A mRNA-LNP encoded APC-targeting neoantigen vaccine elicits stronger and broader T cell responses, and superior tumor control

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nykode therapeutics

Background

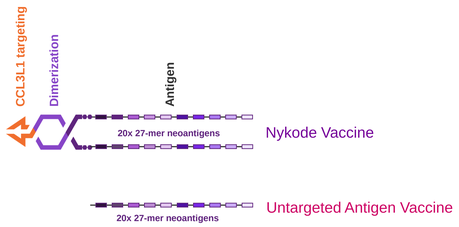
Individualized cancer vaccines based on tumor-specific neoantigens is a groundbreaking approach in oncology that has shown promising efficacy in recent clinical trials. Nykode Therapeutics developed a vaccine platform that targets antigens directly to antigen presenting cells (APCs). Here we used a modular fusion protein containing Chemokine ligand 3-like 1 (CCL3L1) to bind and attract APCs, a dimerization domain to facilitate strong bivalent binding, and an antigen unit encoding 20 neoantigens. Individualized neoantigen vaccines encoded in plasmid DNA induce strong and broad T cell responses in pre-clinical and clinical settings.

In the study presented here, we compared the immunogenicity and tumor control of Nykode's mRNA-encoded APC-targeting vaccine to an untargeted antigen vaccine. Both vaccines encoded the same 20 neoantigens derived from the murine MC38 tumor model and were administered intramuscularly in a lipid nanoparticle (LNP) format.

Find out more about our neoantigen vaccines at our website:
https://nykode.com/research-and-development/scientific-papers-and-presentations/

Vaccine Constructs

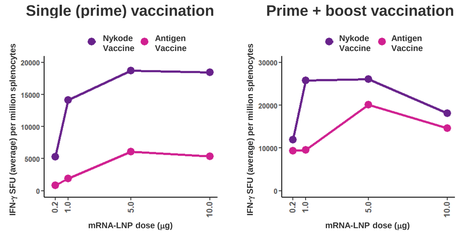
Vaccine constructs used in these studies



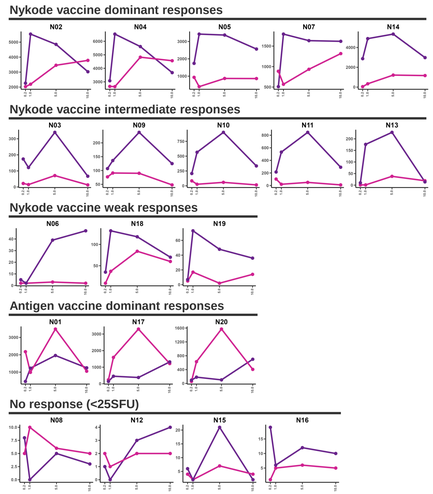
Vaccines were administered as mRNA formulated in lipid nanoparticles (LNPs) and injected intramuscularly.

Nykode neoantigen vaccines induce stronger and broader T cell responses

The Nykode neoantigen vaccine elicited stronger IFN-γ T cell responses than the untargeted Antigen vaccine

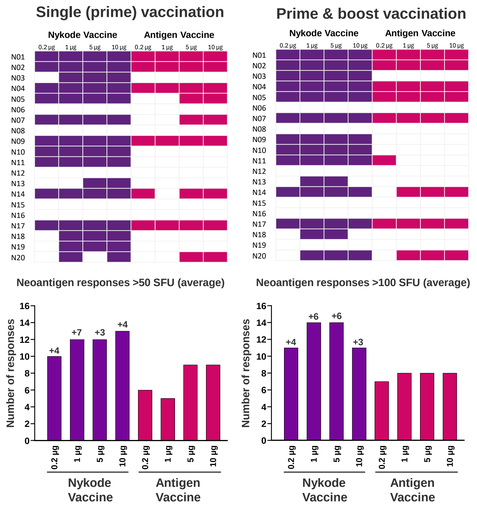


Dose response to individual neoantigens (prime + boost)



C57BL/6, n = 5 per group, IFN-γ FluoroSpot assay of splenocytes using peptide pools covering each of the 20 neoantigens individually. Vaccination on days 0, 21. Fluorospot on days 7 (prime), 28 (prime & boost).

Nykode vaccines elicited responses to a greater number of neoantigens compared to the untargeted Antigen vaccine

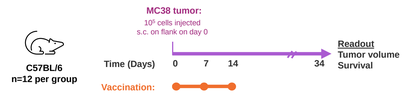


Strength: The Nykode vaccine elicited a much stronger response (up to 7.5x stronger) than the antigen vaccine on day 7 following a single (prime) vaccination. After a second (boost) vaccination the Nykode vaccine still elicited a stronger response, although the magnitude of this difference was reduced.

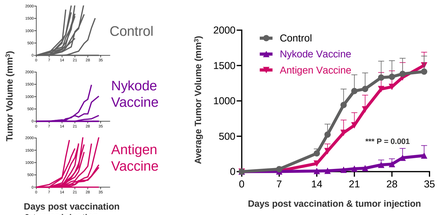
Breadth: The Nykode vaccine elicited responses to substantially more neoantigens than the untargeted neoantigen vaccine after both single (prime) and two (prime & boost) vaccinations. The heatmaps show neoantigen responses above a cutoff of 50 SFU (prime) or 100 SFU (prime & boost). The total number of neoantigen response for each dose and vaccine are shown in the column charts. The Nykode vaccine elicited a greater number of responses at all doses tested (numbers above column values), with +6 neoantigen responses (75% increase) at the 1ug & 5µg dose after prime & boost when both vaccines showed the greatest magnitude of responses.

Nykode neoantigen vaccines mediate improved tumor control

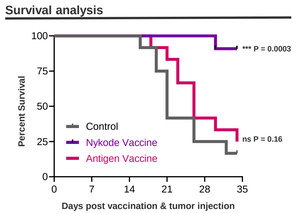
The Nykode neoantigen vaccine elicited superior tumor control compared to the untargeted neoantigen vaccine



Tumor volume



Survival analysis

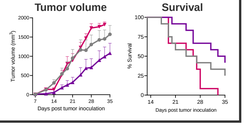


Tumor rejection

Group	Tumors Rejected	P-value (Fisher test)
Control	2/12	NA
Nykode Vaccine	8/11	0.01
Antigen Vaccine	1/12	1.00

Additional Tumor Study

A second study was performed using a 2-fold higher dose of tumor cells. The Nykode vaccine still elicited tumor control under these more challenging conditions while the Antigen vaccine did not.



The Nykode vaccine led to significantly enhanced tumor rejection (Fisher), significantly reduced tumor growth (P=0.001, Tukey), significantly increased survival (Gehan-Breslow-Wilcoxon test), while the untargeted Antigen vaccine displayed no significant differences compared to control (LNP buffer) vaccine.

Conclusions

- **The Nykode neoantigen vaccine, delivered in a mRNA-LNP format, elicits stronger and broader T cell responses compared to an untargeted neoantigen vaccine.**
- **The Nykode neoantigen vaccine reached a peak response at a lower dose (1 µg) after prime & boost vaccination than the antigen vaccine, highlighting the increased potency of the Nykode vaccine.**
- **The Nykode neoantigen vaccine elicited T cell responses to substantially more neoantigens than the untargeted neoantigen vaccine (14 vs 8 at peak dose).**
- **The Nykode neoantigen vaccine provided far better tumor control with tumor rejection in 72% of animals, while the untargeted neoantigen vaccine and control (PBS) vaccination resulted in a similar low frequency of tumor rejection.**

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