



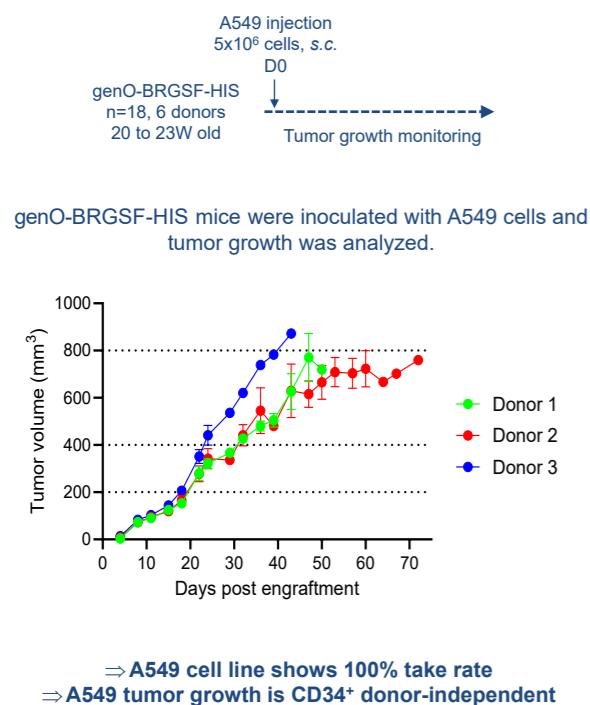
NK cell recruitment into A549 TME in genO-BRGSF-HIS mice

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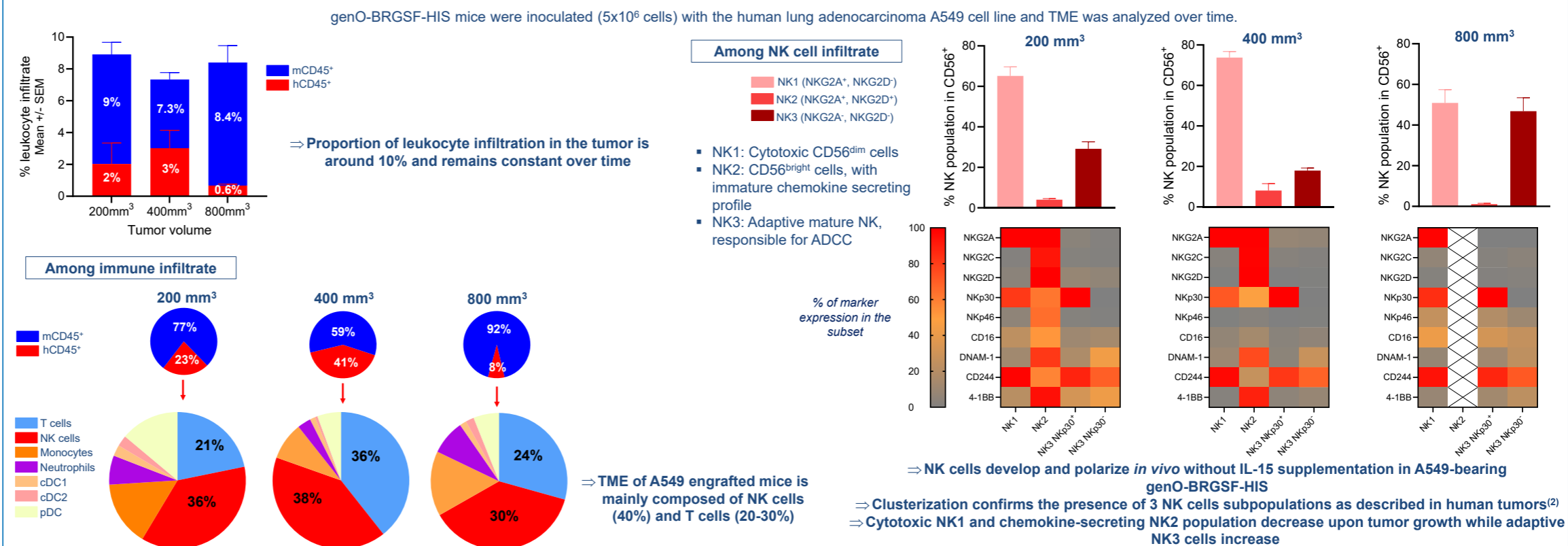
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Background: Natural killer (NK) cells are key components of the innate system, and their high cytotoxicity has been associated to a more favorable prognosis of cancer. Therefore, strategies focusing on enhancing the effector function of NK cells are being investigated. Assessment of NK-targeting therapies in humanized mice is often challenging, as human NK cell levels are low, requiring supplementation with human IL-15 to enhance their development. Here we describe the recruitment of NK cells in the tumor microenvironment (TME) of A549 lung cancer tumor model in genO-BRGSF-HIS mice (BALB/c Rag2^{-/-}, IL2Rγ^{-/-}, SIRPα^{NOD} and Flt3^{-/-} immunodeficient mice reconstituted with human cord blood CD34⁺ cells), without the need of supplementation with human IL-15⁽¹⁾.

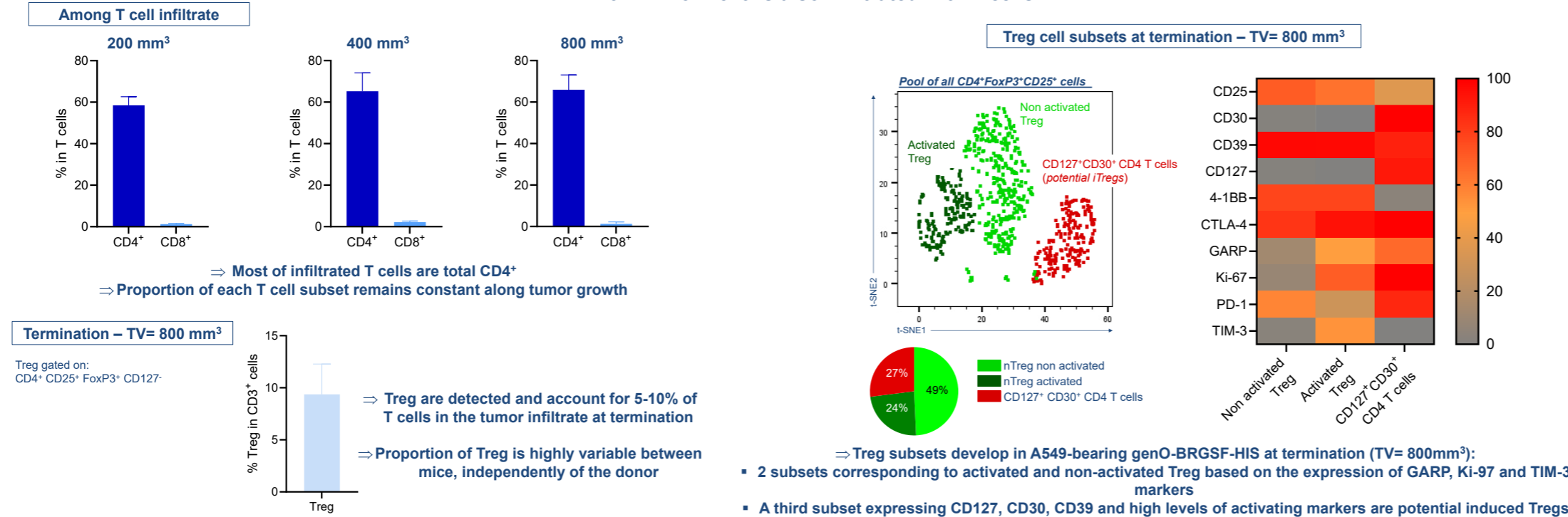
1. Permissiveness of genO-BRGSF-HIS mice to A549 xenograft engraftment



2. TME of A549 is highly infiltrated with NK cells



3. TME of A549 is also infiltrated with T cells



Conclusion: Overall, NK cells respond to environmental stimulus and are recruited into the TME of A549-bearing genO-BRGSF-HIS mice, without the supplementation with human IL-15. NK cells functionality remains to be investigated in future studies and would make genO-BRGSF-HIS mouse model a valuable tool to assess NK-targeting immunotherapies. The A549 TME is also highly infiltrated in T cells. Among T cells, Treg are present and found at different activation status at termination, suggesting that the model could also be used for assessment of therapies targeting Treg.

References:
(1): Martin *et al.*, Front. Immunol., 2025
(2): Rebuffet *et al.*, Nat. Immunol., 2024

