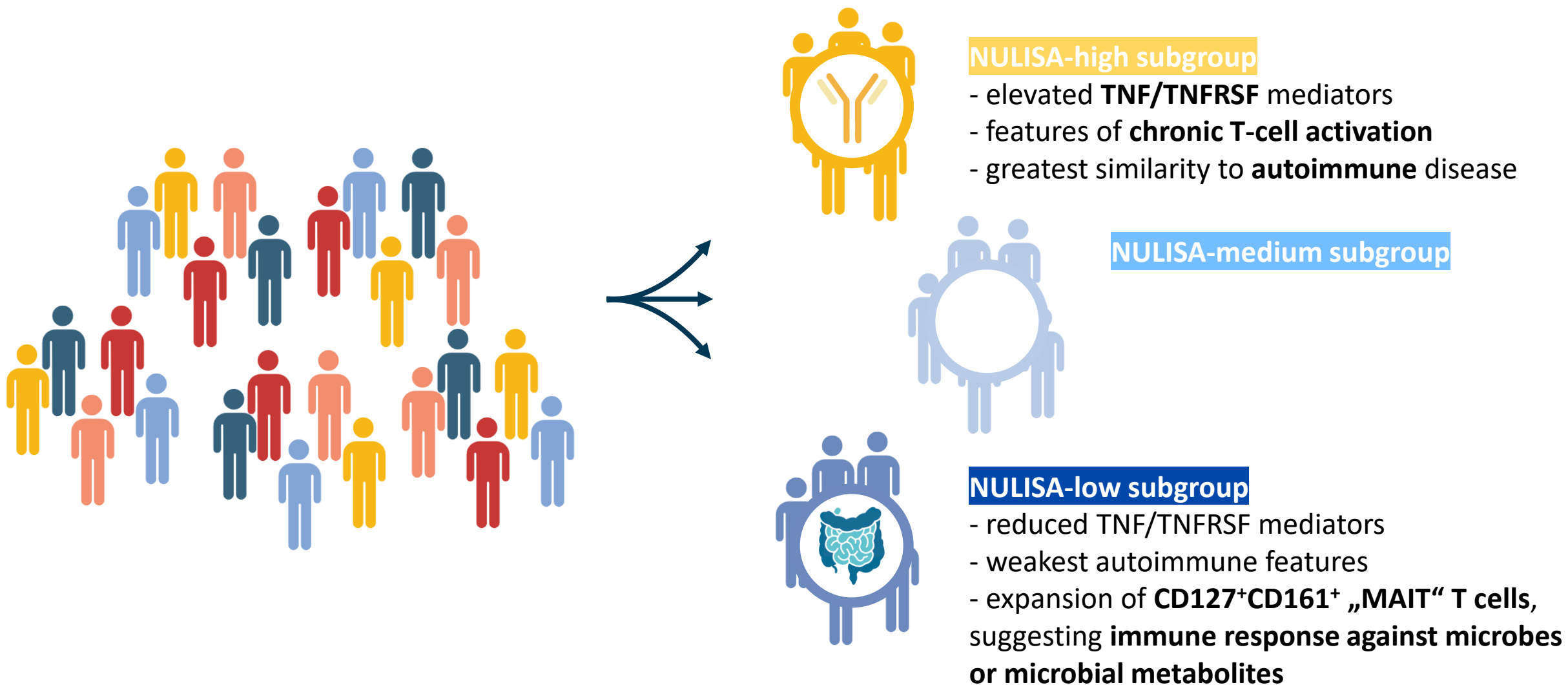
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Summary Aim 1: Multi-layered immune profiling identifies distinct LC-ME/CFS patient subgroups.



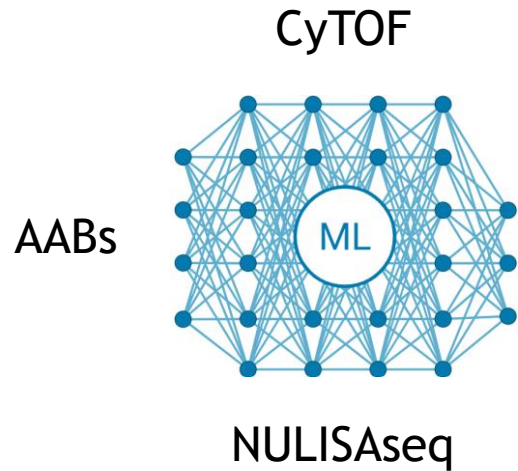
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Summary Aim 2: Linking subgroups to immune cell phenotypes yields candidate treatment-relevant endotypes.

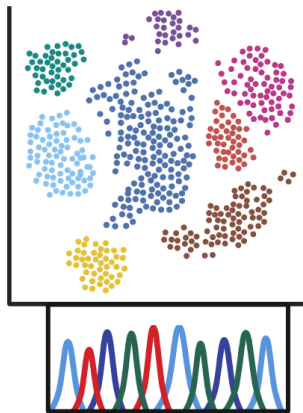


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Outlook



comprehensive cross-method immune profile clustering and analysis involving the plasma proteome, the circulating immune cells and the autoantibodies



elucidate the role of B cells, the B-T cell interaction and antigen specificity in ME/CFS through scRNAseq analysis of ~ 2 mio cells from 60 patients

- PBMCs and enriched B- and T cell populations
- whole transcriptome, BCR and TCR

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Thanks to

AG Sawitzki

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Carmen Scheibenbogen

AG Finke

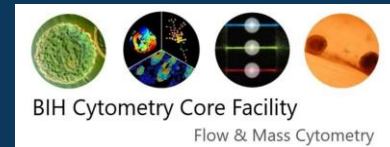
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Carsten Finke

AG Mashreghi

Pawel Durek, Gabriella Guerra, Katrin Lehmann
Mir-Farzin Mashreghi

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Anna Aschenbrenner



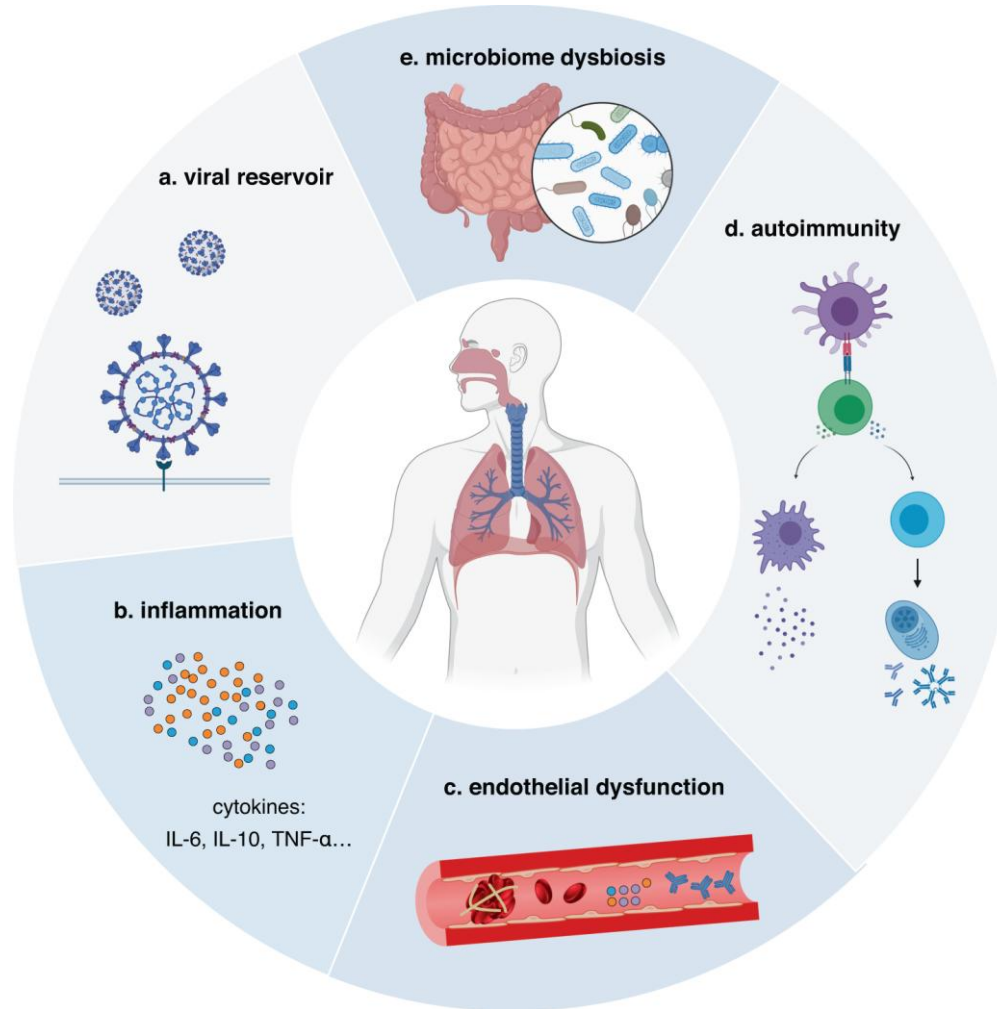
Bundesministerium
für Forschung, Technologie
und Raumfahrt



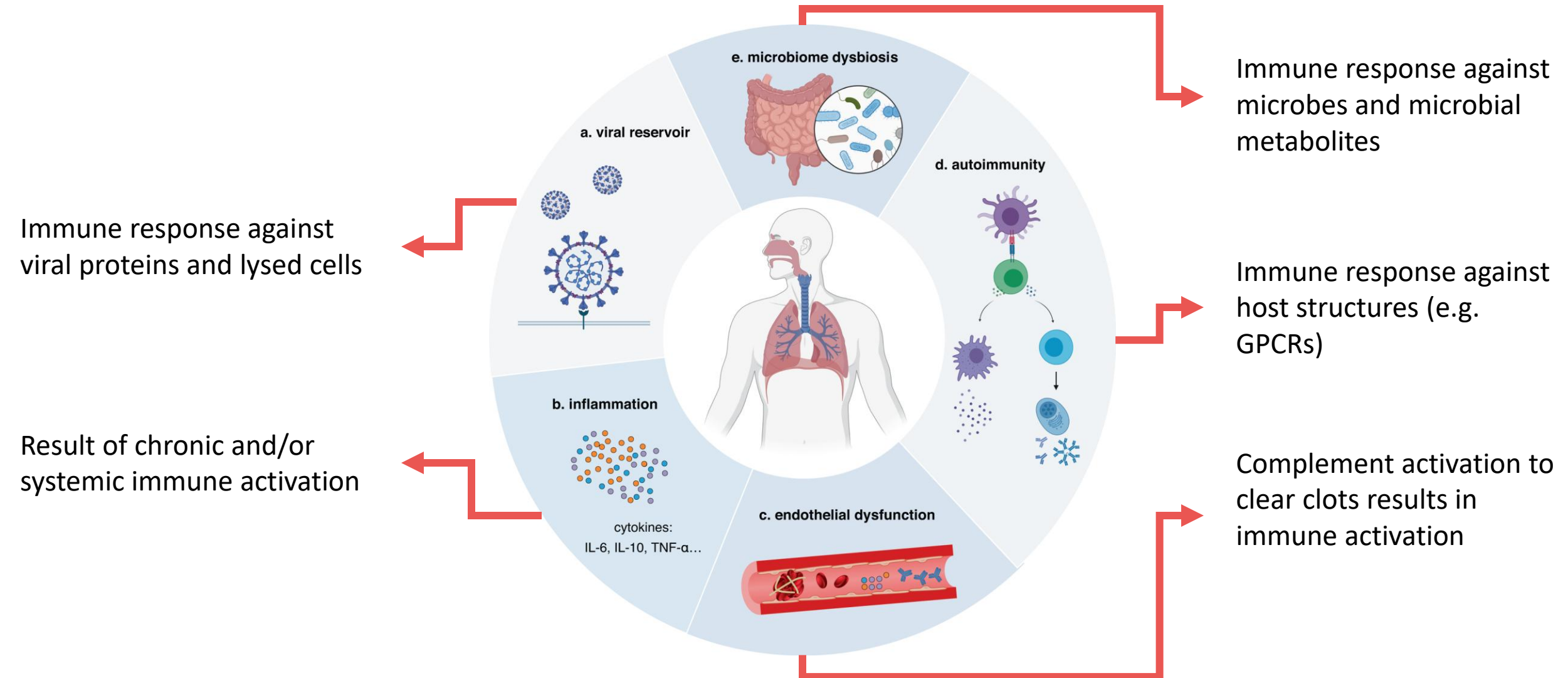
figures created with BioRender.com



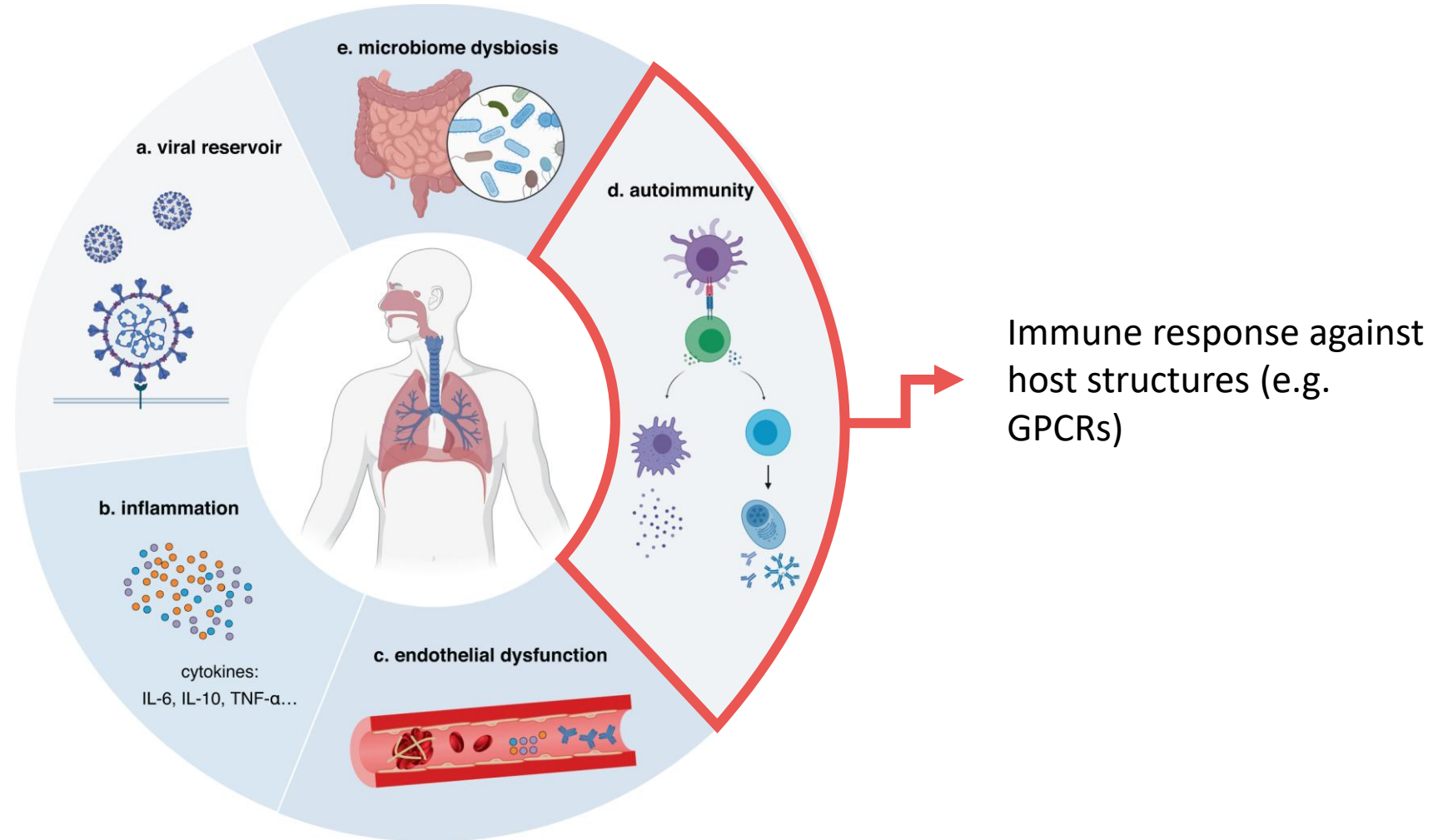
The immune response is the key to decode PAIS

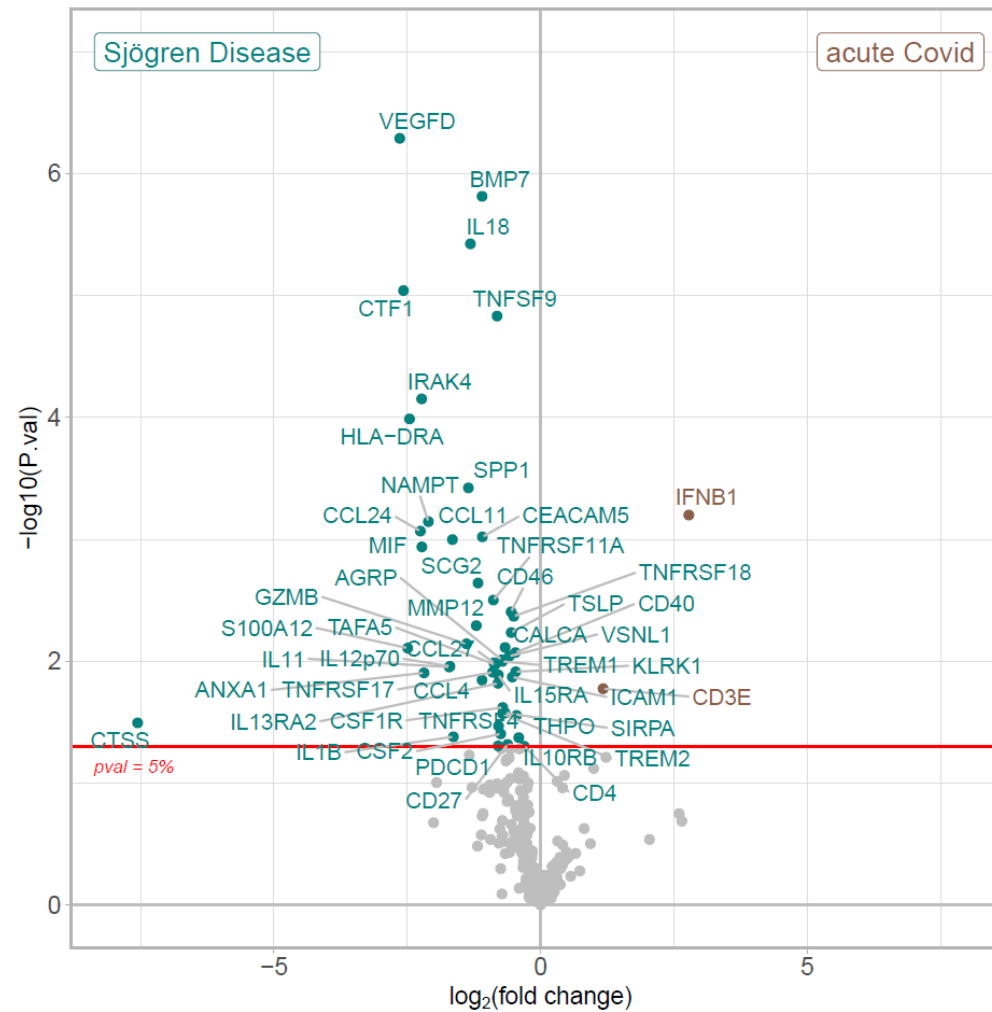


The immune response is the key to decode PAIS

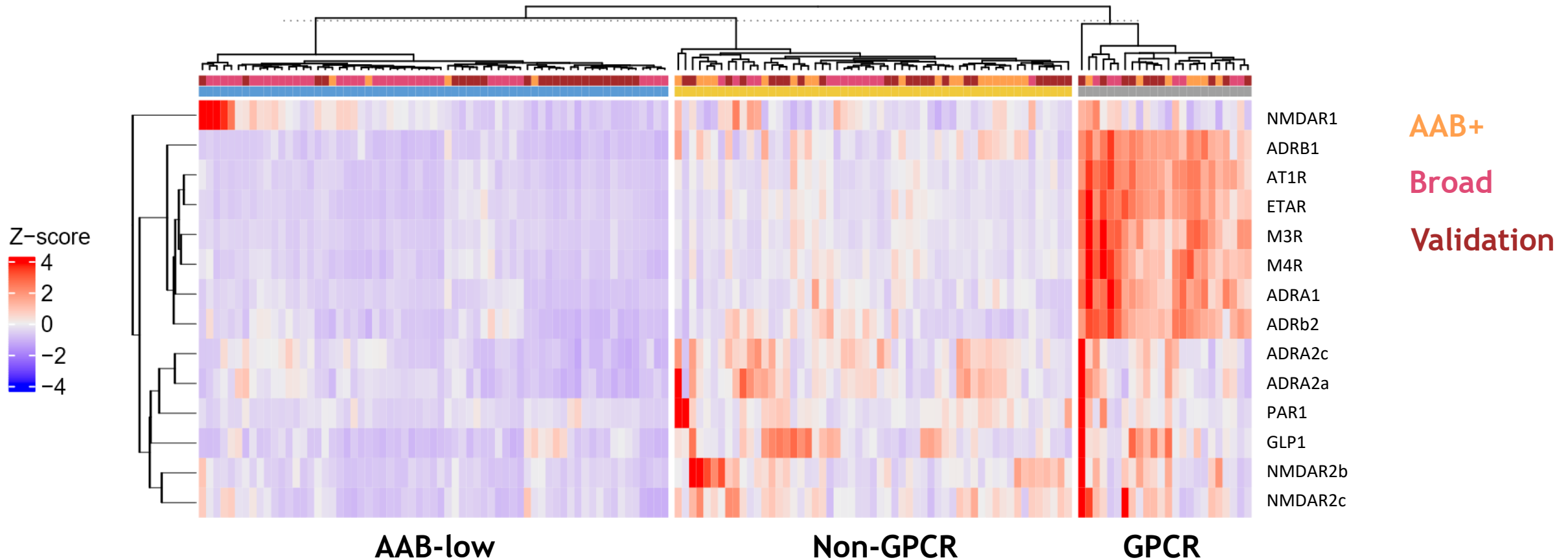


PAI-acquired autoimmunity is a potential cause of PAIS





AABs in patients define clusters based around GPCRs



AAB clusters differ in B cell response

