After clinical lung transplantation, NK cells with a lung-resident phenotype represent the most prominent donor passenger leukocyte

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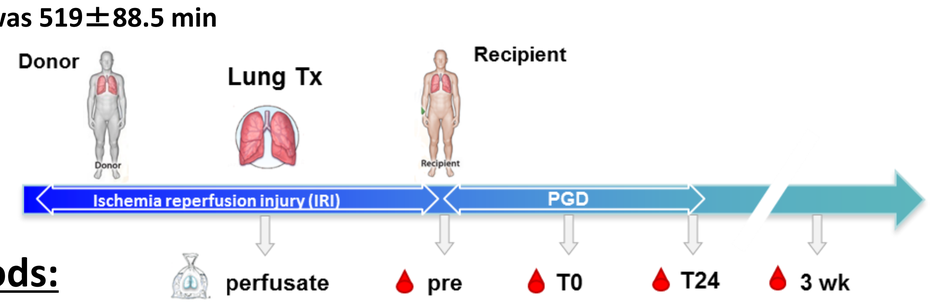
Introduction:

- Lung transplantation is often the only treatment option for end-stage lung diseases
- Survival rates for lung transplants are very limited compared to other solid organ transplants
- Ischemia reperfusion injury remains a major contributor to early post-transplant graft dysfunction and mortality after lung transplantation
- Monitoring of the longitudinal dynamics of T and NK cell subsets after lung transplantation represents a feasible strategy for the identification of potential biomarkers for rejection
- Presence of donor-derived passenger leucocytes in lung transplant recipients has been described long time ago
- However, kinetics, distribution of T vs. NK cells, specific subsets and their potential origin from tissue-resident cells have not been investigated in detail

Aim: Identify donor NK and T cells, define their early kinetics as well as their phenotype and correlation to cold ischemic time

Study cohort:

- 17 male, 23 female patients (mean age of 50.1±11.6 years) with diagnoses of idiopathic fibrosis (n=22), cystic fibrosis (n=8), idiopathic pulmonary hypertension (n=2) and emphysema (n=8) were included; mean cold ischemic time was 519±88.5 min



Methods:

- Isolation of lymphocytes from peripheral blood (PBMC) and perfusion solution by Ficoll
- Analysis of T and NK cell subsets by flow cytometry
- Analysis of donor leukocytes by specific mAb for donor HLA class I alleles

NK cells increase in the periphery of lung transplant recipients after transplantation

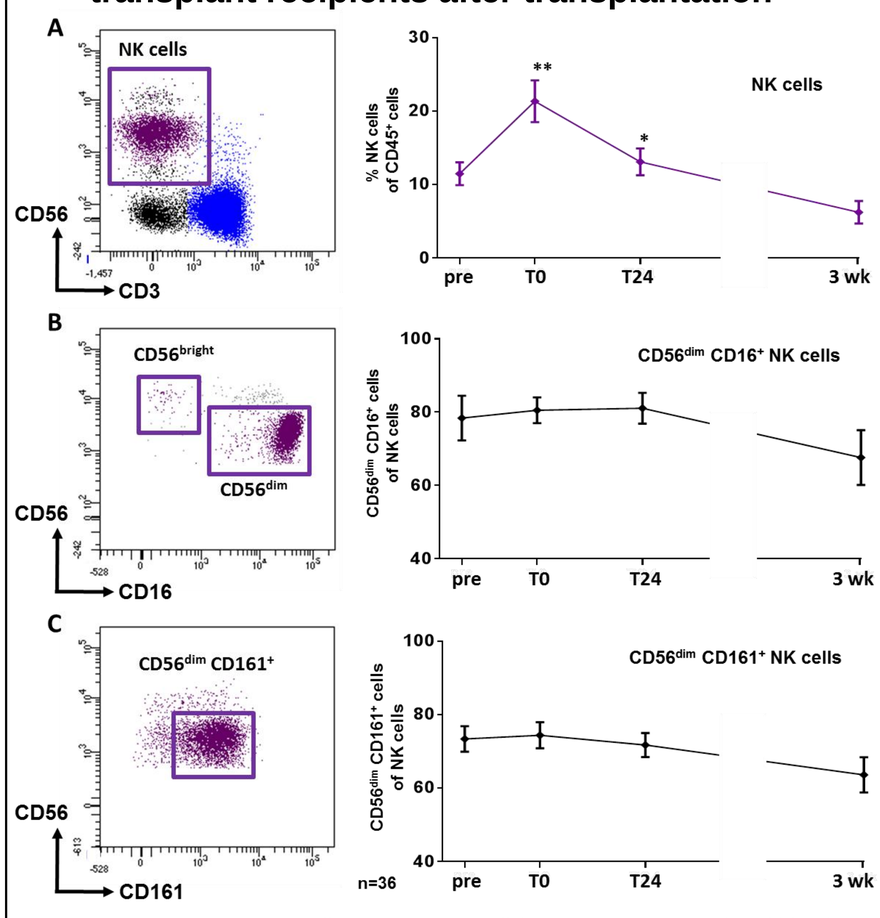
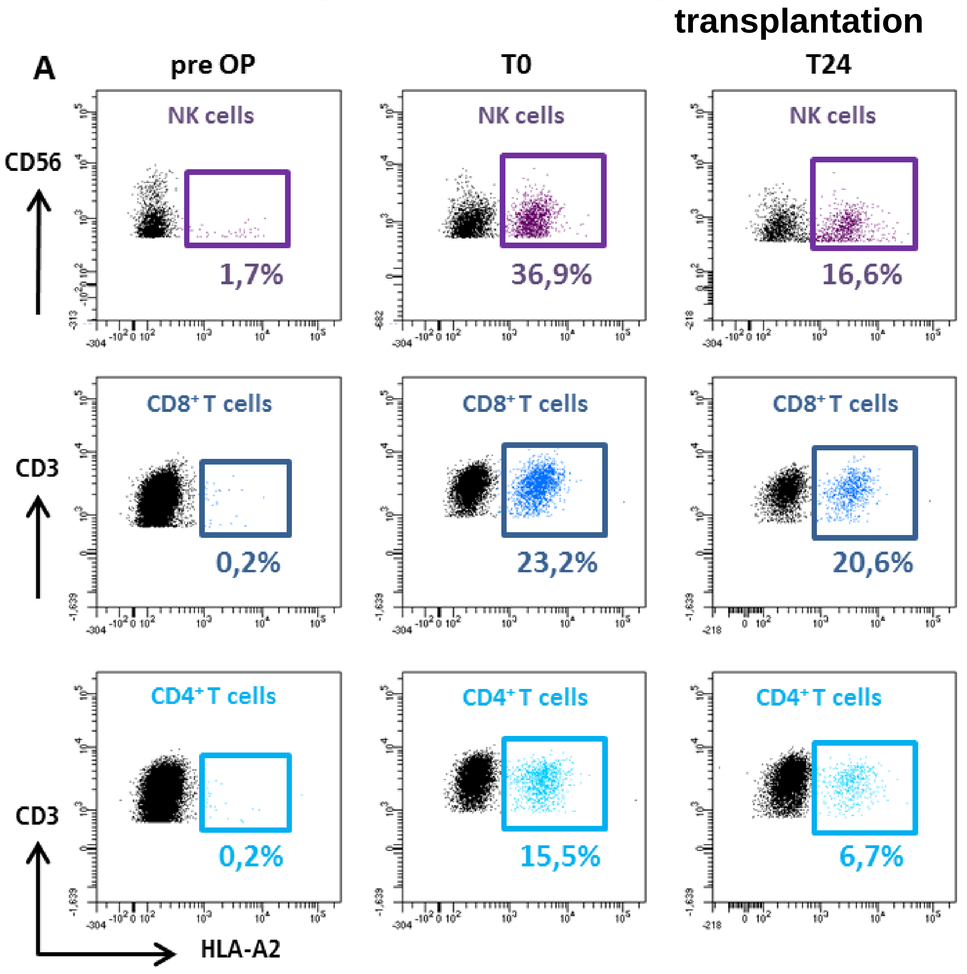


Figure 1. Percentage of NK cells ($CD56^+$ $CD3^-$ cells) among $CD45^+$ peripheral blood (A); percentage of $CD56^{dim}$ $CD16^+$ cells (B) and $CD56^{dim}$ $CD161^+$ cells (C) among NK cells before transplantation (pre), directly after (T0), 24h (T24) and 3 weeks (3 wk) after transplantation

Donor passenger leukocytes emerge in the periphery of lung transplant recipients after transplantation



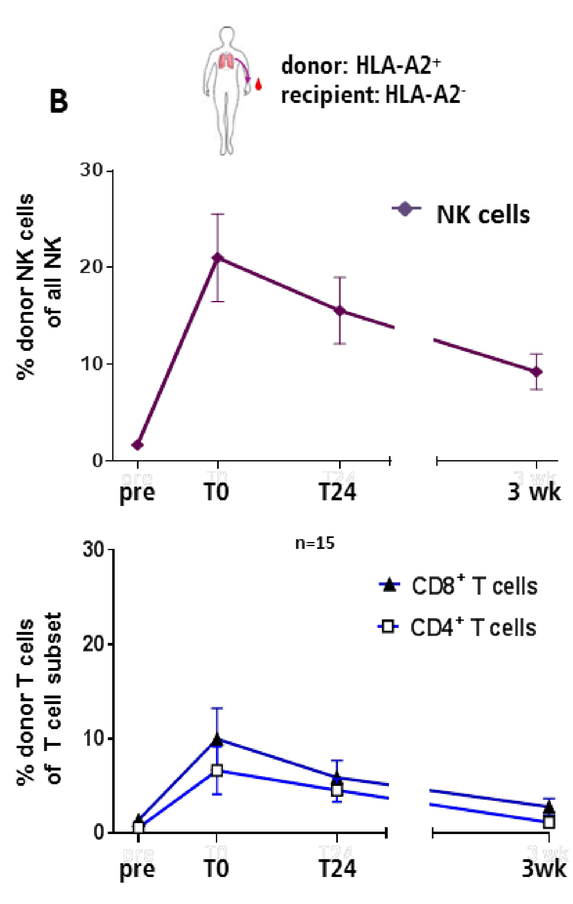


Figure 2. A-B. Percentage of HLA-A2 cells (donor cells) among NK cells, $CD8^+$ T cells and $CD4^+$ T cells before transplantation (pre), directly after (T0), 24h (T24) and 3 weeks (3 wk) after transplantation.

A new population of $CD56^{dim}$ NK cells appears after transplantation and is identical to $CD56^{dim}$ perfusate NK cells

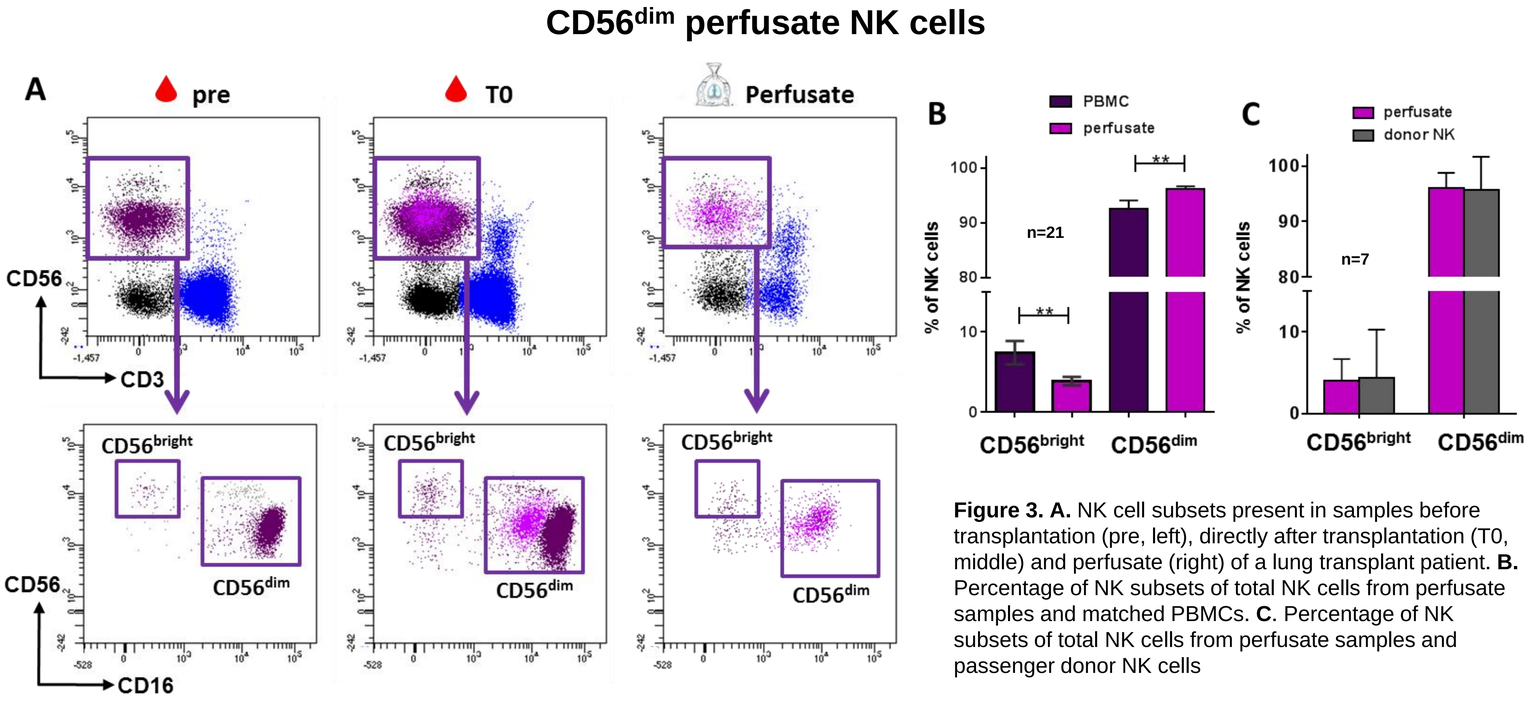


Figure 3. A. NK cell subsets present in samples before transplantation (pre, left), directly after transplantation (T0, middle) and perfusate (right) of a lung transplant patient. **B.** Percentage of NK subsets of total NK cells from perfusate samples and matched PBMCs. **C.** Percentage of NK subsets of total NK cells from perfusate samples and passenger donor NK cells

The proportion of donor leukocytes does not correlate with cold ischemic time

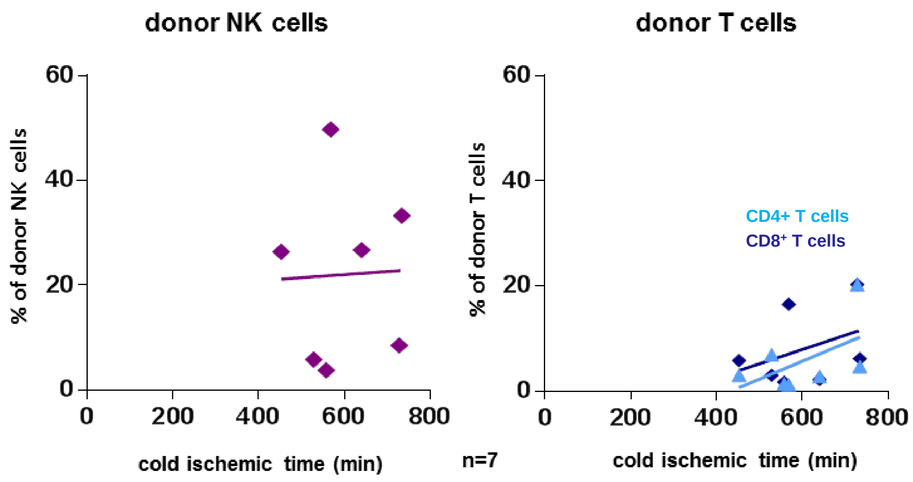


Figure 4 Correlation between the percentage of donor T and NK cells present in the periphery of lung transplant recipients with the cold ischemic time

Conclusions and perspectives:

- Donor NK cells represent the major passenger leukocyte after lung transplantation and peak directly after transplantation independently of cold ischemic time
- Donor passenger T and NK cells have a similar phenotype to perfusate T and NK cells, which indicates their origin as tissue-resident memory T and NK cells
- The association of donor leukocytes with early graft function is currently being investigated