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SITEMAN CANCER CENTER
BARNES-JEWISH HOSPITAL • WASHINGTON UNIVERSITY SCHOOL OF MEDICINE
A National Cancer Institute Comprehensive Cancer Center

NT-I7 as an adjuvant to DNA neoantigen vaccination enhances and prolongs neoantigen-specific anti-tumor immunity

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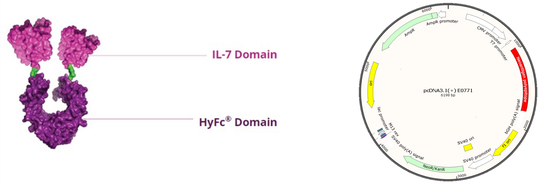
Background

IL-7 is a non-redundant cytokine essential for T cell survival, proliferation and function. NT-I7 (efineptakin alfa; NeoImmuneTech, Inc, Rockville, MD), is a long-acting IL-7 composed of recombinant human IL-7 (rhIL-7) fused to a hybrid Fc antibody platform that has significantly improved the *in vivo* stability and half-life compared to rhIL-7.

DNA cancer neoantigen vaccines are a promising personalized cancer immunotherapy capable of generating strong anti-tumor immunity currently under investigation in clinical trials (e.g. NCT03199040, NCT03122106). A limitation of the platform is the short duration of neoantigen-specific T cell immunity.

NT-I7
(efineptakin alfa; a long-acting IL-7)

DNA Vaccine
Plasmid containing E0771 neoantigens



In this study, we test the addition of NT-I7 as an adjuvant to a validated polyepitope DNA neoantigen vaccine for the E0771 murine breast cancer model (DNA-E0771) containing three immunogenic neoantigens (Lrrc27, Plekho1, Pttg1)[1].

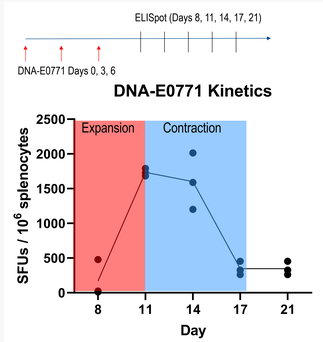
Hypothesis

- The addition of NT-I7 as an adjuvant to DNA neoantigen vaccine will prolong the duration of neoantigen-specific T cell immunity
- DNA neoantigen vaccine plus NT-I7 will generate improved anti-tumor responses compared to DNA vaccine alone

References

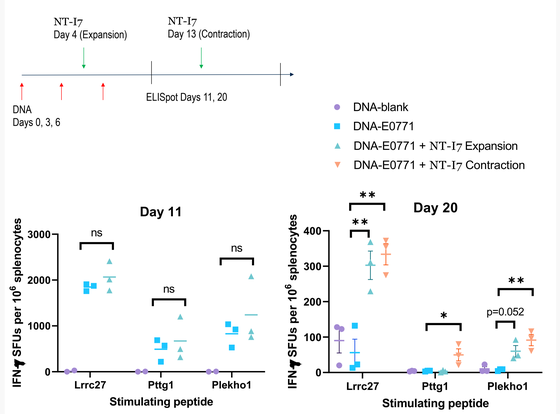
1. Li, Lijin, et al. "Optimized polyepitope neoantigen DNA vaccines elicit neoantigen-specific immune responses in preclinical models and in clinical translation." Genome medicine 13 (2021): 1-13.

DNA-E0771 confers robust, but short-lived neoantigen-specific T cell immunity



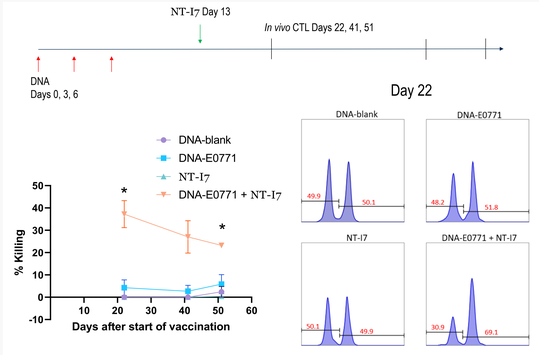
C57BL/6 mice were vaccinated with DNA-E0771 per optimized regimen (4 µg DNA delivered by Helios gene gun on days 0, 3, and 6). ELISpot assays were performed every 3 days starting 8 days after the start of vaccination.

NT-I7 administered during T cell expansion or contraction phase prolongs neoantigen-specific T cell immunity



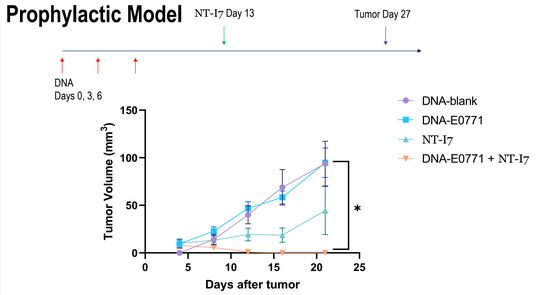
NT-I7 (5 mg/kg) was administered subcutaneously on day 4 or day 13 during the T cell expansion or contraction phase, respectively. The addition of NT-I7 to DNA vaccination during the expansion or contraction phase enhanced the magnitude of the neoantigen specific immunity on Day 20.

DNA-E0771 + NT-I7 generates stronger neoantigen-specific killing and memory CD8⁺ T cell responses



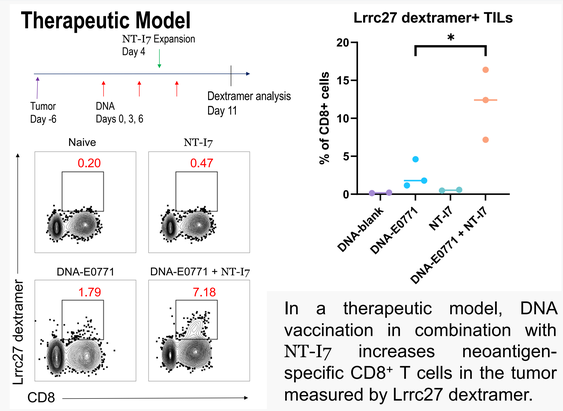
Mice were vaccinated with DNA vaccine with/without NT-I7. Then, 22, 41, and 51 days after start of vaccination, CFSE-labeled syngeneic splenocytes were pulsed with neoantigen peptides (low CFSE) and mixed with naïve splenocytes (high CFSE), then adoptively transferred into vaccinated mice. Flow cytometry was performed 16 hours later. Neoantigen-specific cytotoxicity is calculated by: $\%\ specific\ lysis = 1 - (\%CFSElo\ /\ \%CFSEhi) \times 100$

DNA-E0771 + NT-I7 protects from tumor challenge



C57BL/6 mice were vaccinated with DNA vaccine on days 0, 3, and 6 and NT-I7 (5mg/kg) administered on day 13. 5*10^5 E0771 cells were inoculated subcutaneously on day 27 and tumor growth were tracked with electronic caliper.

DNA-E0771 + NT-I7 increases neoantigen-specific TILs



In a therapeutic model, DNA vaccination in combination with NT-I7 increases neoantigen-specific CD8⁺ T cells in the tumor measured by Lrrc27 dextramer.

Conclusion

NT-I7 as an adjuvant to a DNA neoantigen vaccine:

1) Increases the duration of neoantigen-specific anti-tumor immunity,
2) Protects from tumor challenge in a prophylactic murine model, and
3) Promotes neoantigen-specific TILs in a therapeutic murine model.

Clinical application of NT-I7 may help overcome immunologic shortcomings of current neoantigen vaccines.

Future Directions

- Determine the efficacy and mechanism of DNA-E0771 + NT-I7 in the therapeutic setting, and
- Continue to test DNA-E0771 + NT-I7 in the prophylactic setting to increase sample size and further define the mechanism of action

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NEOIMMUNETECH
NeoImmuneTech, Inc. (NIT) is a clinical-stage T cell-focused biotech company