Molecular alterations before, during and after sepsis/pneumonia

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PI Team-6 CR2TI

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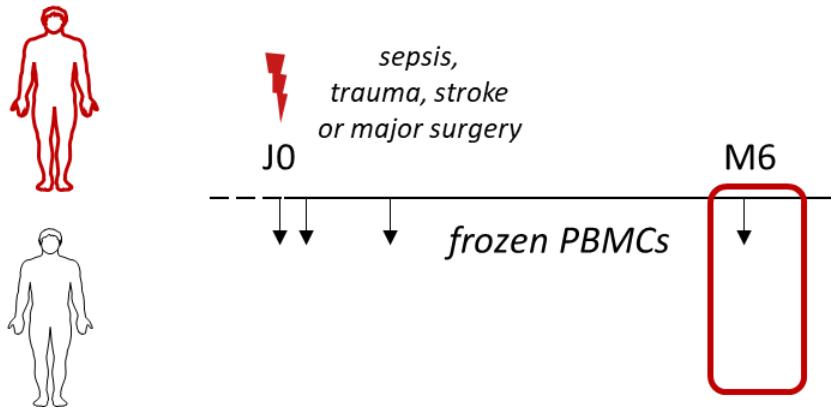
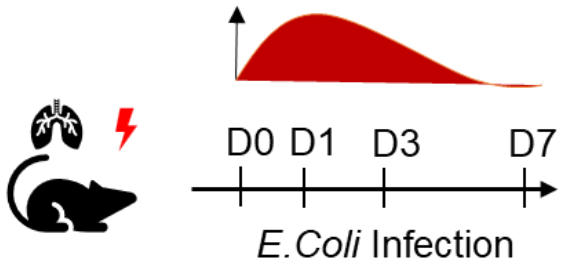


1) **The molecular state of Traumatic brain injury patients**

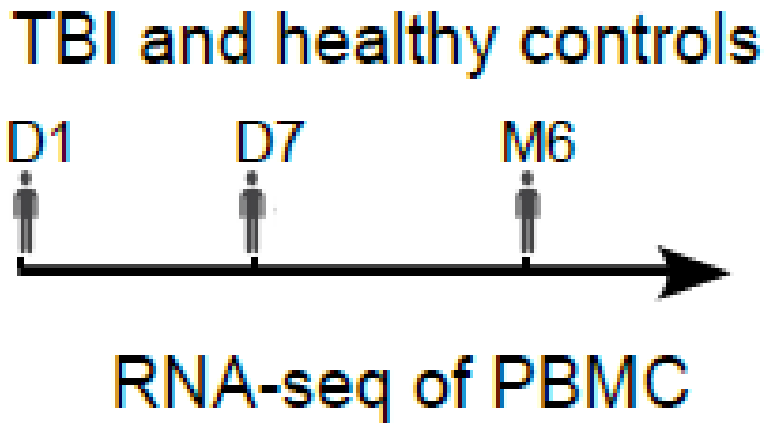
2) **Risk of hospital-acquired Pneumonia**

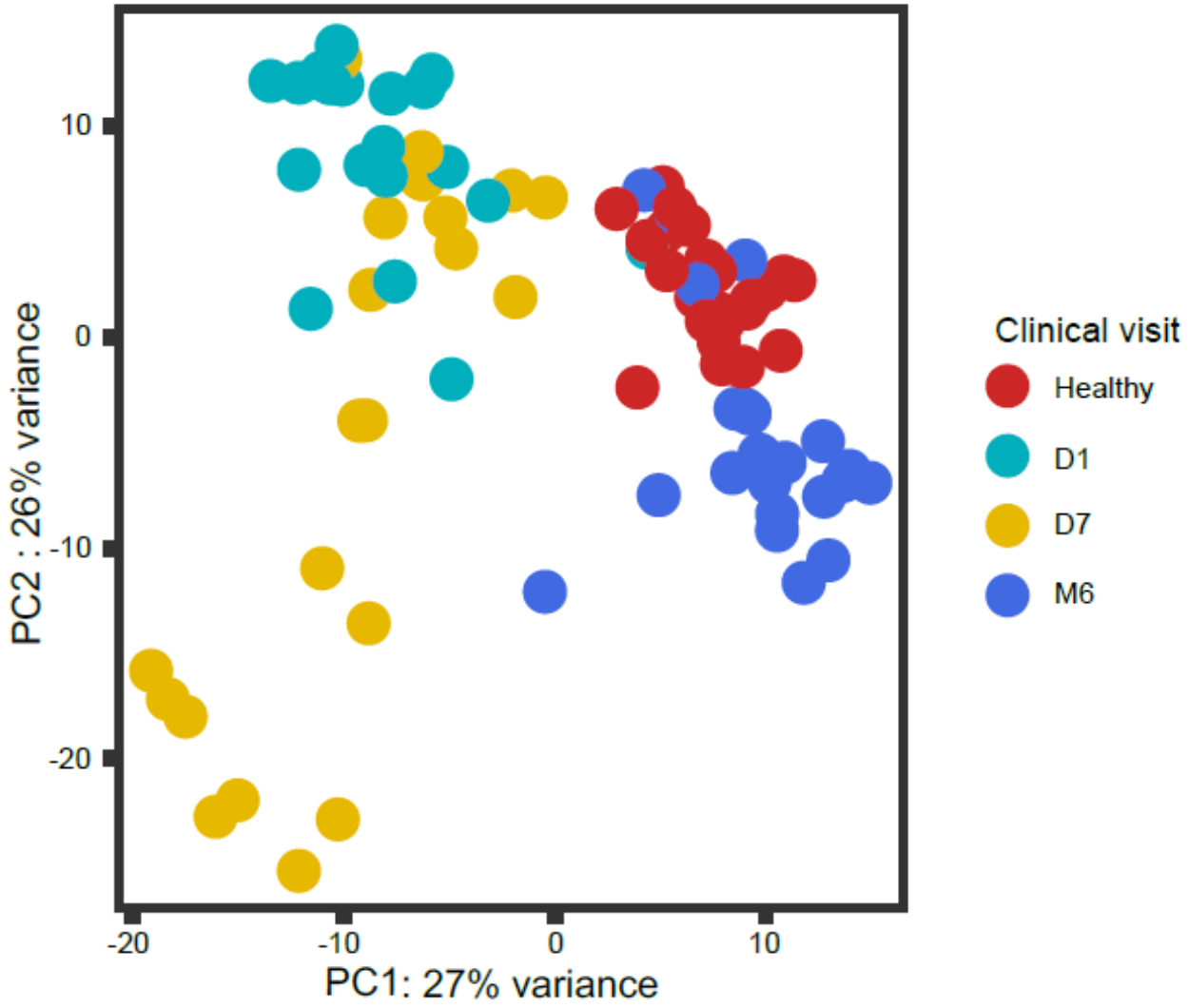
3) **Long-term consequences of Pneumonia**



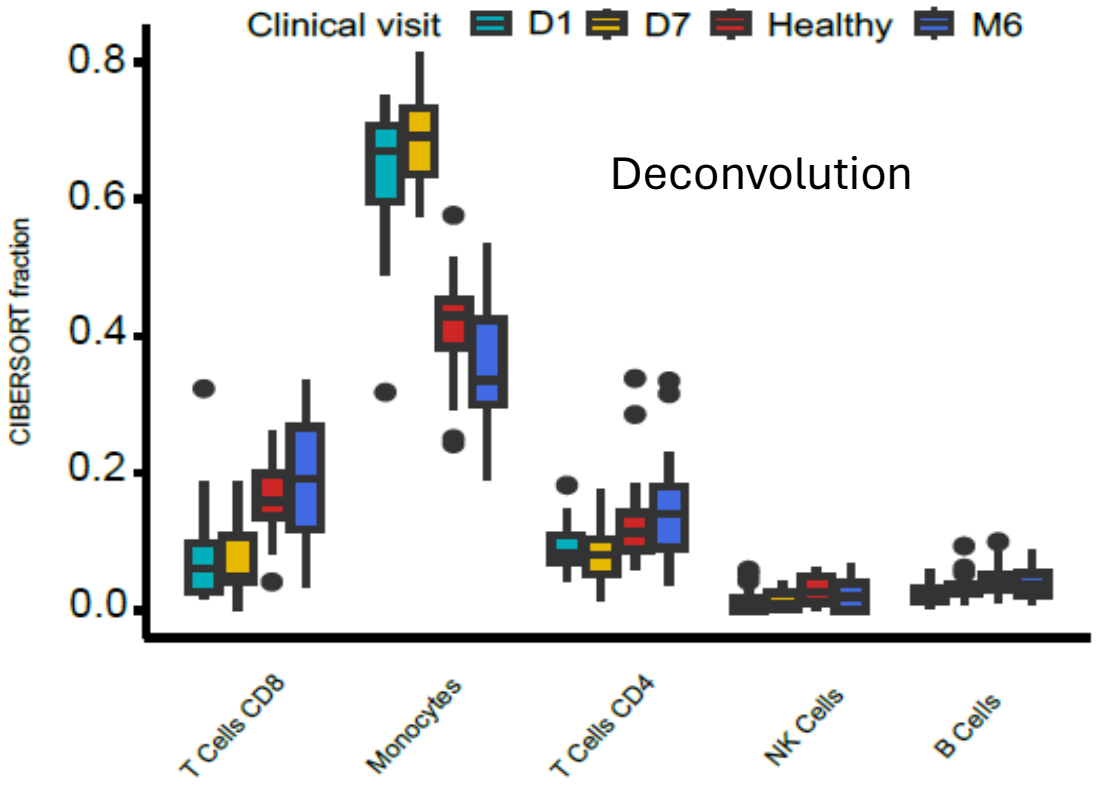
Pandora's box

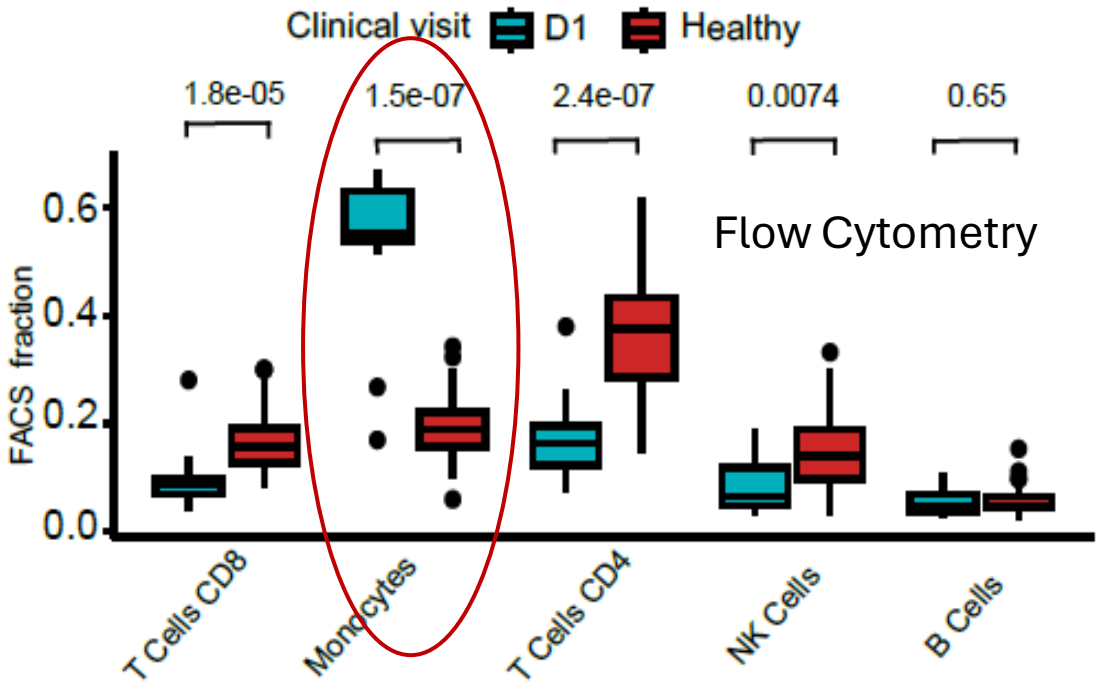
The transcriptomic profile of PBMCs in TBI patients



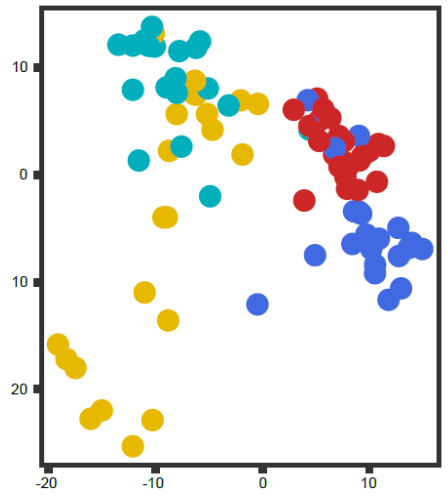


Quantifying the expression heterogeneity

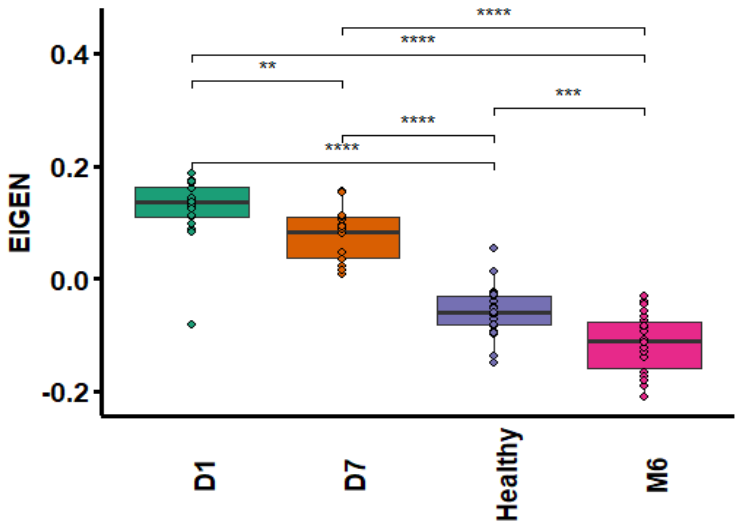




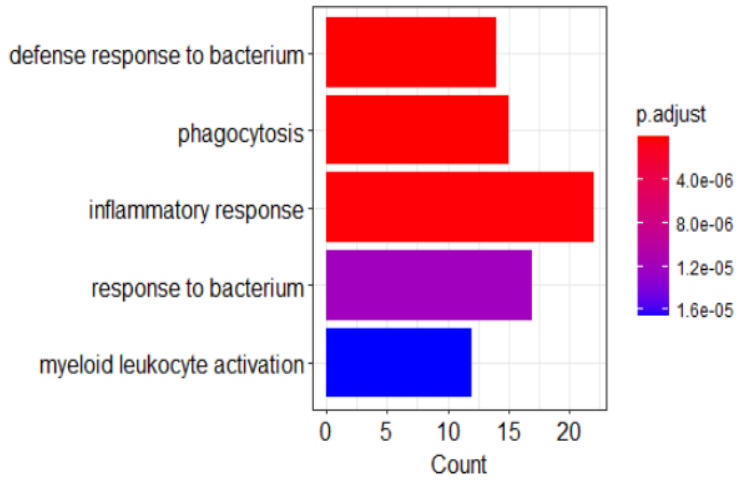
Identifying co-expression modules associated to TBI



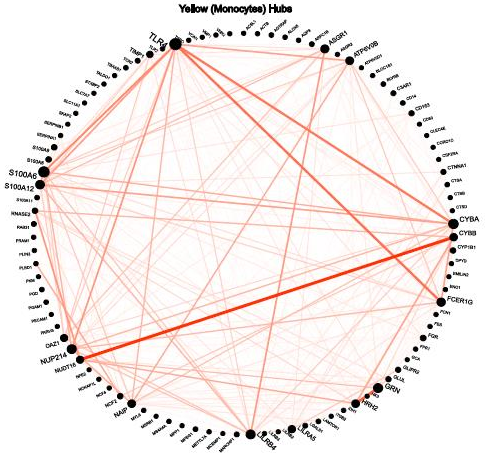
Yellow Module across conditions

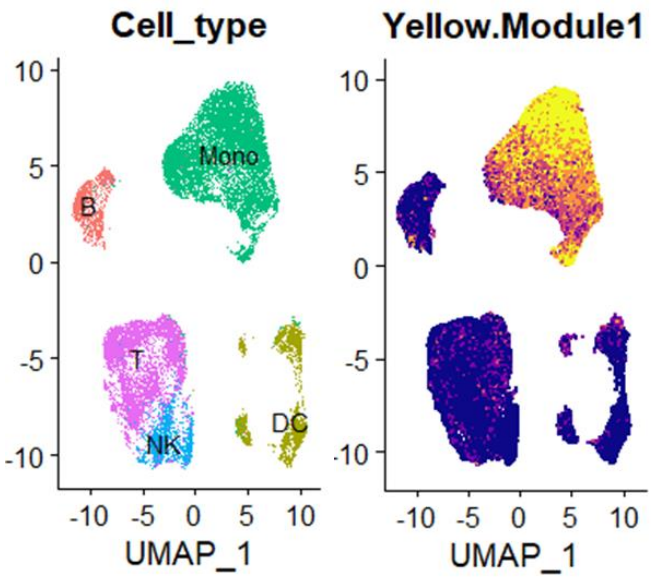


Gene Ontology Yellow Module

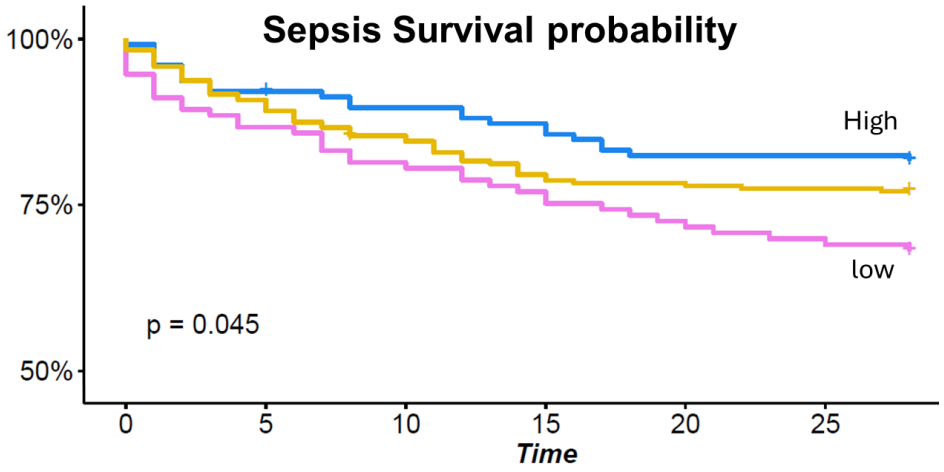


Gene expression module

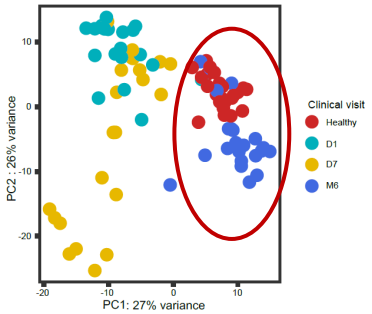




Yellow module expression in ICU patients

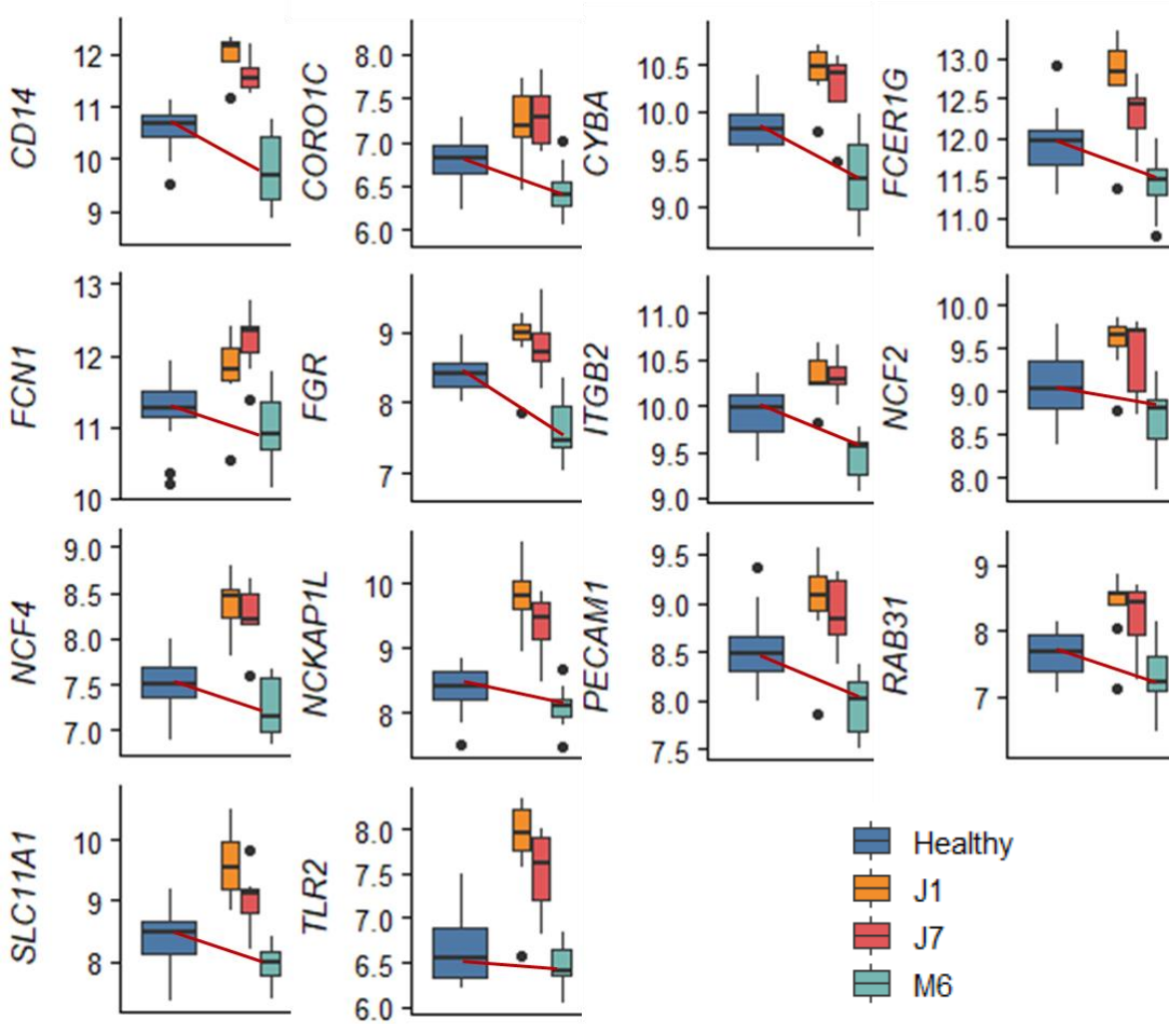


MARS consortium

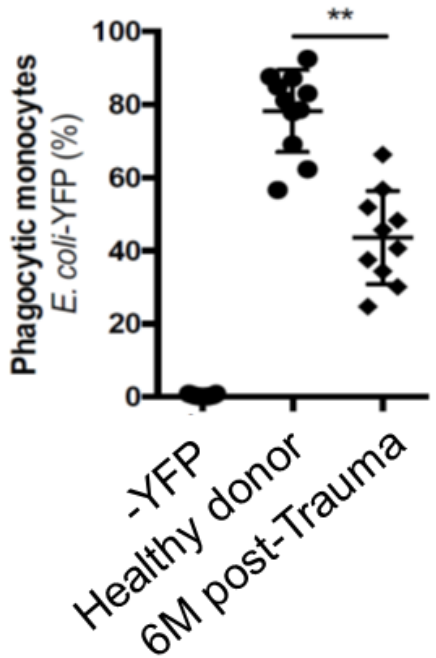


Long-term consequences of TBI

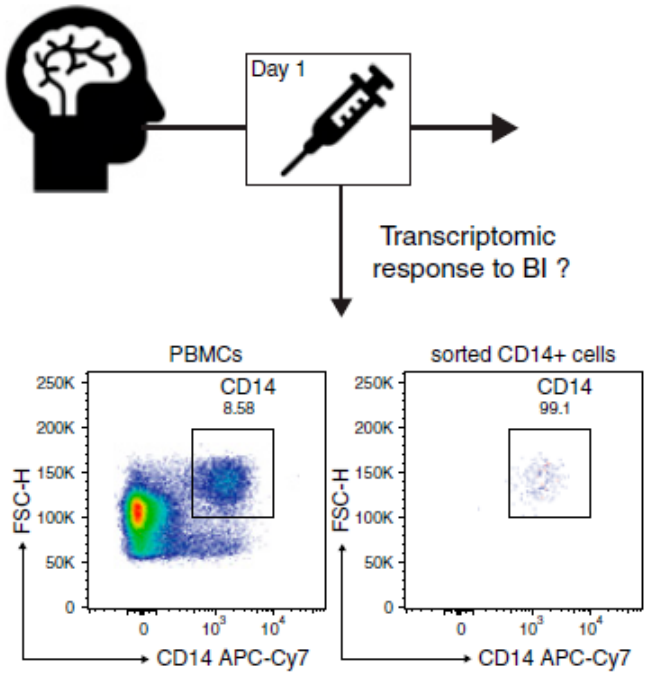
Phagocytosis gene expression (Yellow module)

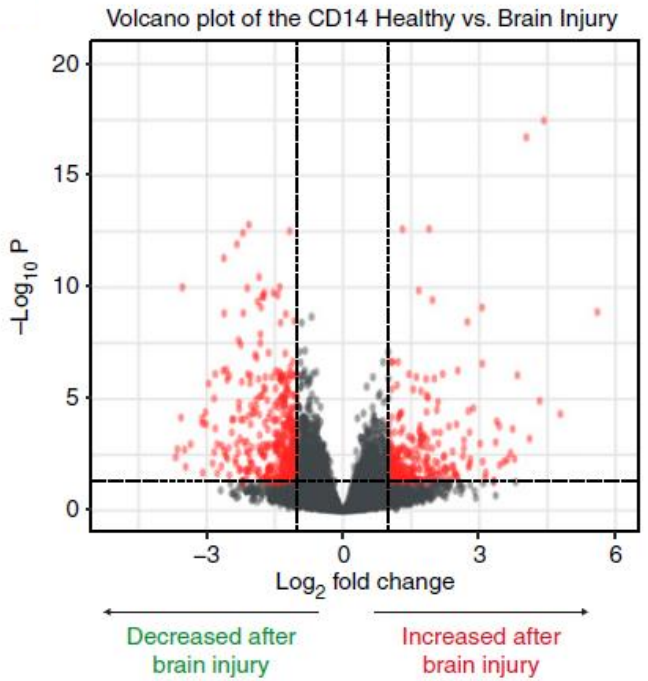


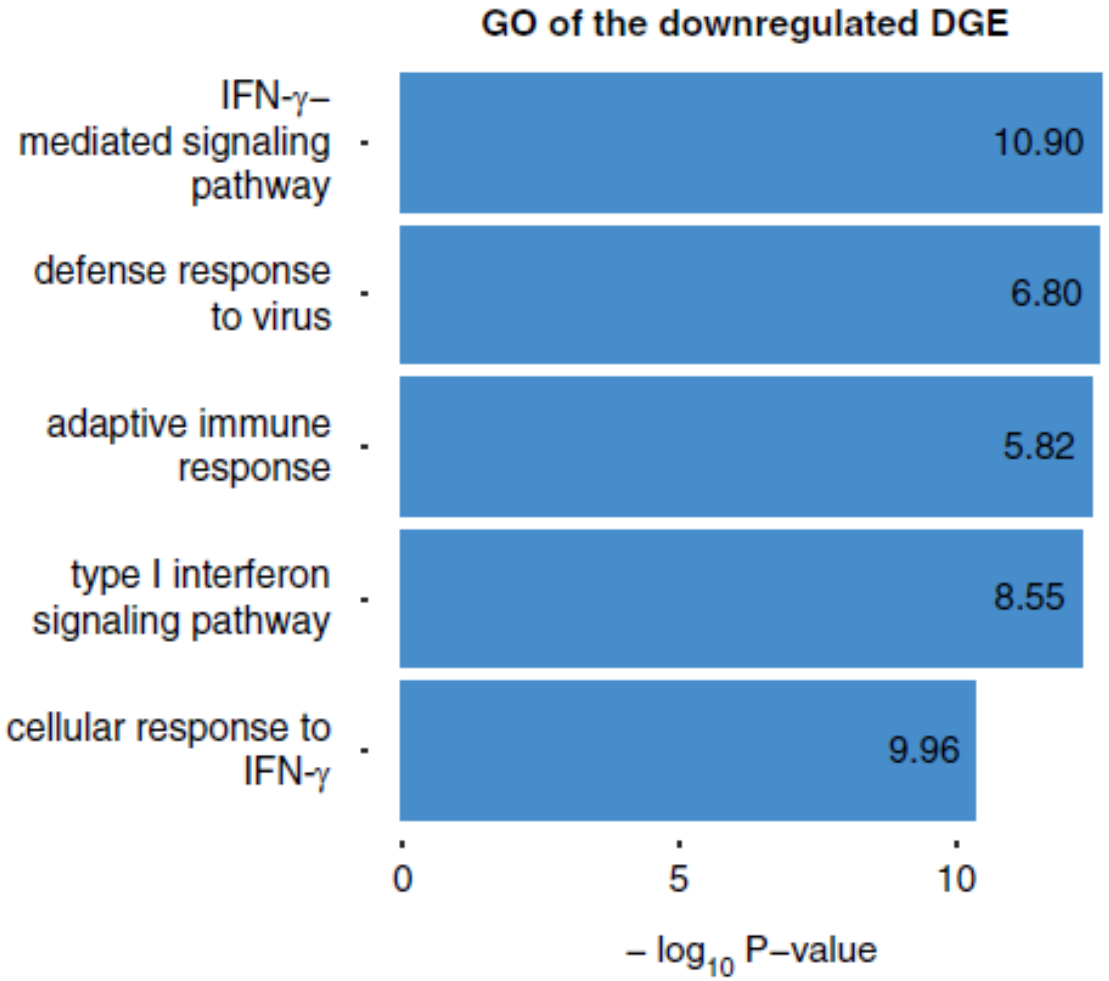
Phagocytosis in Monocytes 6 month post TBI



Monocyte gene expression at Day 1







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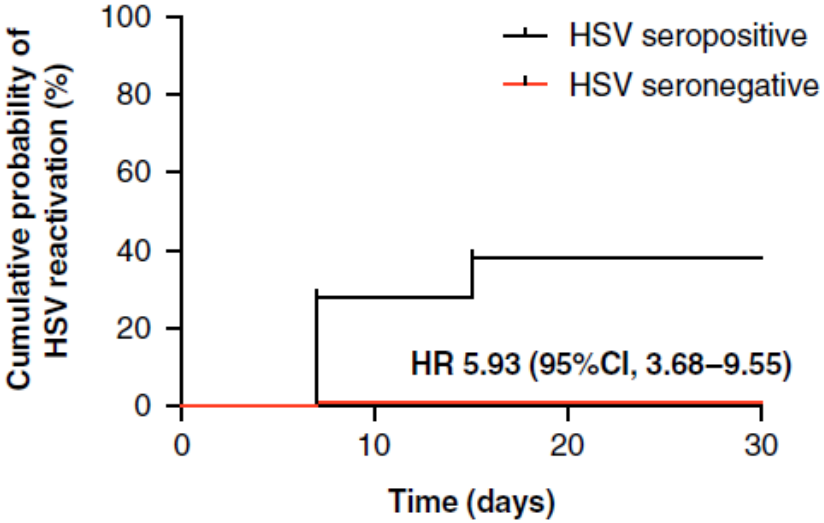
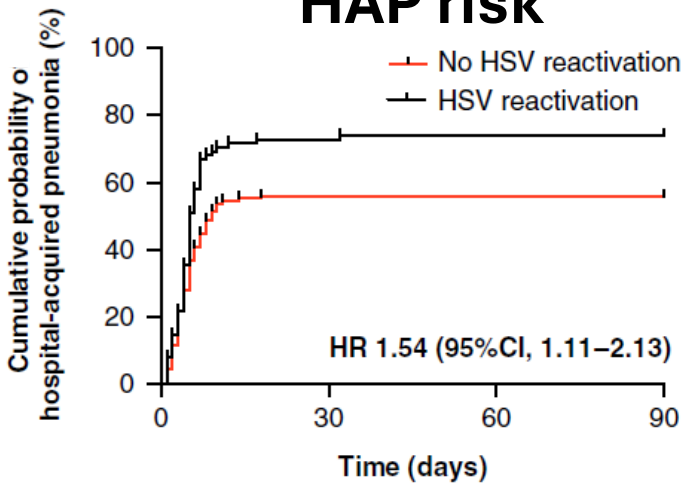
Viral reactivation in TBI patients

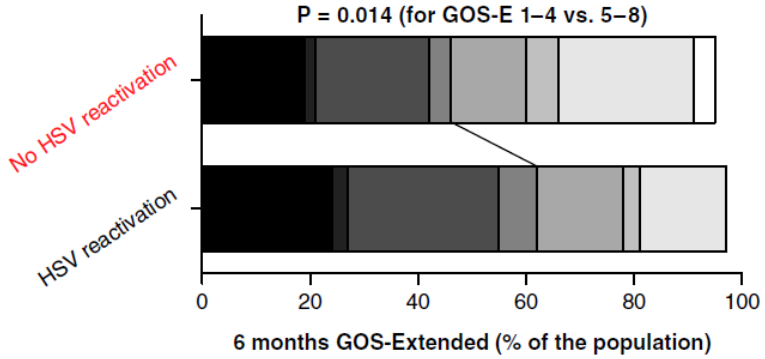
Herpes virus



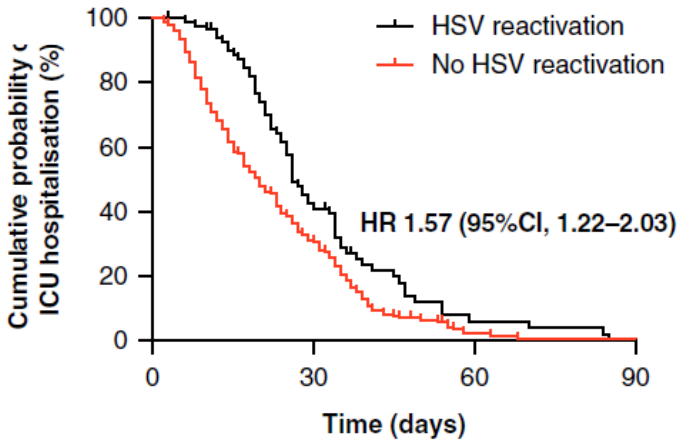
HAP risk



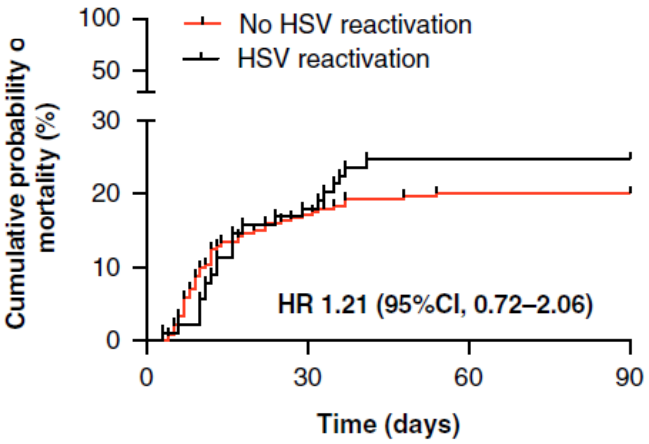
TBI recovery



Length of ICU stay



Mortality



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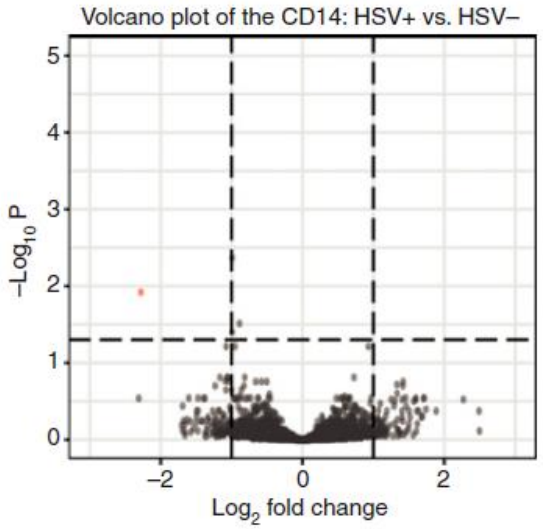
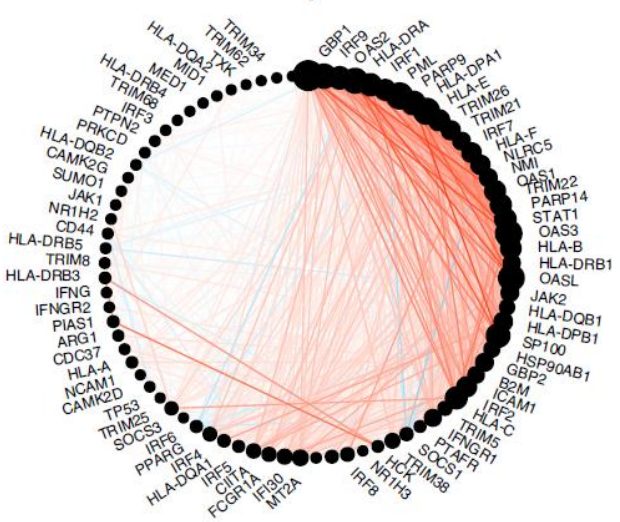
Monocyte gene expression and viral reactivation

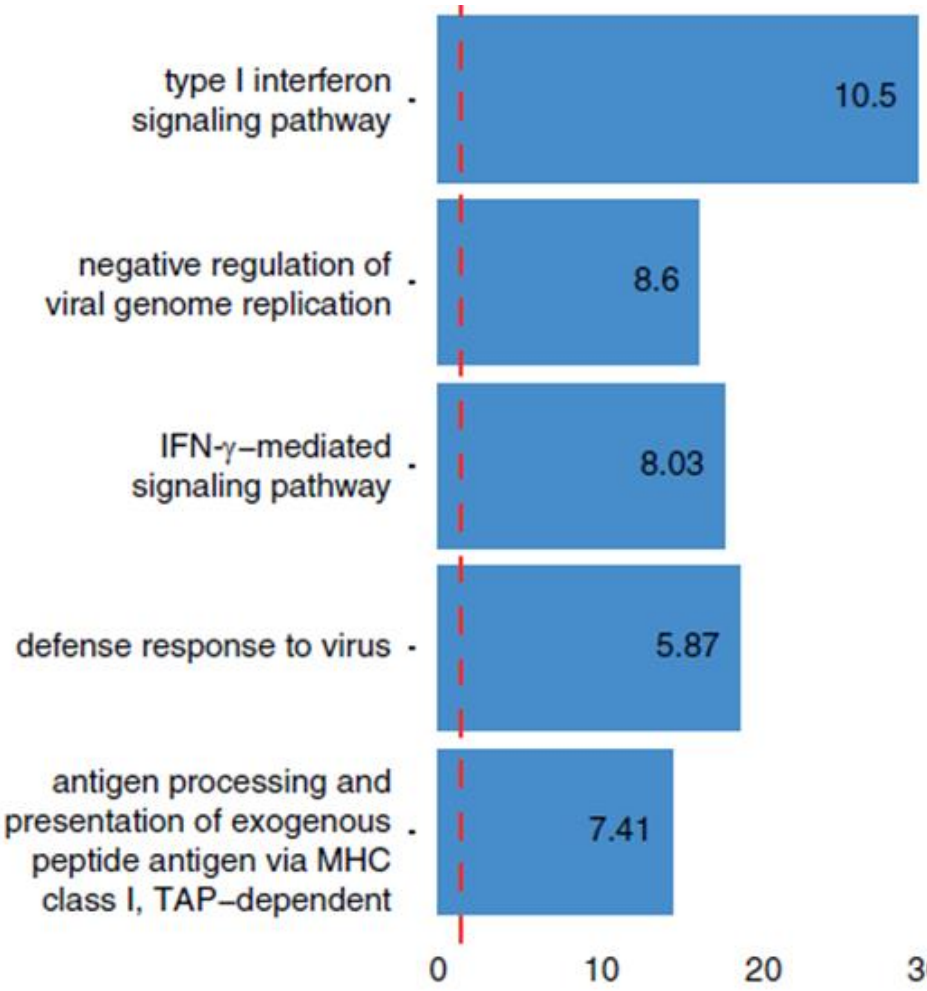
Differential expression



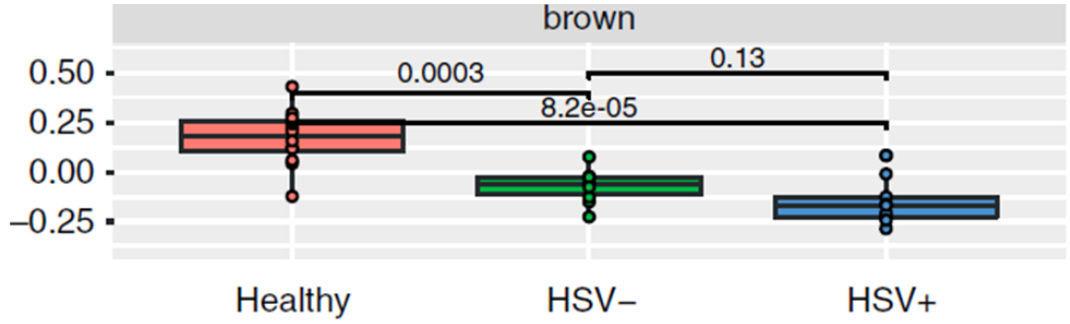
Co-expression module



Gene ontology



Module expression and HSV reactivation



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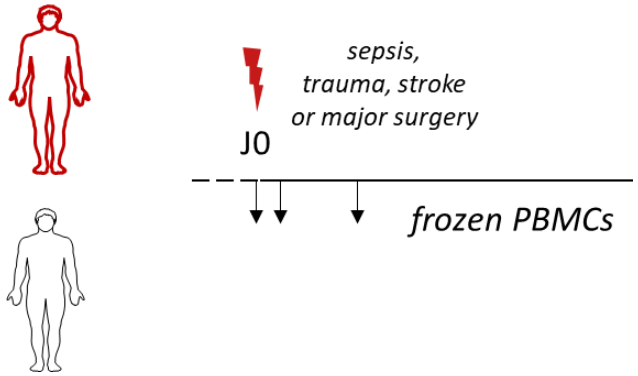
2) Risk of hospital-acquired Pneumonia

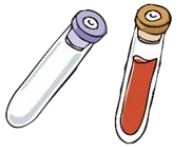


Cytokines

Metabolome

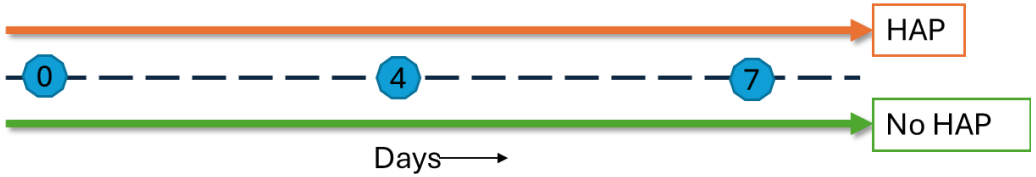
Cytometry

Microbiome



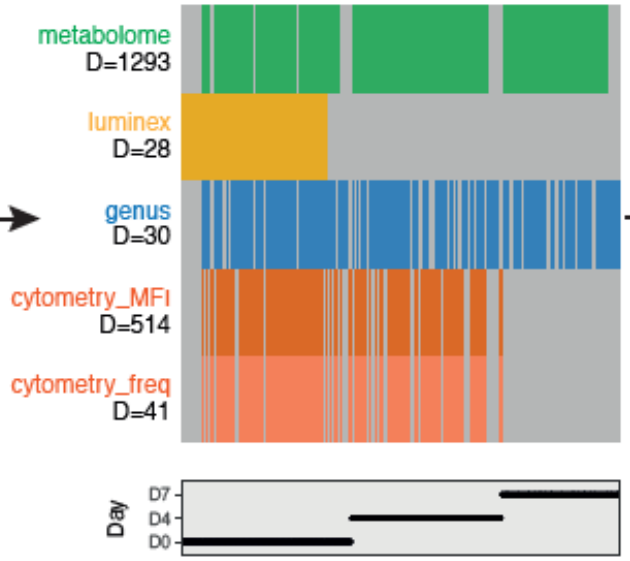
Serum

Tracheal aspirates

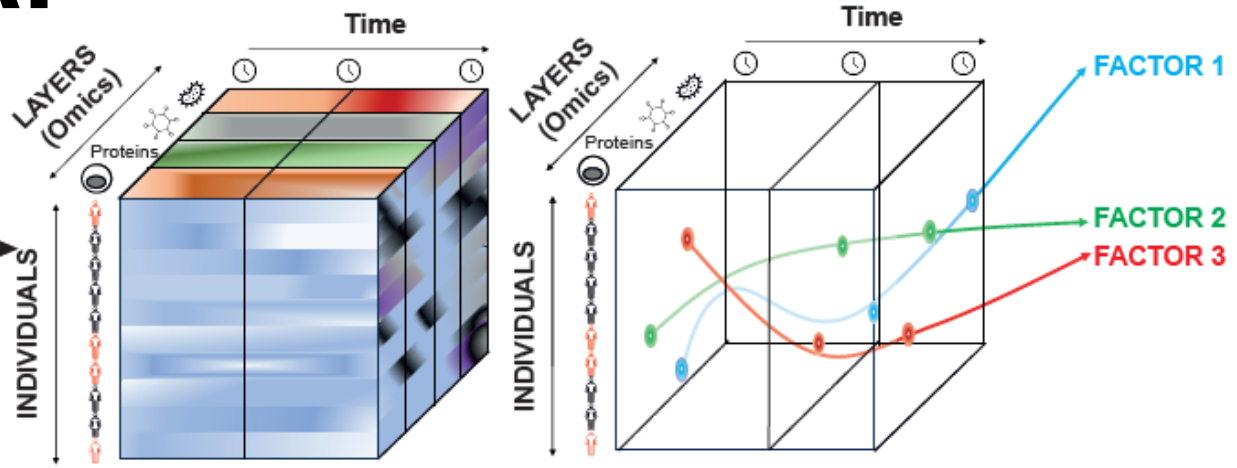


Inferring pathophysiological mechanims of AI-based multi-omics prediction of HAP

158 BI patients
(73 with HAP, 23 with
HAP-inudced ARDS)



655 samples (361 blood and 294 ETAs)
collected upon admission, day 4 and day 7



Identification of temporal and spatial patterns
of variation (MEFISTO)

Train/Test Split

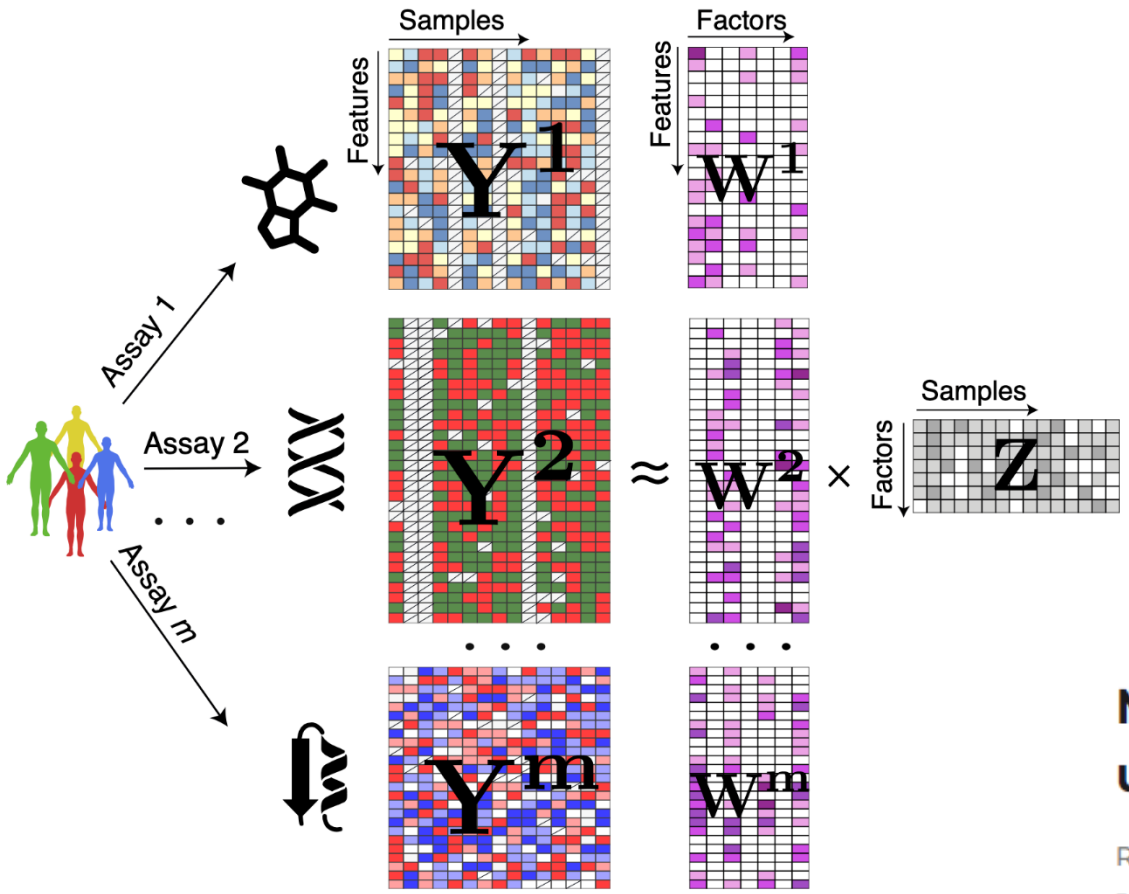
-ML Based
{DTC, BC, LR, NB}

-LR
-NB

HAP²

Unpublished data

Inferring temporal variation in multi-omics data



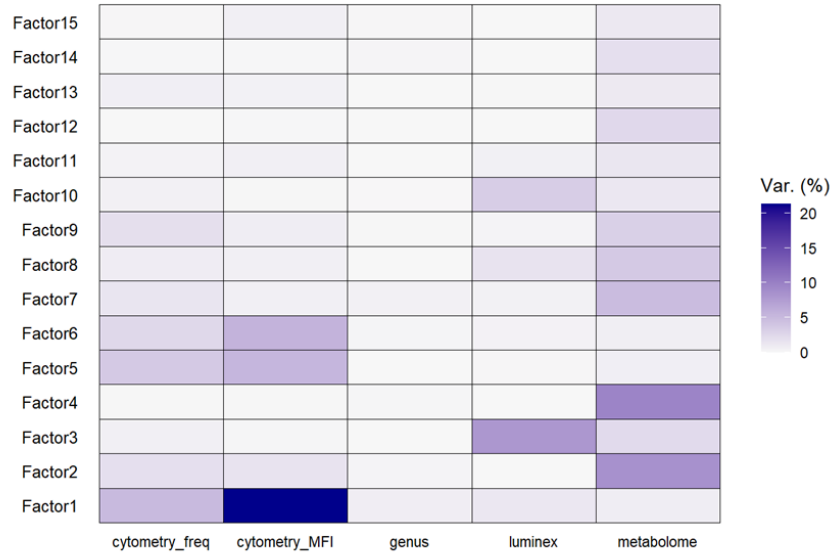
- Generalization of principal component analysis to multi-omics data
- Infers low-dimensional representation in terms of a few latent factors
- The learnt factors represent the driving sources of variation across data modalities
- integrate multi-modal data with continuous structures among the samples
- **Identify factors which capture variation**

Multi-Omics Factor Analysis—a framework for unsupervised integration of multi-omics data sets

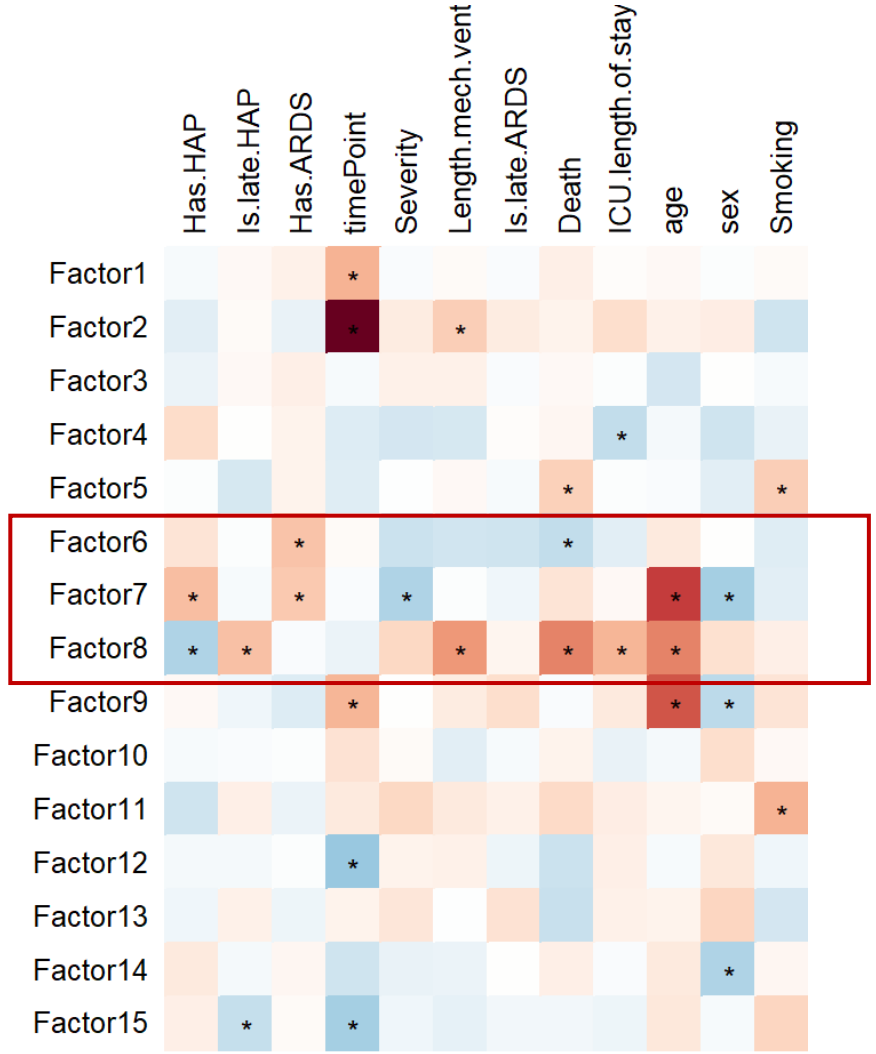
Ricard Argelaguet, Britta Velten, Damien Arnol, Sascha Dietrich, Thorsten Zenz, John C Marioni, Florian Buettner, Wolfgang Huber, Oliver Stegle

Association between factors and clinical variables

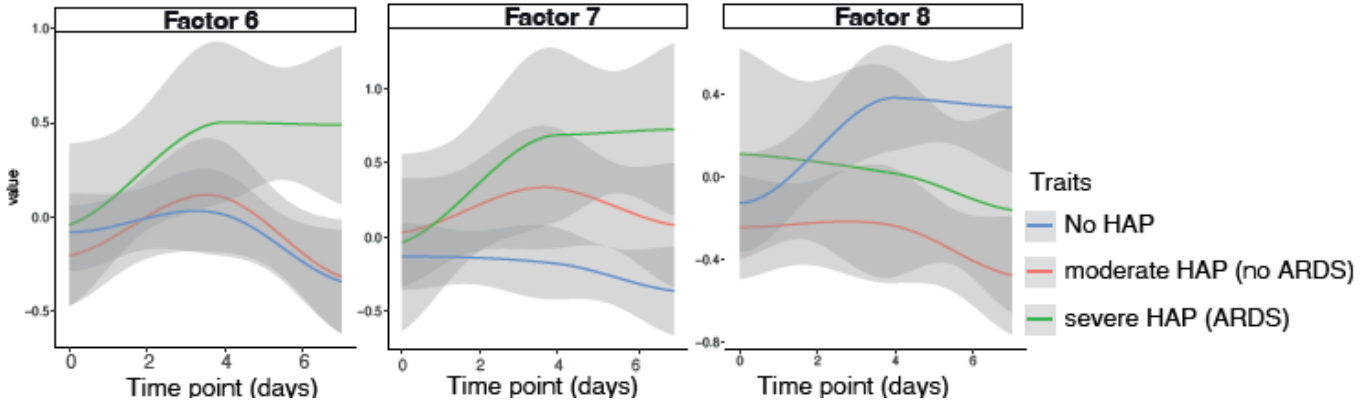
Identification of Factors



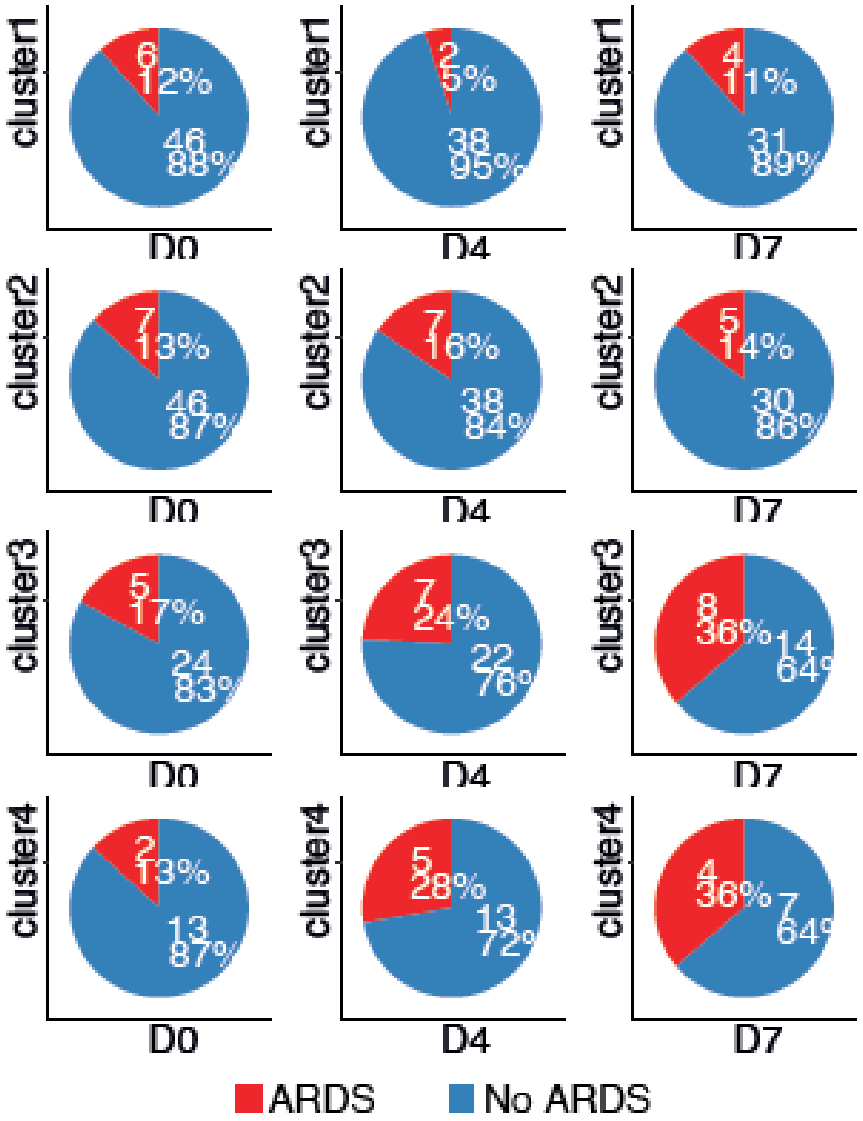
Factors and clinical variables

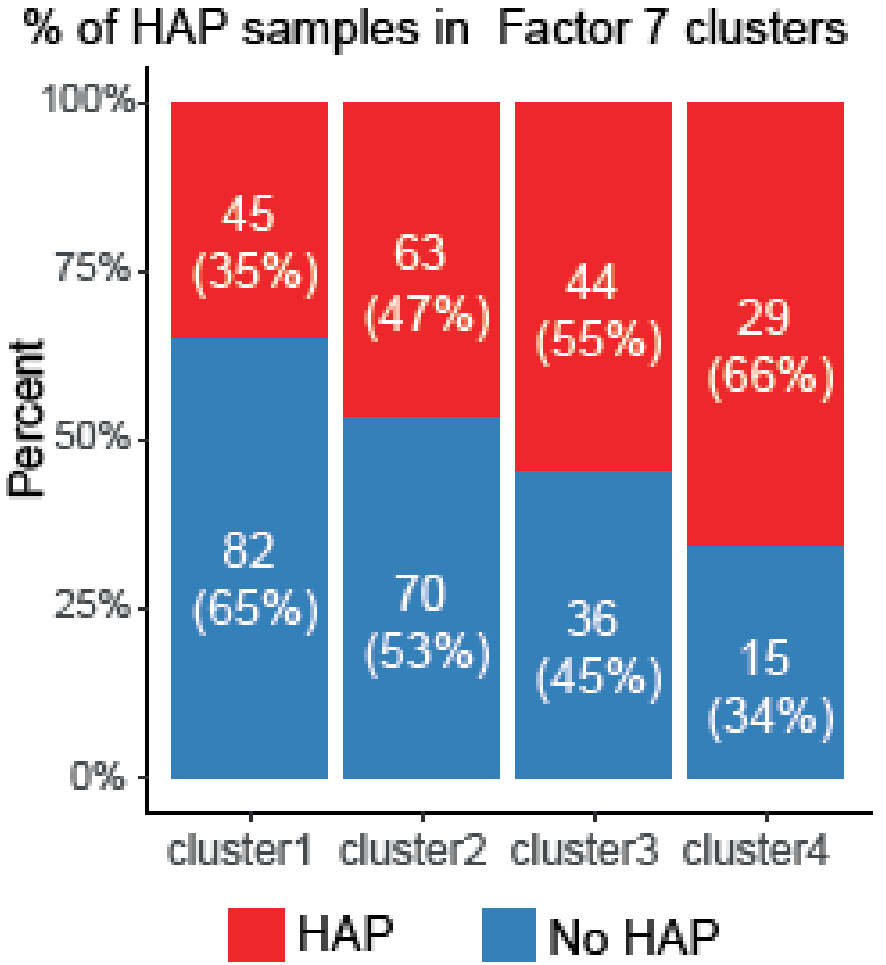


Temporal evolution of Factors

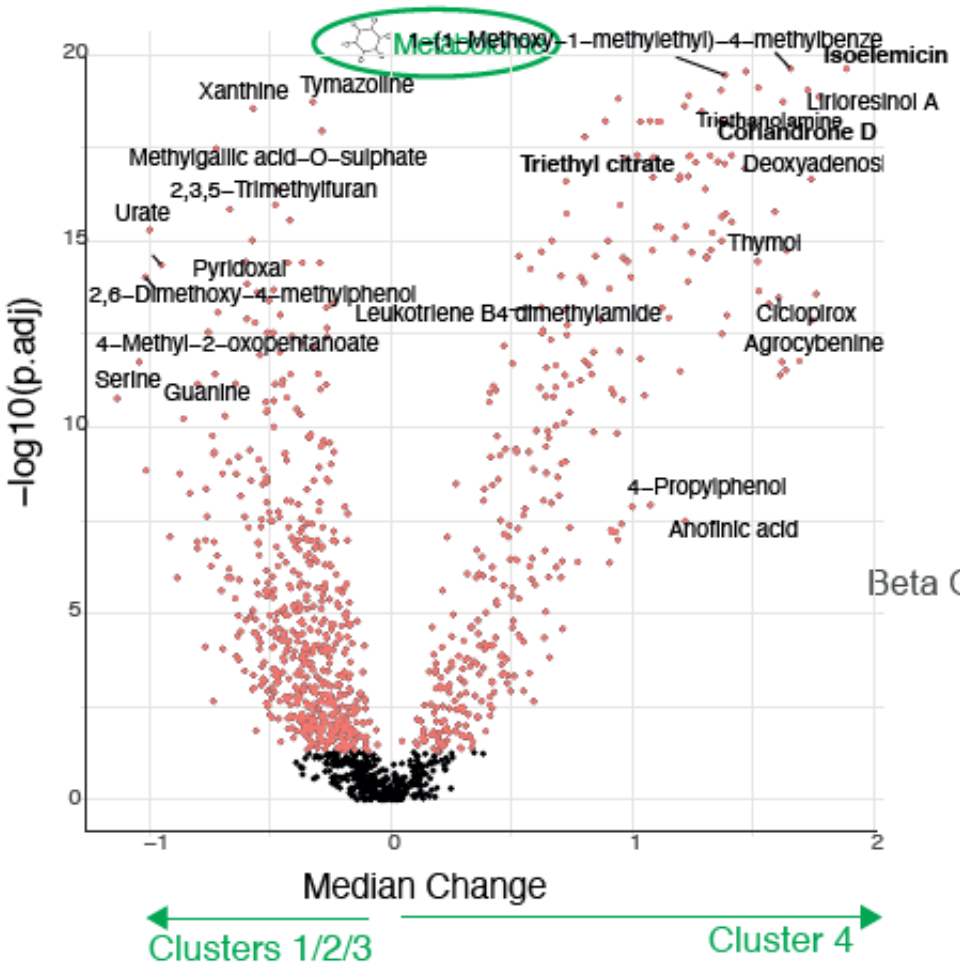


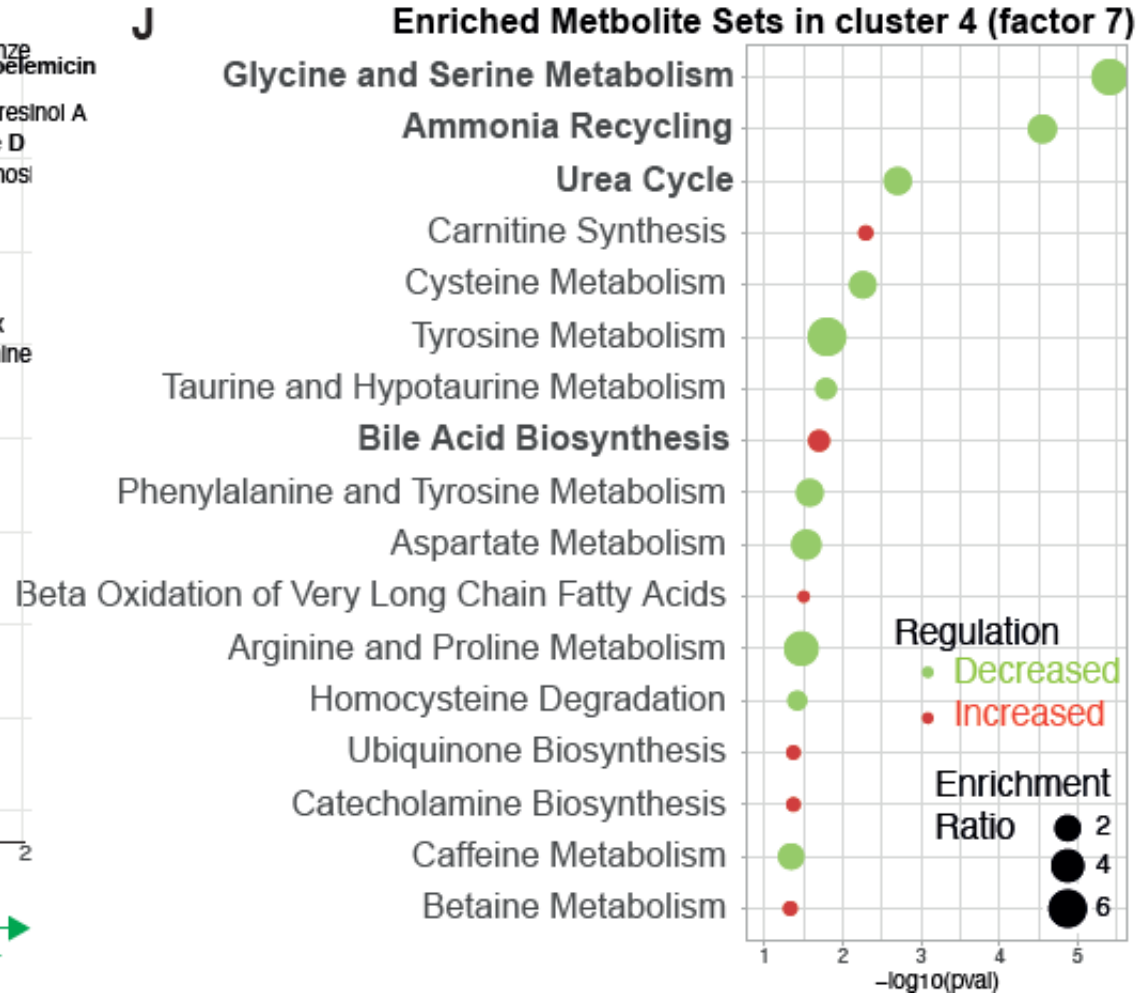
K-mean **actor 7 values**



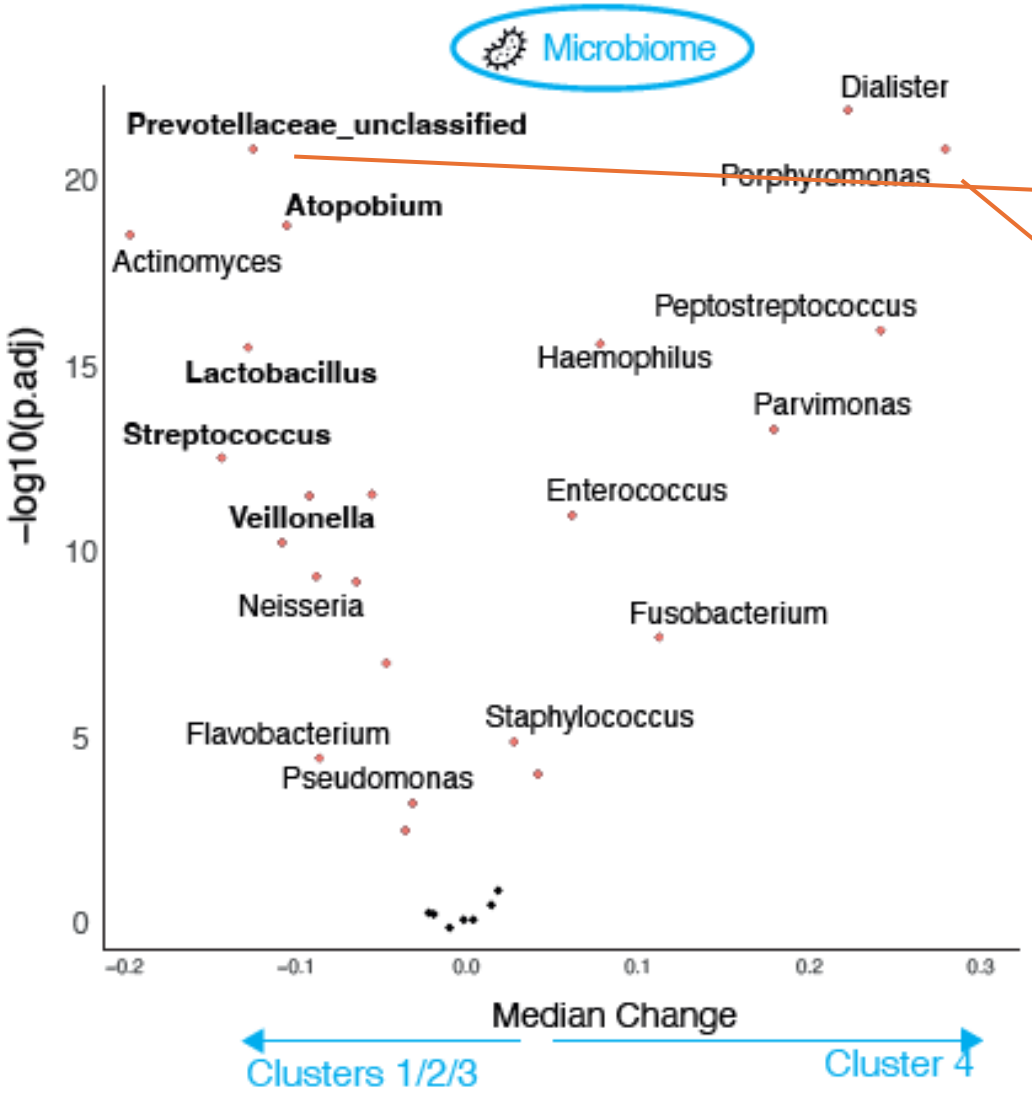


Metabolomic alterations in cluster 4

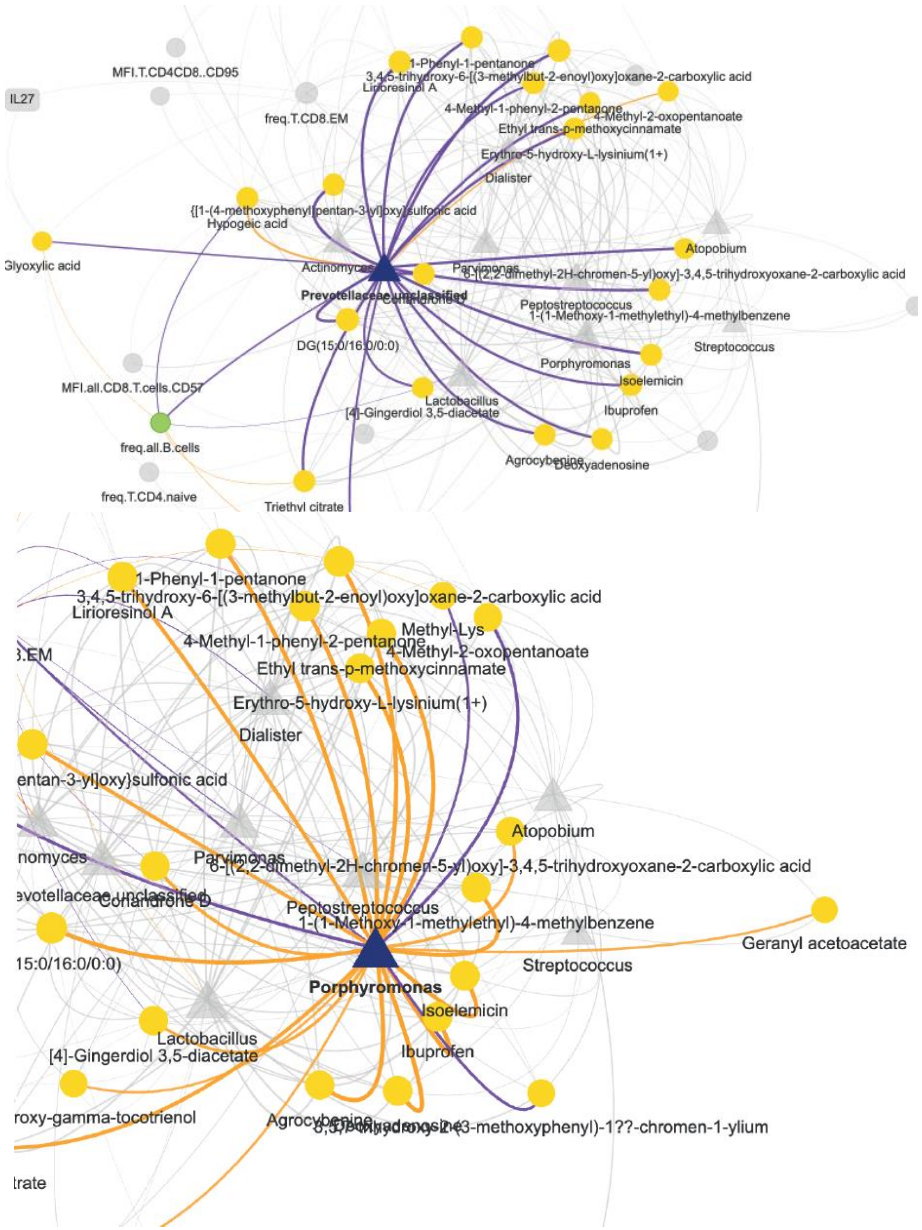




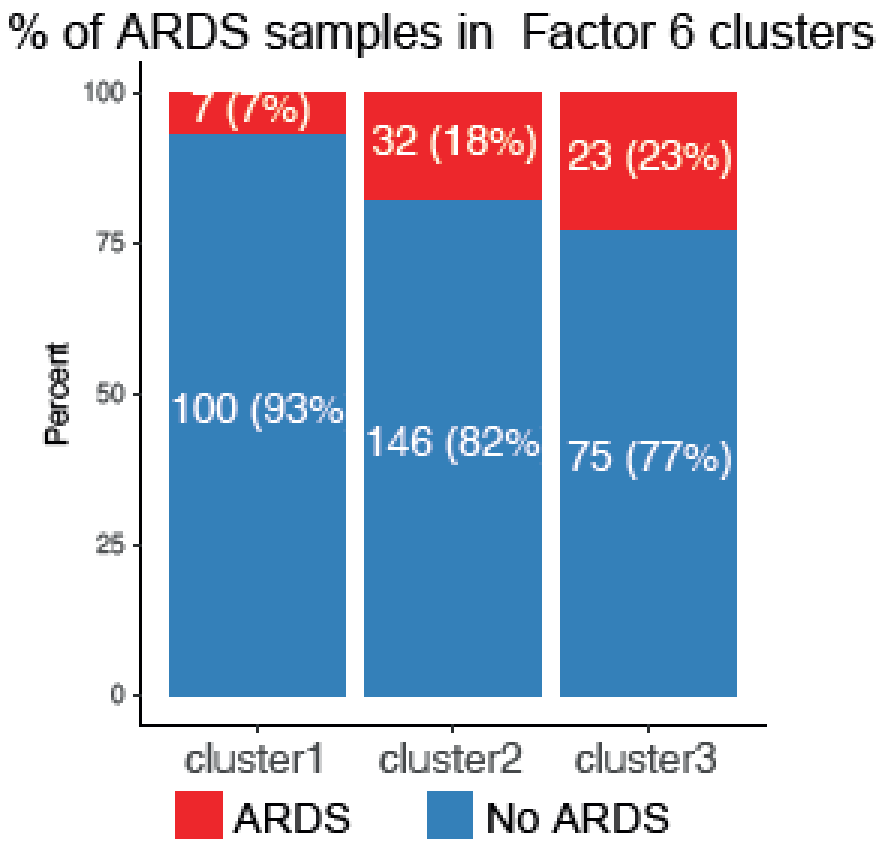
Microbiome alterations in cluster 4



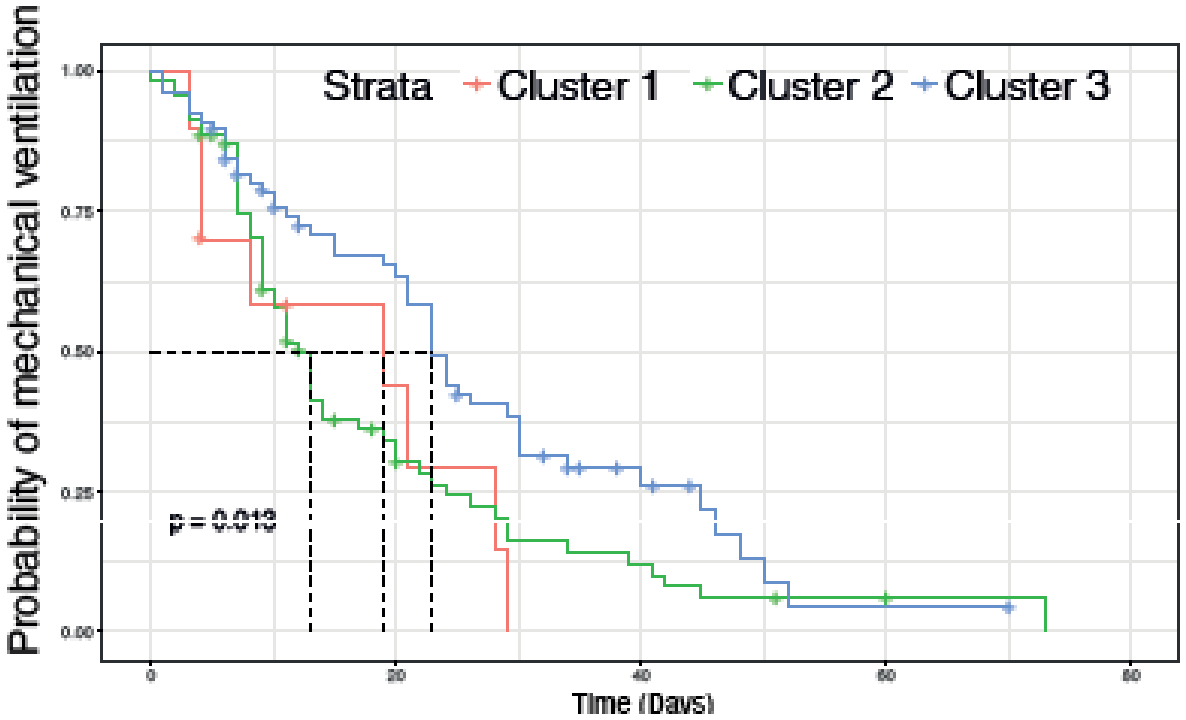
Correlation of Metabolome & Microbiome



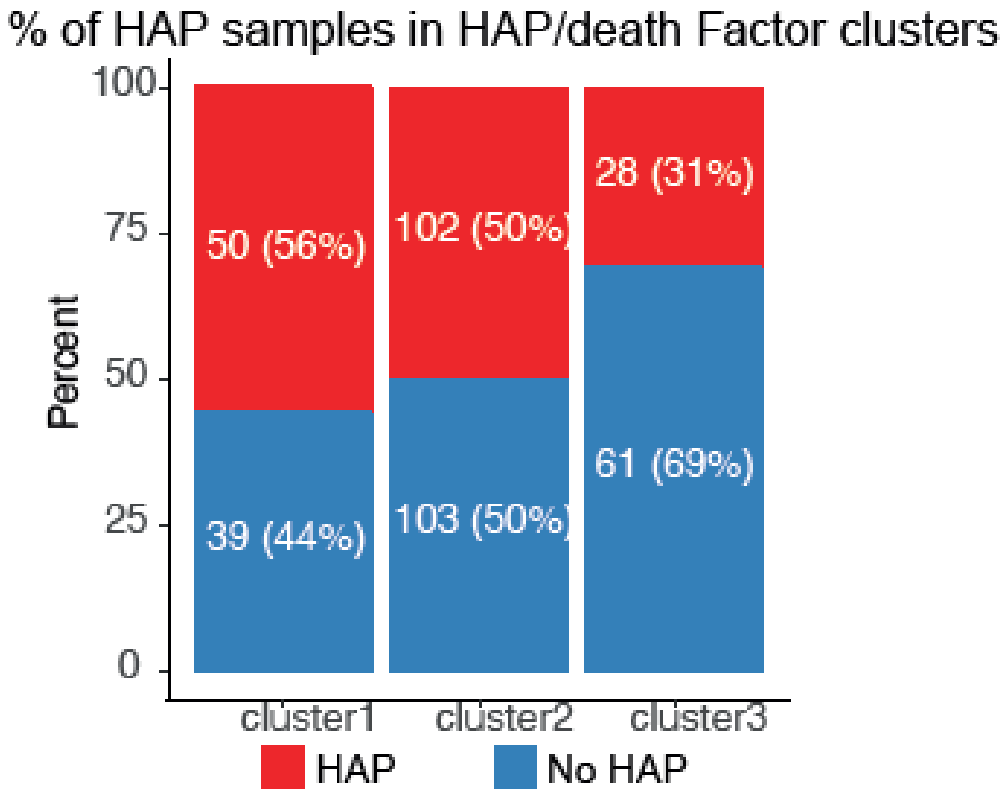
Association of Factor 6 with HAP severity

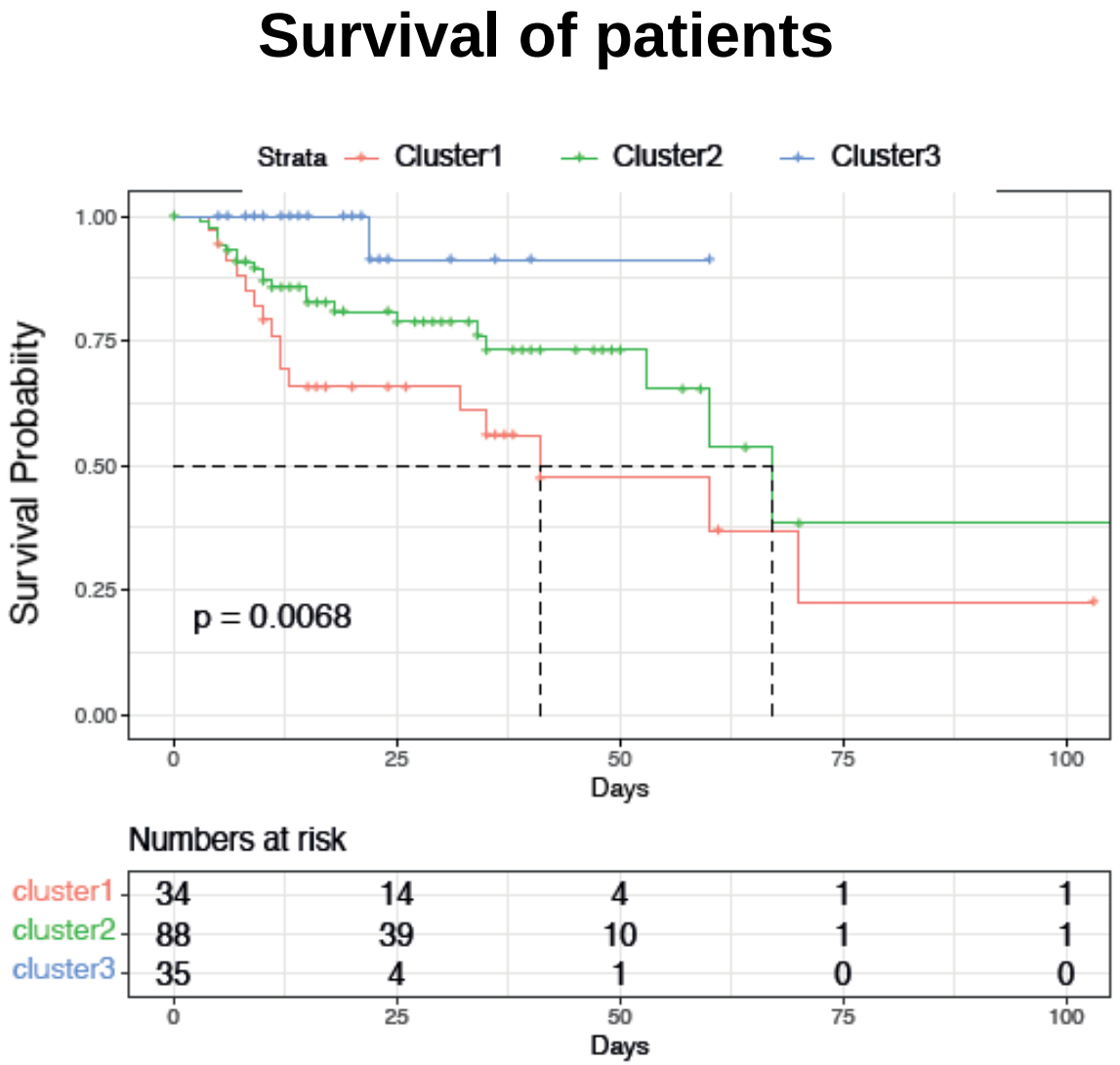


Length of mechanical ventilation



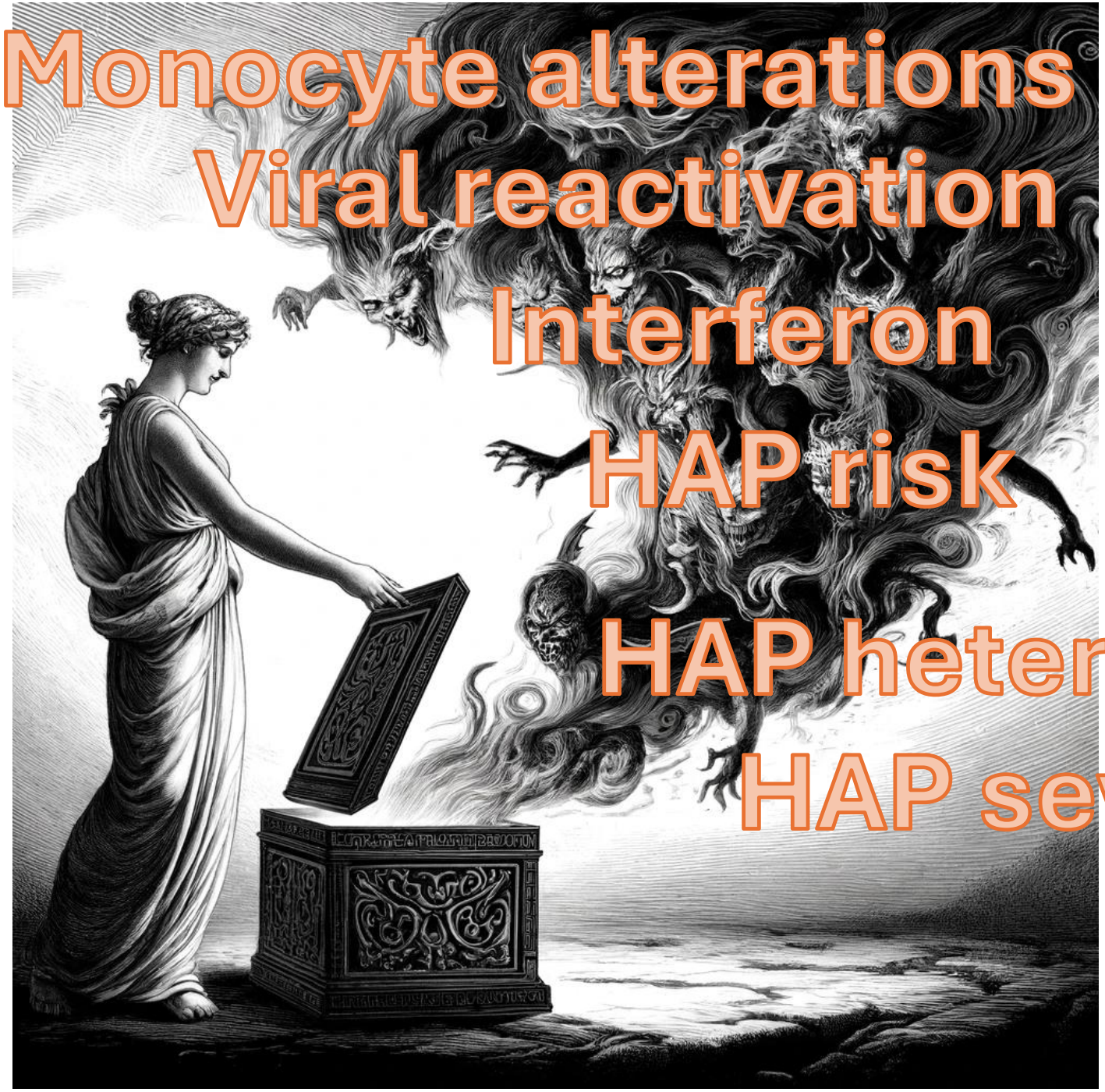
Association of Factor 8 with survival





Validation and Prediction?

To be followed up by Melanie Petrier tomorrow morning !



Monocyte alterations

Viral reactivation

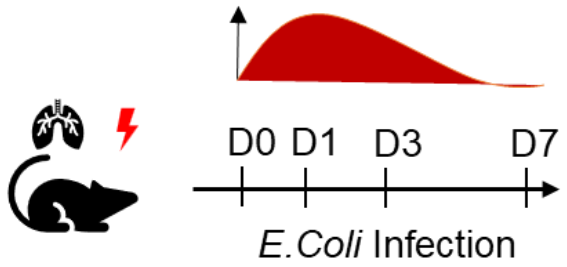
Interferon

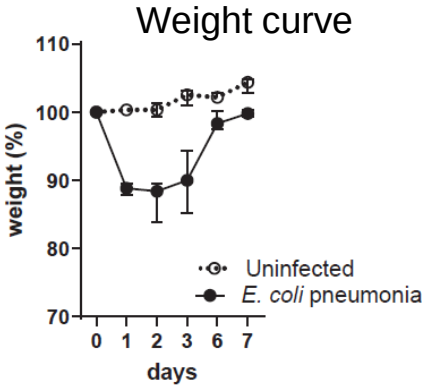
HAP risk

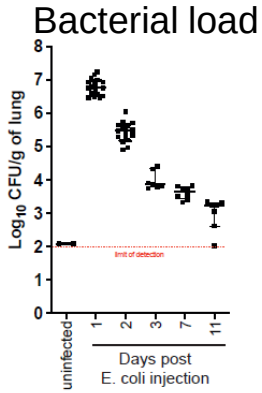
HAP heterogeneity

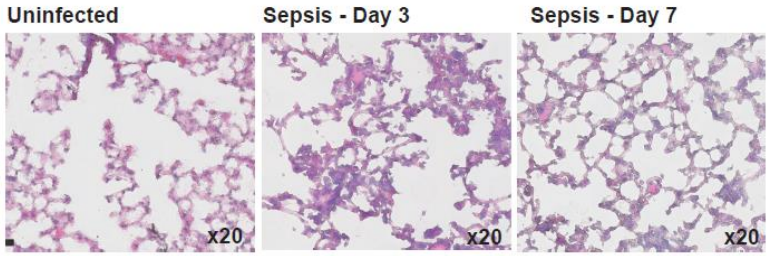
HAP severity

A Pneumonia/sepsis model to study their long-term consequences

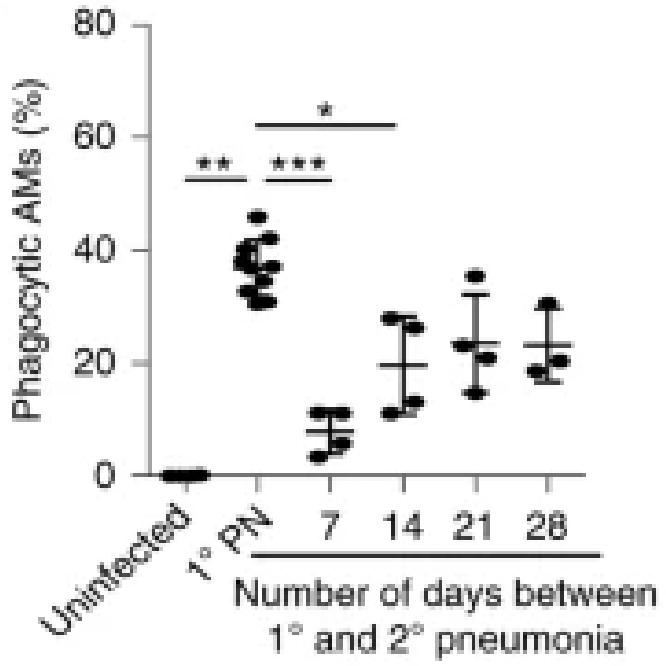




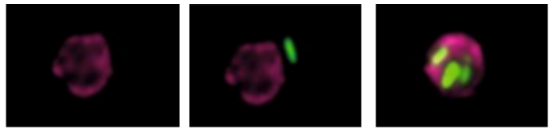


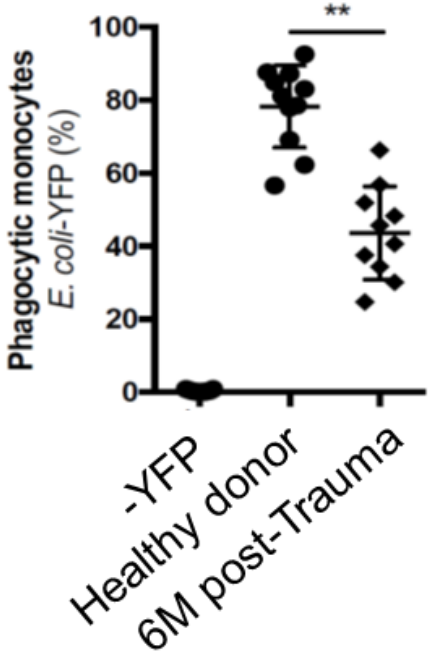


Reduced phagocytosis in AM After 1st Pneumonia



Reduced phagocytosis in Monocytes post-TBI





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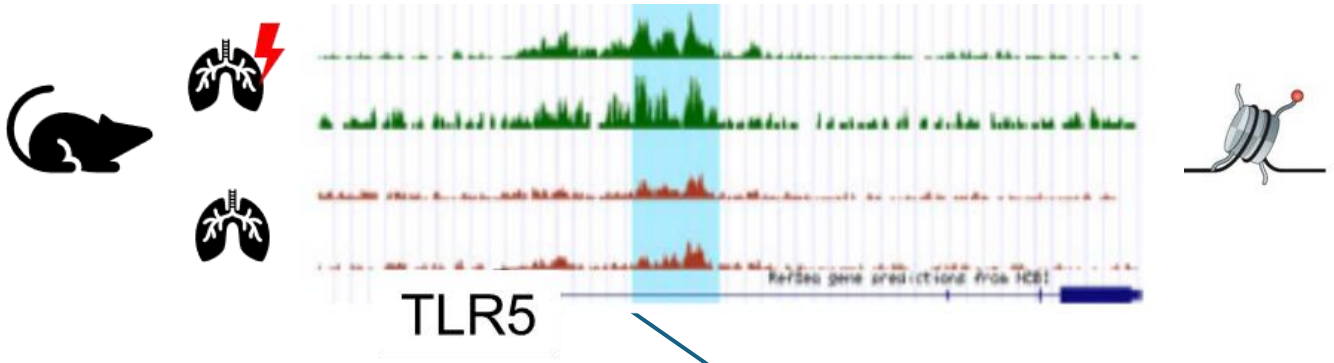
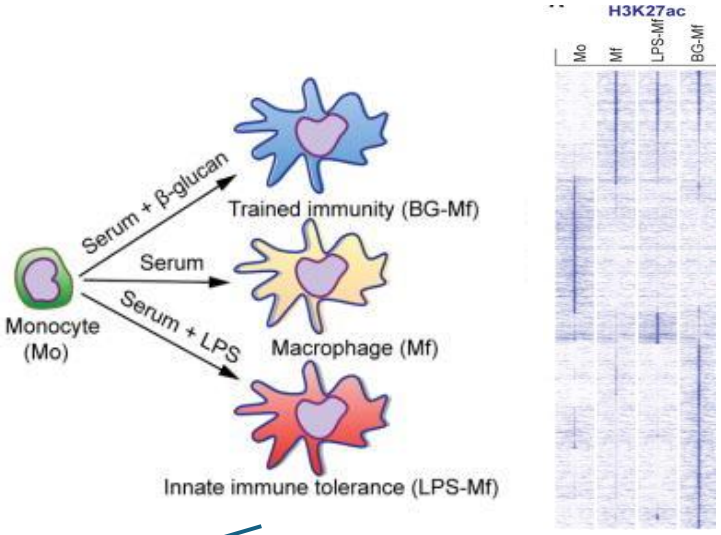
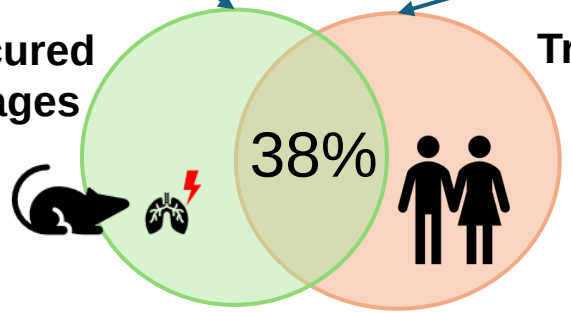
AM are epigenetically altered post-sepsis

Epigenetic alterations in AM post-Pneumonia



Human trained immunity epigenetic state





$P = 2.2 \times 10^{-16}$

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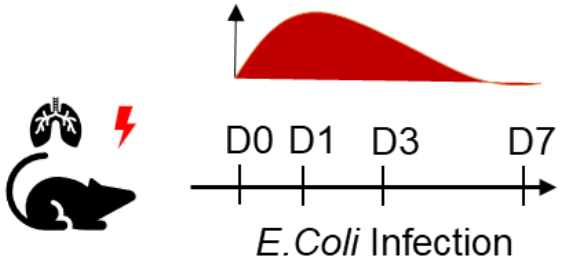
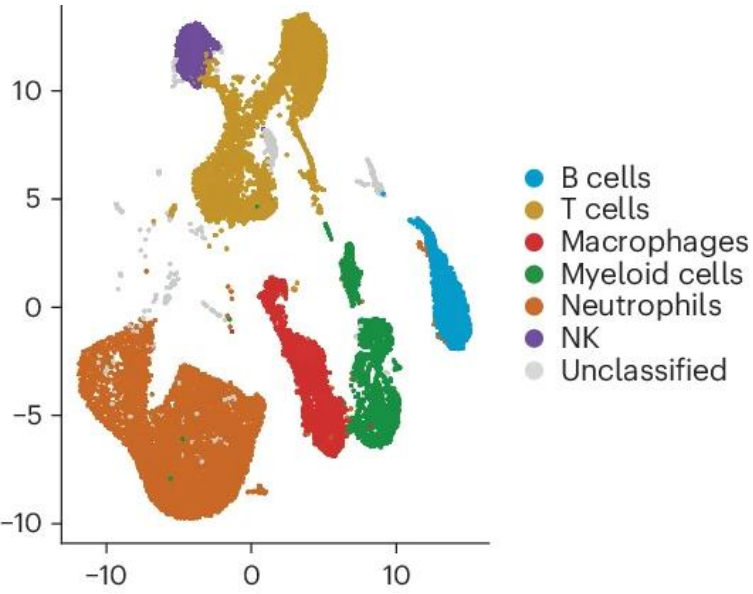
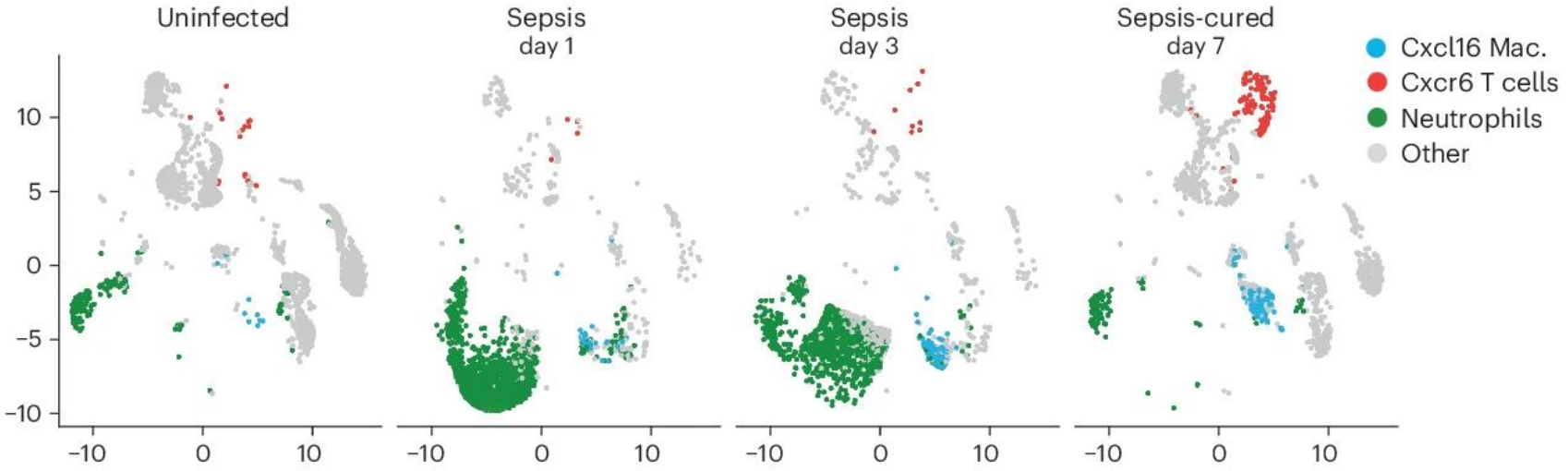
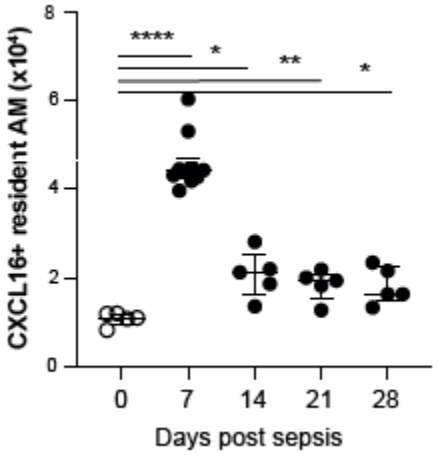
Immune reorganisation after sepsis



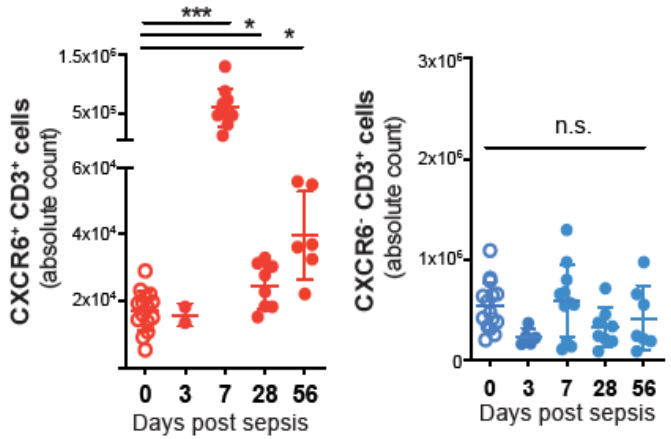




CXCL16 expression by AM



CXCR6+ TRM cells over time



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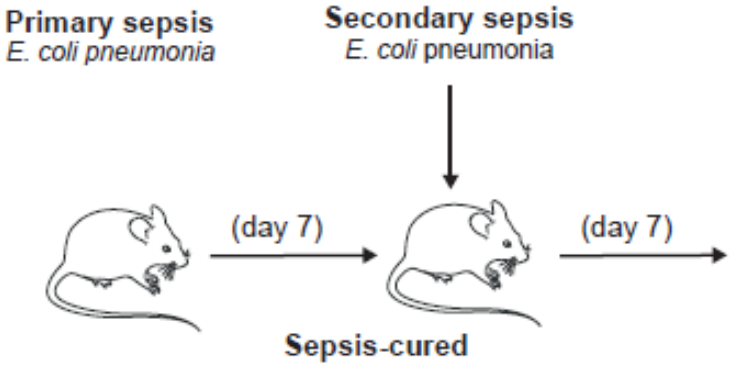
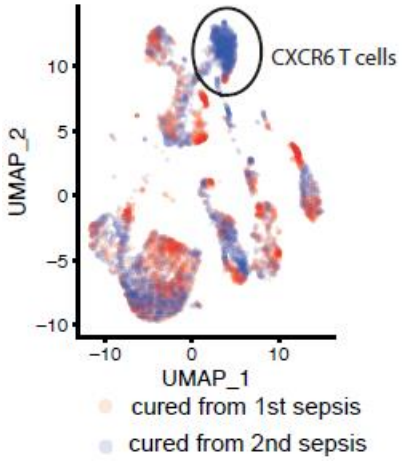
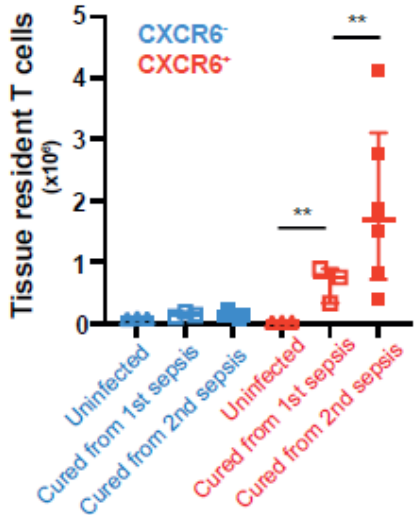
Sepsis-trained AM role in secondary infections



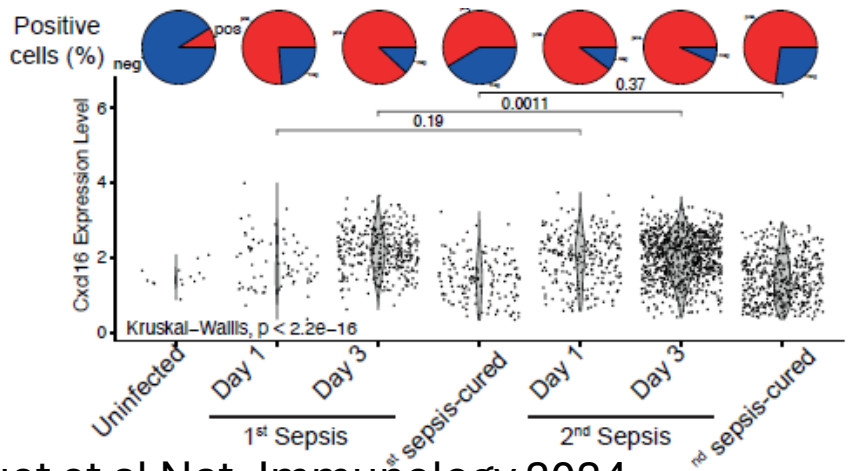
single cell transcriptome



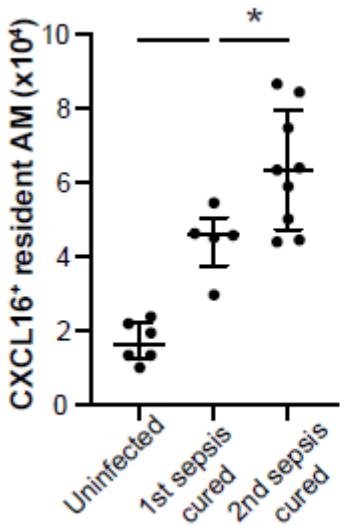
Trm quantification

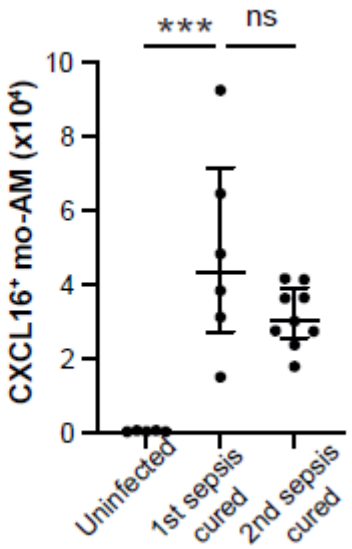


Expression of CXCL16 in Macs



AM quantification





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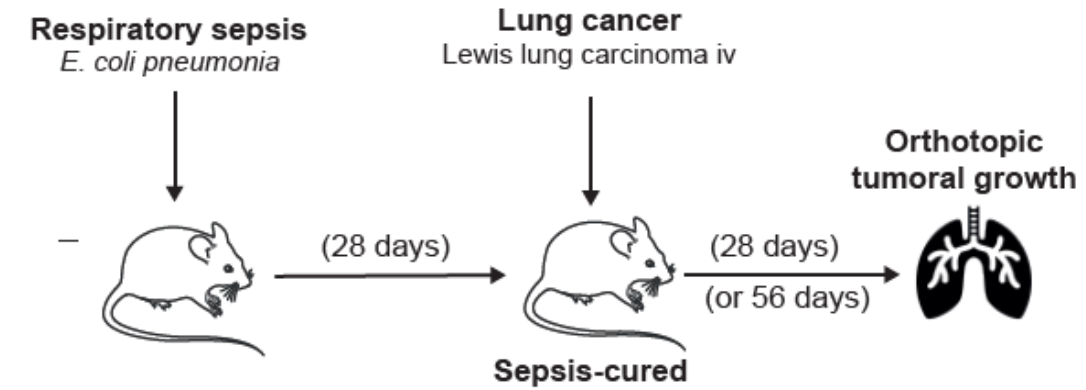
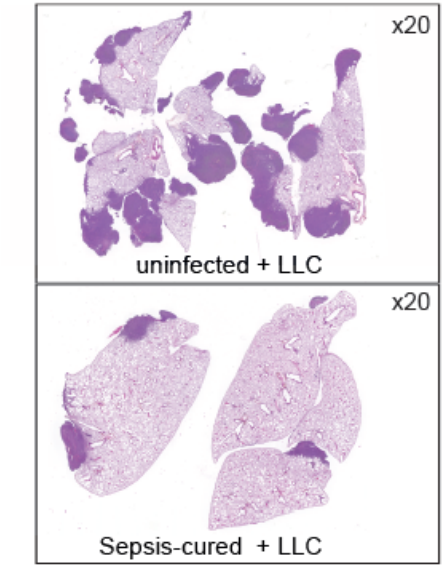
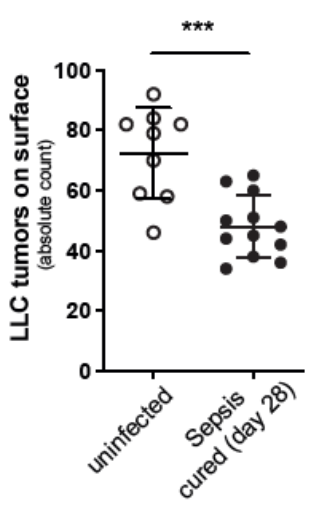
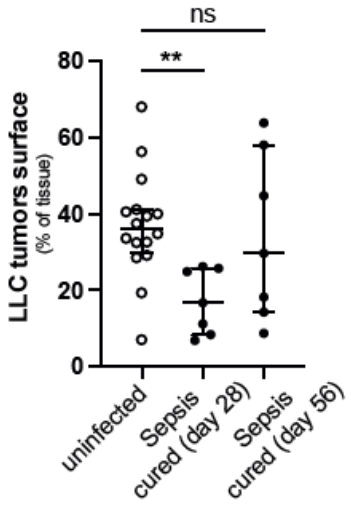
Sepsis-trained AM role in response to cancer









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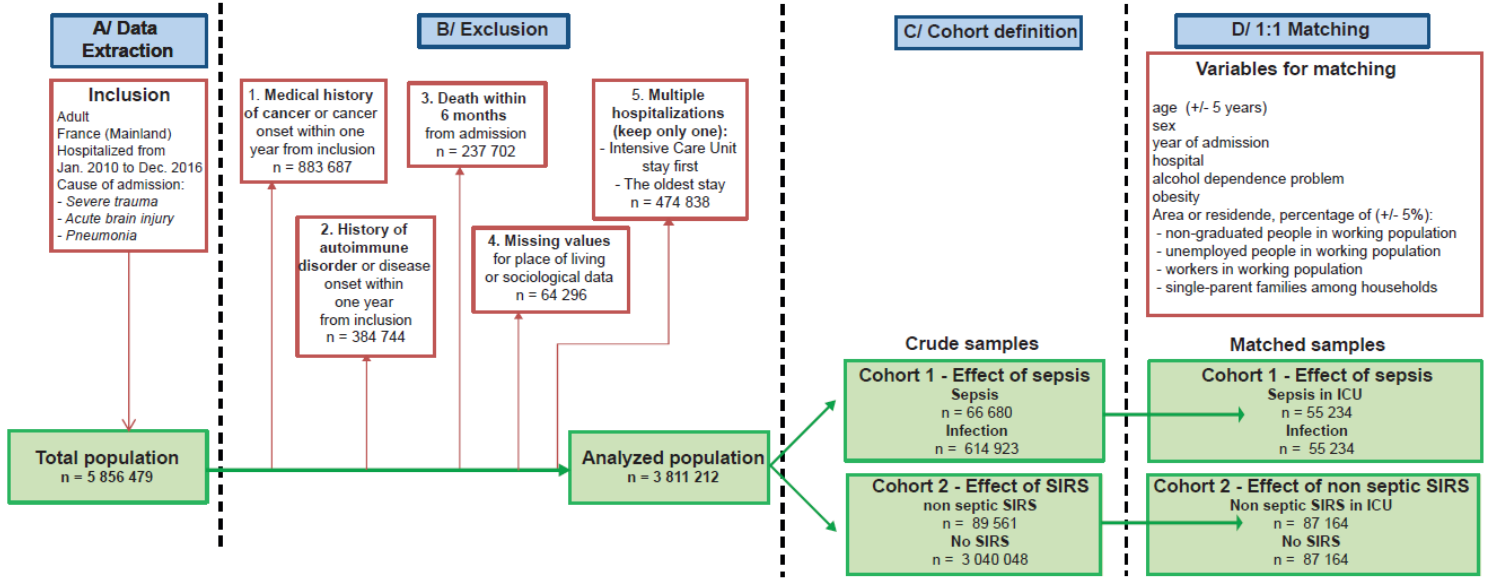
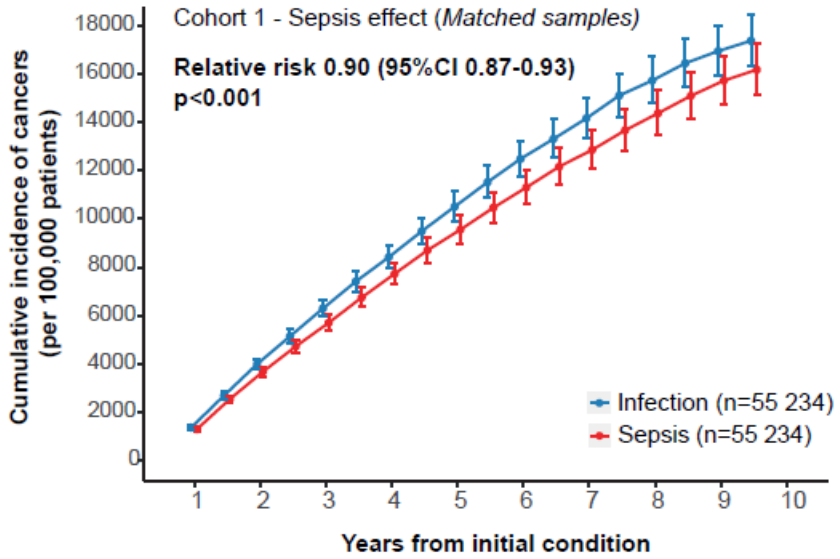
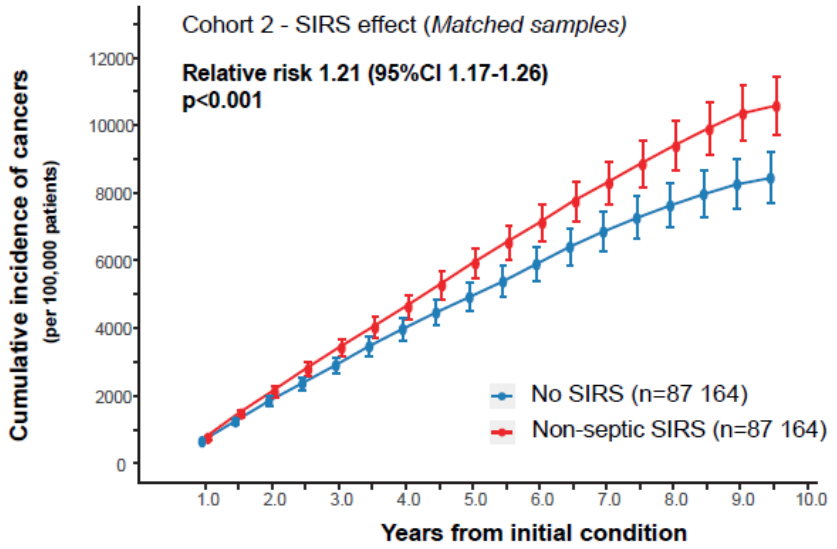
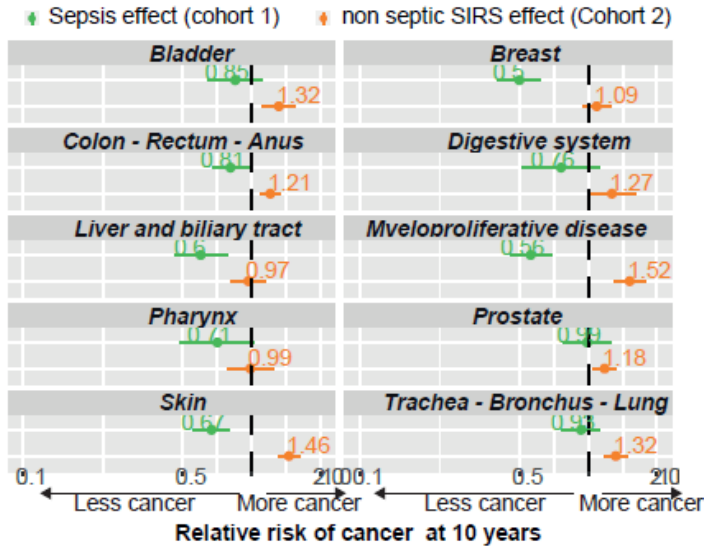
Post-Septic cancer risk in France

SNDS
Système national des données de santé









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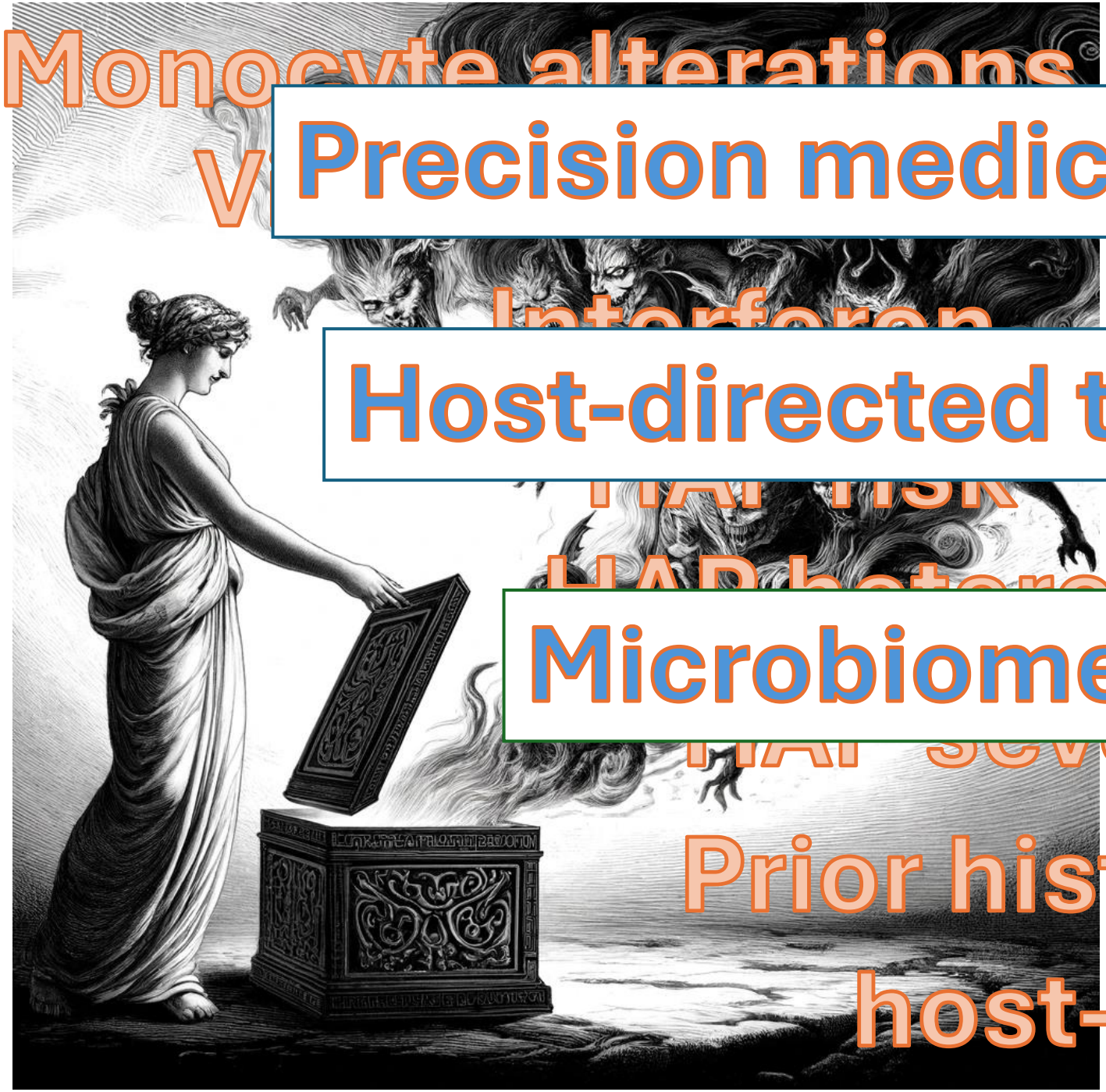

Monocyte alterations

V

Interferon

TIAR risk

LIAR heterogeneity

TIAR severity

Precision medicine

Host-directed therapy

Microbiome modification

Prior history increases host-responses

Acknowledgment

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Inserm

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