APC-Targeted Vaccines Deliver Antigen Specific Immune Tolerance in Mouse Models of Autoimmune Disease

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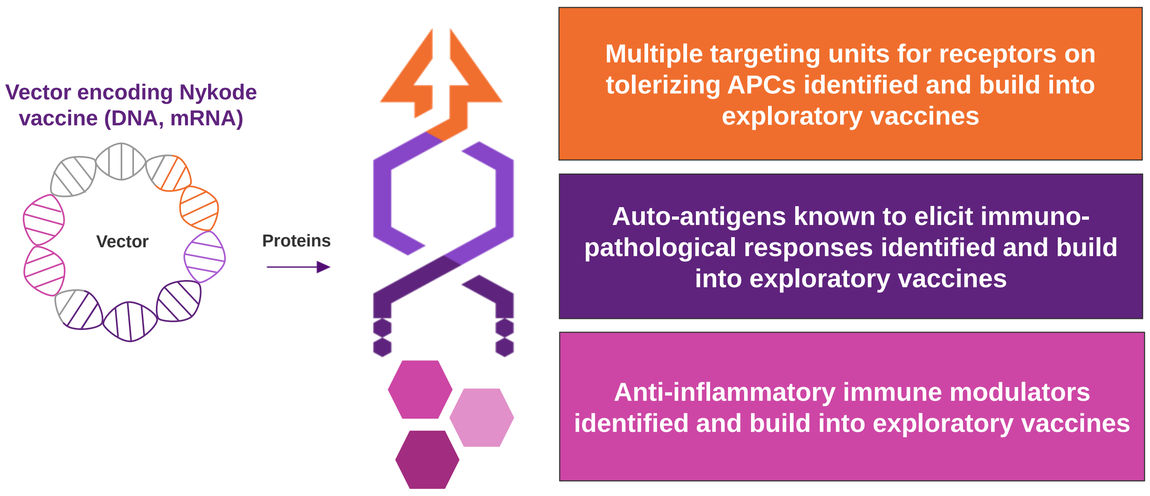
Introduction

Nykode Therapeutics has developed a platform that targets antigens directly to antigen presenting cells (APCs) using a modular dimeric protein format for effective delivery of antigen specific immune tolerance (ASIT)

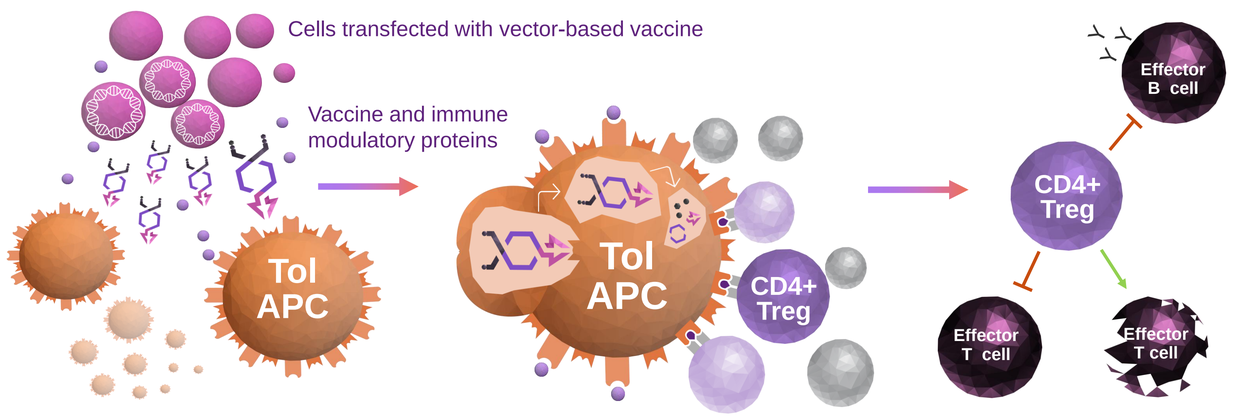
Here, vaccines were designed to deliver a tolerogenic response toward disease-associated antigens via specific APC-receptor-targeting. The vaccines were tested for their tolerogenic potential in Experimental Autoimmune Encephalomyelitis (EAE) models and in Non-Obese Diabetic (NOD) mice either alone or combined with co-expression of immune-modulatory proteins in a multicistronic plasmid DNA.

NYKODE MODULAR VACCINE DESIGN



- Numerous exploratory vaccines build on above modules and evaluated experimentally
- Several patent applications covering these concepts filed
- Nykode's vaccine is clinically validated: VB10.16 Therapeutic vaccine candidate for HPV16+ cancers

NYKODE: TOLERANCE INDUCTION MOA



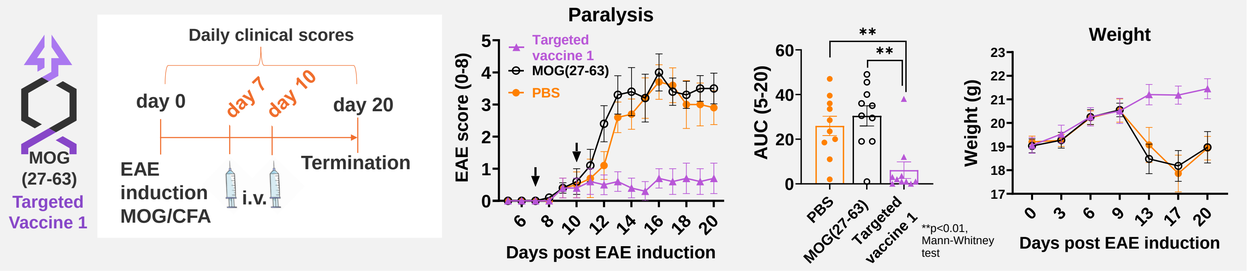
1 Cells encode and secrete tolerogenic APC-targeted proteins together with immunomodulatory molecules to enhance tolerogenic effect.

2 Tol APCs present vaccine antigens in a tolerogenic milieu supported by co-encoded immune modulatory molecules, and prime regulatory T cell (Treg) activation and expansion.

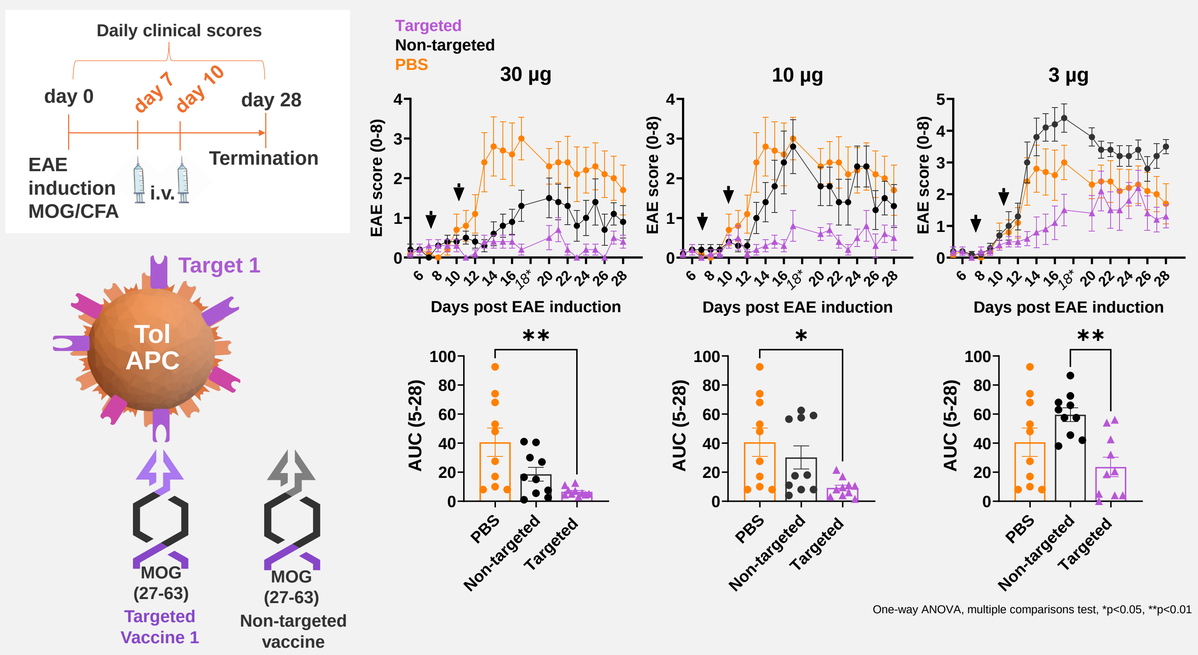
3 Tregs inhibit or delete disease-specific effector T cells and inhibit effector B cells

EFFECT OF NYKODE VACCINE IN EAE MOUSE MODELS

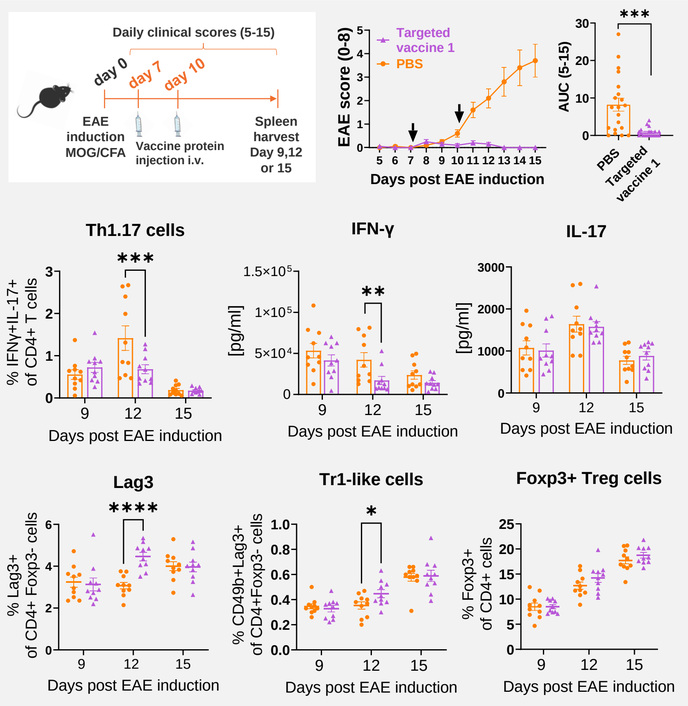
1. Nykode vaccine delivers effective disease therapy versus equimolar dose of antigen peptide alone



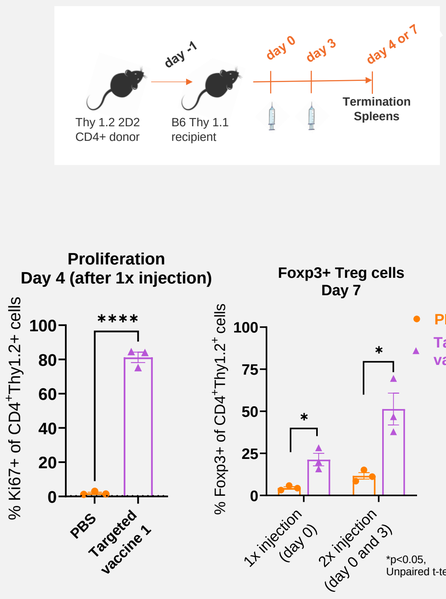
2. APC targeting is required for effective early therapy of EAE disease



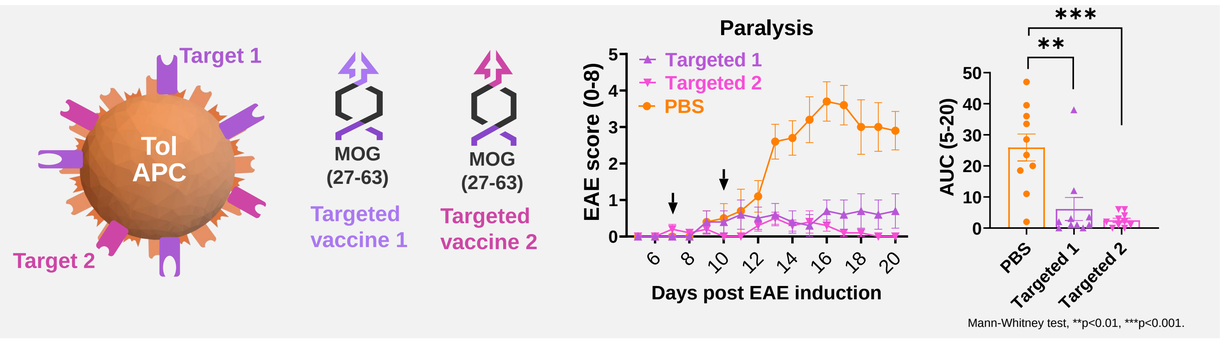
3. Nykode vaccine reduce Ag-specific effector T cell responses and increases frequency of T cells with immune inhibitor



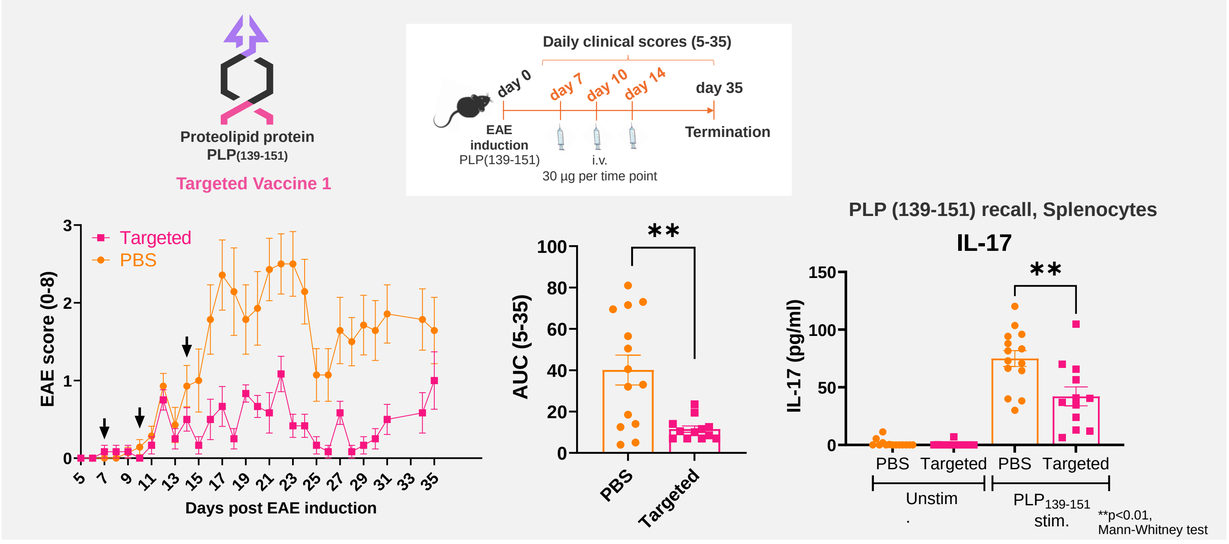
4. Nykode vaccine potently expands and induces Ag-specific Foxp3+ T cells *in vivo*



5. Nykode vaccines targeting different receptors on APCs are effective as early therapy in EAE

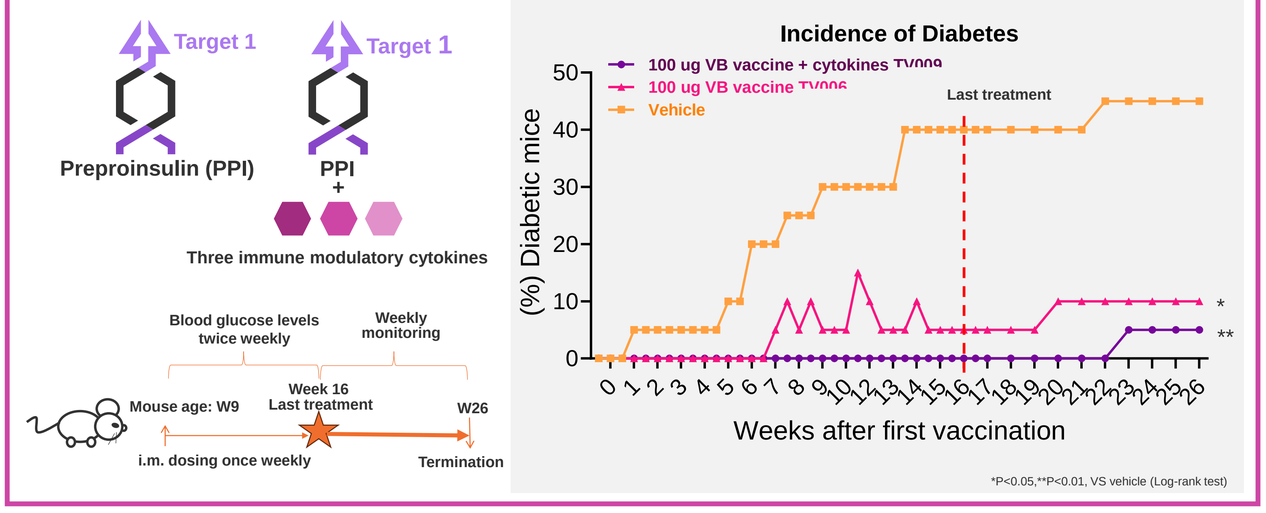


6. Early therapeutic treatment with Nykode vaccine alleviates disease progression in relapsing-remitting EAE



EFFECT OF NYKODE VACCINE IN NOD MOUSE MODEL

7. DNA vaccination with APC-targeting vaccine show durable prevention of diabetes in NOD mice



CONCLUSION

These data demonstrate the flexibility of novel APC-targeted vaccines tailored to target specific APC receptors and deliver potent tolerogenic responses in two different mouse models of autoimmune disease.

NEXT AND ONGOING

In-depth analysis to further dissect the immunological and molecular mechanisms behind the disease control mediated by Nykode's APC targeted vaccines, including:

- Address mechanism of immune modulation in disease tissue
- Further evaluate potency and efficacy of later therapeutic delivery of vaccines
- Assess APC-targeted vaccines potential for inducing bystander suppression

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