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IMMUNE PARAMETERS ASSOCIATED WITH LOWER SARS-CoV-2 VACCINATION RESPONSE IN OLD PEOPLE

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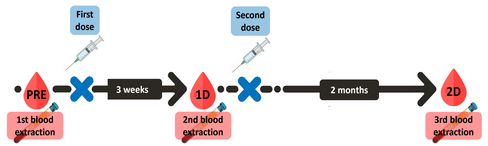
Background

Previous studies described lower frequencies of SARS-CoV-2 neutralizing antibodies in old people after the vaccination with SARS-CoV-2 BNT162b2 mRNA vaccine[1].

The aim of the study was to investigate the major immune alterations in old people, in terms of both SARS-CoV-2 specific adaptive and innate immunity, associated to a lower response to the SARS-CoV-2 BNT162b2 mRNA vaccine.

Methods

DESIGN AND PARTICIPANTS



	All participants (n=54)	Elderly participants (n=21)	Young participants (n=33)
Age (years)	49.5 [28 – 73]	73 [72 – 74]	29 [26 –48.5]
Sex (Female sex), n (%)	35 (64.8)	13 (61.9)	22 (66.7)

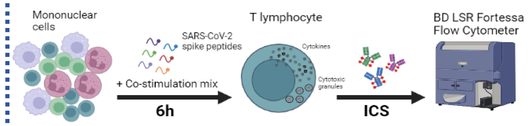
HUMORAL RESPONSE

ELISA: Antibodies (IgG) against receptor-binding domain (RBD) of the spike protein of SARS-CoV-2 in plasma

STUDIED IMMUNE CELL TYPES

- **T lymphocytes**
  - CD4+T: Naïve (CD45RA+ CD27+); Central Memory (CD45RA- CD27+); Effector Memory (CD45RA- CD27-); TEMRA (CD45RA+ CD27-)
  - CD8+T
- **Dendritic Cells**
  - mDCs: CD1c+ mDCs; CD141+ mDCs; CD16+ mDCs
  - pDCs
- **Monocytes**: Classical (CD14++ CD16-); Intermediate (CD14++ CD16+); Non classical (CD14+ CD16++)

SARS-CoV-2 SPECIFIC T CELL RESPONSE



R10 medium: 10% FBS, 1% Pen/Strep, 1% L-Glu in RPMI

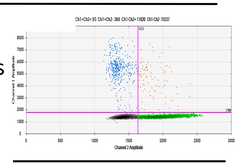
Co-stimulation mix: anti-CD49d, anti-CD28, Monensin, Brefeldin, anti-CD107a BV650

ICS (Intracellular Cytokine Staining): Degranulation (CD107a), Cytotoxicity (Perforin, PRF), Cytokines (IFN-γ, TNF-α and IL-2)

THYMIC FUNCTION

DNA extraction

Droplet digital PCR: T cell receptor excision circles (TRECs) measurement, ratio sj-TREC/DβJβ-TRECs
→ Reference gene: RPP30



INNATE CELLS FUNCTION

	Stimulation	Incubation
pDCs	**TLR9:** 1uM CpG-A	18h
mDCs	**TLR3:** 2ug/ml Poly I:C	24h
Monocytes	**TLR4:** 0.5ng/ml LPS	5h

- IFNα production (ELISA)
- Activation markers CD86+CD40+, CD83+ and IDO+ (Flow Cytometry)
- IL-6, IL-1α and TNFα (ICS, Flow Cytometry)

Results

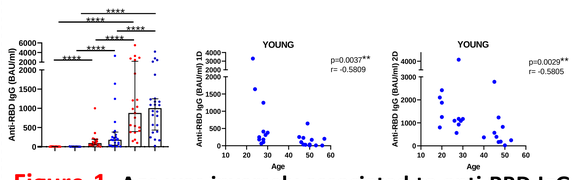


Figure 1. Age was inversely associated to anti-RBD IgG levels in plasma after BNT162b2 mRNA SARS-CoV-2 vaccination.

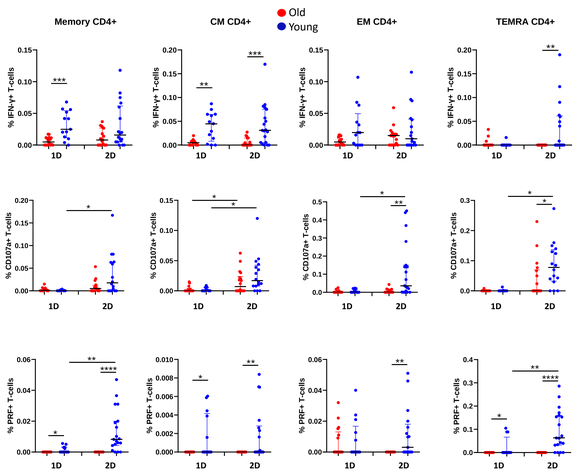


Figure 2. Old people showed lower SARS-CoV-2 spike-specific T cell degranulation (CD107a), cytotoxic capacity (PRF) and IFN-γ production after vaccination.

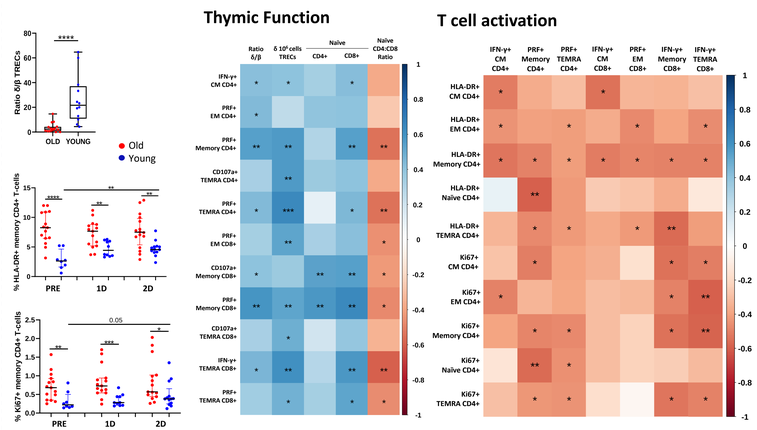


Figure 3. Lower thymic function and higher activated (HLA-DR+) and proliferating (Ki67+) T cell levels found in old people were associated to a lower SARS-CoV-2 spike-specific T cell response after vaccination.

The lower specific T cell response to SARS-CoV-2 BNT162b2 mRNA vaccine in elderly people is associated to a thymic dysfunction, an impaired DC function and monocyte-mediated pro-inflammatory profile.

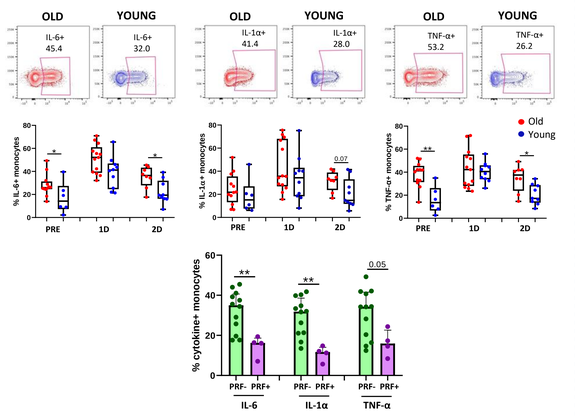


Figure 5. Higher production of pro-inflammatory cytokines (IL-6, IL-1α and TNFα) by monocytes observed in old people was associated to a lower SARS-CoV-2 spike-specific T cell response after vaccination.

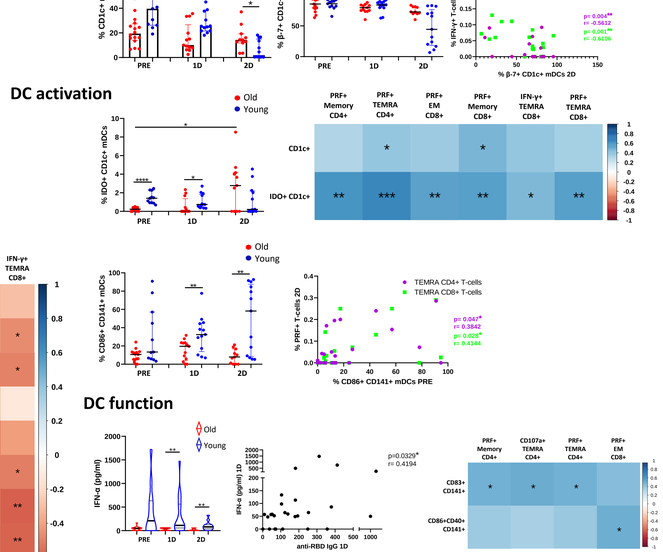


Figure 4. Young people presented higher DC homing (lower % of integrin β7+ cells in peripheral blood) and higher activation (IDO+ and CD86+) and TLR-mediated functional capacity (IFNα in pDCs and CD86+40+ and CD83+ in CD141+ mDCs). This was associated with a higher SARS-CoV-2 spike-specific T cell response after vaccination.

Conclusions

1. **Old people showed a lower SARS-CoV-2 specific T cell response to BNT162b2 mRNA vaccination**
2. **Thymic dysfunction and subsequent alteration of T cell homeostasis is associated to a lower SARS-CoV-2 spike-specific T cell response after vaccination.**
3. **Lower DC homing, activation and functional capacity are related to a lower SARS-CoV-2 spike-specific T cell response after vaccination.**
4. **The monocyte-mediated pro-inflammatory profile observed in old people is associated to a lower SARS-CoV-2 spike-specific T cell response after vaccination.**

REFERENCES

1- Müller L., et al. (2021). Age-dependent Immune Response to the Biontech/Pfizer BNT162b2 Coronavirus Disease 2019 Vaccination. Clin. Infect. Dis. 73, 2065–2072.

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