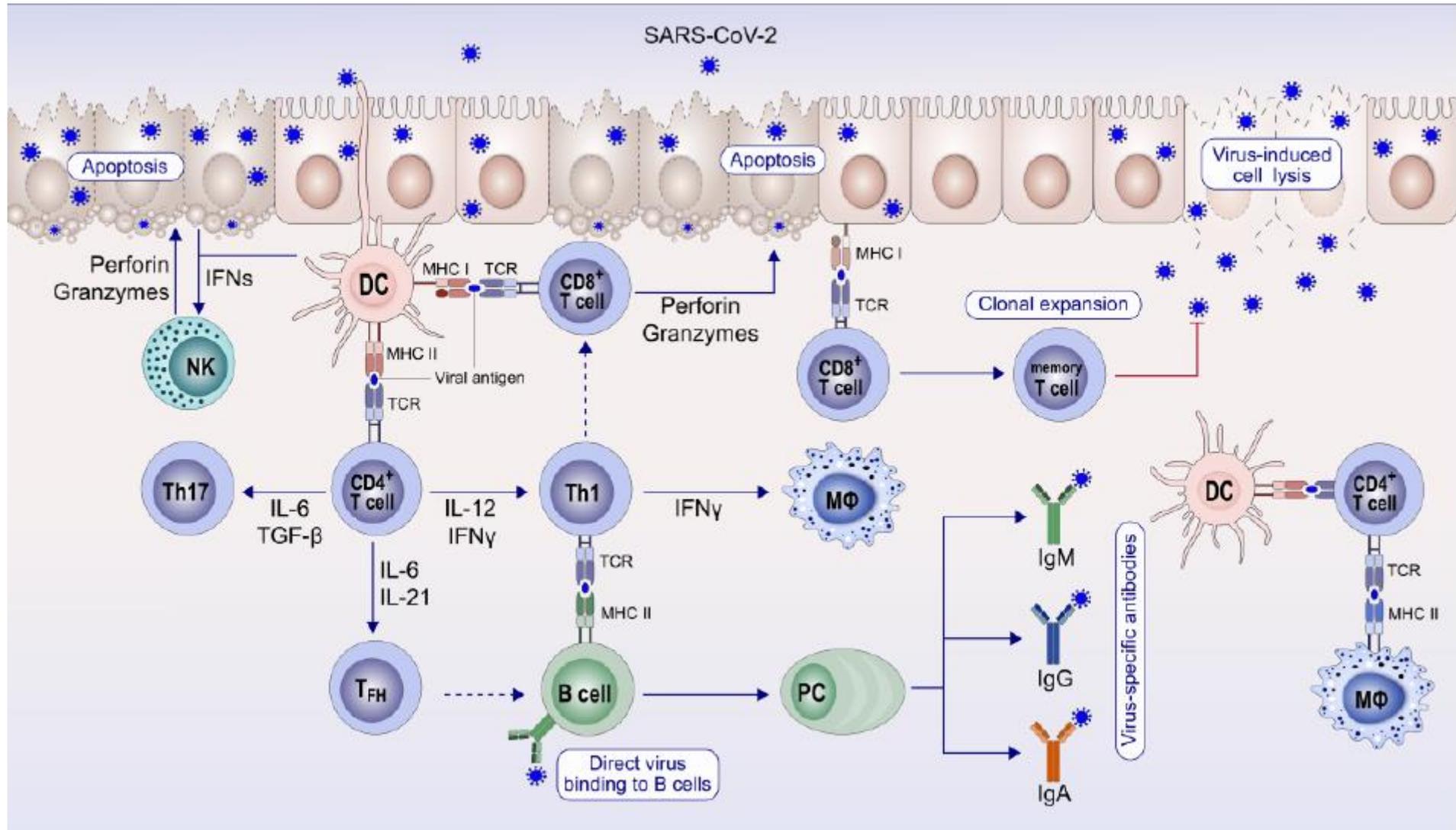


Particularités de l'infection par SARS-CoV-2 et Stratégies vaccinales

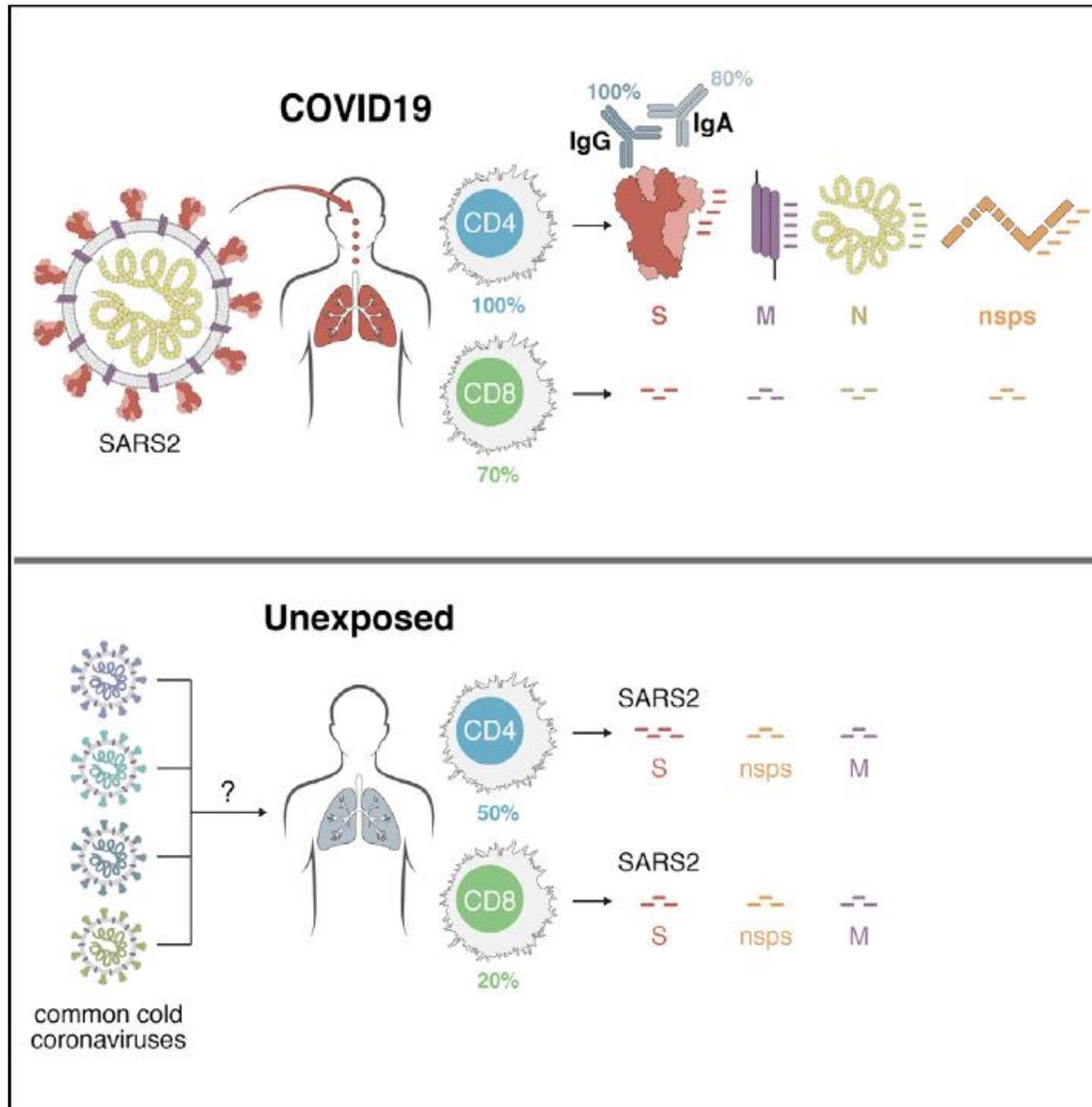
Hechmi Louzir

Institut Pasteur de Tunis

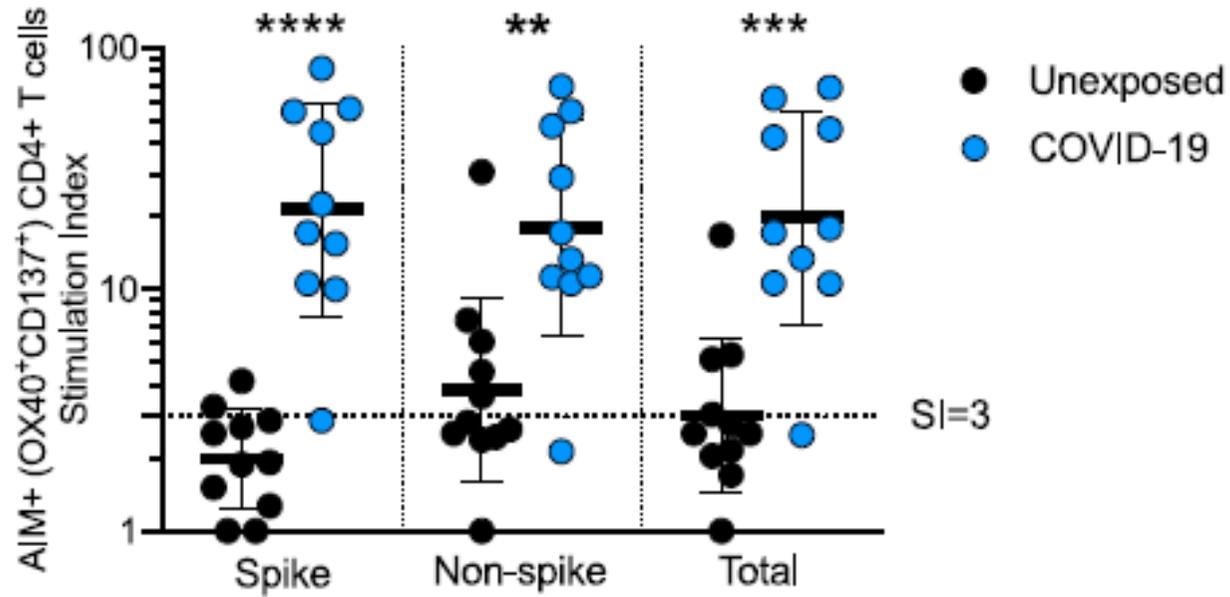
Réponse immunitaire: naturelle (NK) et spécifique (T, B)



Grifoni A, et al. Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. Cell. 2020 May 20:S0092-8674(20)30610-3



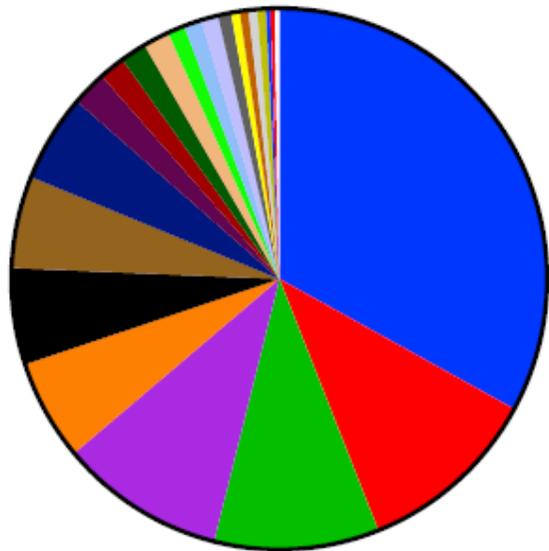
Grifoni A, et al. Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. Cell. 2020 May 20:S0092-8674(20)30610-3



Distribution of CD4 and CD8 epitopes by SARS-CoV-2 antigen

A

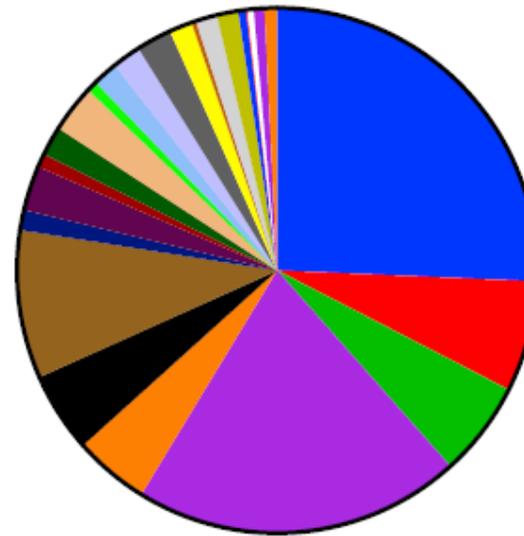
CD4⁺ T cells



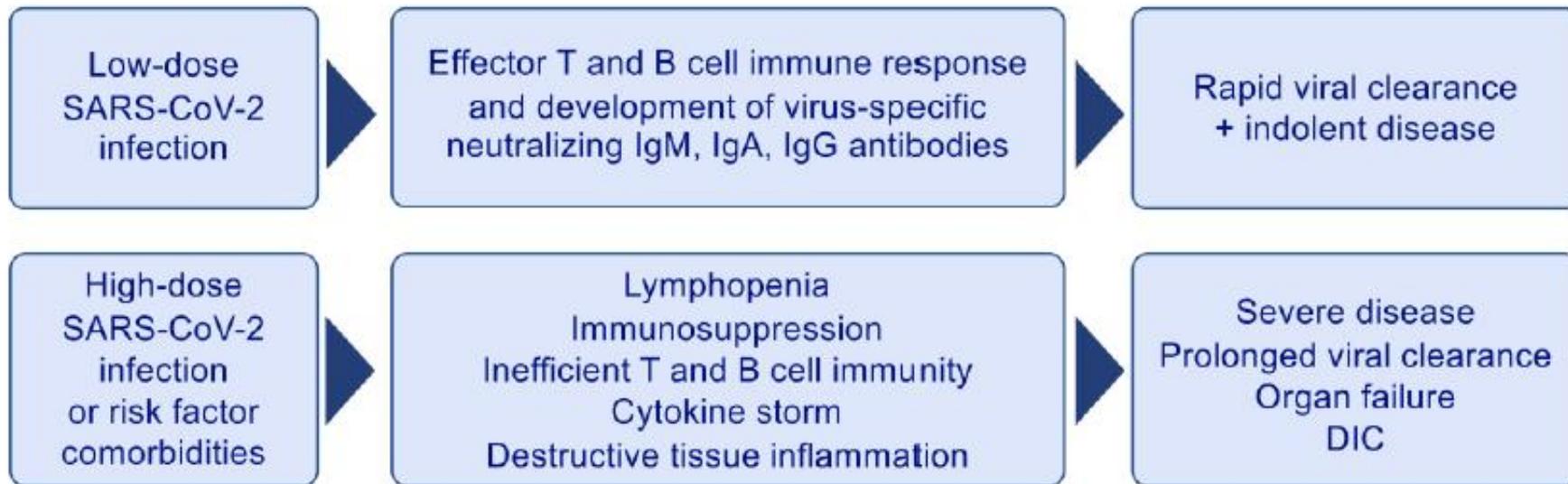
- 33% S
- 11% N
- 10% M
- 10% nsp3
- 6% nsp4
- 6% ORF3a
- 5% nsp12
- 5% ORF8
- 2% nsp13
- 2% ORF6
- 2% nsp2
- 2% nsp6
- 1% E
- 1% ORF7a
- 1% nsp16
- 1% nsp14
- 0.5% nsp5
- 0.5% nsp7
- 0.5% nsp8
- 0.5% nsp15

B

CD8⁺ T cells

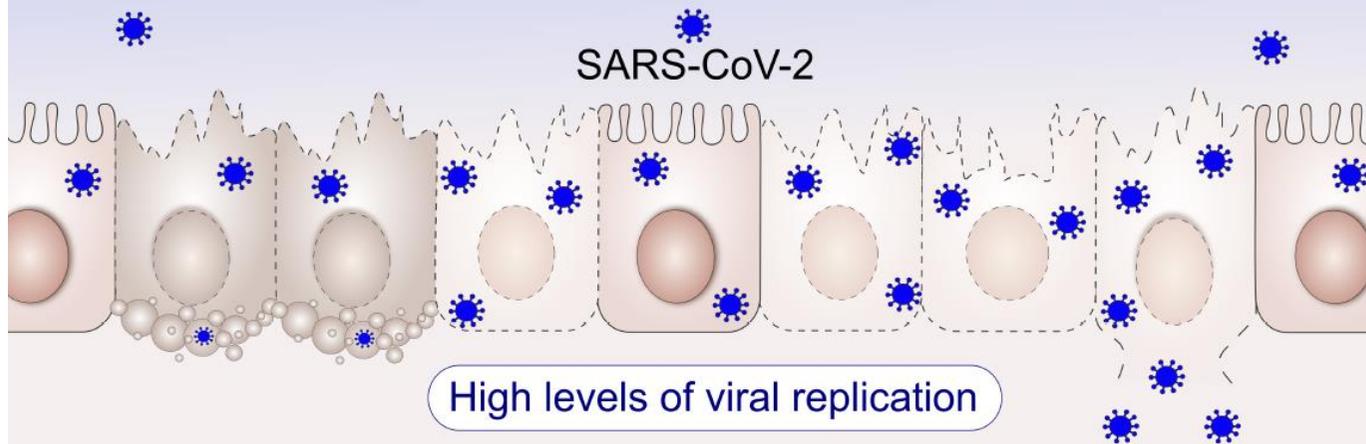


- 26% S
- 20% nsp3
- 9% nsp12
- 7% N
- 6% M
- 5% ORF3a
- 5% nsp4
- 3% nsp6
- 3% nsp13
- 2% nsp14
- 2% nsp16
- 2% nsp2
- 2% ORF7a
- 1% nsp5
- 1% nsp8
- 1% nsp15
- 1% ORF8
- 1% ORF6
- 1% nsp9
- 1% nsp1
- 1% E
- 0.5% nsp10
- 0.5% ORF10



Tay MZ et al. The trinity of COVID-19: immunity, inflammation and intervention. Nat Rev Immunol. 2020 Apr 28.

Severe COVID-19



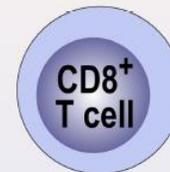
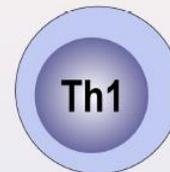
Cytokine storm: IFN- γ , IL-1 β , IL-6, IL-12, IL-17, IL-18, TNF- α

ARDS

High acute phase reactants

Cell free hemoglobin

Lymphopenia and eosinopenia



Microinflammed endothelium and DIC



Virus-infected endothelium?

Particularités de l'infection par SARS-CoV-2

- “ Hétérogénéité de l'**expression clinique** de l'infection (forme asymptomatique-maladie sévère)
- “ Hétérogénéité et intensité de la **réponse immune** (réponse anticorps et cellulaire)
- “ Rôle de la **charge virale** (dans l'expression clinique et la transmission)

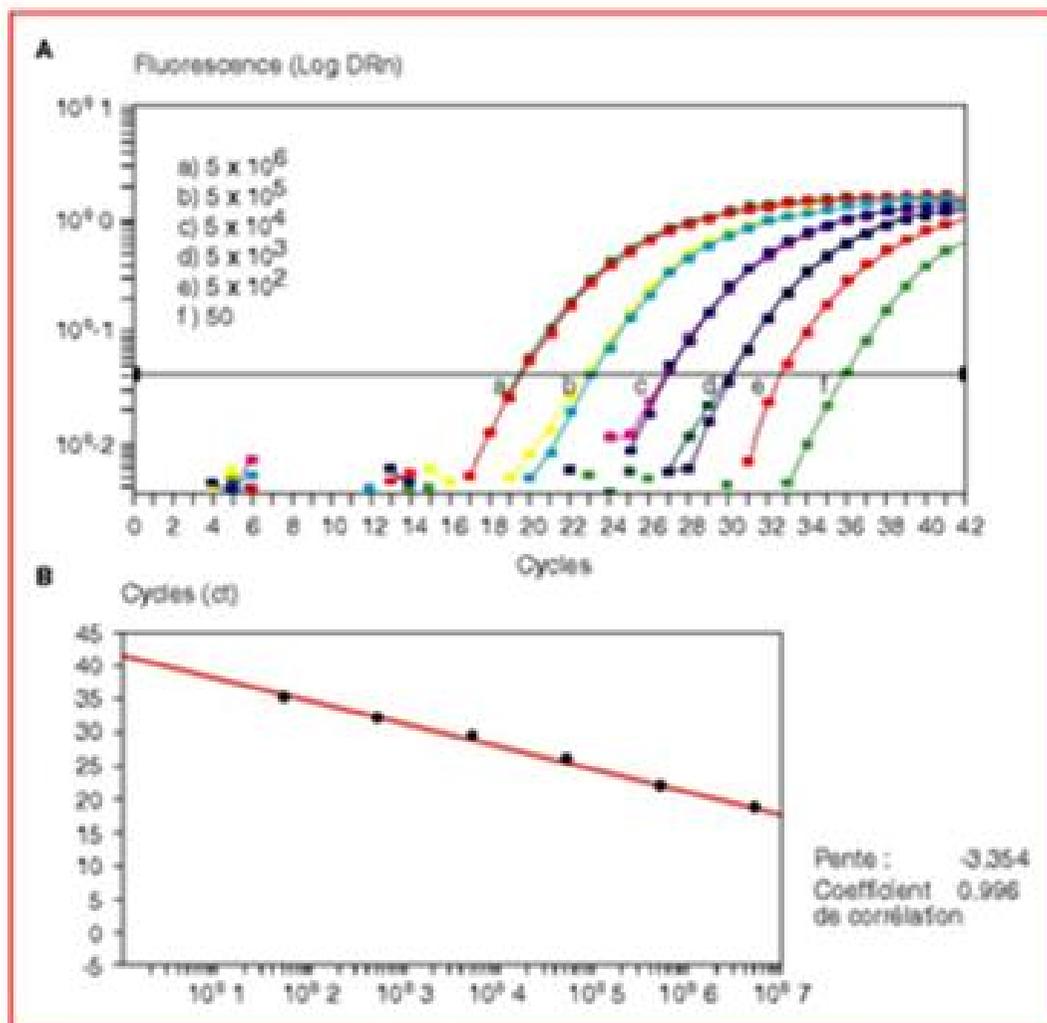
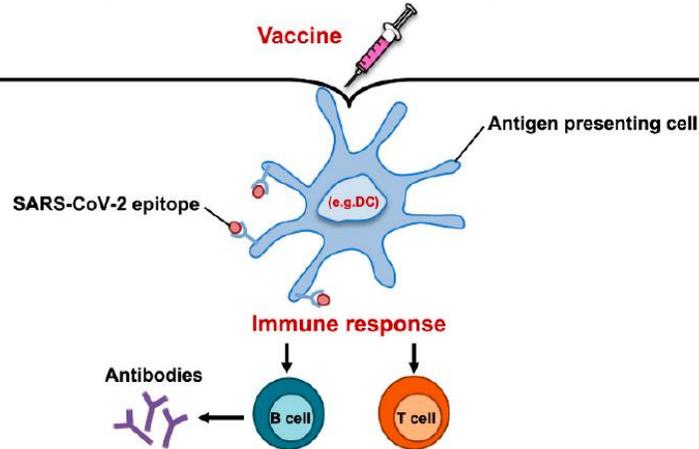
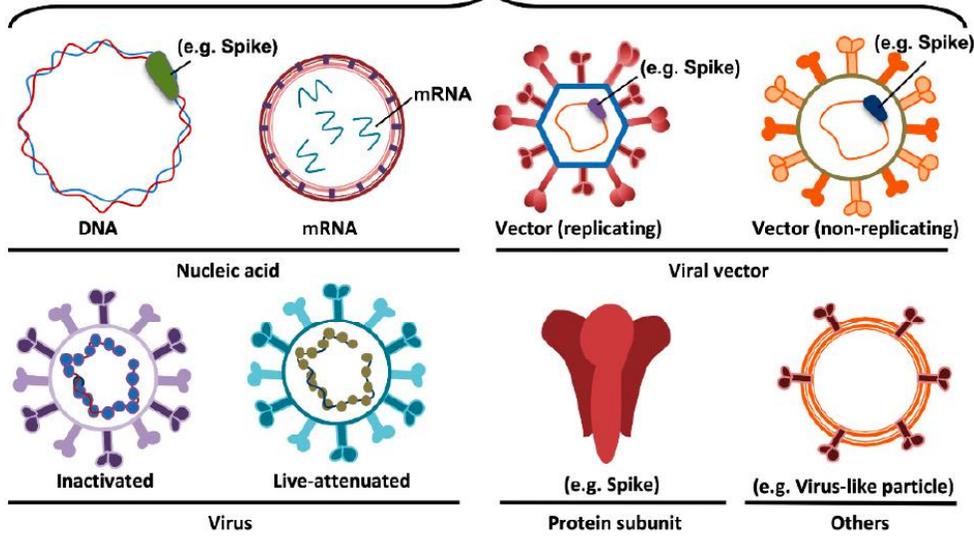
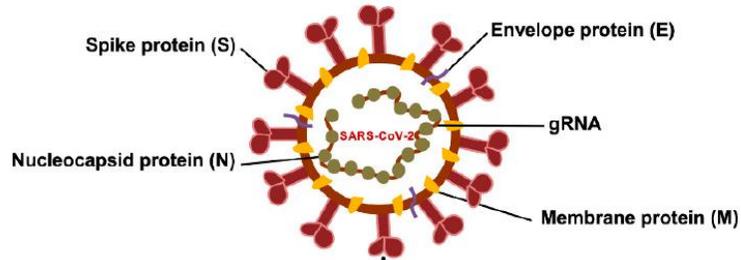


Figure 3 : Schéma PCR en temps réel

Notion de « corrélats de protection »

- “ Après infection par SARS-CoV-2 (avec ou sans symptômes): il y a le développement d'une réponse immune humorale (**anticorps neutralisants**, notamment contre la protéine S) et d'une **réponse cellulaire T** (TCD4+ et **TCD8+**).
- “ Cette réponse immune est associée à une résistance à la réinfection (durée > 12 mois).
- “ Les mécanismes précis ainsi que leurs parts dans la contribution à la résistance contre le virus ne sont pas bien connus.
- “ Protection contre l'**infection/maladie**

Vaccine platforms



Effacité d'un vaccin

Vaccine efficacy is measured by calculating the incidence rates (attack rates) of disease among vaccinated and unvaccinated persons and determining the percentage reduction in the incidence rate of disease among vaccinated persons compared to unvaccinated persons. The basic formula is:

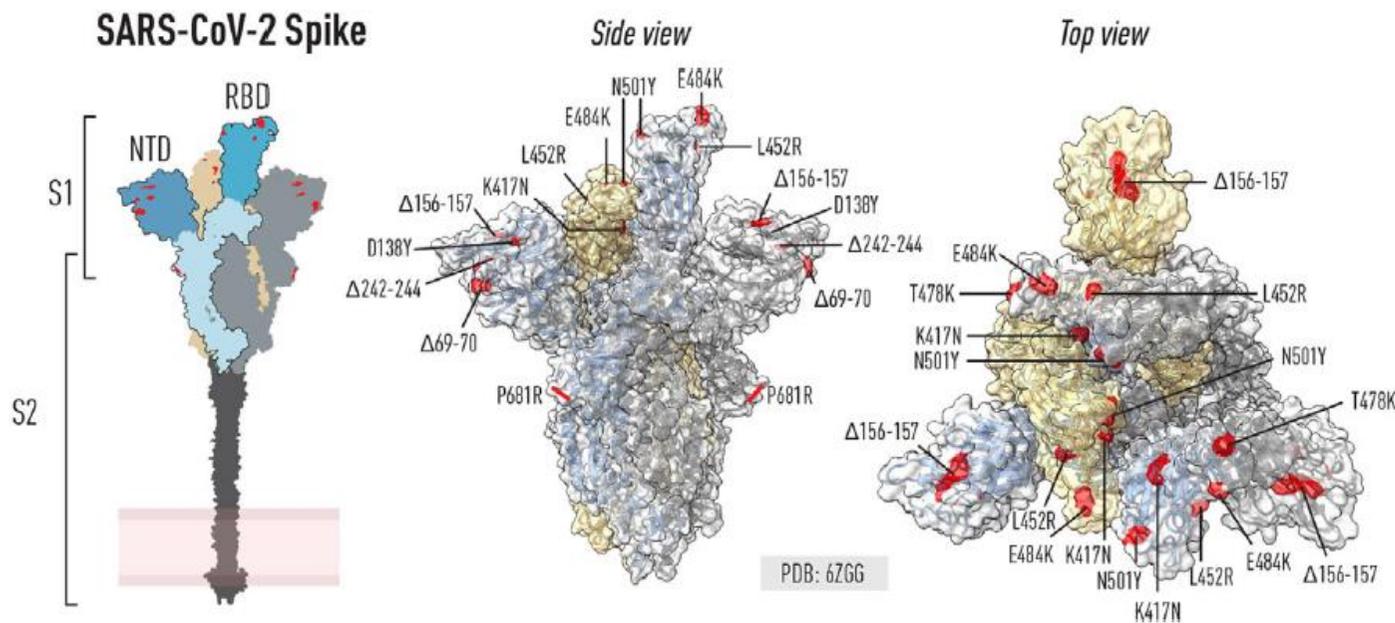
$$VE = \frac{ARU - ARV}{ARU} \times 100$$

where VE = vaccine efficacy, ARU = attack rate in the unvaccinated population, and ARV = attack rate in the vaccinated population.

VOCs



Immunity to SARS-CoV-2 induced by infection or vaccination / Castro Dopico et al.



Variants of concern

Alpha (B.1.1.7)

N501Y, Δ69-70

Beta (B.1.351)

Δ242-244, K417N, E484K, N501Y

Gamma (P.1)

D138Y, K417N, E484K, N501Y

Delta (B.1.617.2)

Δ156-157, T478K, L452R, P681R

Alpha (B.1.1.7) variant (United Kingdom)

Possesses the *N501Y* mutation

Efficacy of convalescent sera, monoclonal antibody(mAb) therapy, & vaccines:

- **Refractory** to mAb therapy
- **Retained activity** of REGN-COV2 & bamlanivimab/etesevimab
- **Normal efficacy** of vaccines & convalescent sera



Beta (B.1.351) variant (South Africa)

Possesses characteristic mutations *N501Y, E484K, K417N*

Efficacy of convalescent sera, monoclonal antibody(mAb) therapy, & vaccines:

- **Resistant** to mAb therapy, convalescent sera, & Oxford-AstraZeneca
- **Retained activity** of REGN-COV2 & bamlanivimab/etesevimab
- **Moderate resistance** to Pfizer-BioNTech, Moderna, Novavax, and J&J



SARS-CoV-2 Variants of Concern

Delta (B.1.617) variant (India)

Possesses characteristic *DIID, G14D, L45R, E484q and P681R* mutations

Efficacy of convalescent sera, monoclonal antibody(mAb) therapy, & vaccines:

- **Refractory** to mAb therapy
- **Resistant** to convalescent sera
- **Mild resistance** to two-dose Pfizer and AstraZeneca regimens



Gamma (P.1) variant (Brazil)

Possesses characteristic mutations *N501Y, E484K*

Efficacy of convalescent sera, monoclonal antibody(mAb) therapy, & vaccines:

- **Reduced neutralization** by mAb therapy
- **Resistant** to convalescent sera
- **Normal efficacy** of Pfizer-BioNTech



Objectif de la Vaccination/Résultats attendus

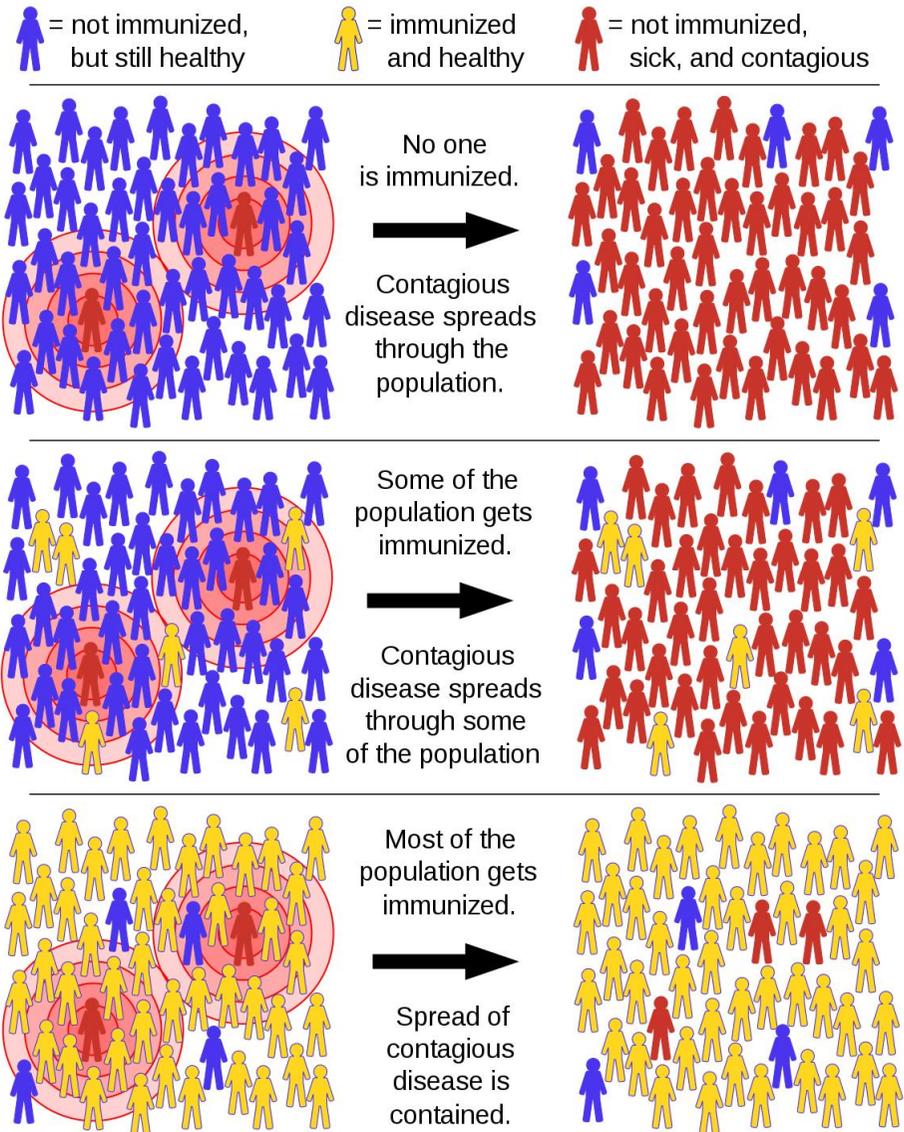
- ” Réduire la morbidité par SARS-CoV-2
- ” Réduire la mortalité par SARS-CoV-2
- ” Freiner la circulation du virus.
- ” Vaccination massive permet (?) d'éviter l'émergence de variants.
- ” Reprise de la vie normale

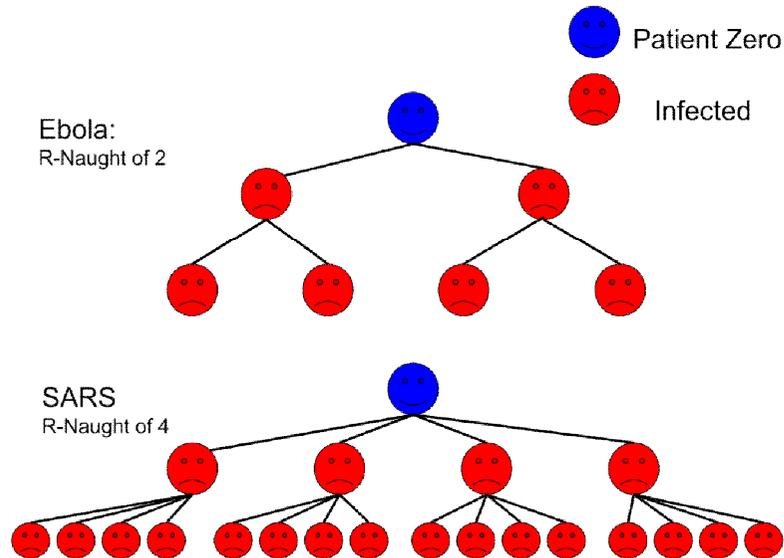
Il faut à ce stade distinguer:

- 1- La protection individuelle, directe
- 2- La protection de groupe, indirecte

Herd Immunity

Herd immunity occurs **when a large portion of a community (the herd) becomes immune to a disease**, making the spread of disease from person to person unlikely. As a result, the whole community becomes protected — not just those who are immune.





R_0

- R_0 : peut varier en fonction de la durée de la phase contagieuse, la probabilité d'une transmission lors du contact, le nombre de contacts, etc. (facteurs socio-économiques, environnementaux).
- Le R_0 décrit l'évolution de la maladie à ses débuts, lorsqu'une fraction $(1 - f)$ d'une population a été infectée (et immunisée), les contacts de cette fraction ne conduit pas à des contaminations supplémentaires et seule la fraction f reste susceptible.
- $R = f * R_0$
- Le R_0 permet de calculer la proportion minimale au sein d'une population (P) qui doit être immunisée.
- $P = 1 - 1/R_0$, ou encore : $f = 1/R_0$



non-immune



disease



immune

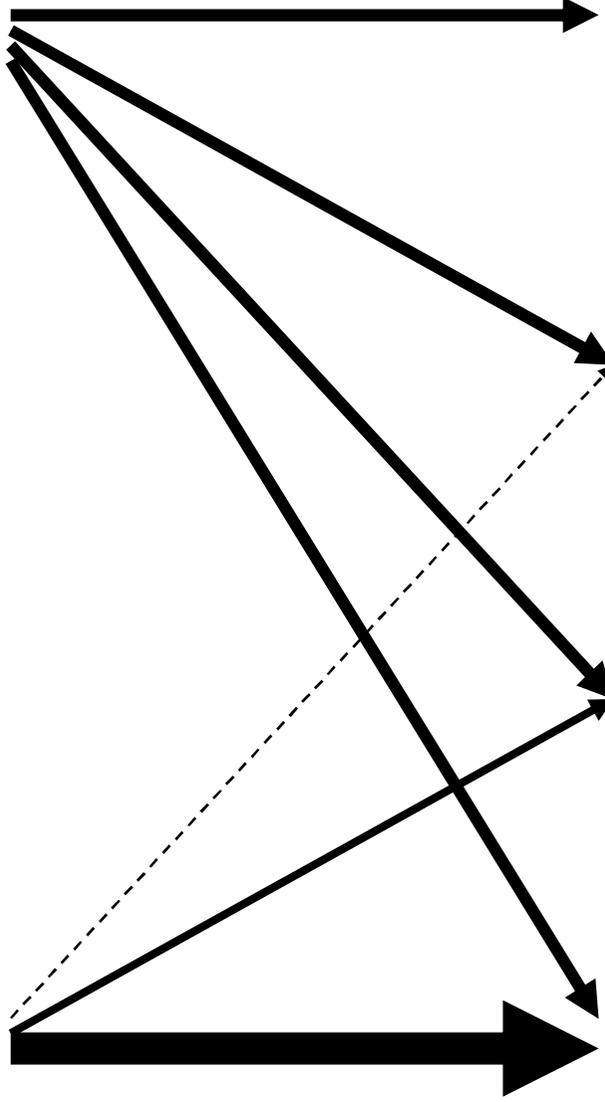


healthy

Increasing immunity



Low force of infection

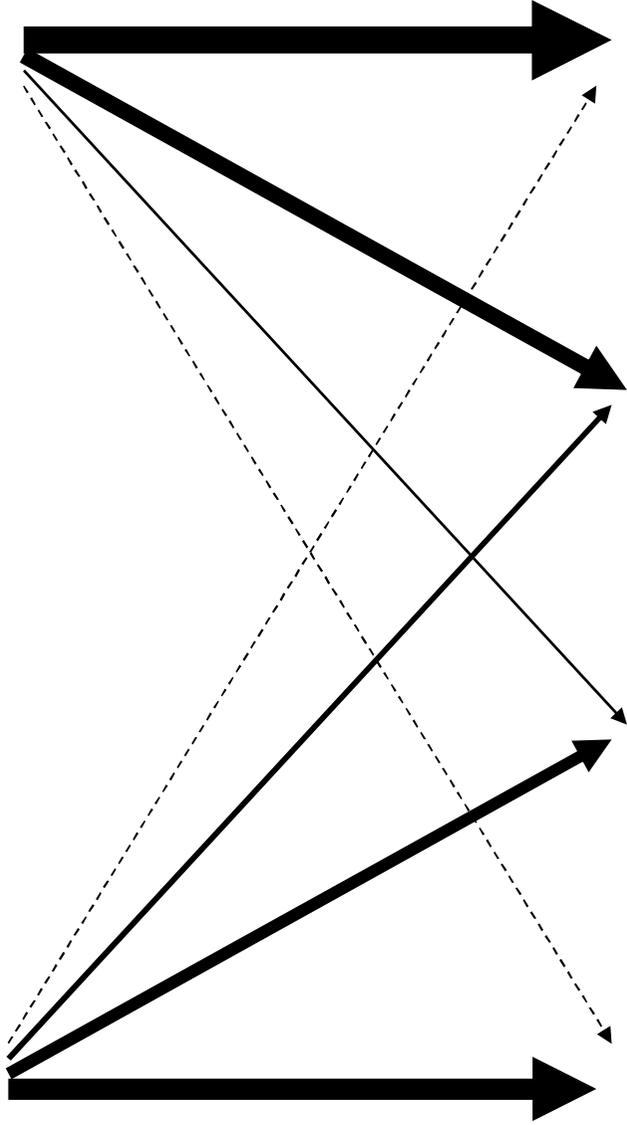


Increasing severity

Increasing immunity



High force of infection



Increasing severity

