COVID-19 : une maladie immunologique ?
Réponse cellulaire au SARS-CoV-2

4es Journées de la Fédération d'Immunologie Médicale

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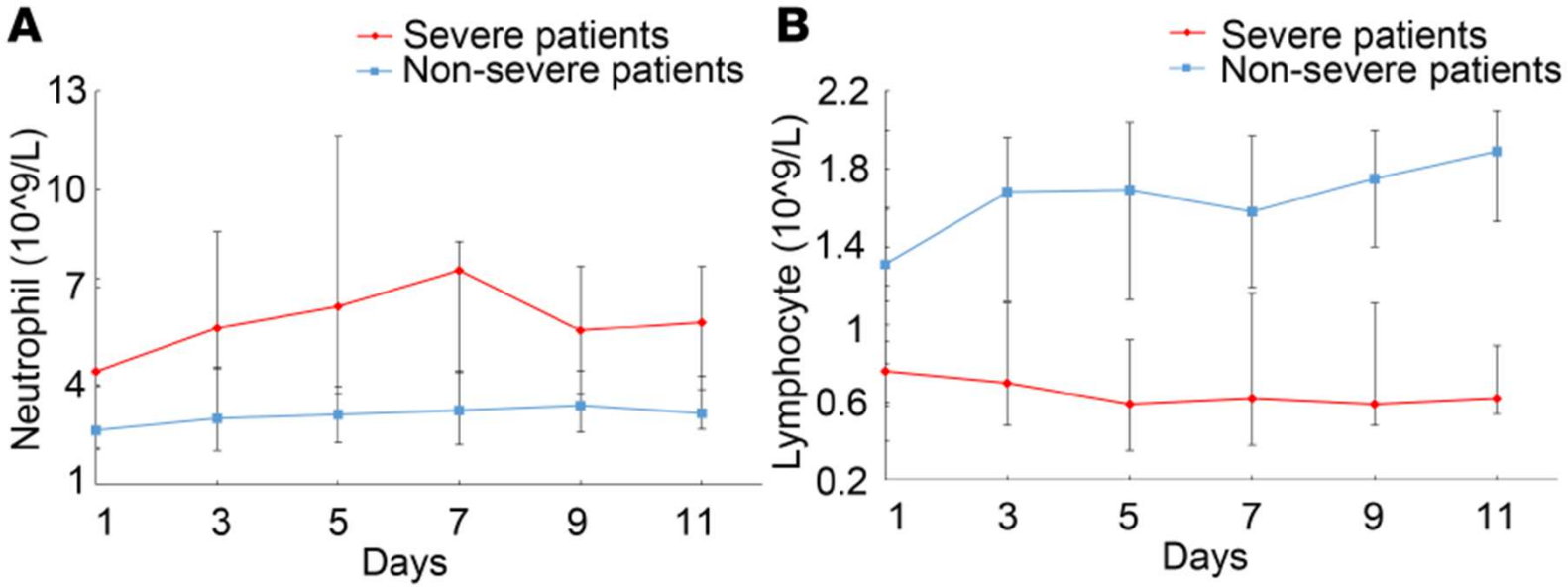
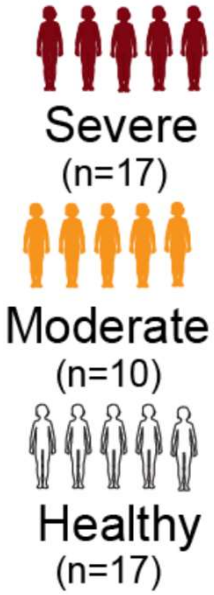
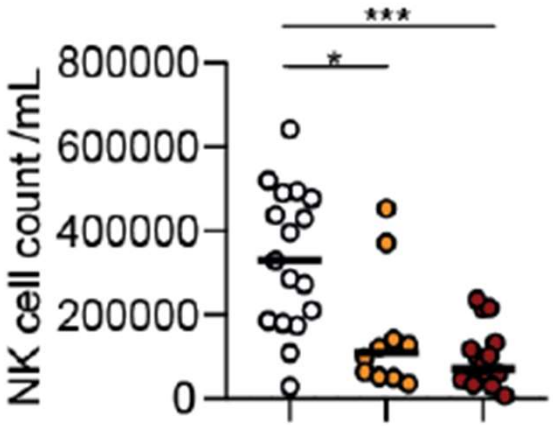
Hyperneutrophilia and Lymphopenia during severe COVID-19 infection

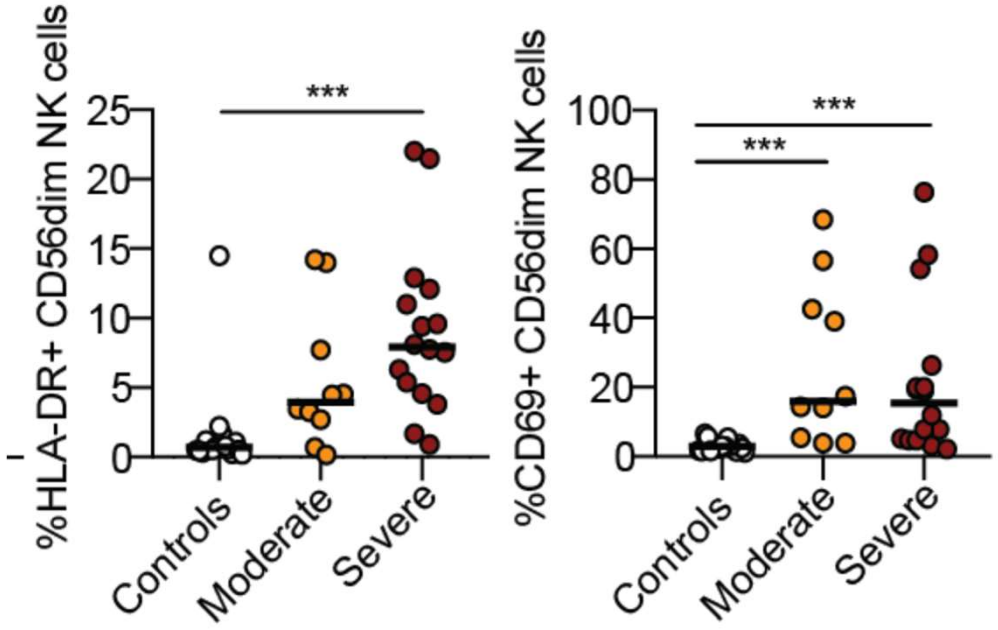


Shaohua et al, JCI Insight 2020

NK cells are activated during moderate and severe COVID-19 infection

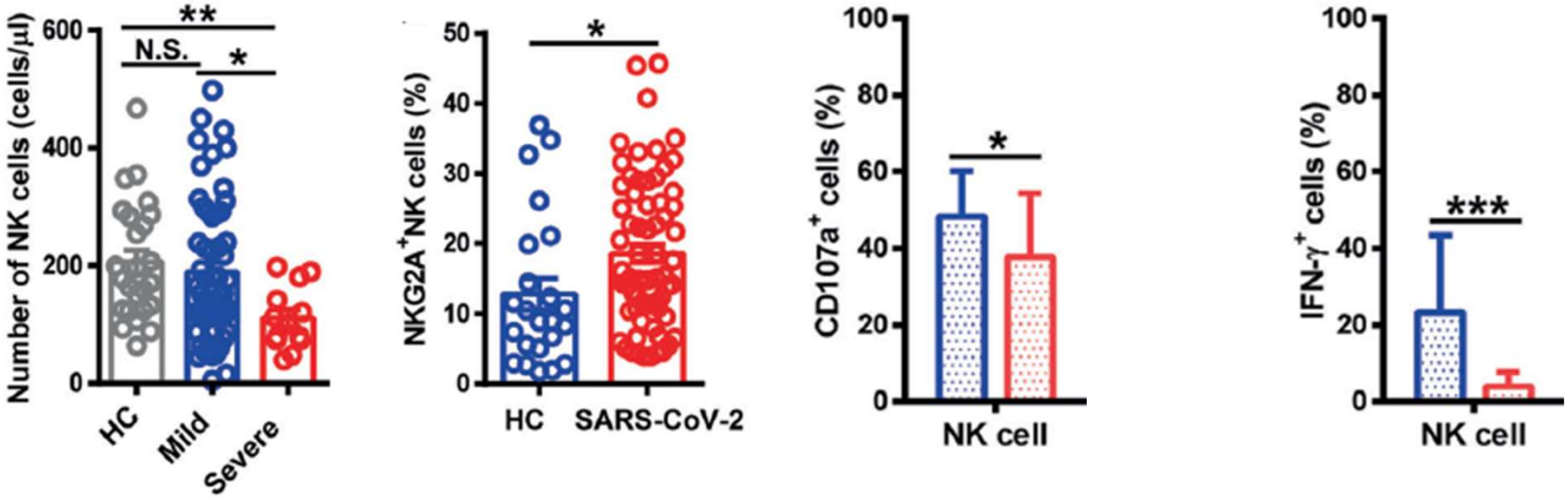






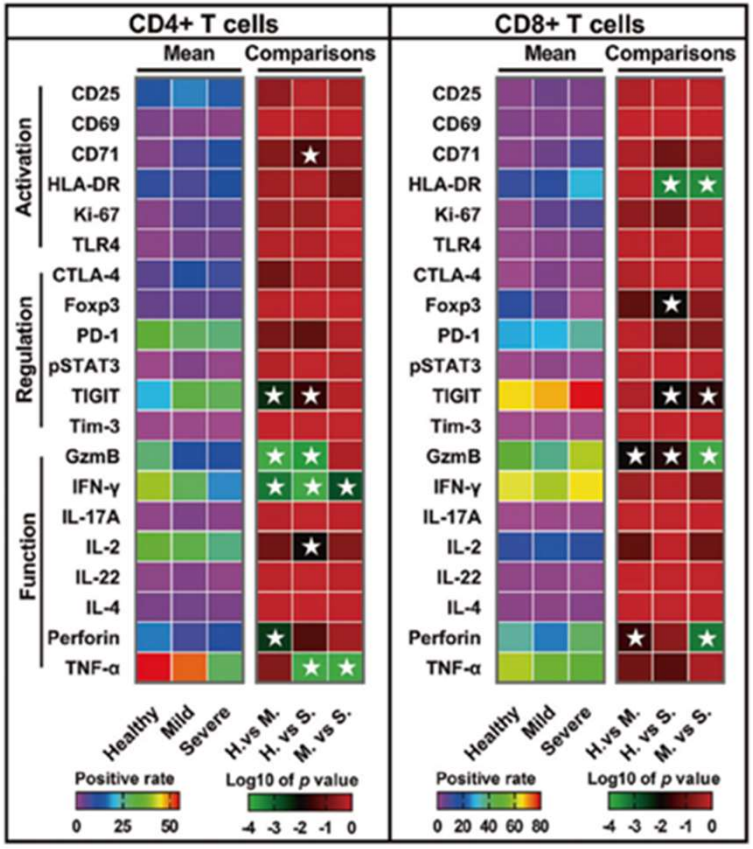
Maucourant et al, Sci Immunol 2020

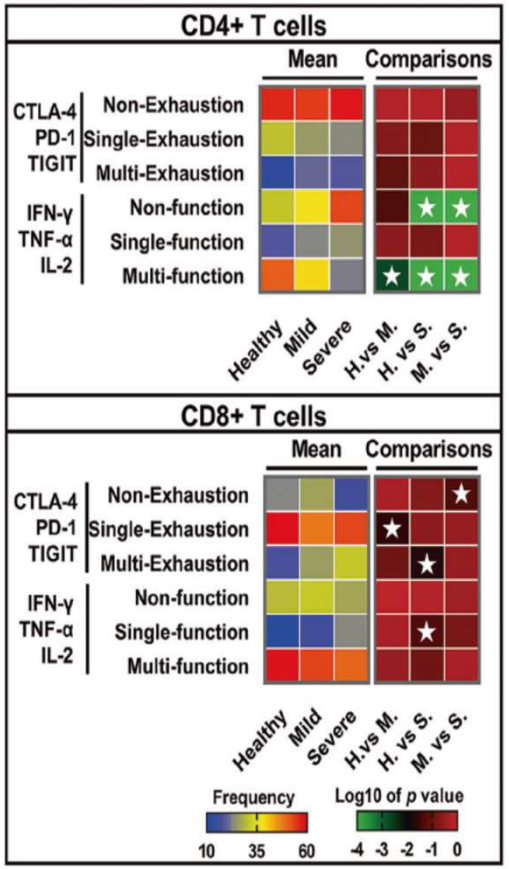
NK cells shows an hypofonctionnal phenotype during severe COVID-19 infection



Zheng et al, Cell Mol Immunol 2020

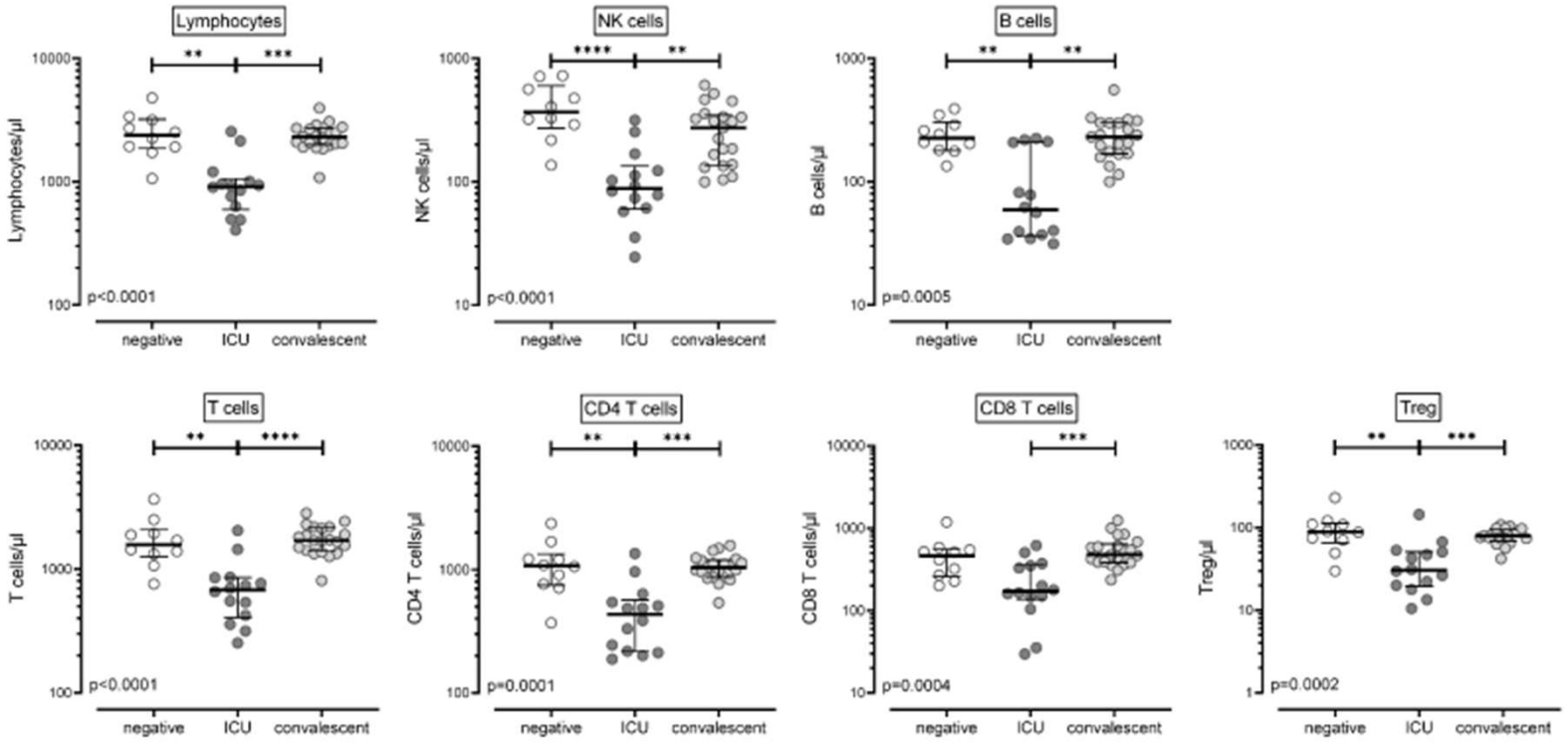
Peripheral CD4 T cell functions are lacking during mild/severe COVID-19 infection





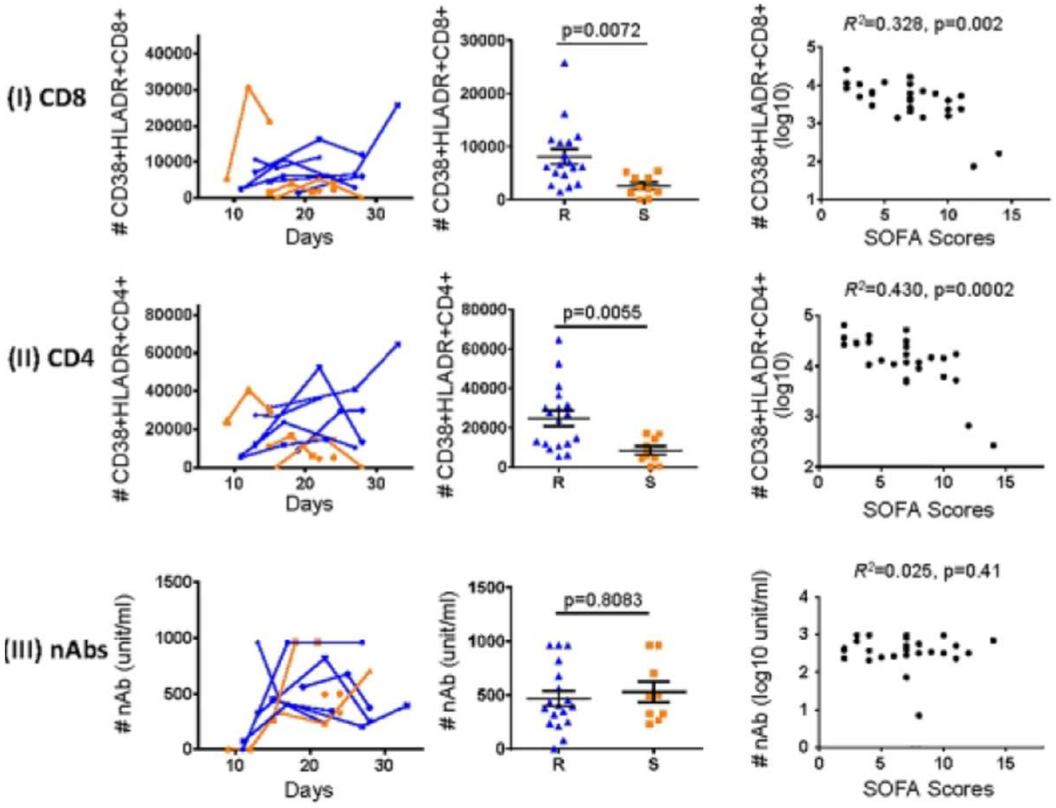
Zheng et al, Cell and Mol Immunol, 2020

The lymphopenia is reversible after severe COVID-19 infection



Schub et al, JCI Insight 2020

T cell activation is associated with recovery after mild COVID-19 infection

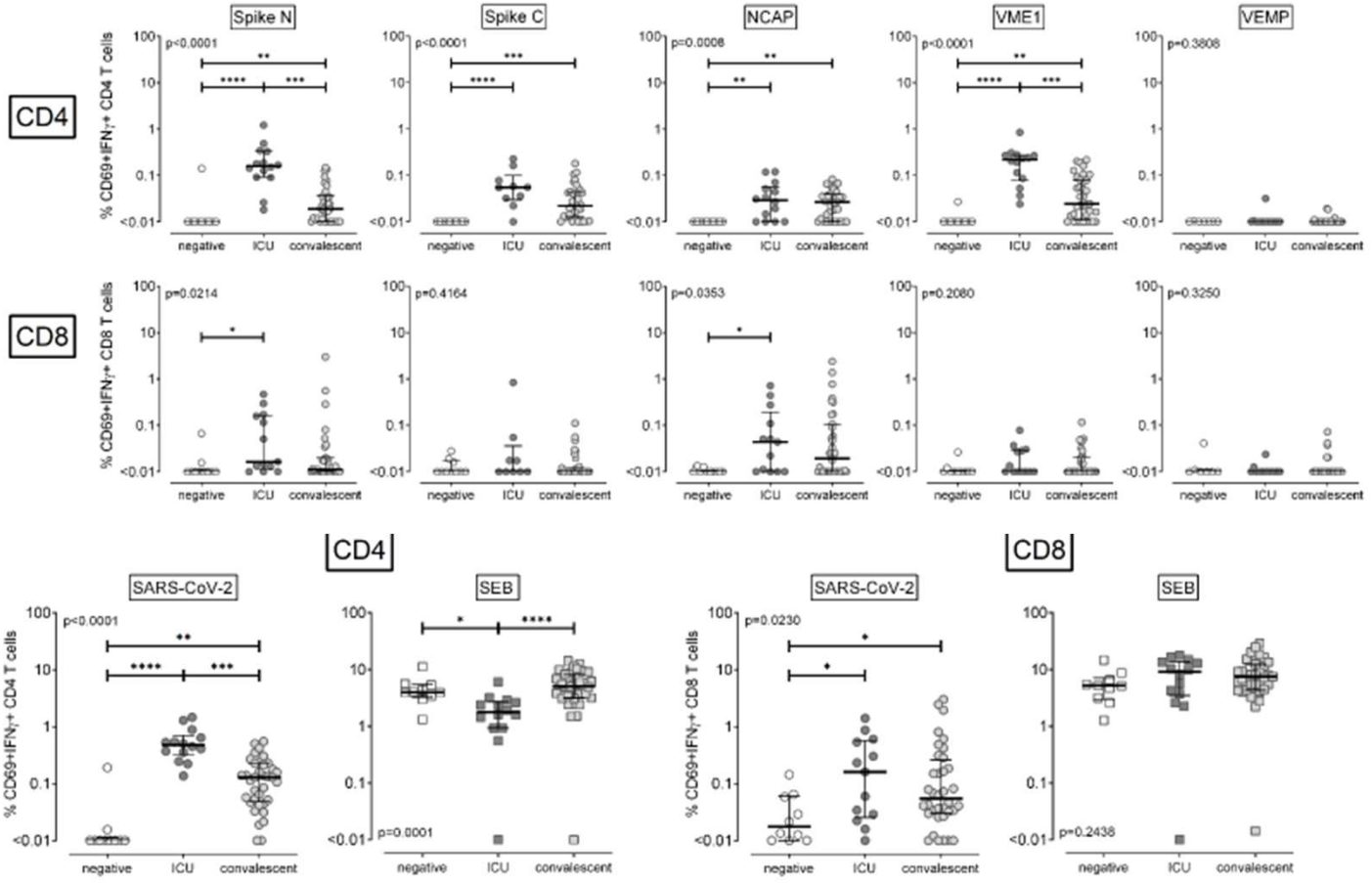


(B) Comparison of absolute numbers of CD38+HLA-DR+CD8+ T cells (I), CD38+HLADR+CD4+ T cells (II) and nAbs (III) in 1 ml blood samples. The data are presented as the mean ± SEM (18 measurements from the 6 patients in R group and 9 measurements from the 5 patients excluding patient S6 in S group)

Recovering group (R); Severe persistence group (S)

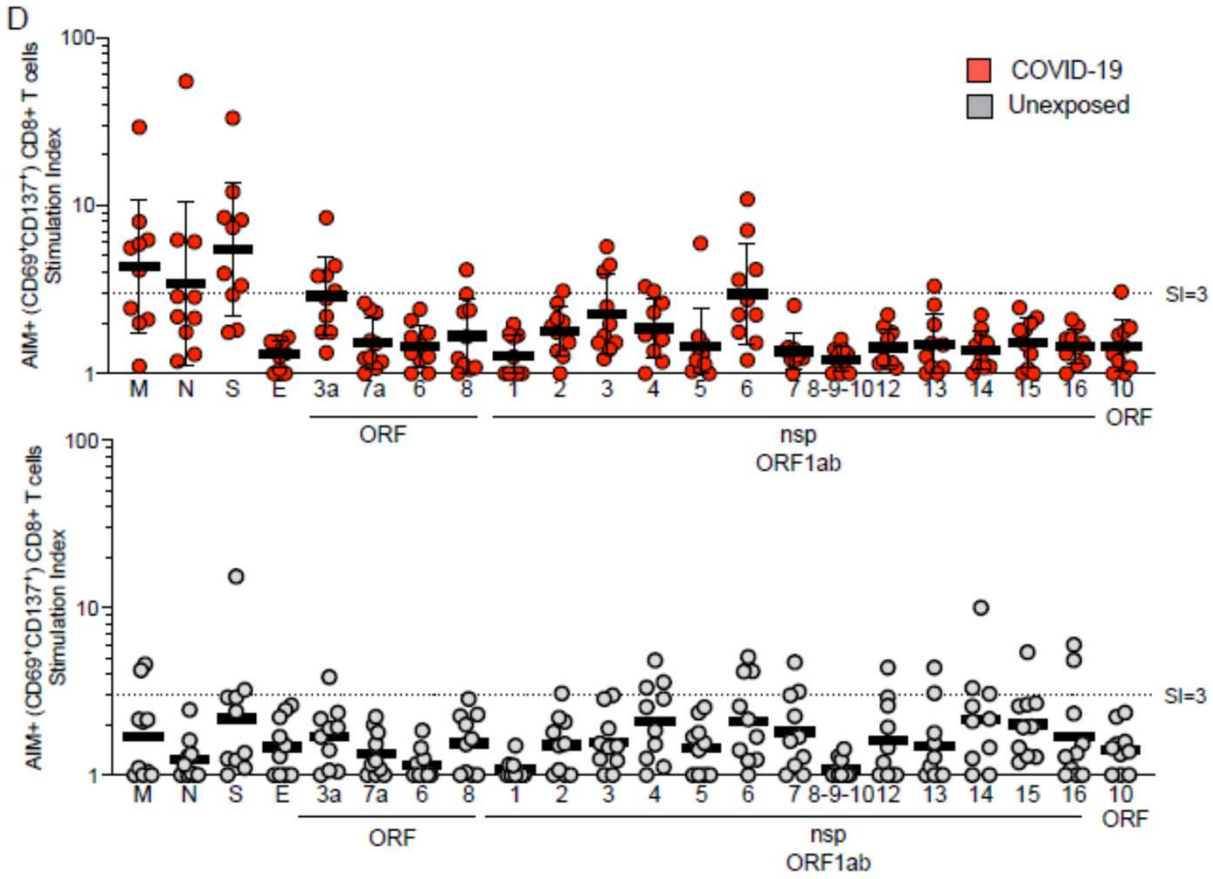
Wang et al, AJRCCM 2020

Peripheral CD8 and mostly CD4 SARS-CoV2 –specific T cell responses are detectable during severe COVID-19 infection



Schub et al, JCI Insight 2020

Peripheral CD8 SARS-CoV2 –specific T cell responses are detectable after recovery from COVID-19 infection

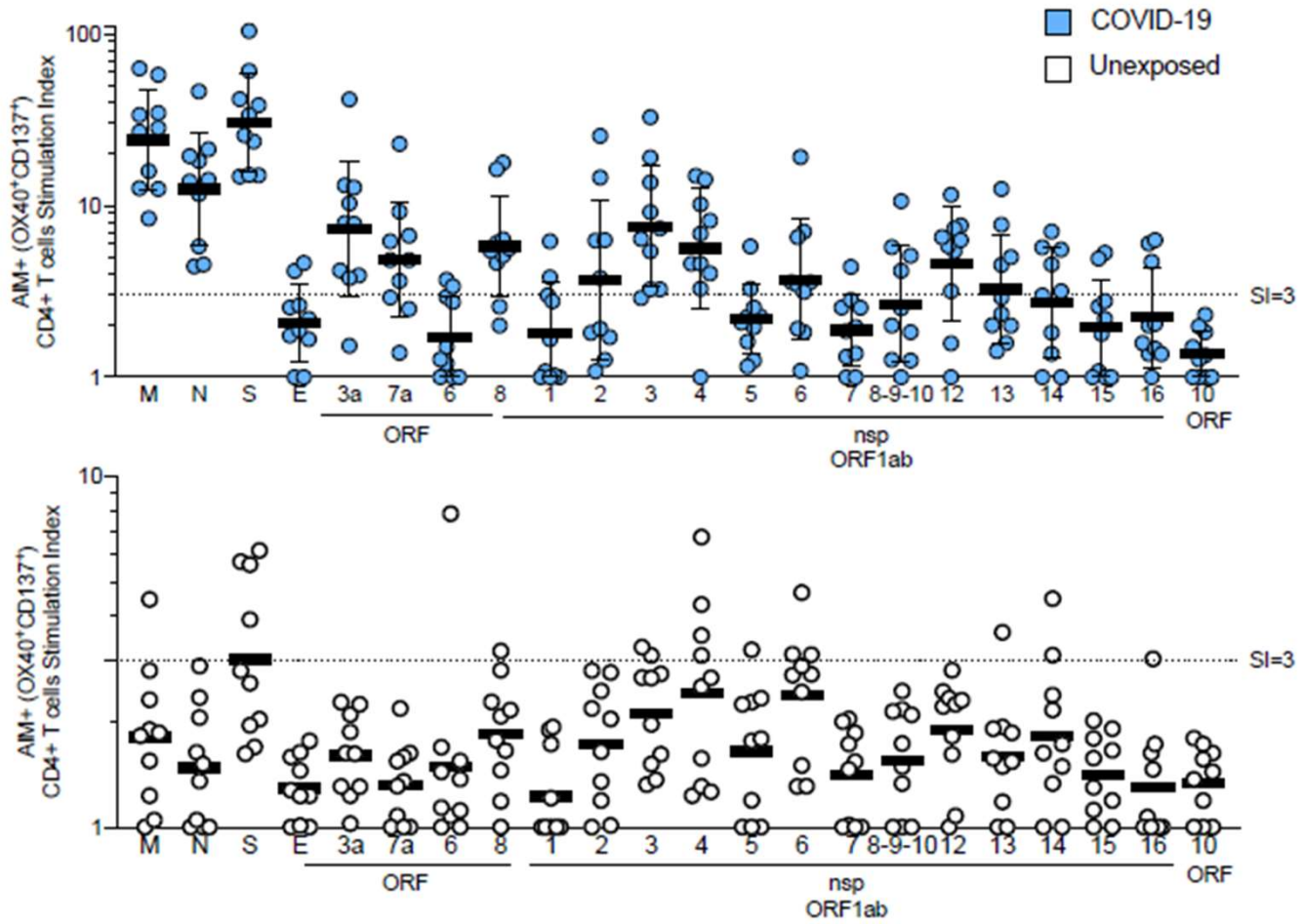


20 adult patients who had recovered from COVID-19 disease

Disease Severity
Mild 70% (14/20)
Moderate 20% (4/20)
Severe 10% (2/20)
Critical 0% (0/20)

Grifoni et al, Cell 2020

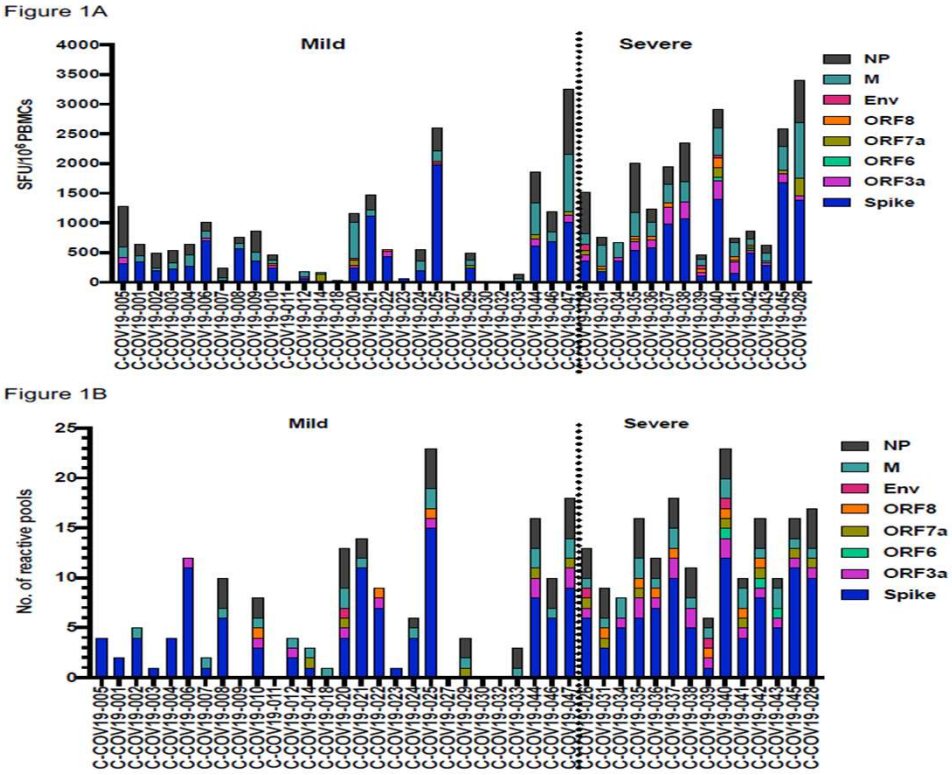
Peripheral CD4 SARS-CoV2 –specific T cell responses are detectable after recovery from COVID-19 infection



20 adult patients who had recovered from COVID-19 disease

Grifoni et al, Cell 2020

Peripheral SARS-CoV2 –specific T cell responses are detectable after mild and mostly severe COVID-19 infection



A total of 423 15- to 18-mer peptides overlapping by 10 amino acid residues and spanning the full proteome of the SARS-CoV-2 except ORF-1 (253 spike, 29 M, 9 E, 35 ORF3a, 7ORF6, 15 ORF7a, 16 ORF8, 59 NP)

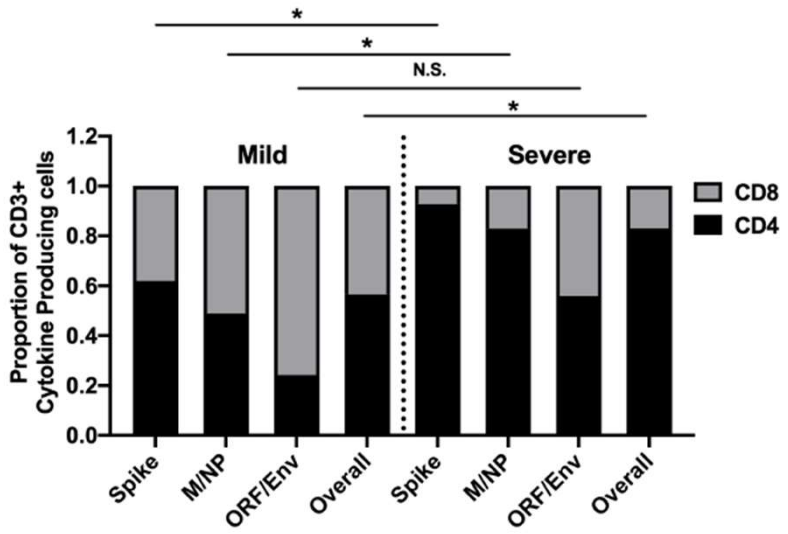


Figure 4: Distribution of SARS-CoV-2–specific CD4$^+$ and CD8$^+$ memory T cell responses Cytokine producing T cells were detected by intracellular cytokine staining (ICS) after incubation with SARS-CoV-2 peptides. A) and B) FACS plots representative of CD4$^+$T cell and CD8$^+$ T cells response respectively upon stimulation with respective SARS-CoV-2 peptide pools. C) The relative proportion of SARS-CoV-2 peptide pool-reactive CD4$^+$ and CD8$^+$ T cells. The SARS-CoV-2 peptide pool-reactive CD4$^+$ or CD8$^+$ T cells were identified with at least one of the three cytokines detected: IFN-γ, TNF-α and IL-2. Data shown are from 14 subjects with previously mild COVID-19 symptoms and 8 with severe symptoms. Mann-Whitney test was used for the analysis. * P<0.05

Peng et al, Nat Immunol 2020

Local pulmonary viral replication during severe forms leads to systemic replication and immune cell recruitment

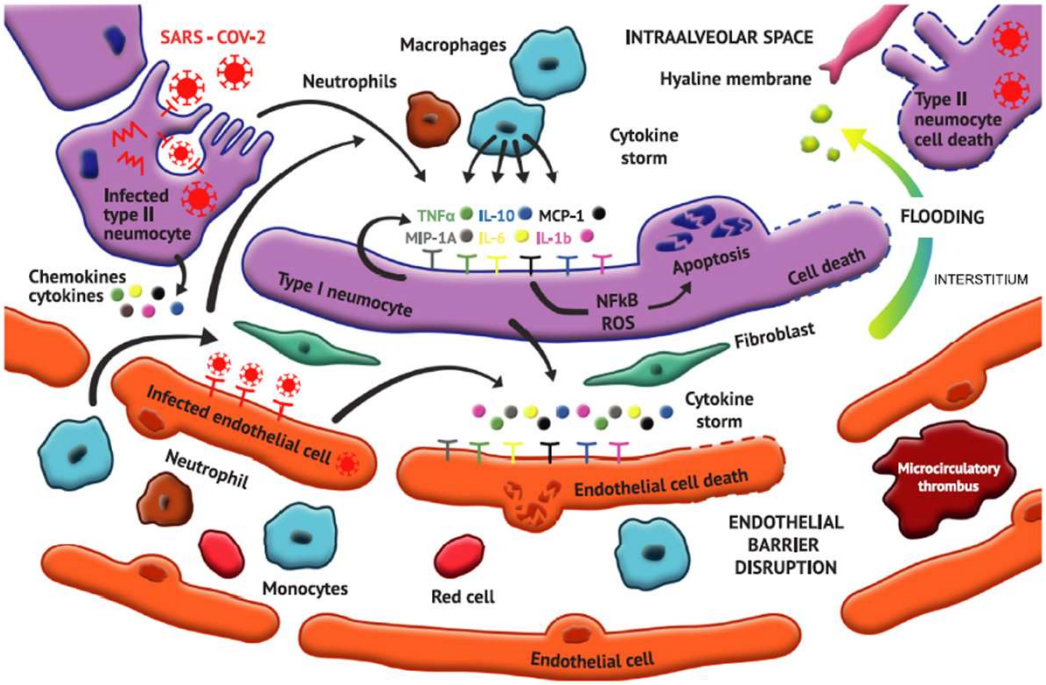
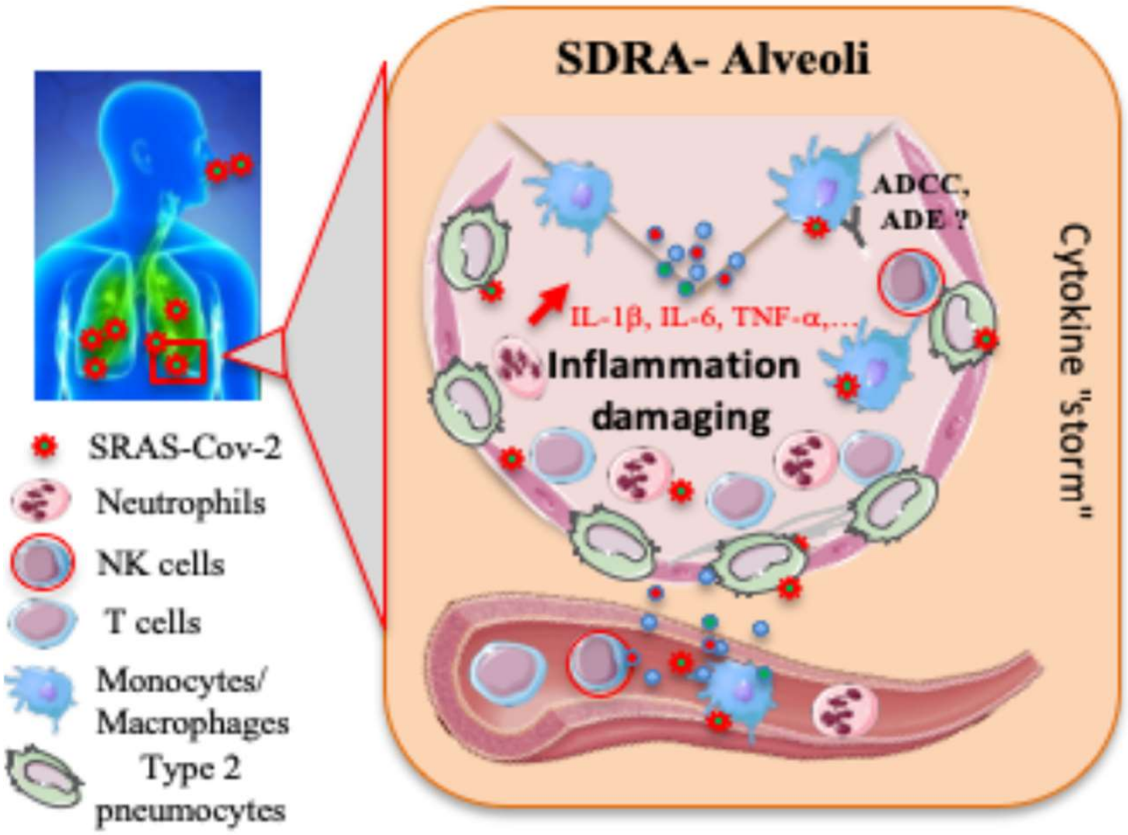


Fig. 2. *Physiopathology of acute lung injury in SARS-CoV-2 infection (COVID-19).*

SARS-CoV-2 infects primarily type II pneumocytes through binding to the ACE2 receptor. The infected and surrounding pneumocytes secret cytokine and chemokines, which attract monocyte-macrophages and neutrophils to the alveolar space, which secrete additional cytokines and chemokines. Ultimately the pneumocytes suffer apoptosis/pyroptosis releasing large amounts of proinflammatory factors. Endothelial cells are infected, overexpress adhesion molecules, and release chemokines and cytokines. Endothelial cells undergo apoptosis, which, together with alveolar cell apoptosis, increases vascular leakage and breaks the alveolar-capillary barrier. The hyperinflammatory milieu and endothelial dysfunction activate coagulation cascades through tissue factor expression, platelet activation, and NETosis all of them promoting microcirculatory thrombi formation. The break of endothelial-alveolar barrier further promotes vascular leakage resulting in interstitial and alveolar space flooding. Downregulation of the ACE2/Ang-(1–7)/Mas1R axis contributes to increasing vasoconstriction, inflammatory signals, endothelial dysfunction, vascular leakage, and prothrombotic state.

Domingo et al, E Biomedicine 2020

Local pulmonary viral replication during severe forms leads to systemic inflammation and immune cell recruitment



Guihot et al, Frontiers Immunol 2020

Conclusion : Réponses cellulaires T au cours des formes sévères de COVID-19

- Lymphopénie T/B/NK prédominant sur les CD4 réversible après résolution de la maladie malgré une activation T persistante
- Les cellules NK sont activées mais leur fonction est altérée
- Présence d'une réponse T spécifique du SARS-COV-2 systémique
- Avec migration des effecteurs au site de l'infection
- La réponse cellulaire T est plutôt CD4 localement et en périphérie

→ Les mécanismes immunopathologiques des formes létales restent à déterminer

Immunology, Pitié-Salpêtrière

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