

1. Introduction & Aims

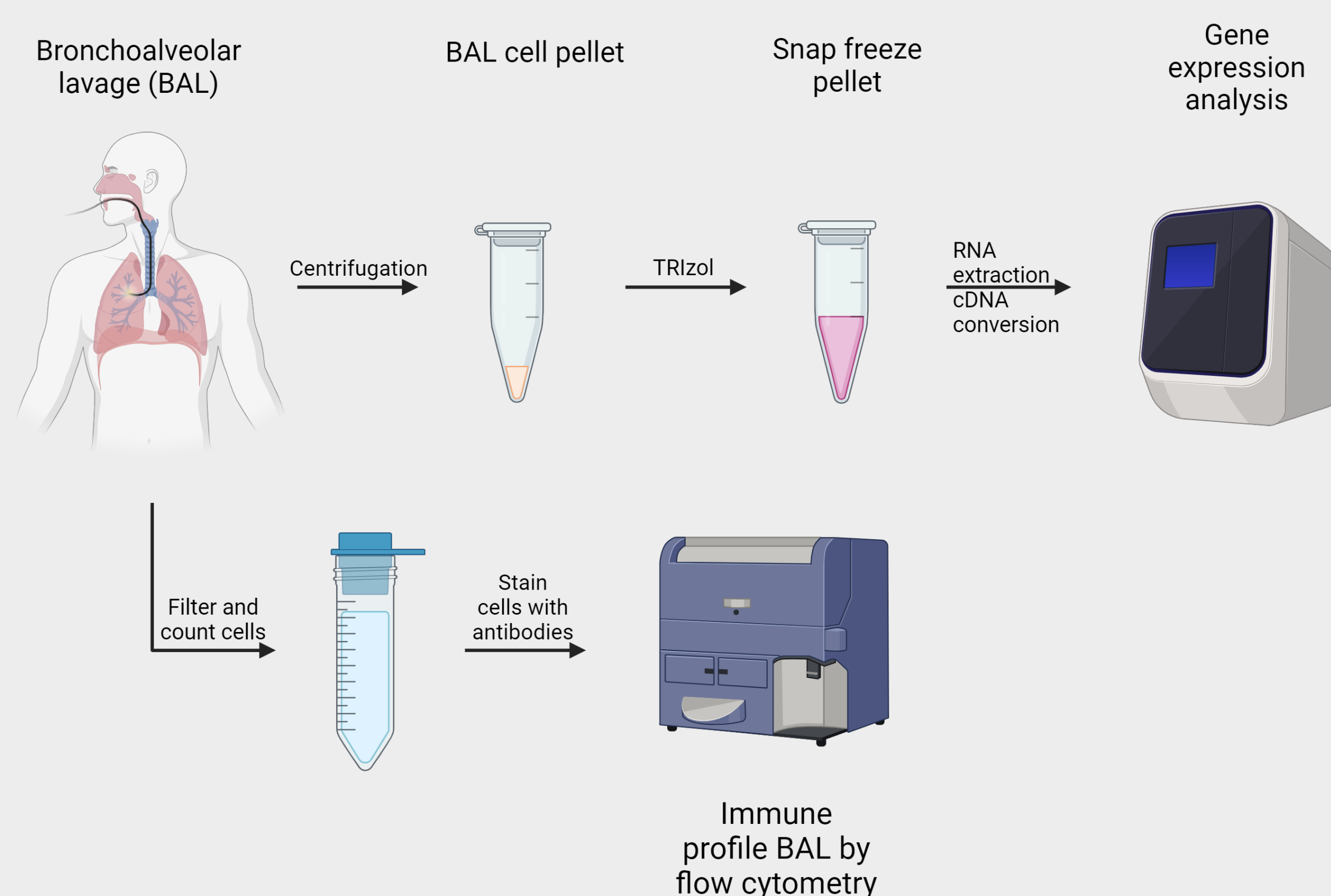
- Idiopathic pulmonary fibrosis (IPF) is the most common form of interstitial lung disease. It is characterised by the excessive deposition of extracellular matrix (ECM) in the lung parenchyma leading to impaired gas exchange¹
- Therapeutic options for IPF are limited, therefore there is an urgent need to understand the mechanism underlying IPF²
- Invariant natural killer T (iNKT) cells are a subset of T cells that express the T-cell receptor (TCR) V α 24/J α 18 chain in humans. Upon activation, NKT cells produce multiple cytokines, including those that have been implicated in IPF pathogenesis³
- NKT cells have been shown to drive IPF pathology in animal models of lung fibrosis³. **However, their role in human IPF remains unknown.**

Aims:

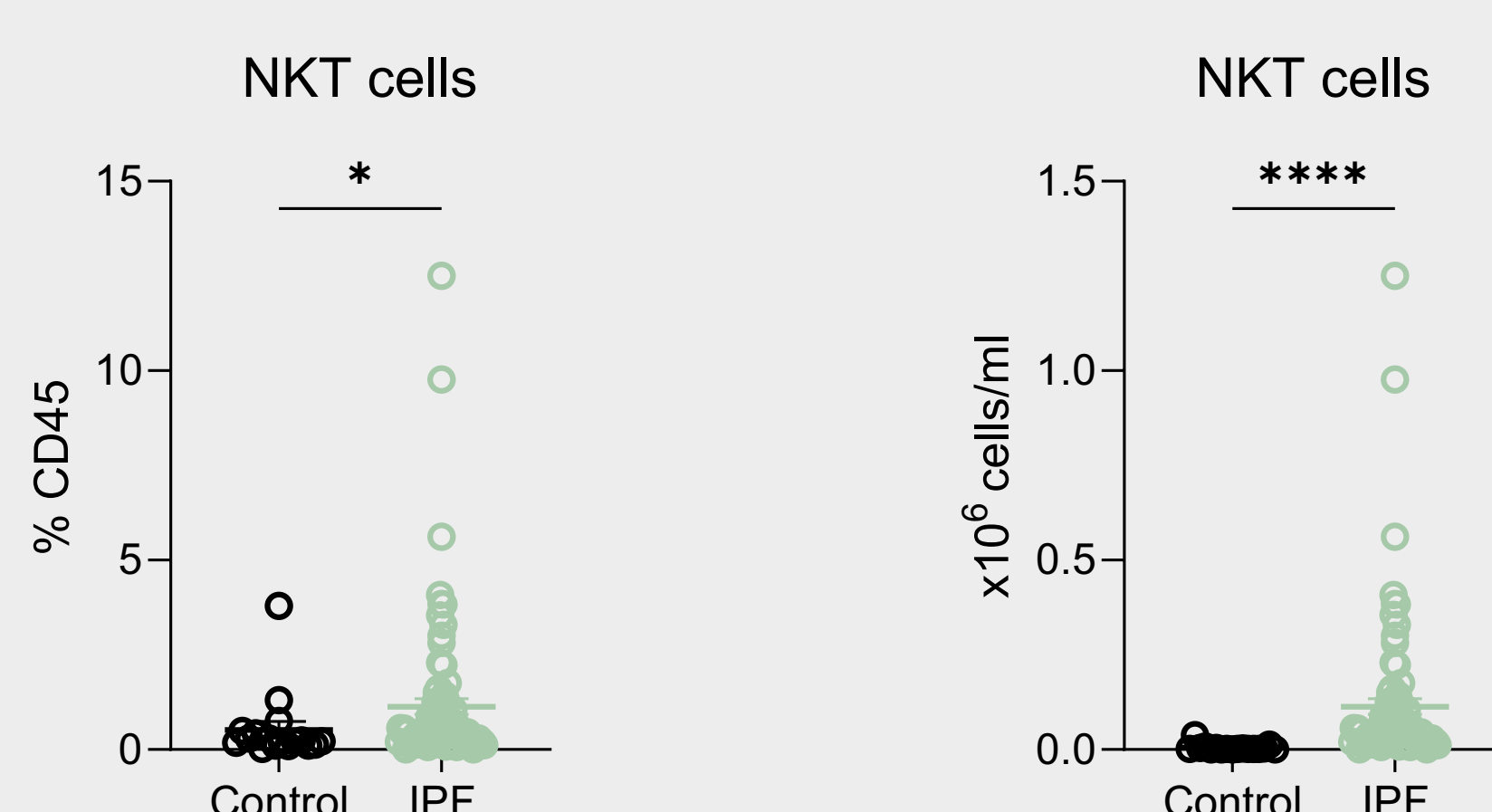
- Characterise the NKT population in IPF bronchoalveolar lavage (BAL)
- Investigate the phenotype of NKT cells and the relationship of these populations to disease parameters

2. Methods

BAL from healthy controls and IPF patients was obtained. BAL cell pellet was collected, RNA was extracted from the cells and gene expression analysis was conducted by real-time PCR. Surface and intracellular flow cytometry of cells isolated from BAL of healthy donors and IPF patients was also conducted to characterise their NKT cell compartment.

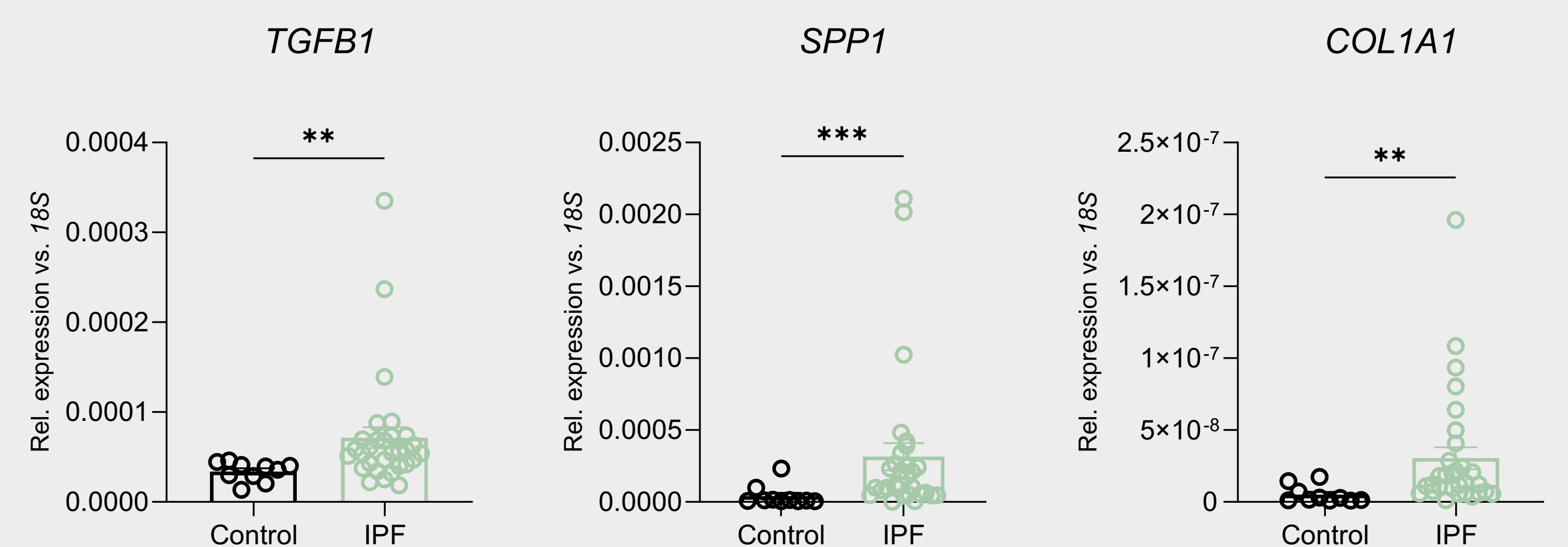


3. The proportion and number of NKT cells significantly increase in BAL of IPF patients



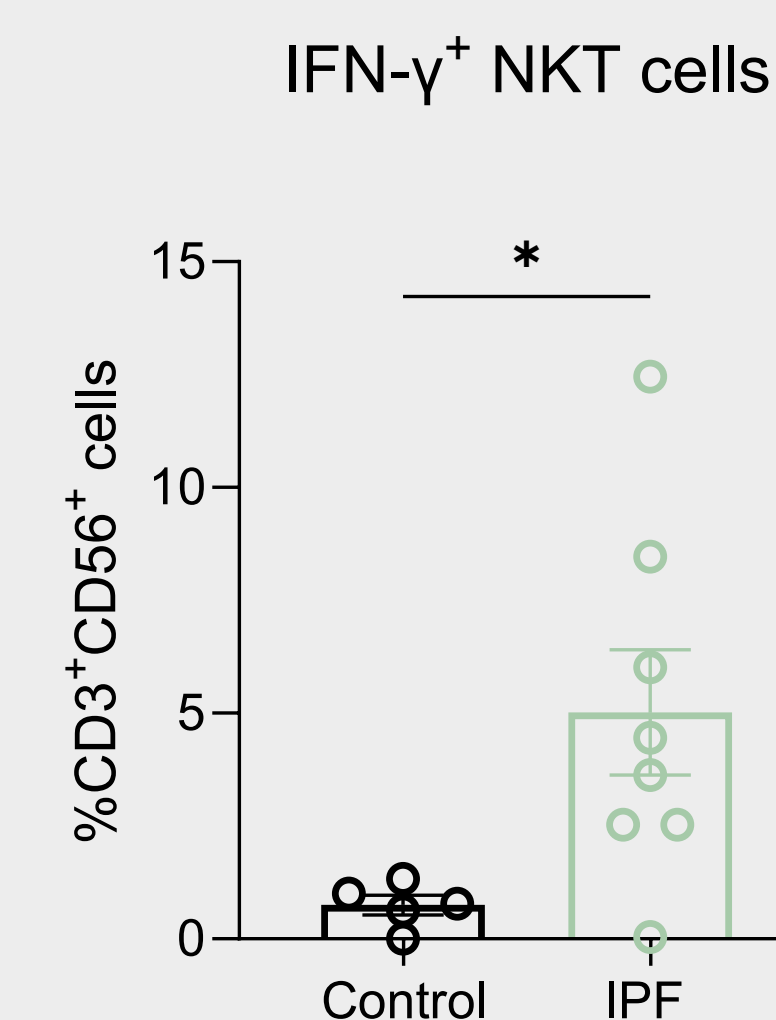
Proportion of live, CD45⁺ and total number of NKT cells isolated from BAL of healthy controls and IPF patients (Kolmogorov-Smirnov test: *p=0.05, ****p=0.0001)

4. Gene expression of TGFB1, Osteopontin and Collagen Type I α 1 significantly increase in IPF patients



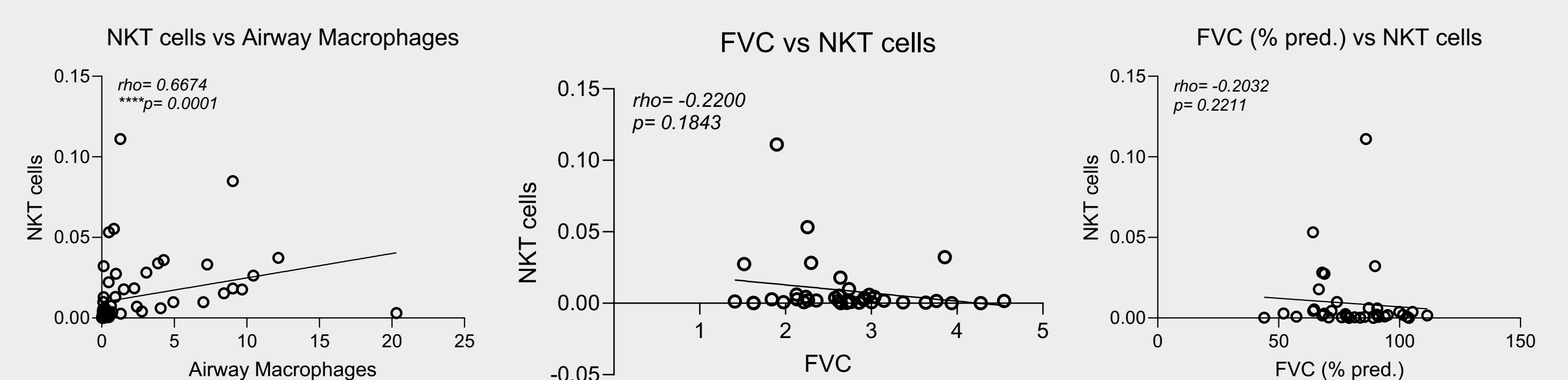
Gene expression determined by real-time PCR of cells isolated from BAL of healthy controls and IPF patients (Kolmogorov-Smirnov test: **p=0.01, ***p=0.001)

5. IFN- γ ⁺ NKT cell expression increases in BAL of IPF patients



Proportion of IFN- γ ⁺ NKT cells (CD3⁺, CD56⁺) present in BAL of healthy controls and IPF patients expressing IFN- γ (Mann-Whitney U test: *p=0.05)

6. Total number of NKT cells correlates with total number of airway macrophages but not with lung function parameters in IPF



The total number of cells isolated from BAL of healthy controls and IPF patients positively correlates with the number of airway macrophages, however it does not correlate with lung function parameters (Spearman Rank correlation: ****p=0.0001)

7. Conclusion

- The number and proportion of NKT cells significantly increase in IPF BAL compared to healthy controls
- TGFB1*, *SPP1* and *COL1A1* significantly increase in IPF patients
- IPF patients show increased expression of IFN- γ ⁺ NKT cells in their BAL
- The number of NKT cells positively correlates with the number of airway macrophages in IPF patients. However, there is no correlation with lung function parameters
- Our data implicate NKT cell populations in the pathogenesis of IPF

References

¹Ogger & Byrne 2021, *Mucosal Immunol.*, ²Spencer et al. 2020, *ERJ Open Research*, ³Kumar et al. 2023, *Front. Immunol*

Data or observed results in earlier studies or trials may not be indicative of results in later studies or trials.