A novel and versatile cytokine empowered DNA vaccine platform with superior immune activating potential

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nykode therapeutics

Introduction

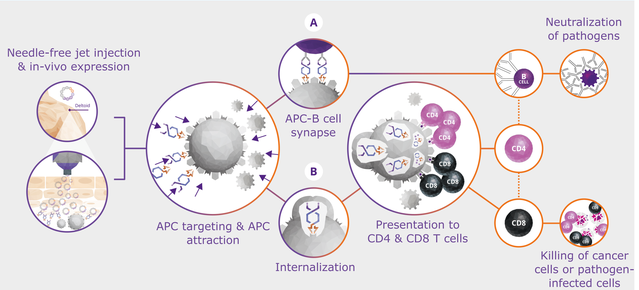
Immunotherapy, in particular Immune Checkpoint Blockade (ICB) has been regarded as the next standard of care for many solid tumor indications. Yet, a significant proportion of patients do not respond to therapy. More specifically, failure of ICB has been linked to the absence of an anti-tumor immune response that can be boosted or revitalized. Cancer vaccines that are designed to elicit such response by educating the host immune system to recognize tumor antigens, are therefore considered a key next generation therapeutic modality for the treatment of human cancers.

Various vaccine platforms have been developed over the years, but recent advances in delivery technologies combined with the intrinsic qualities of the DNA matrix have positioned DNA vaccines as a safe and flexible alternative to other types of vaccine technologies. Nykode Therapeutics is developing DNA vaccines that allows specific targeting of tumors antigens to Antigen Presenting Cells (APCs), thus maximizing the elicited immune response.

Here we present a second-generation version of our DNA platform in which our Vaccibody™ molecule can be co-expressed with immune-stimulatory proteins from one plasmid using a multicistronic design. Compared to the Vaccibody™ molecule alone the simultaneous expression of selected immune stimulatory cytokines was shown to boost the overall immune response almost 3-fold to drive a potent anti-tumor response.

These data demonstrate the flexibility and potential of DNA vaccines as well as the advantages of combining an APC targeted delivery of tumor specific antigens together with a local production of immune stimulatory proteins.

Mechanism of action



Take-home message

- **Nykode Therapeutics is developing its second-generation vaccine.**
- **The new Vaccibody platform encompasses the targeted vaccine and its adjuvants.**
- **The adjuvanted vaccine offers significant advantages in terms of immunogenicity, efficacy, flexibility and fields of application.**

Download our poster!

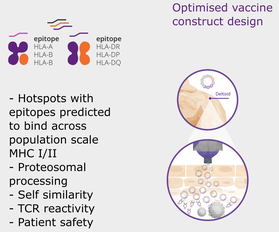
In-house bioinformatics applied to optimal vaccine design across therapeutic areas

OncoSHARED

Identification of shared cancer antigens for off-the -shelf vaccines

Identification of epitopes across patient population/cancer indication

Optimised vaccine construct design



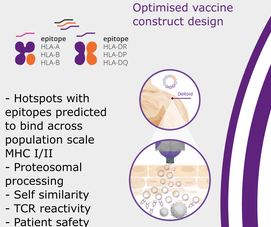
- Hotspots with epitopes predicted to bind across population scale MHC I/II
- Proteosomal processing
- Self similarity
- TCR reactivity
- Patient safety

epicPATH

Identification of conserved epitopes in pathogens

Epitopes mapping and conservation analysis

Optimised vaccine construct design



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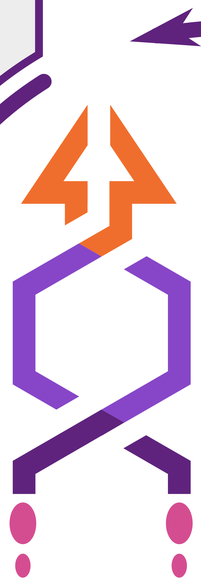
Vaccibody™: A modular vaccine platform



Targeting — **Attract and bind Antigen Presenting Cells (APCs)**
Molecules that bind surface receptors on APCs:
- Natural ligands, including cytokines and chemokines.
- Bacterial proteins
- scFv from mAb binding

Dimerization — **Crosslinking targeted receptor on the surface of the APC**
Favorize essential vaccine mechanisms:
- Molecule internalization
- Endosome escape for optimal HLA-I loading

Antigen(s) — **Mount a target-specific immune response**
Full-length antigens
- Cancer, viral, bacterial, parasitic etc...

Multiple T cell epitopes
- Individualized and shared cancer products
- T cell epitopes for infectious diease
- T cell epitopes for autoimmunity

Adjuvant(s) — **Enhance the immune response**
- Cytokines
- Chemokines
- Growth factors
- Immune modulators
- Receptors agonists

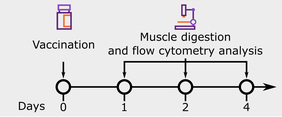
Promotion of APC infiltration, proliferation and differentiation in muscle

Design

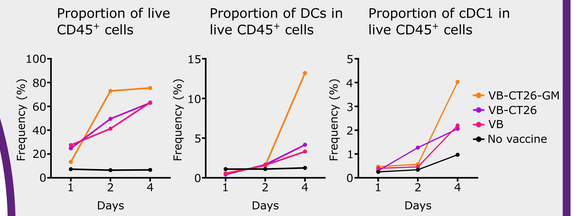
Induction of APC infiltration, proliferation and differentaition are essential steps to ensure the success of a cancer vaccine therapy. Our second-generation platform demonstrates enhanced potency in terms of CD45+ infiltrated cells, proprotion of DCs in general and cDC1 in particular.

BALB/c mice

single 6 µg vaccination i.m.



Results



Second-generation Vaccibody shows a clear enhancement in terms of APC infiltration comparison with the first generation

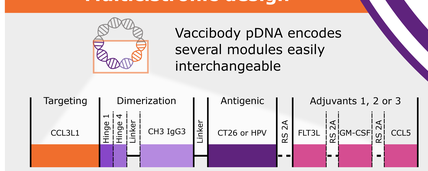
Second-generation Vaccibody is efficiently expressed and secreted

Concept & Rationale

The second-generation of Vaccibody platform consists of an optimized multicistronic format resulting in a high expression and secretion of the different modules.
Each of the module can be replaced to tailor a desired immune response.

pDNA: plasmid DNA

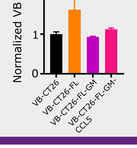
Multicistronic design



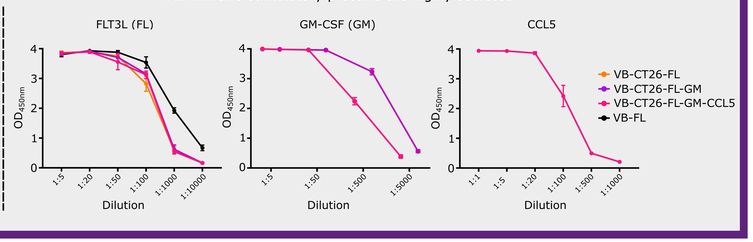
Vaccibody pDNA encodes several modules easily interchangeable

Expression & Secretion

Multicistronic format does not impair VB protein secretion



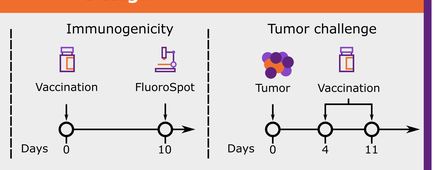
All immune-stimulatory proteins are highly secreted



Enhancement of immunogenicity and long-lasting anti-tumor protection

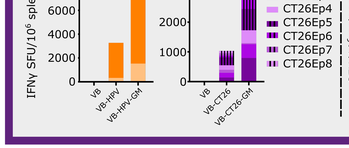
Design

Addition of one or several immuno-modulators to Vaccibody molecule enhances the immune response independently of the antigen nature, leads to an expansion of antigen-specific polyfunctional T cell response and induces a potent anti-tumor response.

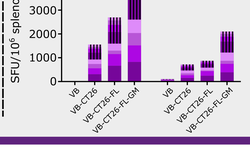


In vivo efficacy

Increased immunity is independent of the antigen nature



Synergy between cytokines elicit a polyfunctional effector T-cells response



Adjuvanted Vaccibody platform inhibits tumor growth in an aggressive cancer model