Investigating the Effect of Therapeutic Peptide–Lipoplex Vaccination on Tumor-Infiltrating Leukocytes

Arbelaez *et al.* A nanoparticle vaccine that targets neoantigen peptides to lymphoid tissues elicits robust antitumor T cell responses (2020) NPJ vaccines (https://doi.org/10.1038/s41541-020-00253-9)

BACKGROUND

Cancer vaccines using synthetic long peptides (SLP) targeting tumor antigens have been tested in the clinic, but the outcomes have been unimpressive. In this study, Arbelaez *et al.* investigated the impact of delivering neoantigen peptides in liposomes on tumor-infiltrating CD8+ T cells in C57BL/6 mice bearing MC38-G12D tumors.

STUDY DESCRIPTION

The mutated neoantigen Adpgk peptide derived from the antigen G12D, and the adjuvant CpG were formulated into liposomes (Neo-Lpx) to immunize mice with MC38-G12D tumors five days after subcutaneous tumor implantation in C57BL/6 mice. Mice were administered Neo-Lpx (50µg CpG/peptide) after randomization on day 14. Tumor-infiltrating leukocytes (TIL) were prepared from harvested MC38-G12D tumors to detect Adpgk-specific CD8+ T cells by flow cytometry using custom Adpgk/H2Db Dextramer® reagents.

RESULTS

CD8+ TILs specific for the neoantigen peptide Adpgk were enriched in tumors after treatment with Neo-Lpx (**Fig. 1a**). Due to heterogeneity in antigen specificity and activity of TILs, it was important to analyze the tumor-infiltrating T cells responding to the tumor antigens. Thus, researchers focused on markers of chronic antigen stimulation that may lead to functional T-cell exhaustion. High levels of PD-1 and Tim3 on all the TILs from Neo-Lpx treated tumors were observed. Using the Adpgk Dextramer® reagents, researchers compared the lipoplex vaccine-expanded TILs to bulk TILs and found that Neo-Lpx treated TILs exhibited a higher dysfunctional signature (**Fig. 1b**).

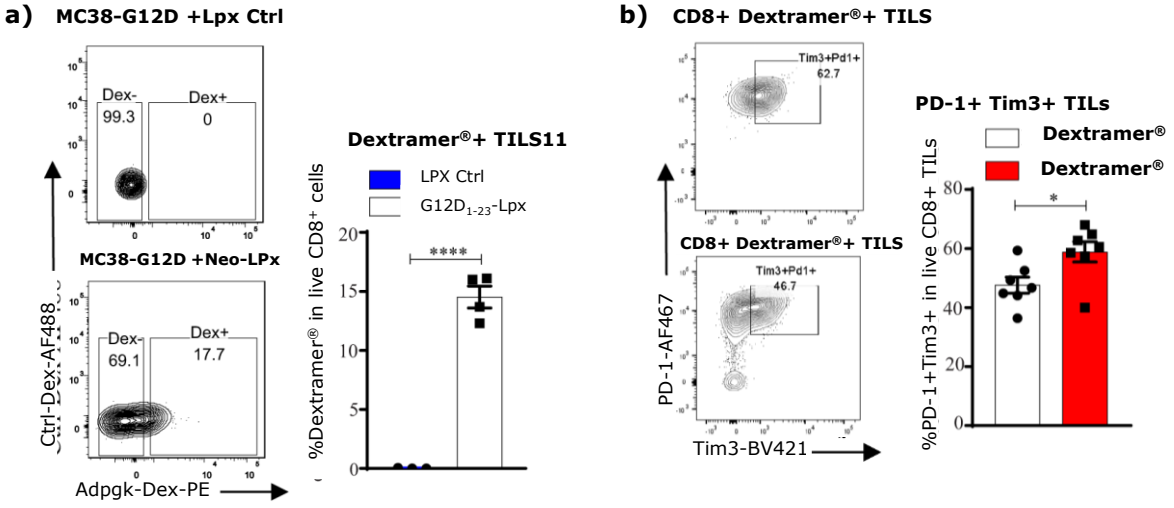

Fig. 1: Detection and checkpoint signature of tumor-infiltrating, Adpgk-specific CD8+ T cells
a) Detection of mutant Adpgk-specific CD8+ TILs in mice immunized with Neo-Lpx using an MHC I Dextramer® specific for the mutated neoantigen peptide Adgk derived from the antigen G12D. b) TILs specific or not for Adpgk using MHC I Dextramer® staining were analyzed for PD-1 and Tim3 expression.

CONCLUSIONS

- Researchers successfully detected Adpgk-specific CD8+ T cells in MC38 tumors from Neo-Lpx immunized C57BL/6 mice using MHC I Dextramer® reagents customized for the purpose
- The higher dysfunctional signature compared to untreated bulk TILs, as measured by PD-1 and Tim3 expression led to further studies combining the Neo-Lpx with checkpoint inhibitor anti-PD-1