

## ***T-CELL EXHAUSTION IMPACTS SPECIFIC ADAPTIVE RESPONSES AFTER VACCINATION IN SOLID ORGAN TRANSPLANT***

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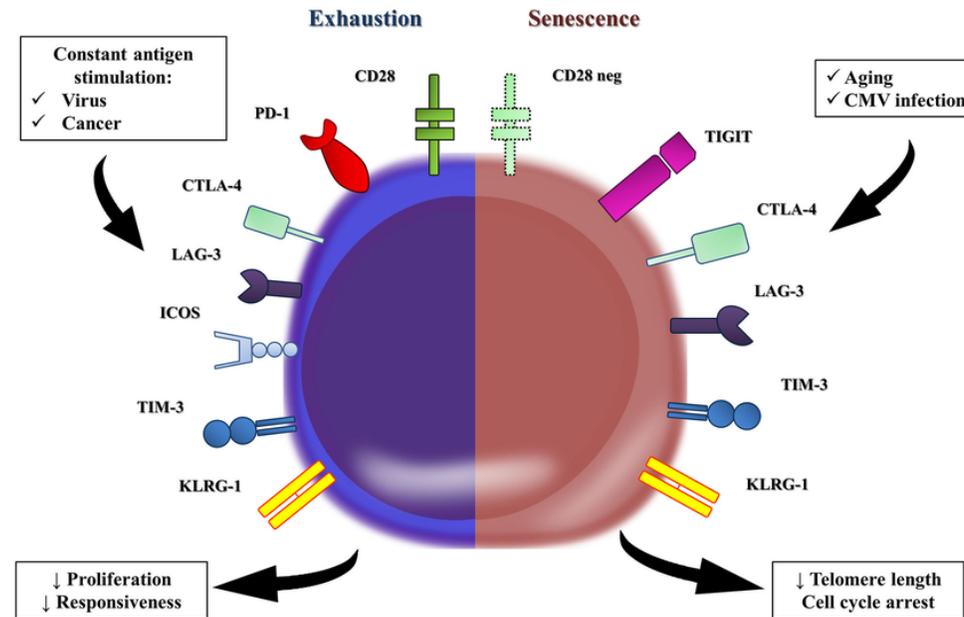
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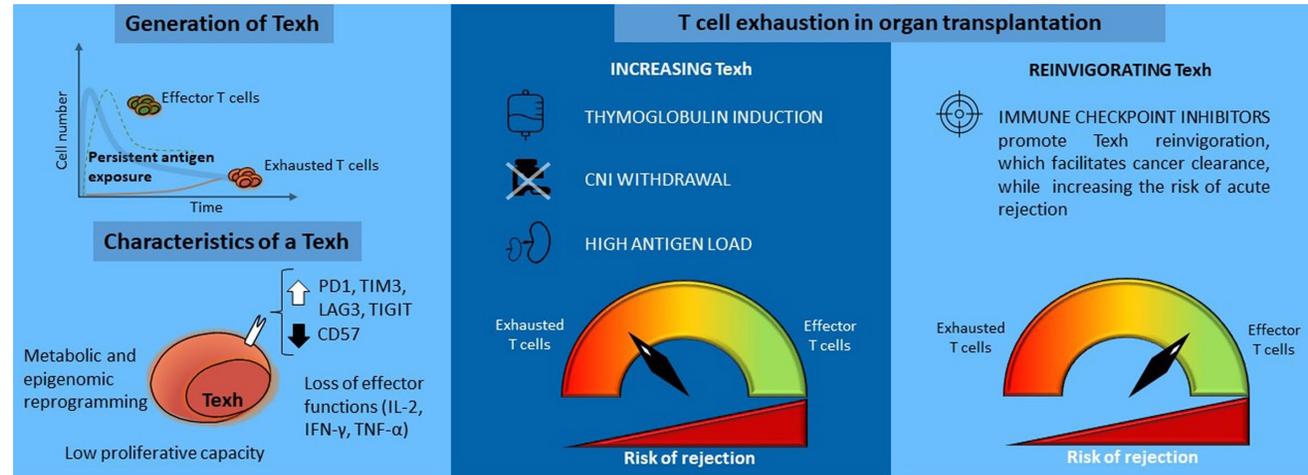
# BACKGROUND: T-cell exhaustion and senescence

Exhaustion in T cells is a dysfunctional state characterized by a progressive loss of effector functions that has been classically associated to repeated exposure to foreign or self-antigens as well as high antigen loads



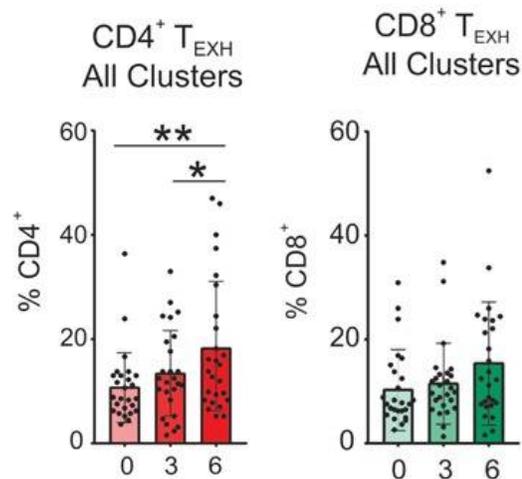
After repetitive antigen stimulation, T cells may also undergo a senescent state, a biological feature defined by a functional immune deficiency characterized by a permanent state of cell cycle arrest

# BACKGROUND: T-cell exhaustion in transplantation

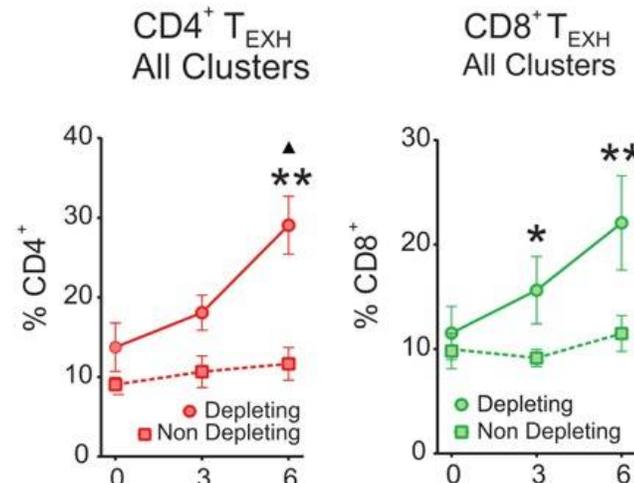


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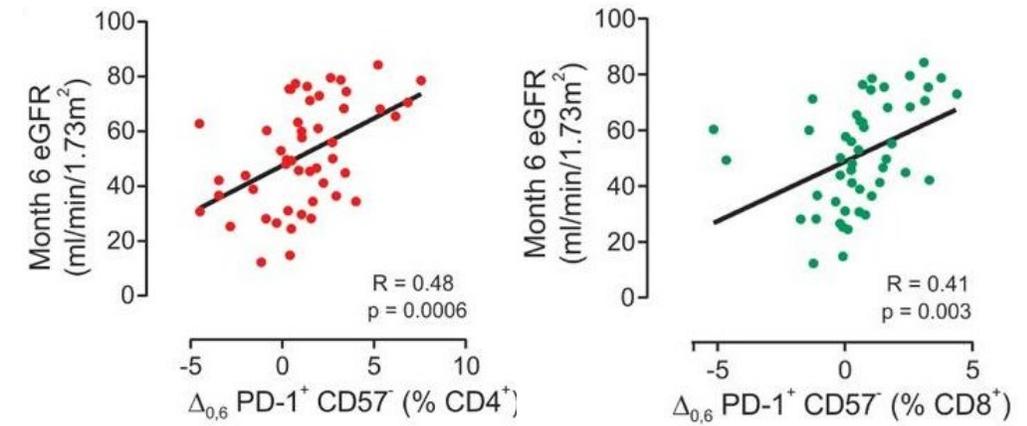
## Time after transplant



## Immunosuppression (ATG)

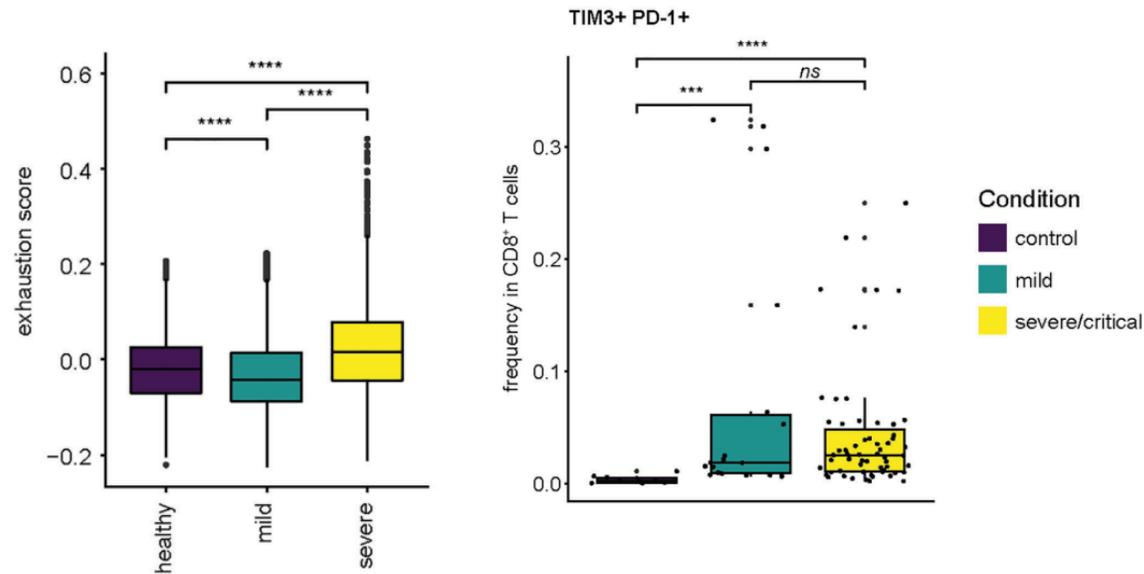


## Renal function

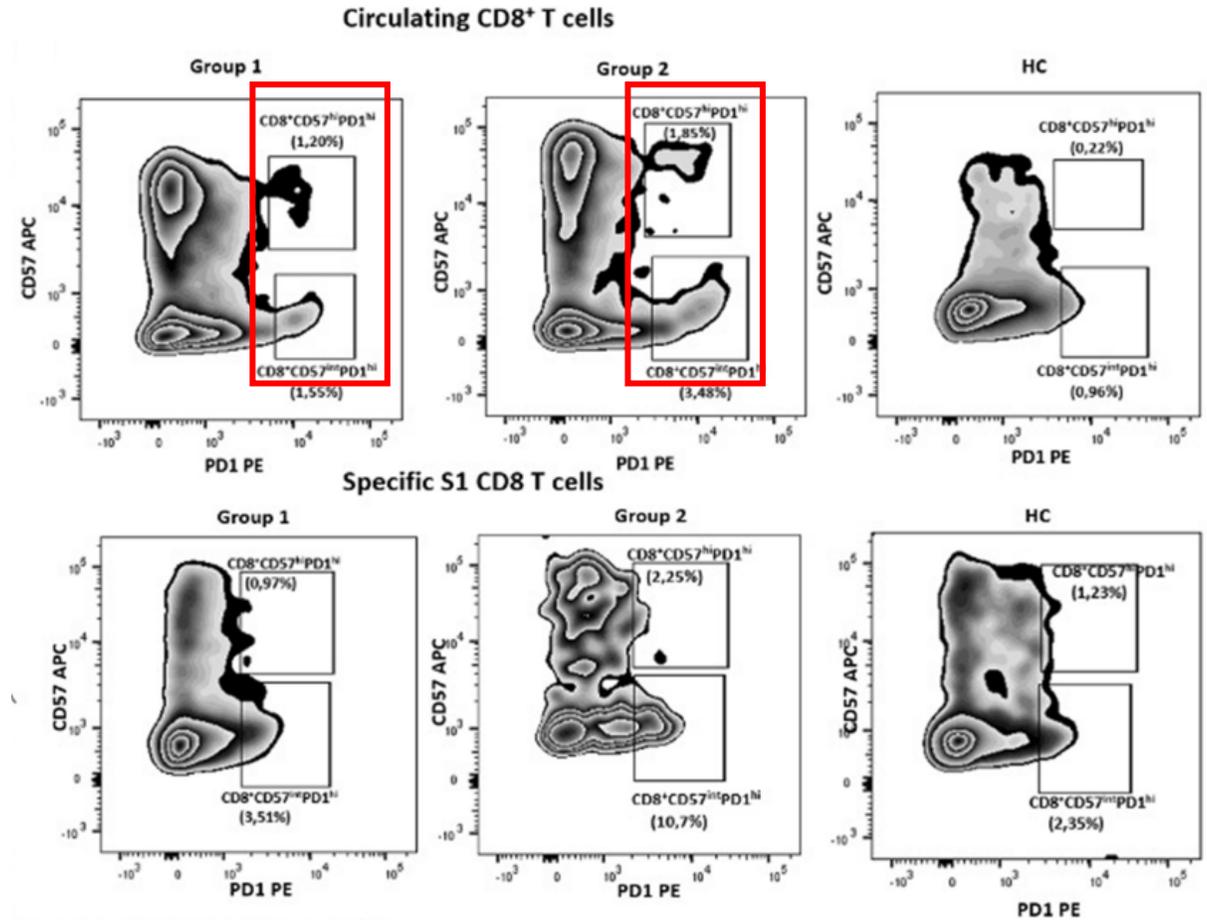


# BACKGROUND: T-cell exhaustion in SARS-CoV-2

## INFECTION



## VACCINATION



# HYPOTHESIS AND OBJECTIVES

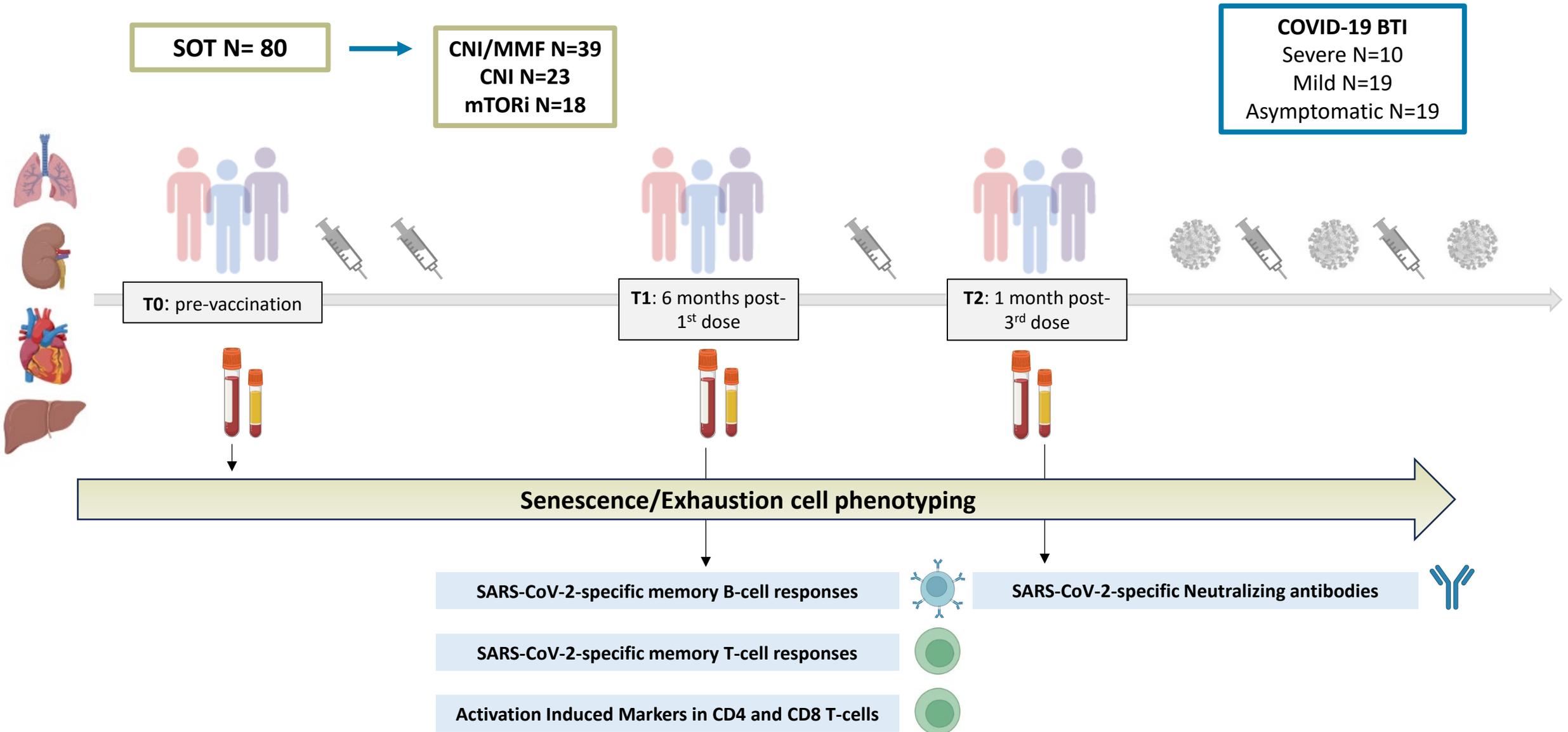
**Exhausted/Senescent T-cells** can impact the adaptive functional response after subsequent **SARS-CoV-2 mRNA vaccine** boosters in **Solid Organ Transplant patients**

## OBJECTIVES:

1. Decipher if the role of T-cell exhaustion/senescence **prior to active immunization** can modulate the development of immune memory responses in SOT
2. Investigate the value of these cell populations in identifying the patients **more susceptible** to develop severe forms of COVID-19 after vaccination



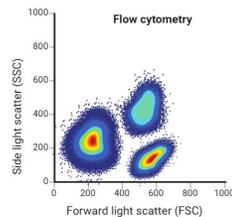
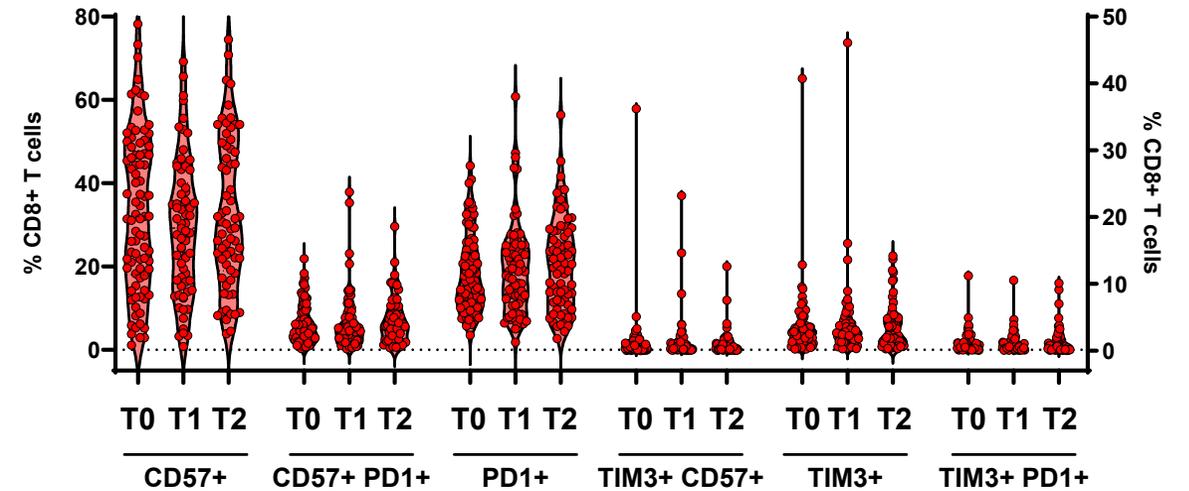
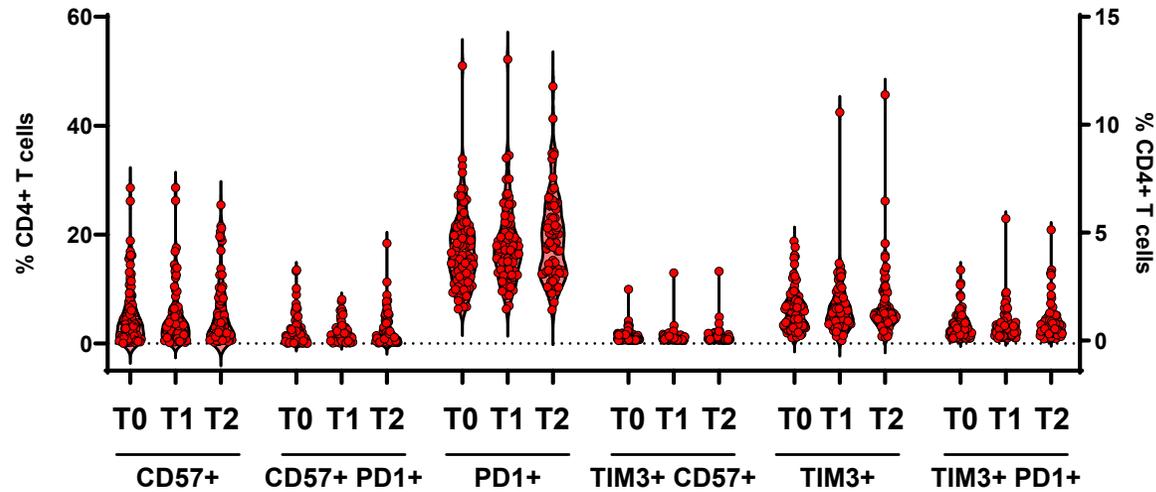
# STUDY DESIGN



# RESULTS: No increase in T-cell exhaustion/senescence after vaccination

CD4 T cells

CD8 T cells

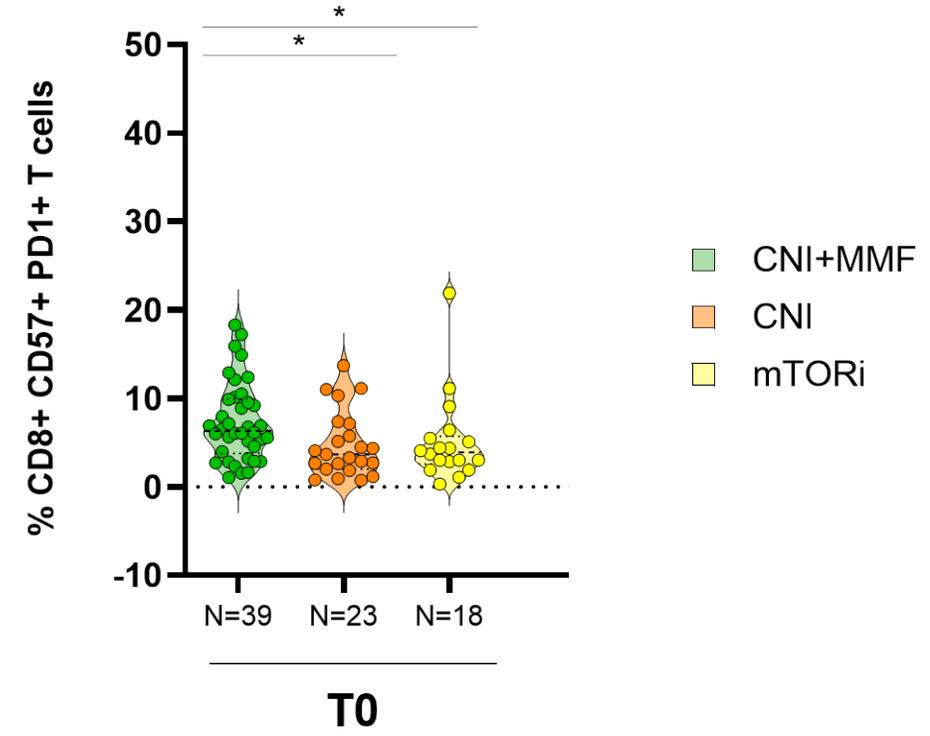
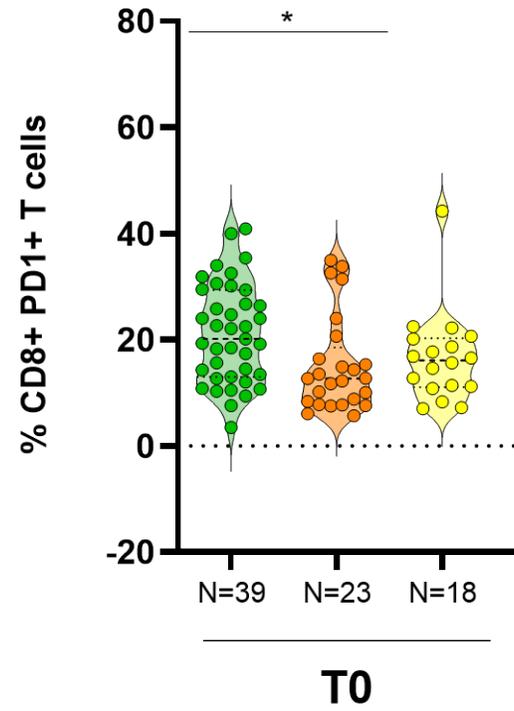
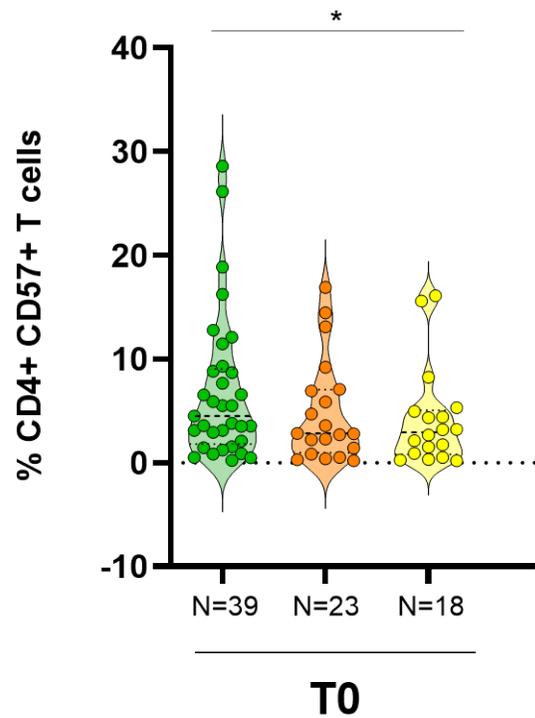


*Exhaustion/Senescence cell phenotyping: CD57, TIM3 and PD1 markers*

# RESULTS: Immunosuppression impacts baseline T-cell exhaustion/senescence

CD4 T cells

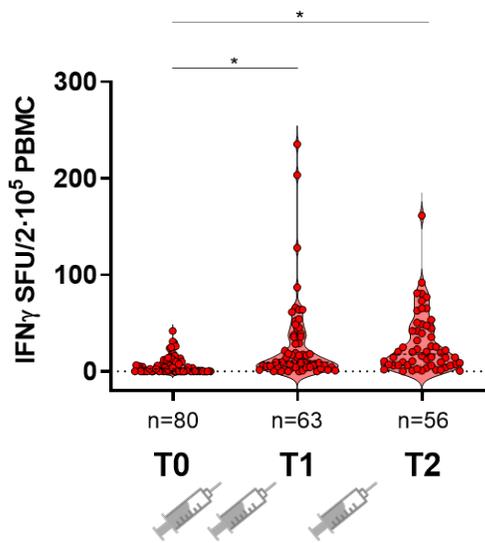
CD8 T cells



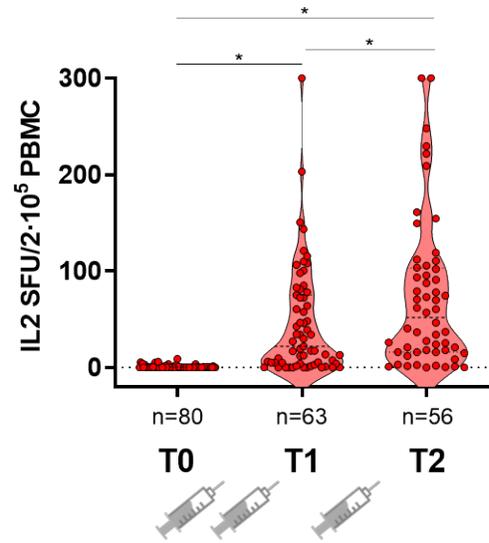
# RESULTS: Functional immune responses after vaccination

## TH1 T CELL FREQUENCIES

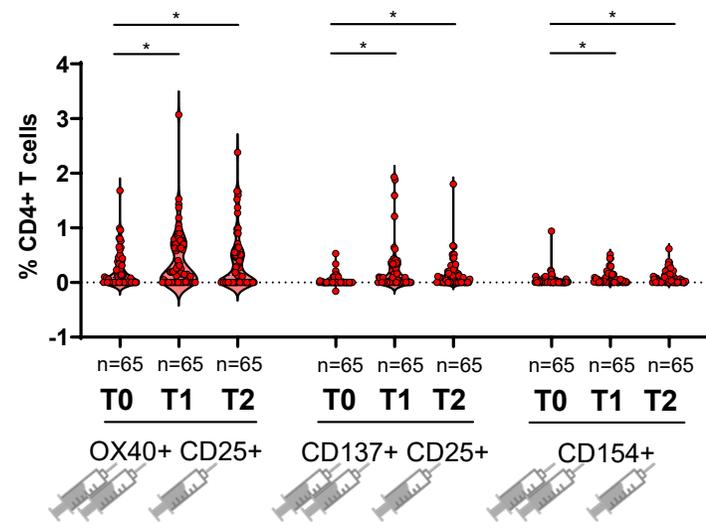
### SARS-CoV-2 specific IFN- $\gamma$ T-cells



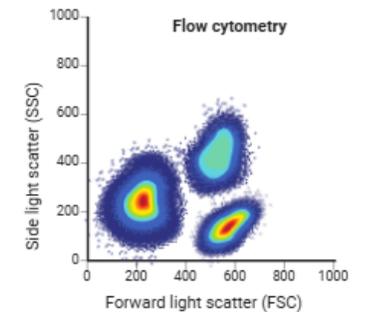
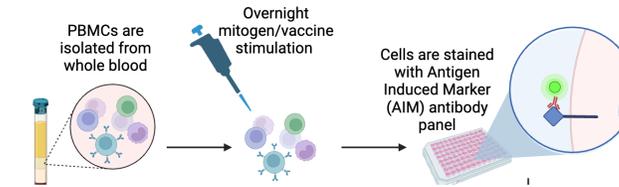
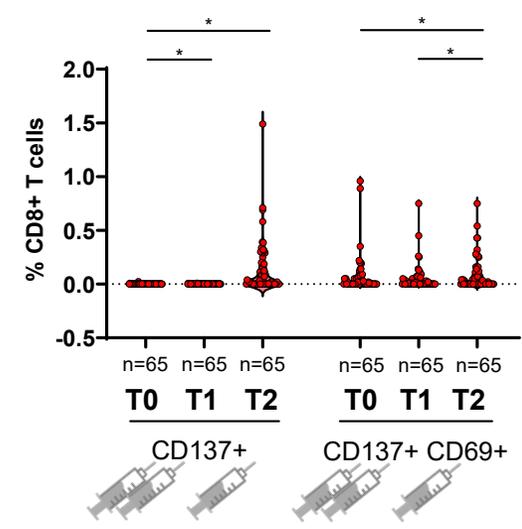
### SARS-CoV-2 specific IL-2 T-cells



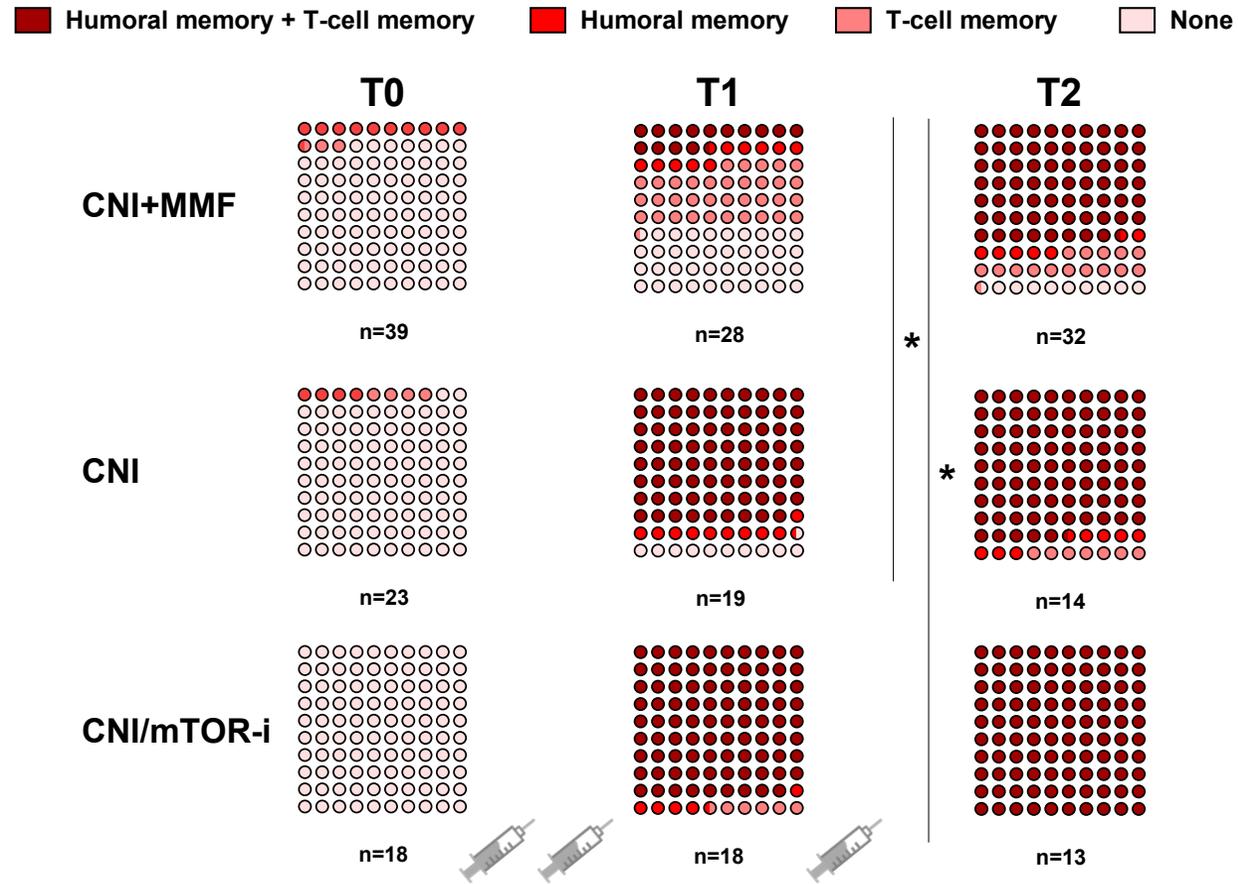
### AIM+ CD4+ T cells



### AIM+ CD8+ T cells



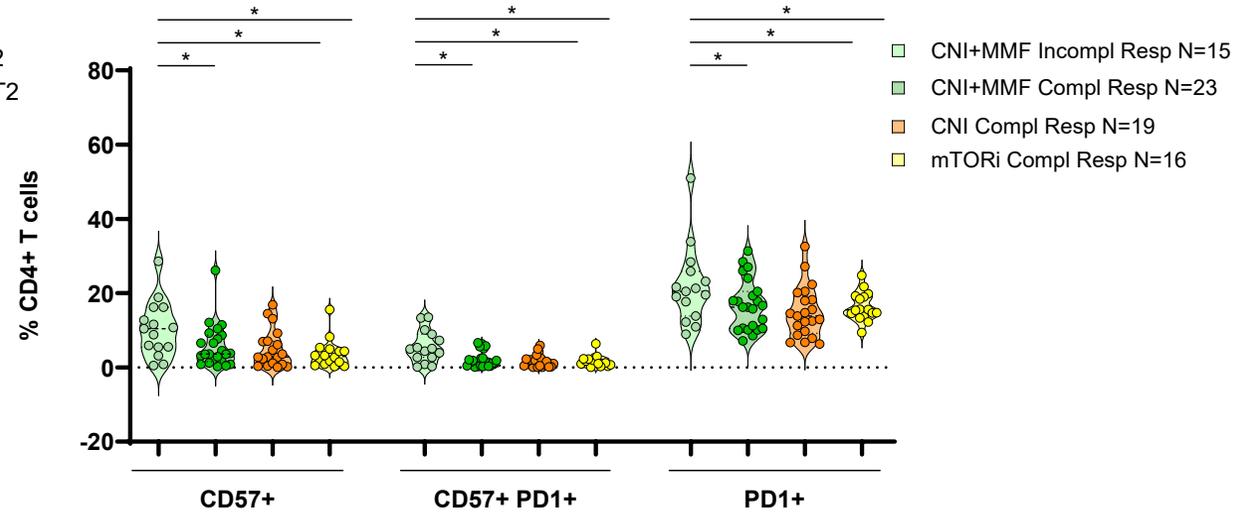
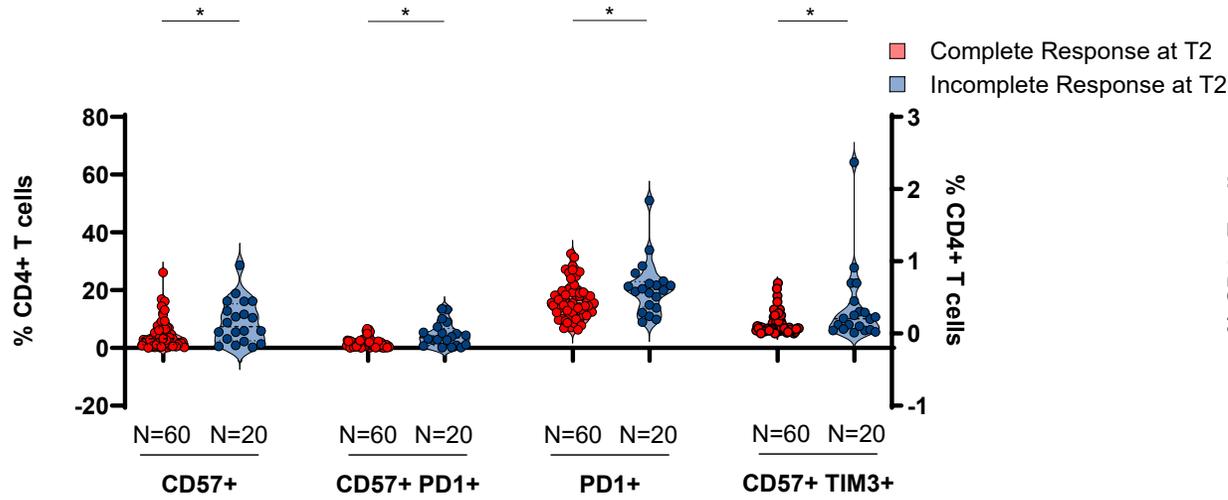
# RESULTS: Functional immune responses after vaccination



**60 COMPLETE RESPONDERS**

**20 NON-RESPONDERS**

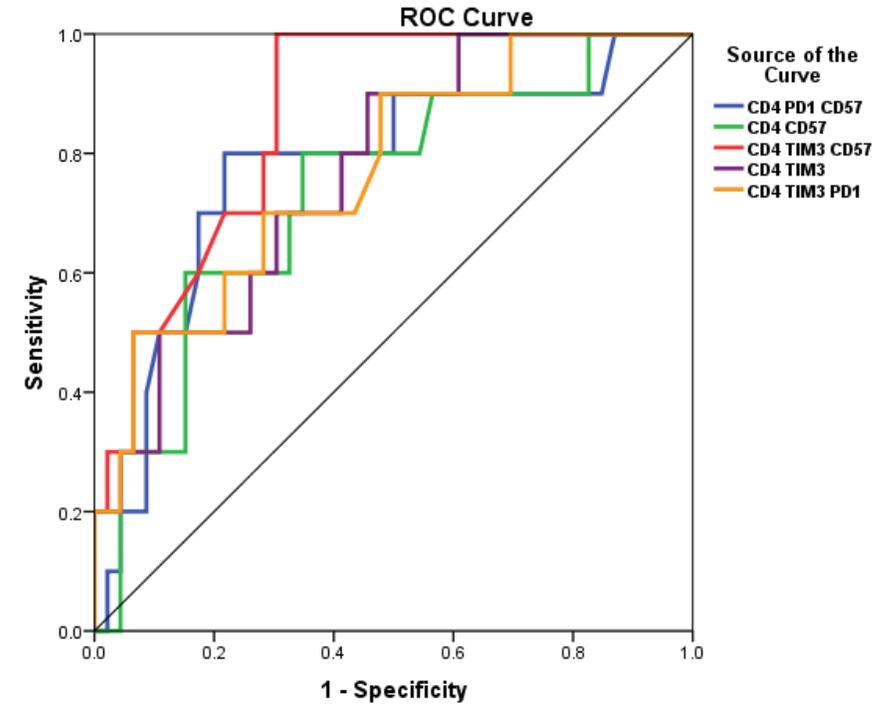
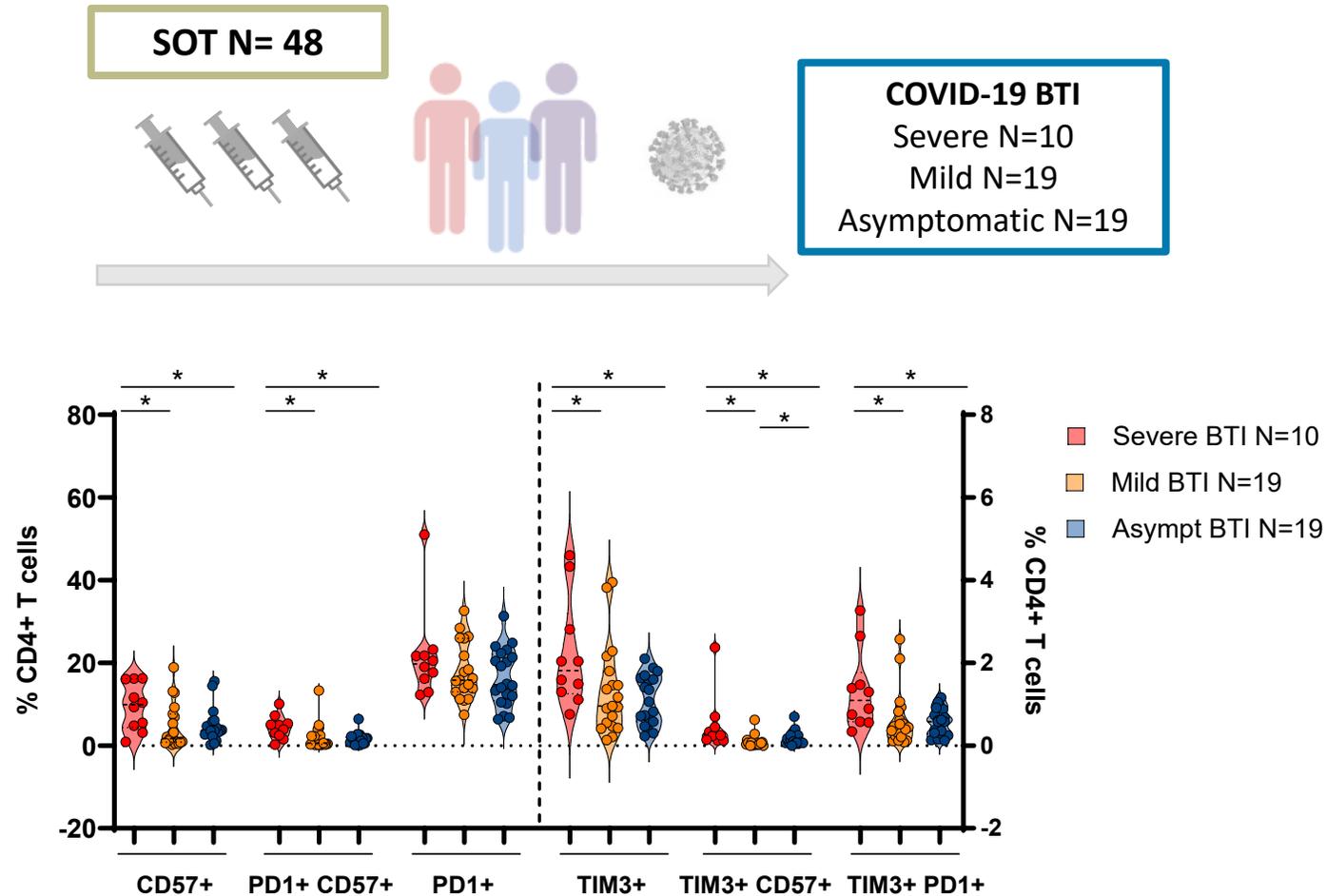
# RESULTS: Interconnection between adaptive immune responses and T-cell exhaustion/senescence



***High percentages of exhausted/senescent CD4 T-cells at baseline associates with incomplete adaptive immune responses***

***Patients in SoC IS non-responding to active immunization display higher levels of dysfunctional T-cells***

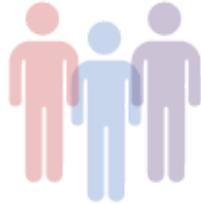
# RESULTS: BTI severity prediction



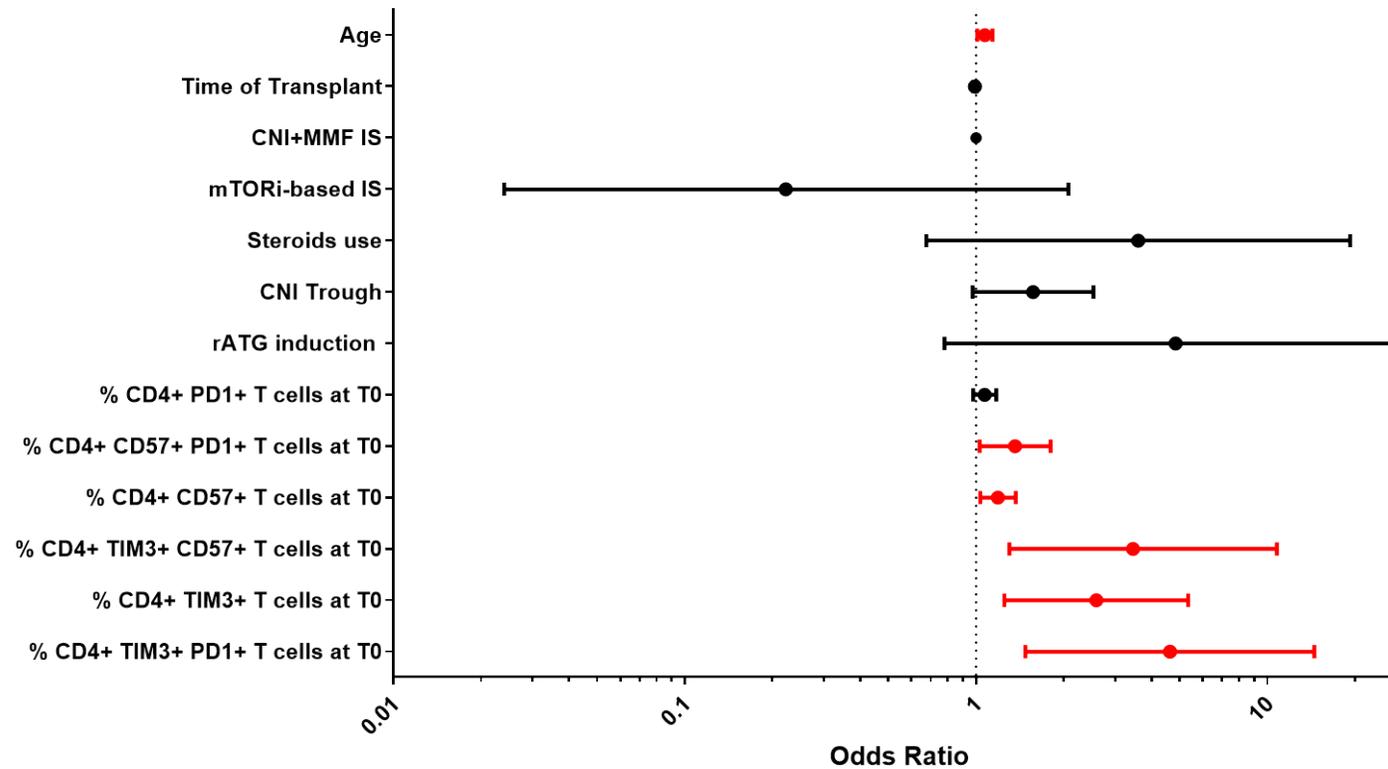
Cell Phenotypes	AUC	Asymptotic Sig.
CD4+ PD1+ CD57+	0.792 (0.608-0.976)	<b>p=0.007</b>
CD4+ CD57+	0.762 (0.578-0.945)	<b>p=0.016</b>
CD4+ TIM3+ CD57+	0.883 (0.783-0.984)	<b>p&lt;0.001</b>
CD4+ TIM3+	0.769 (0.607-0.931)	<b>p=0.013</b>
CD4+ TIM3+ PD1+	0.801 (0.638-0.965)	<b>p=0.005</b>

# RESULTS: BTI severity prediction

SOT N= 48



COVID-19 BTI  
Severe N=10  
Mild N=19  
Asymptomatic N=19



# SUMMARY

- We did not observe an increase in the percentages of exhausted/senescent T-cells after vaccination.
- T-cell exhaustion/senescent phenotypes seem to drive poor antiviral immune responses after SARS-CoV-2 booster vaccination, mainly for CD4+ T cells.
- Patients not developing memory immune responses exhibited a significantly more exhausted/senescent phenotypes prior to vaccination.
- CD4+ exhausted/senescent T cells seem to favour severe BTI if infected.

***Our study adds new insight in the implications of T-cell exhaustion/senescence driving unsuccessful protective immunity after booster vaccination in SOT and may have relevant implications in different anti-viral immunization***

# ACKNOWLEDGEMENTS

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