Targeting of neoantigen cancer vaccines to antigen presenting cells results in faster and broader T cell responses whether encoded in DNA or mRNA

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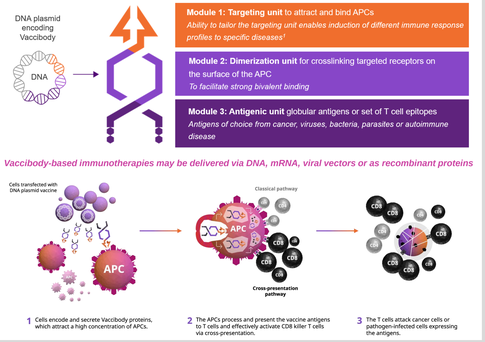
BACKGROUND

Individualized cancer vaccines based on patient-specific neoantigens are a groundbreaking approach in oncology, offering a highly individualized treatment option for cancer patients. Unlike traditional vaccines, which are designed to prevent diseases by stimulating an immune response against a specific pathogen, individualized cancer vaccines are therapeutic, aiming to treat cancer by training the immune system to recognize and attack the patient's own cancer cells. The key is to induce a fast, strong, broad, and persistent CD8+ T cell response.

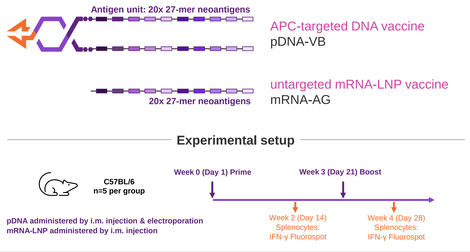
Here we compared the immunogenicity of an Antigen Presenting Cell (APC)-targeted Vaccibody™ vaccine to an untargeted vaccine. Both vaccines encoded the same 20 neoantigens derived from the murine MC38 tumor model. The APC-targeted vaccine was administered in both plasmid DNA and mRNA-lipid nanoparticle (LNP) formats, while the untargeted vaccine was administered in the mRNA-LNP format.

THE VACCIBODY PLATFORM



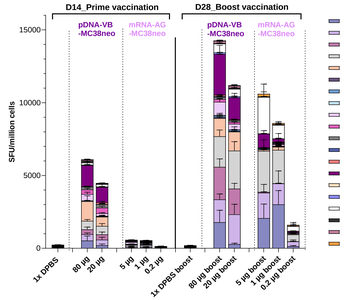
APC-Targeted DNA vaccine compared to untargeted mRNA-LNP vaccine

Here we compared the standard Vaccibody platform (APC-targeted DNA vaccine) to an untargeted mRNA-LNP vaccine



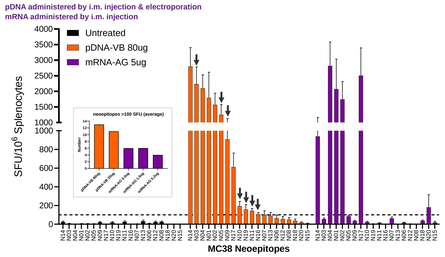
Analysis of immune responses by IFNγ Fluorospot assay

The APC-targeted Vaccibody DNA vaccine induced a significantly stronger immune response already at day 14 after a single vaccination.



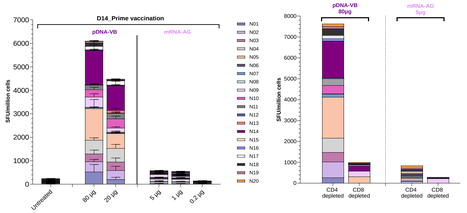
pDNA-VB induces T cell responses against a greater number of neoantigens

The APC-targeted Vaccibody DNA vaccine induced immune responses against more than twice as many neoantigens at the highest doses of each vaccine. Responses only seen in the pDNA-VB vaccine are indicated by arrows. The pDNA-VB vaccine induced responses against a greater number of neoantigens at all doses tested (inset).



APC-targeted DNA vaccine induced a strong immune response to single vaccination that was CD8+ driven

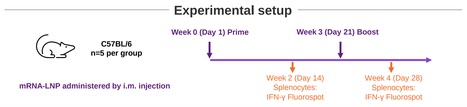
The contribution of CD4+ and CD8+ T cells to the strong response seen after single vaccine (left panel) was analyzed by depletion of CD4+ or CD8+ T cells before IFNγ fluorospot assay (right panel).



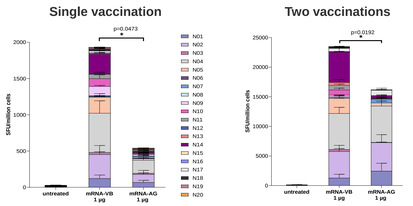
APC-targeted mRNA-LNP vaccine compared to untargeted mRNA-LNP vaccine

Here we compared the Vaccibody platform administered as mRNA-LNP to an untargeted mRNA-LNP vaccine

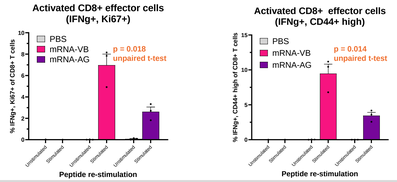
The constructs used were identical to the previous experiment except that the APC-targeting Vaccibody vaccine was administered in a mRNA-LNP format.



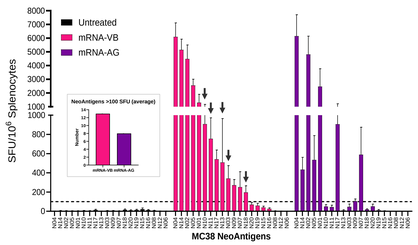
The mRNA-LNP encoded, APC-targeting Vaccibody vaccine induces a stronger immune response after a single (prime) or two (prime & boost) vaccinations



Stronger responses after prime & boost was verified by flow cytometry showing a higher % of activated CD8+ T cells



The mRNA-LNP encoded, APC-targeting Vaccibody induces T cell responses against more neoantigens



SUMMARY

- The Nykode Vaccibody platform can be delivered in a mRNA-LNP vector
- The DNA-encoded Vaccibody vaccine elicits substantially stronger T cell responses than an untargeted mRNA-LNP vaccine already at day 14 following single (prime) vaccination
- The APC-targeting Vaccibody vaccine results in broader T cell responses against a greater number of neoantigens, whether delivered in a DNA or mRNA-LNP format
- The mRNA-LNP APC-targeting Vaccibody vaccine elicits significantly stronger T cell responses than untargeted mRNA-LNP vaccines

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