# Host transcriptome signatures associated with Covid-19 severity and thromboembolic complications

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Mild n=29
(home isolation)

GGD Amsterdam

Moderate n=22
(hospital)

Severe n= 58
(ICU)

Erasmus MC

Matched Controls
n=109
(MERMAIDS
convalescent)

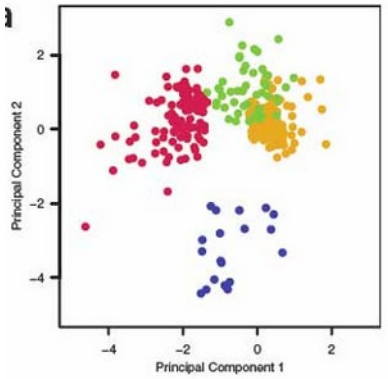
MERMAIDS

Whole blood
tempus tubes

Microarrays scan

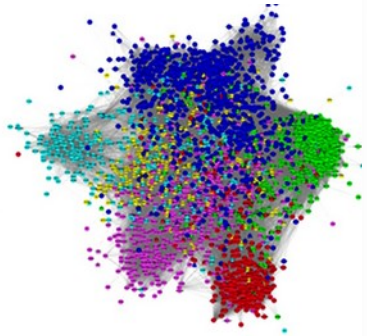
Gene expression data
pre-processing and
normalization

Data visualization and
analysis of variation

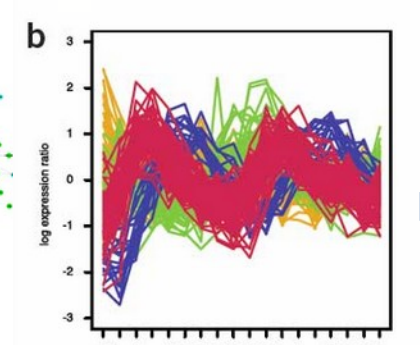



- Study the pathophysiology of Covid-19
- Identify diagnostic /prognostic markers

Modules characterization

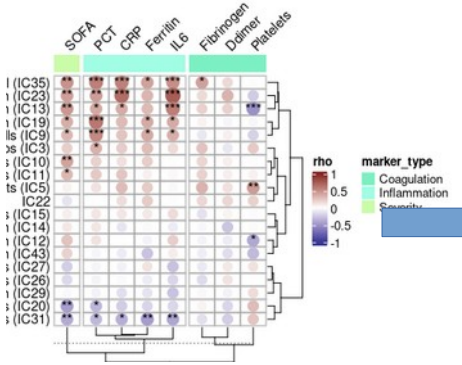


Functional
interpretation

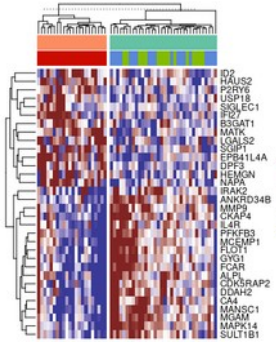



Modules activity across
severity

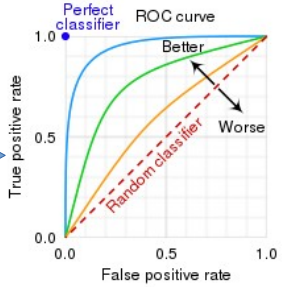
Relate modules to
clinical features




Signature
extraction



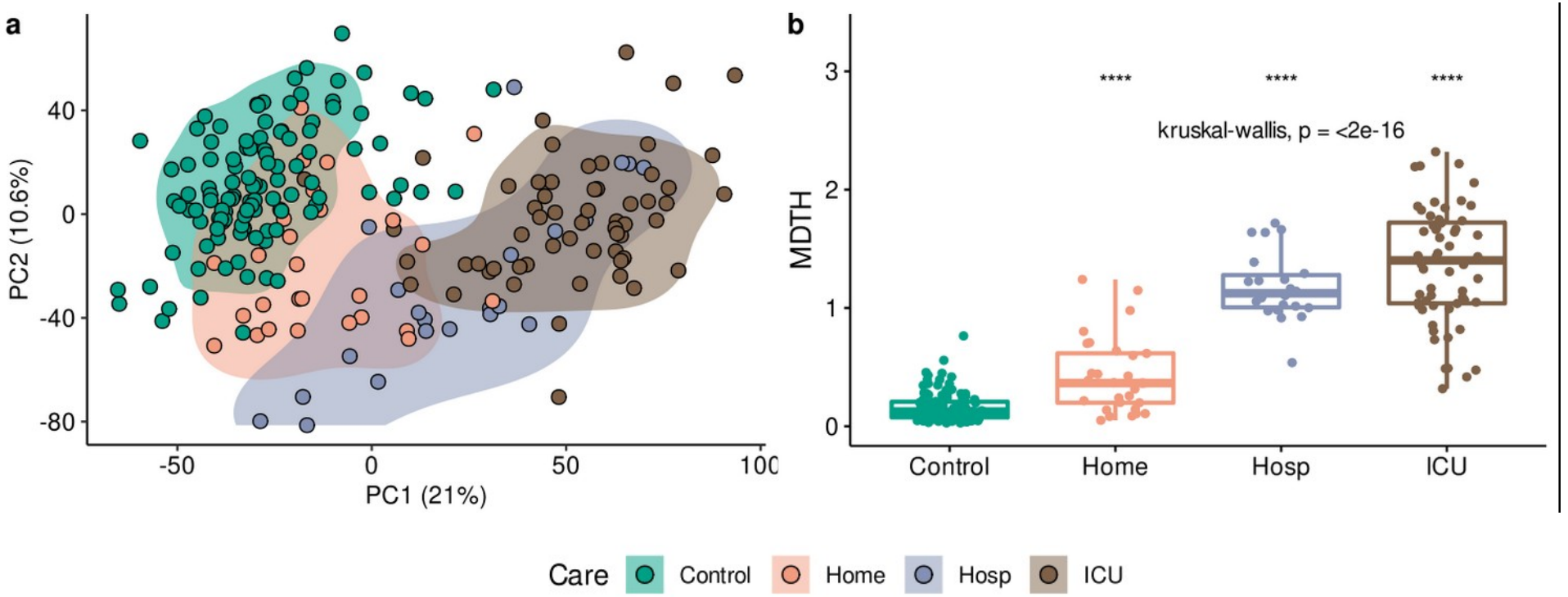
Signature
testing



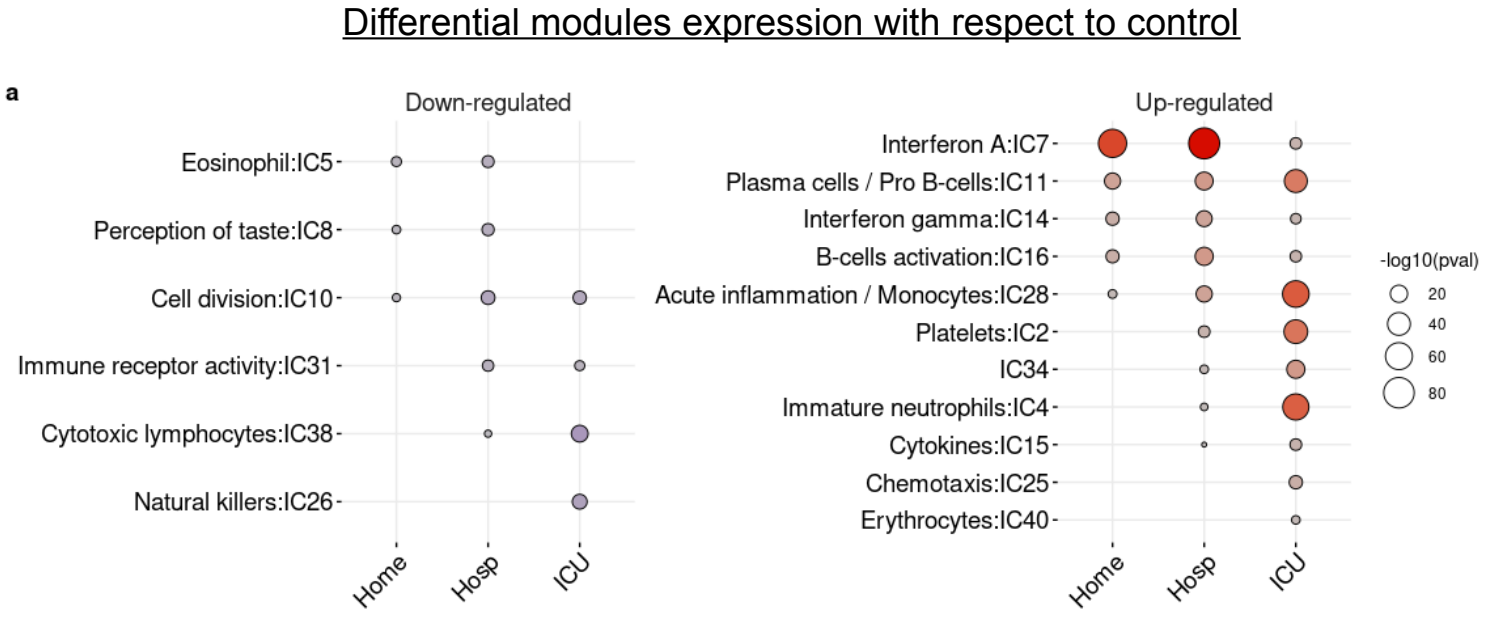
# Variation of transcriptome data reflects severity

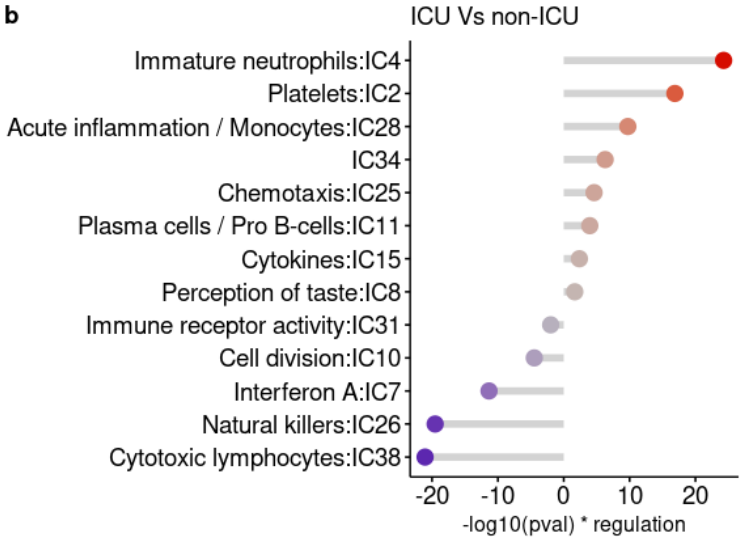
Principal component analysis

Molecular distance to health (MDTH)

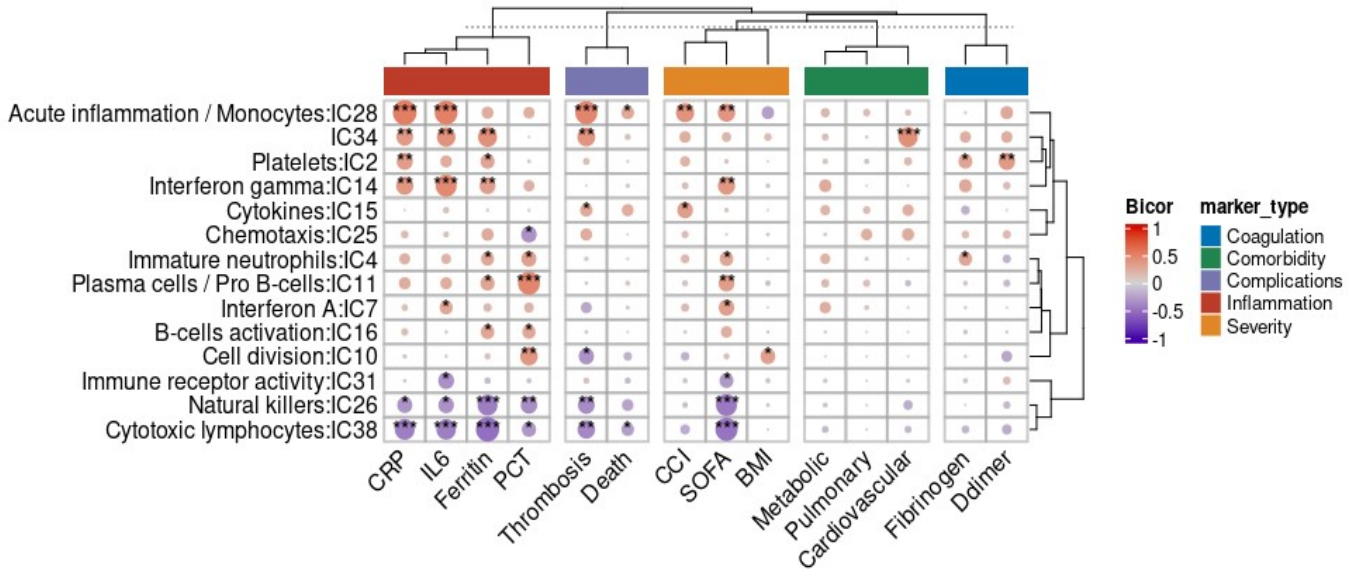


# Differential module expressions reveal common and distinct transcriptional modalities between severity groups

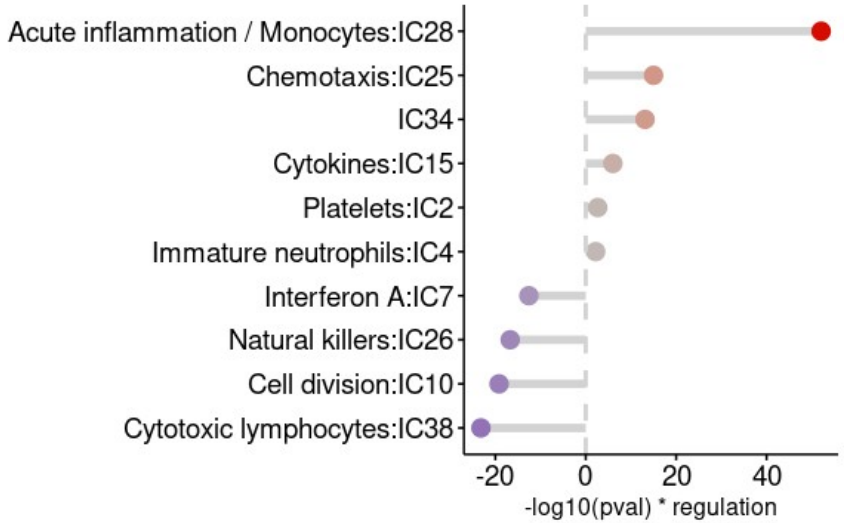


# Correlation of expression modules with clinical markers and complications

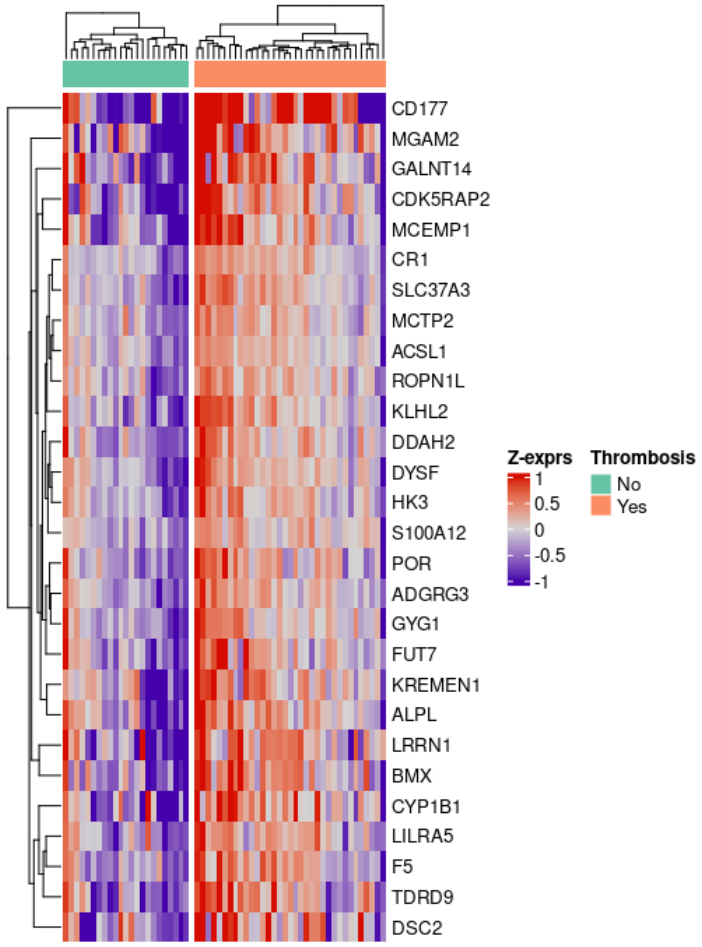



Modules enrichment
thrombotic vs non-thrombotic

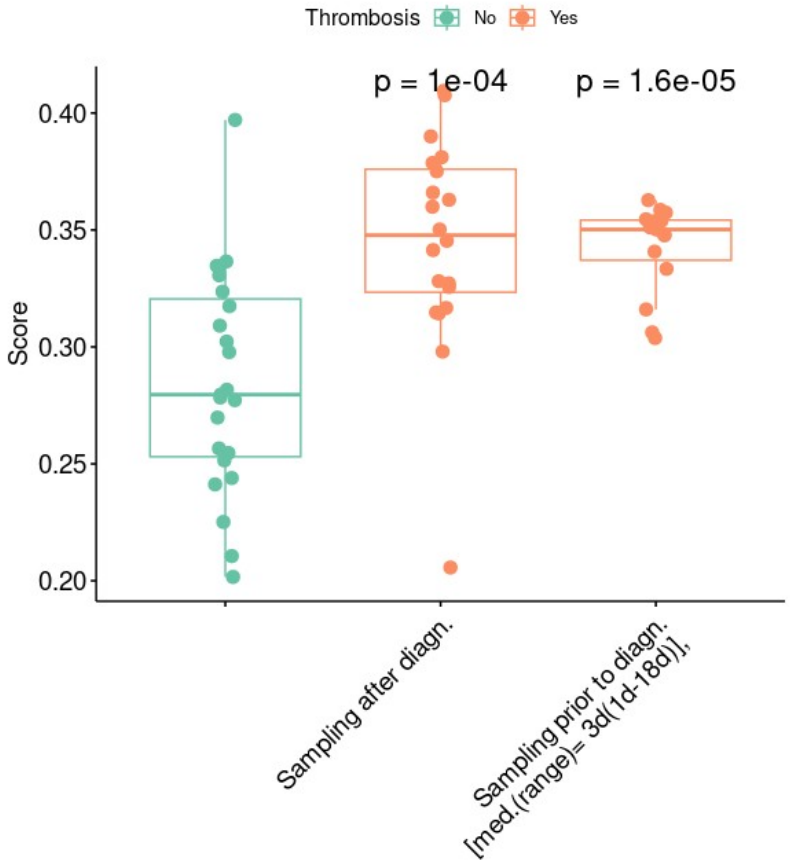


# Discovery of a 28-gene signature associated with thrombotic complications

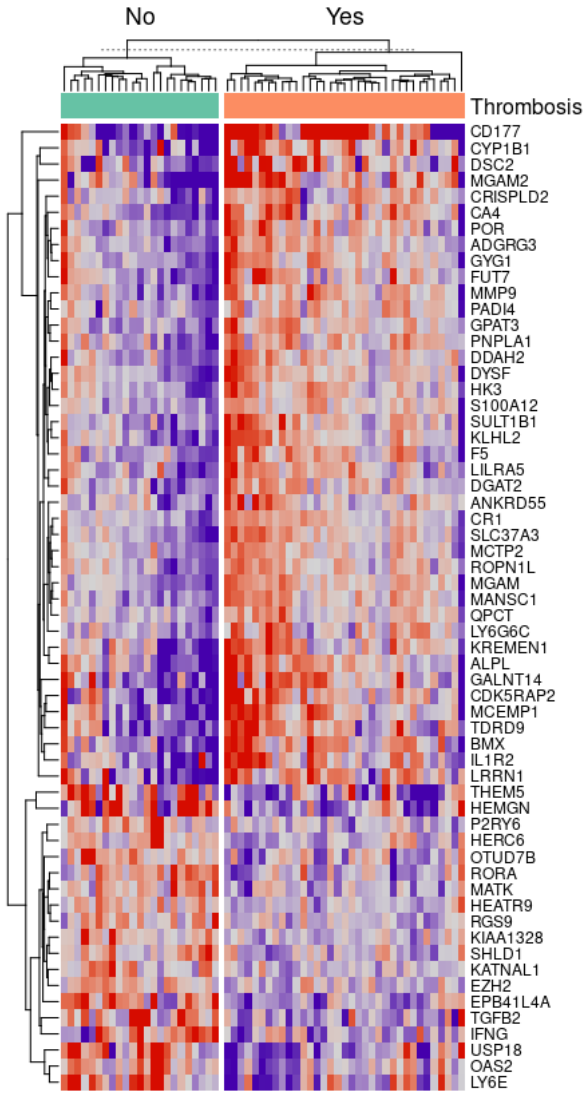
Acute inflammation module:
Thrombosis Vs No thrombosis




Single-subject scoring



# Translating the signature into a feasible 2-gene signature for potential clinical application

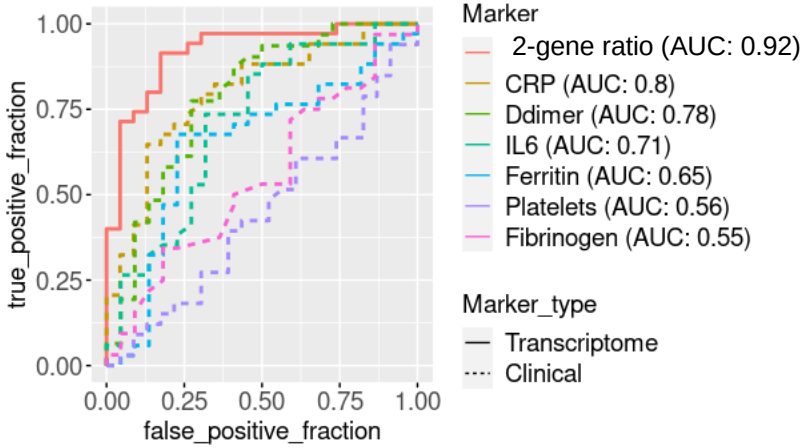



Positively associated genes

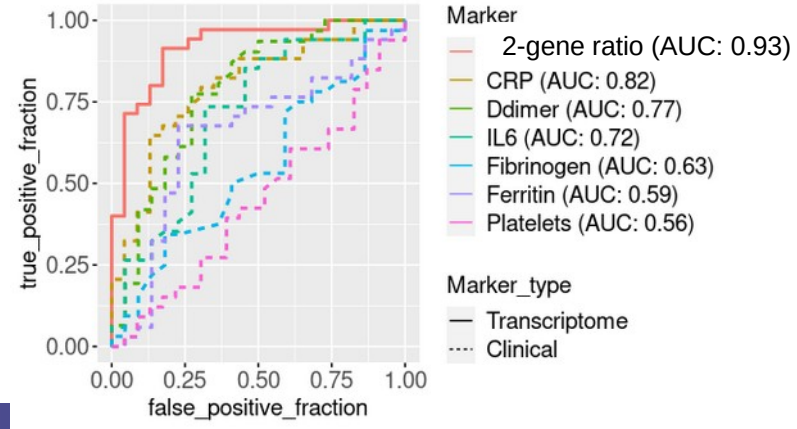
Negatively associated genes

**ROC curves of thrombosis diagnosis**

Sampling after clinical diagnosis




Sampling prior to clinical diagnosis



# Work in progress ...

**Matched case-control study to identify molecular biomarkers of progression to severe disease in Covid-19:**

- **Cases (n=57)**:
  - Died because of Covid-19 or
  - Was admitted to the hospital because of Covid-19 and received mechanical ventilation (and survived)
- **Controls (n=114)**:
  - Was admitted to hospital because of Covid-19 and who received at most supplemental oxygen treatment (for the management of oxygenation problems)
  - Two controls for each case to increase statistical confidence

| Characteristic | Case, N = 57[1] | Control, N = 114[1] |
|---|---|---|
| **sex** | | |
| Female | 18 (32%) | 35 (31%) |
| Male | 39 (68%) | 79 (69%) |
| **Age** | 66 (58, 71) | 63 (57, 69) |
| **Symptoms_duration** | 7 (4, 9) | 7 (5, 9) |
| **Oxy_treatment** | | |
| Invasive mechanical ventilation/ECMO | 40 (70%) | 0 (0%) |
| No additional oxygen or (mechanical) ventilation treatment | 0 (0%) | 7 (6.1%) |
| Non-invasive mechanical ventilation with oxygen | 11 (19%) | 0 (0%) |
| Supplemental oxygen treatment only | 5 (8.8%) | 107 (94%) |
| Unknown | 1 (1.8%) | 0 (0%) |
| **N_Comorbidities** | | |
| 0 | 18 (32%) | 35 (31%) |
| 1 | 14 (25%) | 36 (32%) |
| 2 | 14 (25%) | 31 (27%) |
| 3 | 9 (16%) | 10 (8.8%) |
| 4 | 2 (3.5%) | 2 (1.8%) |
| **Dexamethason** | 31 (54%) | 62 (54%) |
| **Outcome_type** | | |
| Alive, discharged | 4 (7.0%) | 108 (95%) |
| Alive, still admitted | 4 (7.0%) | 0 (0%) |
| Alive, transferred to other hospital | 5 (8.8%) | 4 (3.5%) |
| Deceased | 44 (77%) | 0 (0%) |
| Withdrawal consent | 0 (0%) | 2 (1.8%) |

[1] n (%); Median (IQR)

# Acknowledgments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Rapid European COVID-19 Emergency Research Response

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PREPARE
Platform foR European Preparedness Against (Re-)emerging Epidemics

MERMAIDS
Multi-centre EuRopean study of MAjor Infectious Disease Syndromes