Determination of NKR-P1B Receptor Expression and Its Function in Liver-Resident NK Cells

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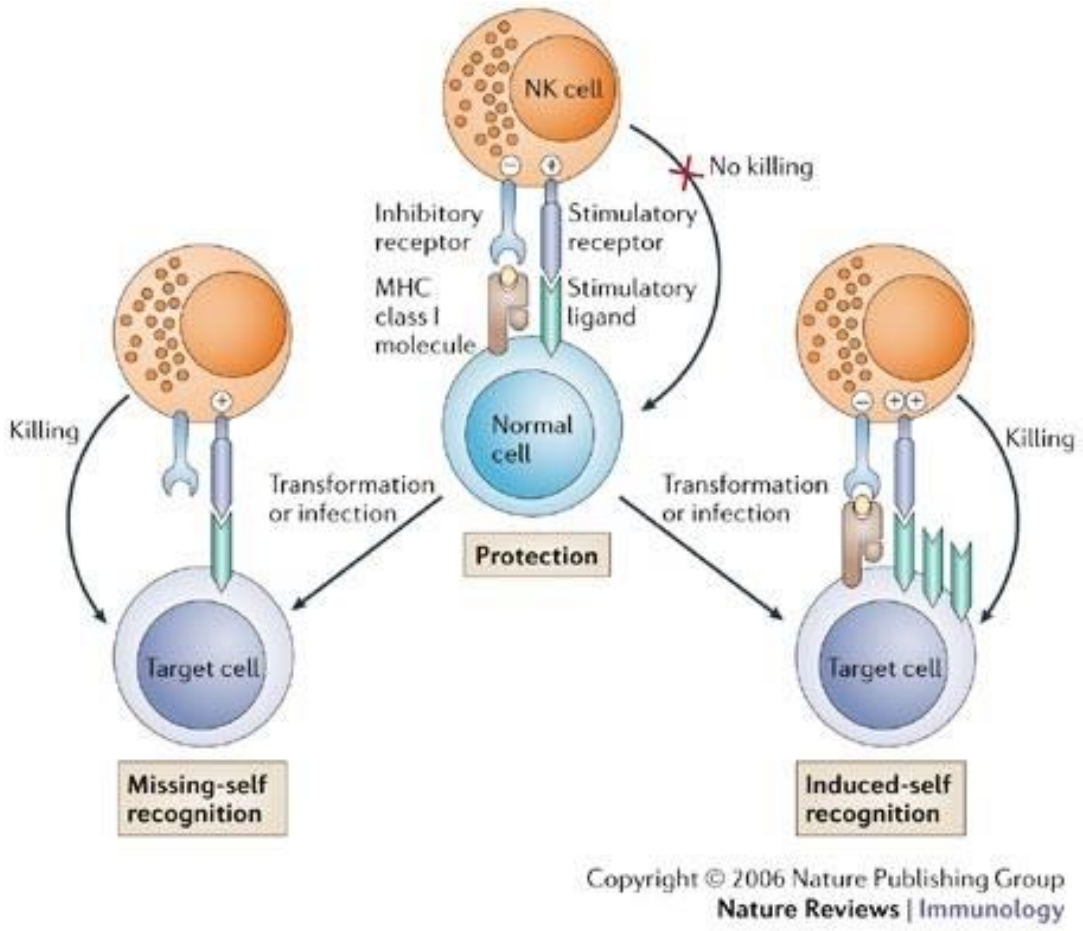
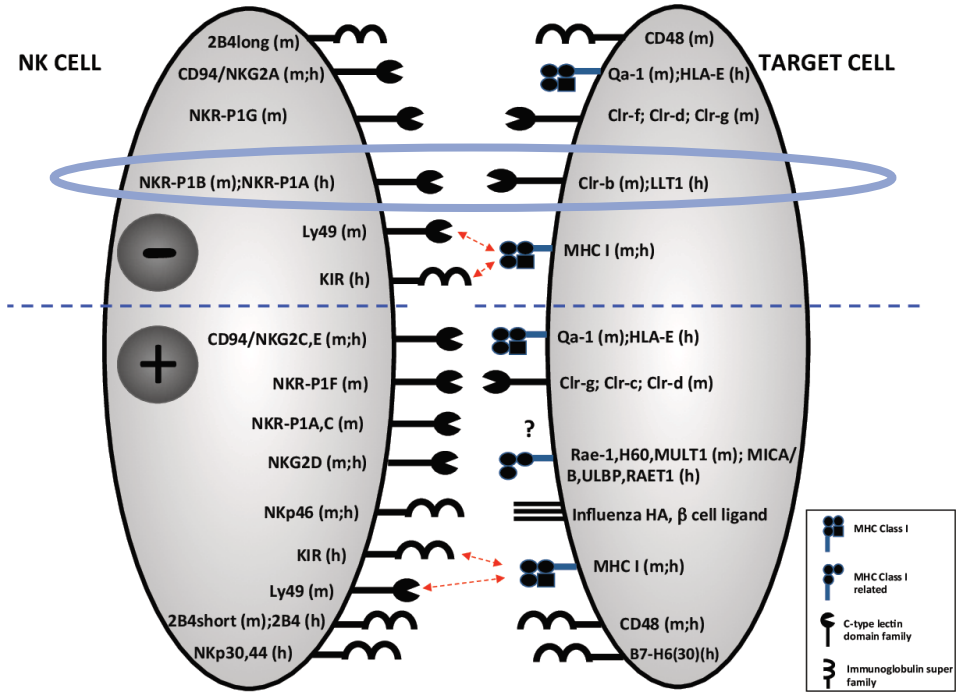
Natural – Killer (NK) Cells



- A subset of lymphocytes which convey "natural cytotoxicity"
- Important members of the innate immune system.
- Able to distinguish target cells that differ only in their expression of MHC class I molecules
- "missing-self" and "induced-self" recognition
- Two distinct subsets, liver-resident NK (lrNK) cells and conventional NK (cNK) cells

The NKR-P1B Receptor

- NK cells can distinguish between normal healthy cells and abnormal cells using a sophisticated repertoire of activating and inhibitory cell surface receptors.
- One of the most unique and earliest identified NK cell inhibitory receptors is the NKR-P1B receptor.
- NKR- P1B is a C-type lectin like receptor that inhibits the function of NK cells upon binging to its cognate C-type related ligand, Clr-b.
- Liver-resident cells harbours large numbers of NK cells but the expression and function of NKR-P1B in these cells have not been explored.



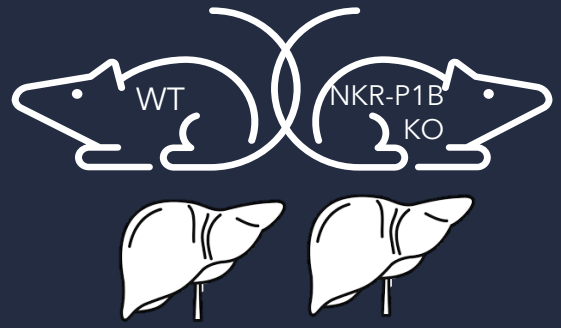
What Does This Thesis Aim To Accomplish?

Identify the expression and distribution of NKR-P1B receptors in liver-resident NK cells

Determine if NKR-P1B plays a role in the development and maturation of liver-resident NK cells

Determine the function of the NKR-P1B:Clr-b recognition system in the liver-resident NK cells

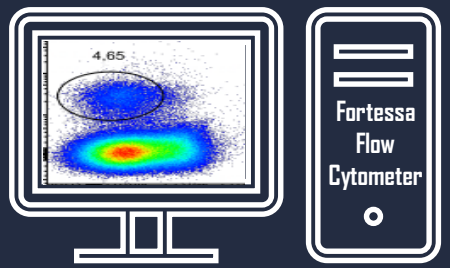
METHODOLOGY



1 C57BL/6 Wild-Type (WT) and NKR-P1B deficient (KO) mouse livers were treated with ACK Lysis Buffer and purified with Percoll to isolate lymphocytes.

2 Cells were counted and approximately 2 millions cells were used for 10-colour flow cytometry analysis.

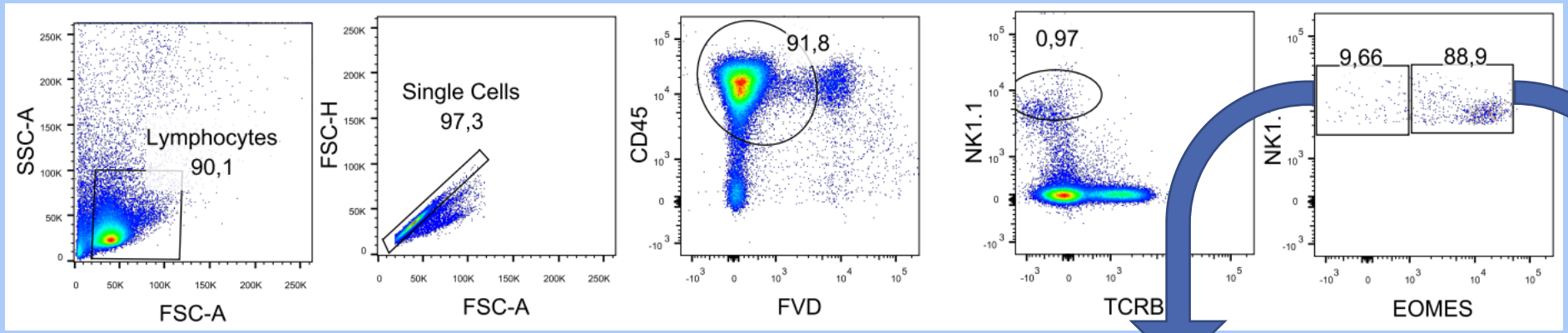
3 Cell were stained with a variety of antibodies to isolate and characterize lymphocyte subsets in the samples.

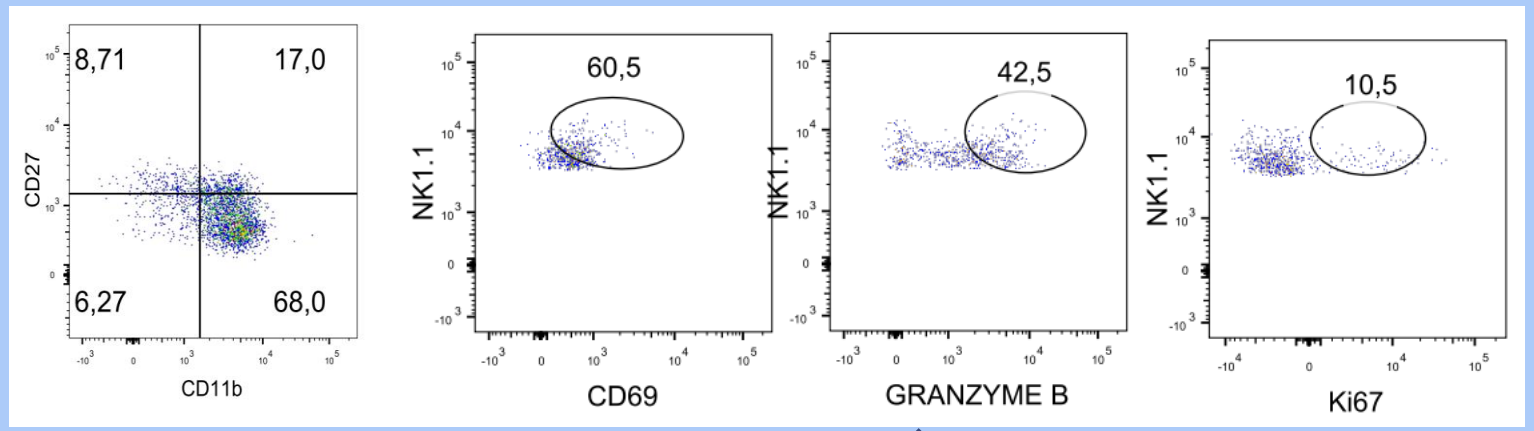


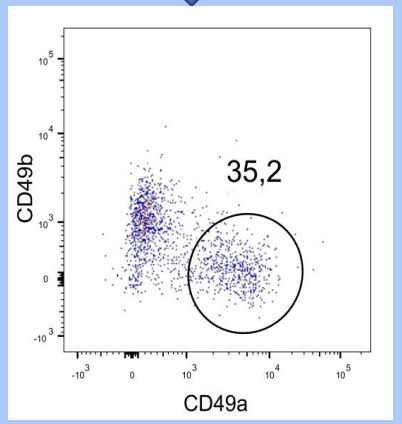
4 Flow cytometry analysis was done using Fortessa X20 flow cytometer and FlowJo vx7.0 software. Specific gating strategies were used to distinguish NK subsets as described in the results section.

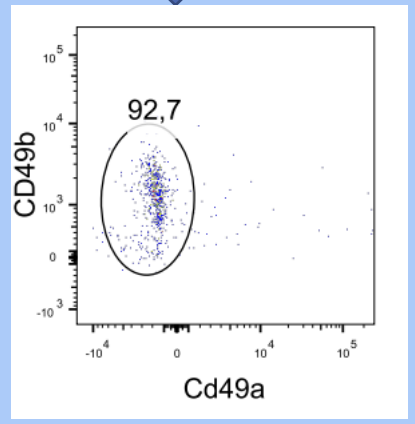
ANALYSIS OF DATA

Gating Strategy

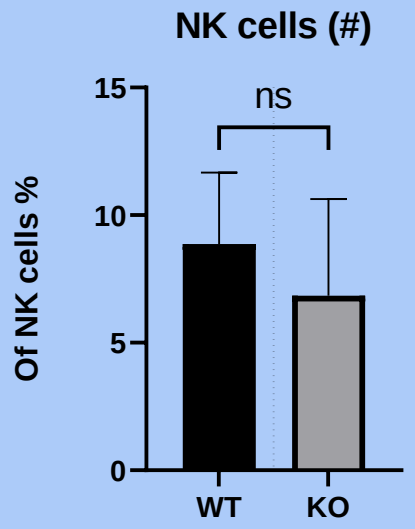


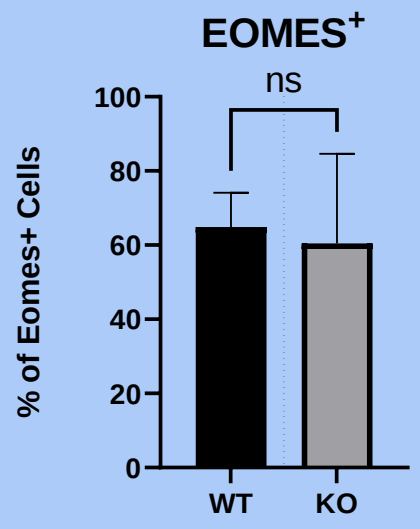


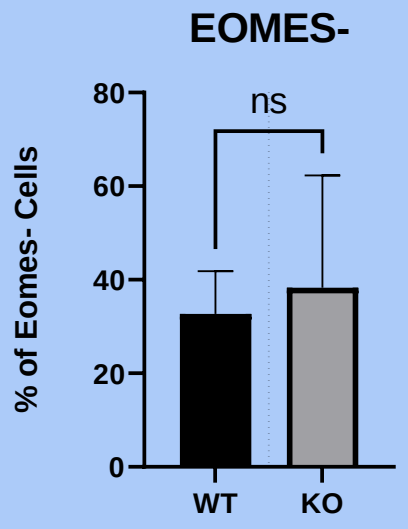


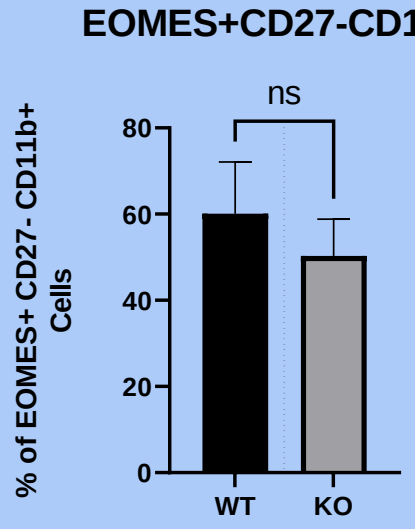


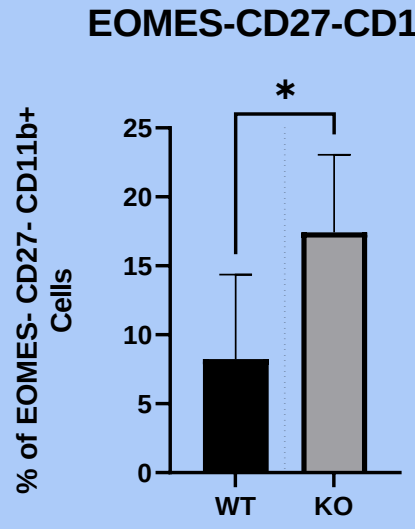
PRELIMINARY RESULTS

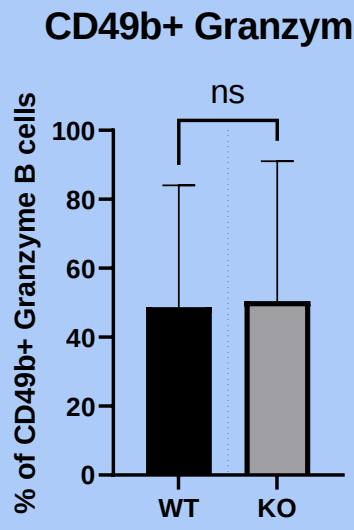


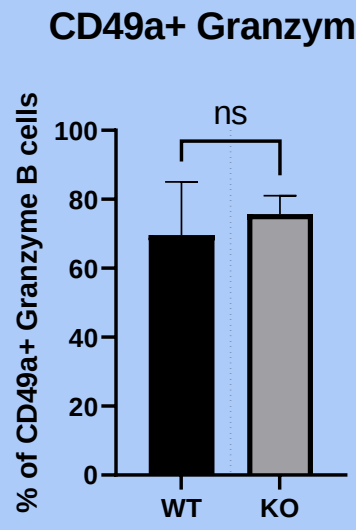












DISCUSSION

- Difference in # of NK Cells is **statistically non-significant** (ns) between Wild-Type (WT) and NKR-P1B Knock-Out (KO) mice.
- **No statistically significant** differences were observed in the numbers and proportions of granzyme B expression in liver resident NK cells between WT and KO mice.
- **Significantly** larger proportion of liver-resident NK cells exhibit a *less mature phenotype* in KO mice compare to the WT mice, suggesting that the NKR-P1B plays a role in the maturation of liver-resident NK cells.
- Future studies will look if the functions of liver-resident cells are affected in NKR-P1B deficient mice compared to the WT

SIGNIFICANCE

These murine studies will give more insight to the function of the human NKR-P1A, which is the homolog of NKR-P1B receptor in humans and could potentially lead to additional research regarding immunological responses in a variety of hepatic inflammatory diseases involving hepatitis, liver fibrosis, liver cirrhosis, and non-alcoholic fatty liver disease (NAFLD).

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