The Immune Landscape of COVID-19 and Cardiovascular Disease

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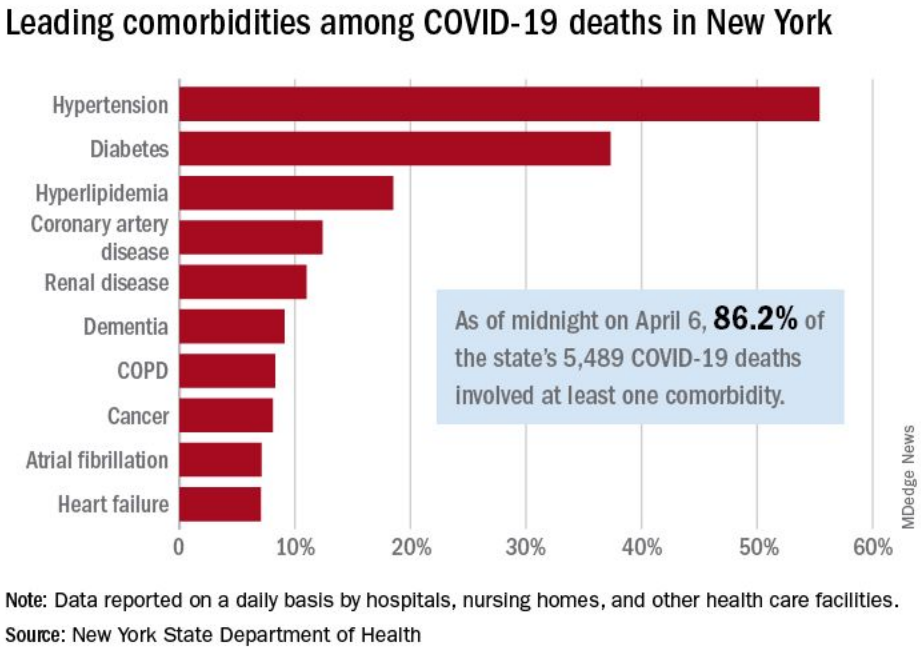
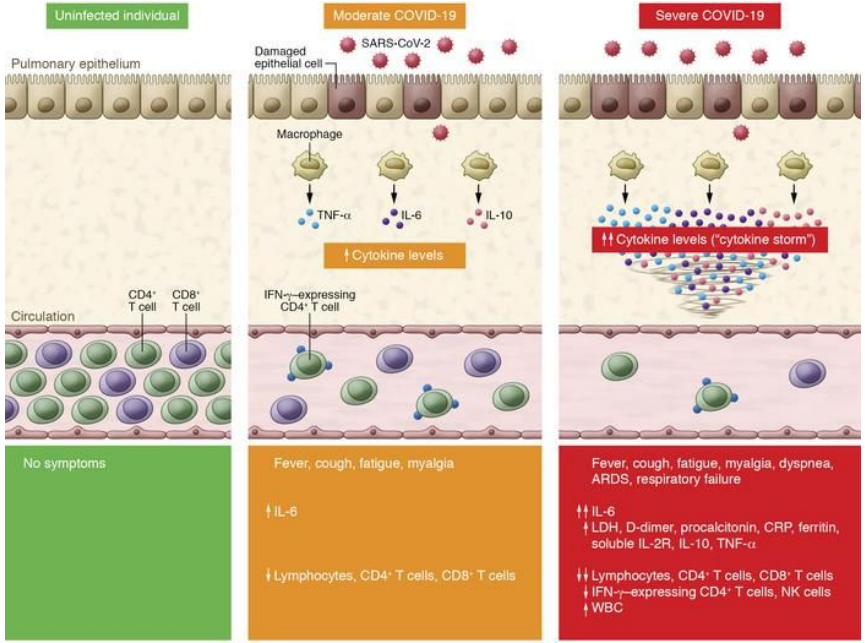
Background: COVID-19 comorbidities



Background: COVID-19 and CVD

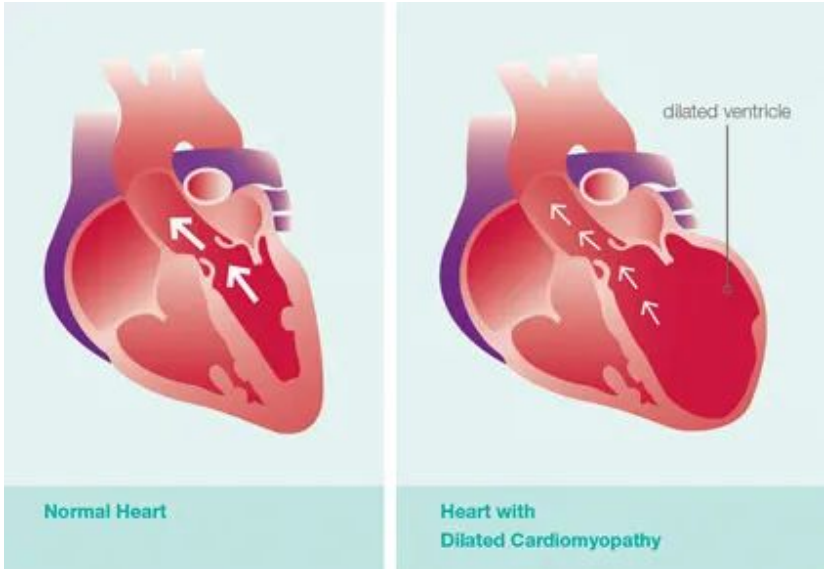
- Triggers cytokine storm
  - Myocardial injury, arrhythmia, acute coronary syndrome, VTE
- COVID-19 patients experience coagulation abnormalities
  - Thromboembolic events (further CVD)
    - May occur in lungs, heart, kidneys, and more (Schurink et al.)



Background: Cardiomyopathy

Cardiomyopathy

- Disease of the myocardium
- Nonischemic Dilated Cardiomyopathy (NIDCM): heart’s ventricles are enlarged
- COVID-19 Commonality: Cytokines and inflammasomes also involved in pathogenesis



Background: VTE

Venous thromboembolism (VTE)

- Blood clotting in veins
- Could lead to pulmonary embolism
- COVID-19 commonalities
  - Increased Oxidative stress, leading to endothelial damage
  - Restriction of venous blood flow recruits neutrophils, monocytes, and platelets
  - Pre-existing immune dysregulation in COVID-19 VTE patients increases their risk of progressing to severe disease

Background: CAD

Coronary Artery Disease (CAD)

- Buildup of plaque and narrowing of of arteries, limiting blood flow to heart
- COVID-19 commonalities
  - CRPs, leukocytes, cytokines upregulated in both CAD and severe COVID-19 patients
  - excessive pro-inflammatory cytokine production associated with vascular damage that induces uncontrolled blood clotting
  - CAD patients likely more vulnerable to COVID-19; COVID-19 may exacerbate CAD

Project Goals

Characterize and compare the dysregulation of the immune landscape in patients with cardiomyopathy, VTE, CAD, and COVID-19

- Cytokine and inflammasome-related gene expression
- Immune infiltration
- Enrichment of immunological pathways

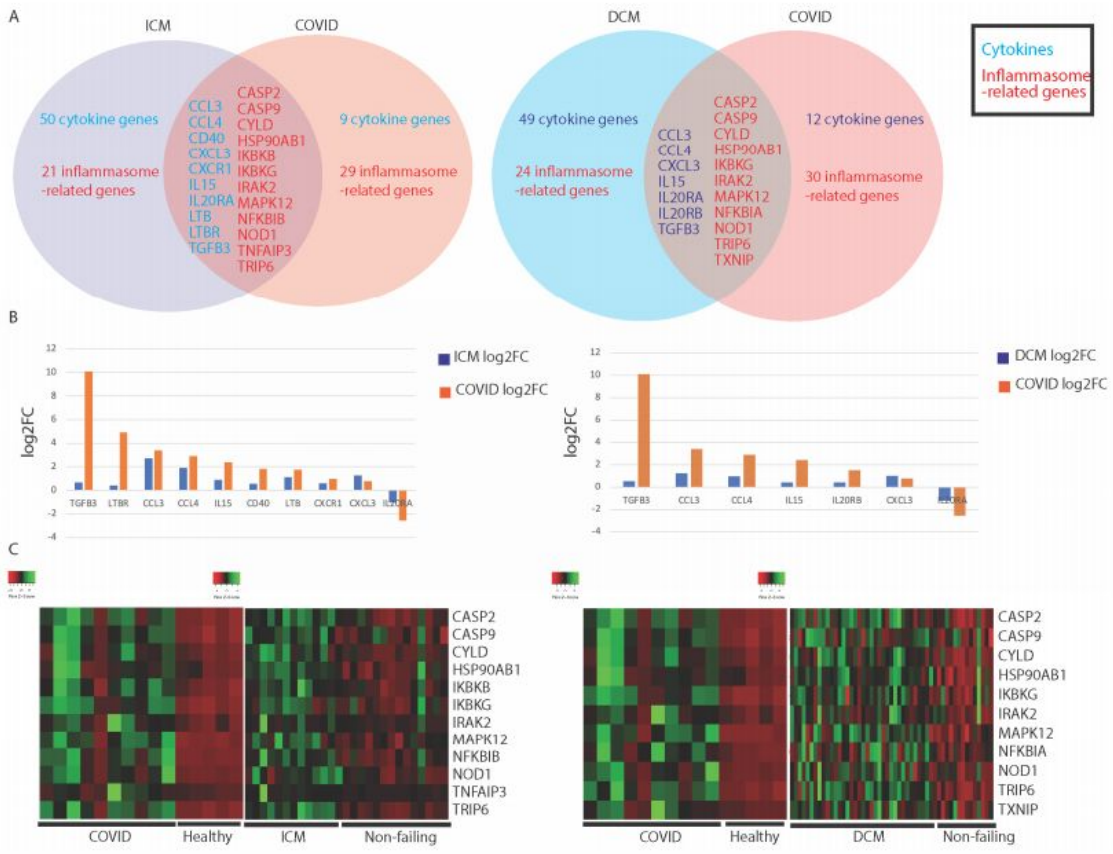
Methods and Data

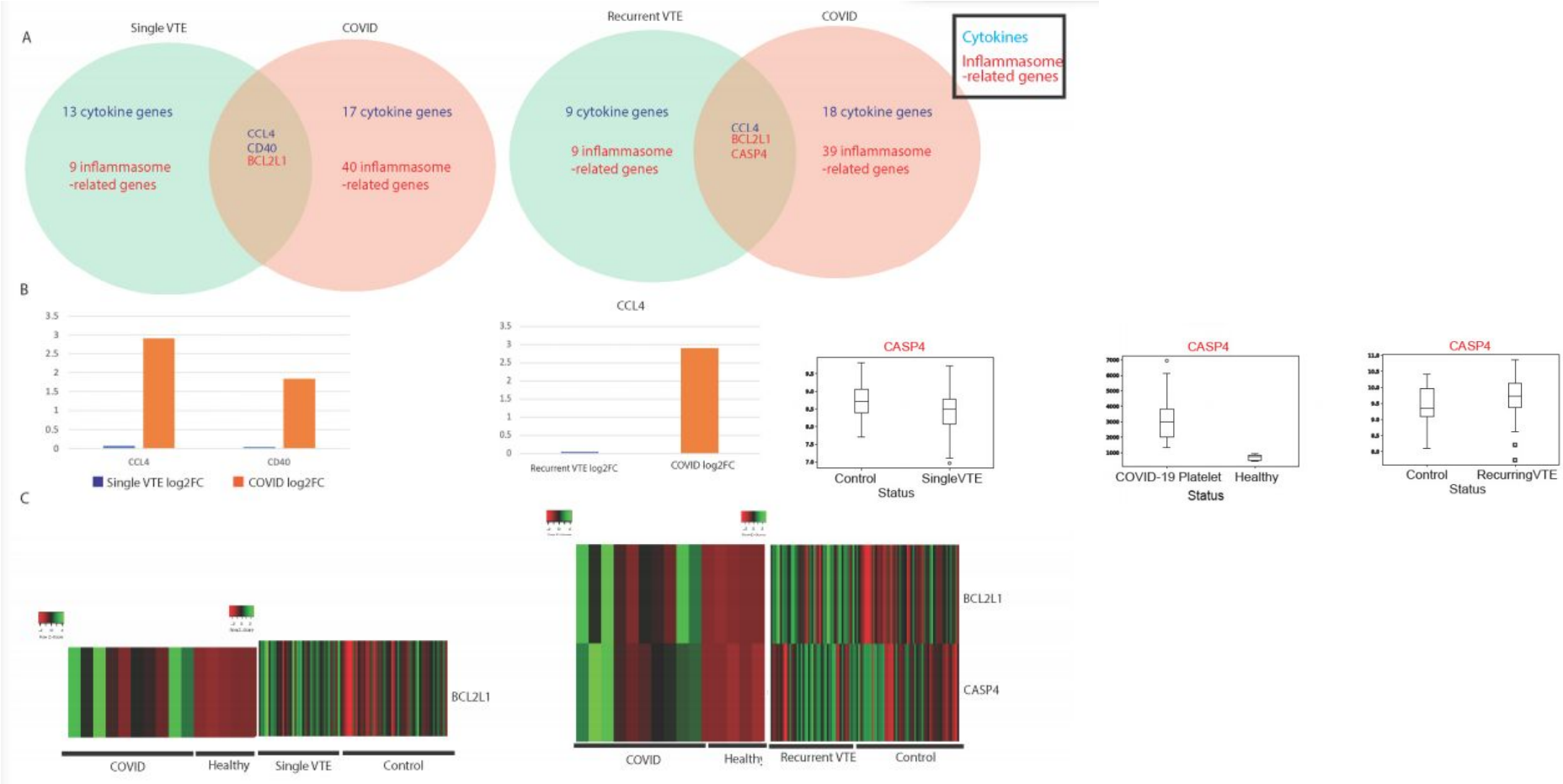
RNA-seq downloaded from GEO omnibus

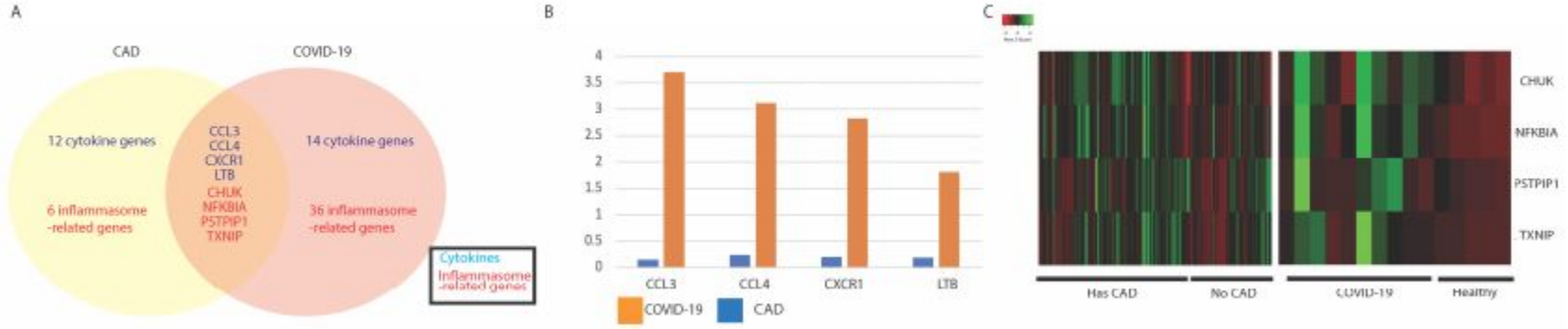
GSE116250	• 14 patients with no major cardiac history • 37 NIDCM patients • 13 ICM patients
GSE19151	• 63 healthy controls • 23 single VTE patients • 17 recurrent VTE patients
GSE90074	• 93 CAD patients • 50 without CAD
SRP262885	• 10 COVID-19 patients • 5 healthy controls

Materials and Data

- Differential Expression: Kruskal-Wallis Test
- Pathway/Signature Enrichment: Gene Set Enrichment Analysis (GSEA)
- Immune Cells from Rna-Seq: Cibersortx


A
ICM
COVID
50 cytokine genes
21 inflammasome -related genes
9 cytokine genes
29 inflammasome -related genes
CCL3
CCL4
CD40
CXCL3
CXCR1
IL15
IL20RA
LTB
LTBR
TGFB3
CASP2
CASP9
CYLD
HSP90AB1
IKBKB
IKBKG
IRAK2
MAPK12
NFKBIB
NOD1
TNFAIP3
TRIP6
DCM
COVID
49 cytokine genes
24 inflammasome -related genes
12 cytokine genes
30 inflammasome -related genes
CCL3
CCL4
CXCL3
IL15
IL20RA
IL20RB
TGFB3
CASP2
CASP9
CYLD
HSP90AB1
IKBKG
IRAK2
MAPK12
NFKBIA
NOD1
TRIP6
TXNIP
Cytokines
Inflammasome -related genes
B
log2FC
ICM log2FC
COVID log2FC
TGFB3
LTBR
CCL3
CCL4
IL15
CD40
LTB
CXCR1
CXCL3
DCM log2FC
COVID log2FC
TGFB3
CCL3
CCL4
IL15
IL20RB
CXCL3
C
CASP2
CASP9
CYLD
HSP90AB1
IKBKB
IKBKG
IRAK2
MAPK12
NFKBIB
NOD1
TNFAIP3
TRIP6
COVID
Healthy
ICM
Non-failing
CASP2
CASP9
CYLD
HSP90AB1
IKBKG
IRAK2
MAPK12
NFKBIA
NOD1
TRIP6
TXNIP
COVID
Healthy
DCM
Non-failing


A
Single VTE
COVID
13 cytokine genes
9 inflammasome
-related genes
CCL4
CD40
BCL2L1
17 cytokine genes
40 inflammasome
-related genes
Recurrent VTE
COVID
9 cytokine genes
9 inflammasome
-related genes
CCL4
BCL2L1
CASP4
18 cytokine genes
39 inflammasome
-related genes
Cytokines
Inflammasome
-related genes
B
CCL4
CD40
Single VTE log2FC
COVID log2FC
CCL4
Recurrent VTE log2FC
COVID log2FC
CASP4
Control
SingleVTE
Status
CASP4
COVID-19 Platelet
Healthy
Status
CASP4
Control
RecurringVTE
Status
C
BCL2L1
COVID
Healthy
Single VTE
Control
BCL2L1
CASP4
COVID
Healthy
Recurrent VTE
Control


A
CAD
COVID-19
12 cytokine genes
6 inflammasome -related genes
CCL3
CCL4
CXCR1
LTB
CHUK
NFKBIA
PSTPIP1
TXNIP
14 cytokine genes
36 inflammasome -related genes
Cytokines
Inflammasome -related genes
B
4
3.5
3
2.5
2
1.5
1
0.5
0
CCL3
CCL4
CXCR1
LTB
COVID-19
CAD
C
CHUK
NFKBIA
PSTPIP1
TXNIP
Has CAD
No CAD
COVID-19
Healthy

Conclusions

- Patients with CVD display significant similarities with inflammation-related genes in COVID-19
- Immune dysregulation provides specific explanations for increased COVID-19 disease severity
- CAD patient display the most similarity to COVID-19 immune landscape
- Identifying immune targets vital to treating COVID-19 patients with CVD comorbidities

Acknowledgements

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