nykode therapeutics

APC-Targeted Vaccines Deliver Antigen Specific Immune Tolerance

ASIT

February 2025

Global leader in antigen presenting cell (APC)-targeted immunotherapy technology

NYKODE THERAPEUTICS

Differentiated immunotherapies targeting antigens to Antigen-Presenting Cells (APCs) direct tailor-made immune responses with focus on oncology and autoimmune diseases

Broad clinical pipeline de-risked through strong durability and survival data

- Lead asset VB10.16 focused on high-unmet need indications, including cervical cancer and head & neck cancer
- Individualized cancer vaccine in 2 basket trials for solid tumors

Strategic multiprogram collaboration in oncology and infectious diseases with Regeneron[1]

Autoimmune diseases constitute a potential new therapeutic vertical in high-unmet need indications

Well-capitalized with a cash position of $115.4m at December 31, 2024

1. Collaboration and license to 5 programs with Regeneron.

Broad pipeline targeting early to late-stage cancer treatment

	Asset	Indication	Rights	Preclinical	Phase 1	Phase 2	Phase 3
Oncology							
Off-the-shelf	VB10.16	HPV16+ cervical cancer	nykode [1]				C-02
		HPV16+ head and neck cancer	nykode [2]			C-03	
	Regeneron programs	Undisclosed	nykode REGENERON [3]				
Individualized	VB10.NEO	Incurable locally advanced and metastatic tumors	nykode [2]			N-02	
Infectious Disease							
Regeneron programs		Undisclosed	nykode REGENERON [3]				
Autoimmune							
Internal		Undisclosed	nykode				

1. Wholly-owned by Nykode. Roche supplies atezolizumab; 2. Wholly-owned by Nykode. Merck (MSD) supplies pembrolizumab; 3. Collaboration with Regeneron

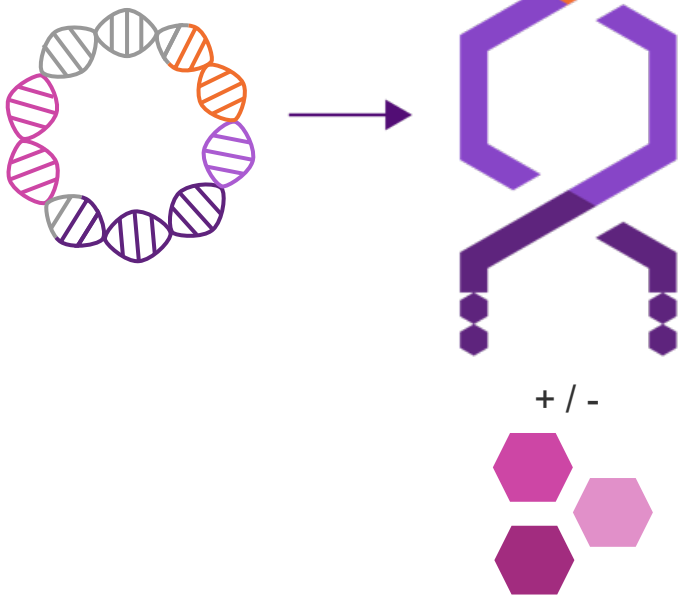
Autoimmune diseases: strong pre-clinical data

The ideal inverse vaccine platform

- Antigen-specific down-regulation of immune responses
- Affecting all major components of the immune system
- Differentiated and versatile MoA allowing adaptation to specific disease
- Long-lasting efficacy both in early stage and late stage disease
- Bystander suppression capacity
- Flexibility to incorporate different antigens coupled with AI solutions for optimal design

Modular design with targeting, antigen and modulatory units able to deliver antigen-specific immune tolerance

Vector encoding
Nykode vaccine



Module 1: Multiple targeting units[1] for receptors on tolerizing APCs identified including natural ligands and other targeting molecules

Module 2: Dimerization unit To facilitate strong bivalent interaction

Module 3: Auto-antigens or allergens known to elicit unwanted immune responses identified

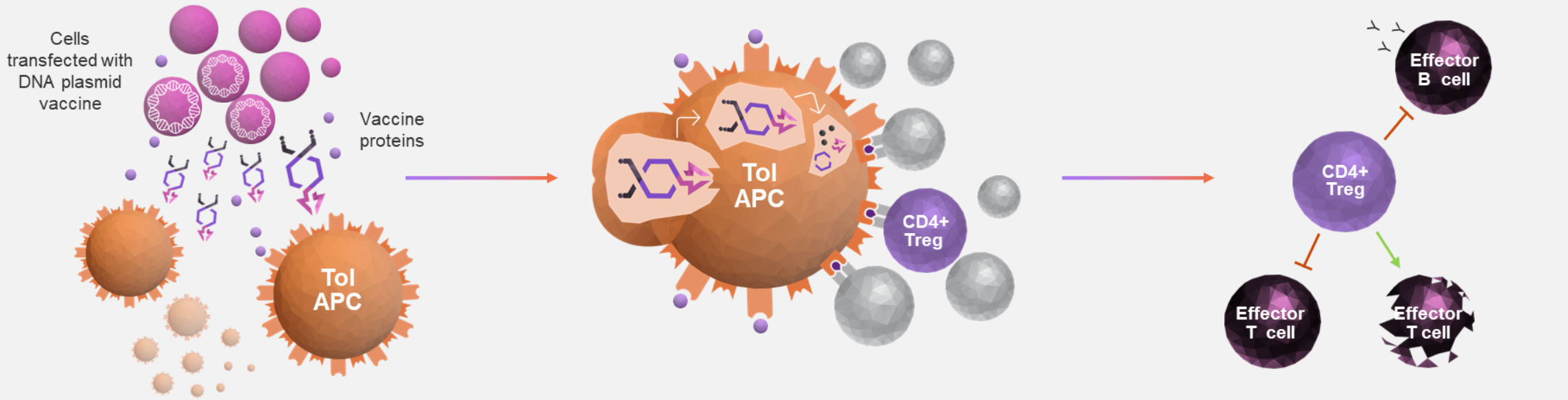
Module 4: Cytokines or modulators playing key roles in mediating anti-inflammatory immune responses

- Numerous exploratory vaccines built on above modules and evaluated experimentally
- Several patent applications covering these concepts filed

Note: [1] Targeting unit can consist of natural ligands, including cytokines/chemokines; bacterial proteins; antibody fragments

Induction of antigen specific tolerance can be achieved by targeting disease causing epitopes to tolerogenic APCs

MECHANISM OF ACTION – TOLERANCE INDUCTION (INVERSE VACCINATION)

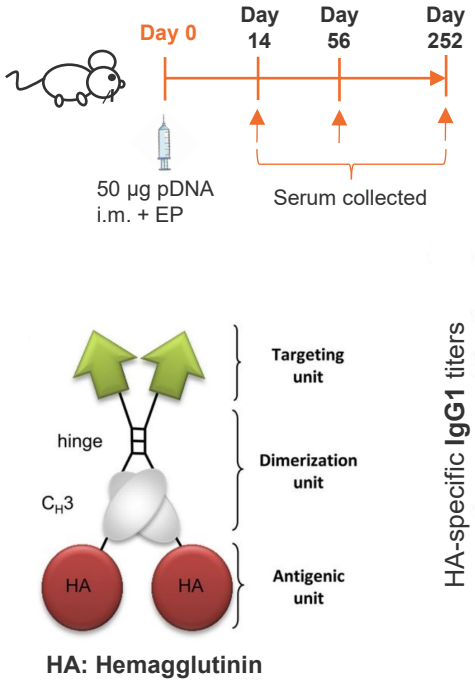


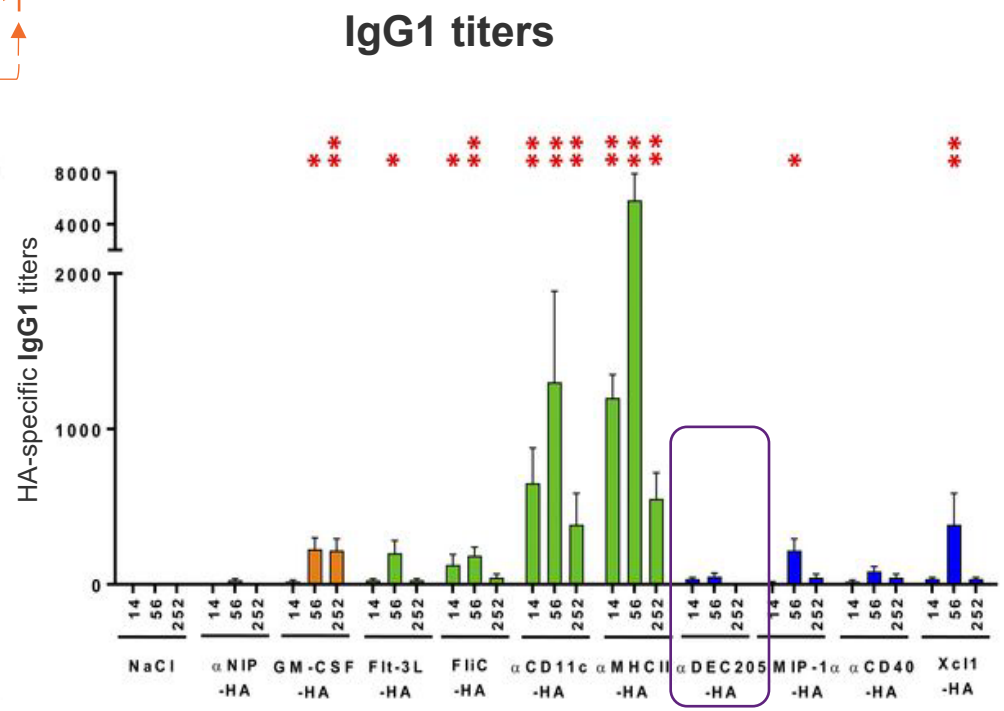
1 Cells encode and secrete Tol APC-targeted Vaccibody proteins together with immunosuppressive molecules/modulators to enhance tolerogenic APC function.

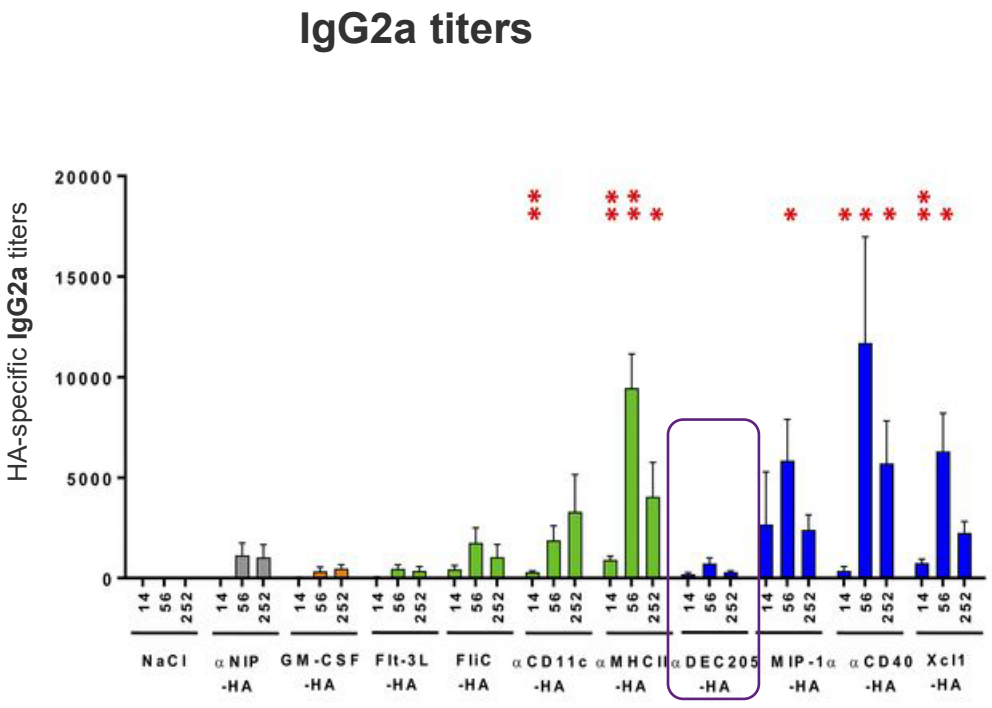
2 The Tol APCs present vaccine antigens in a tolerogenic milieu supported by the vaccine co-encoded suppressive molecules, and prime regulatory T cell (Treg) activation and expansion.

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

Published data demonstrates differential immune responses by targeting distinct receptors on APCs*







* Braathen R et. al. The Magnitude and IgG Subclass of Antibodies Elicited by Targeted DNA Vaccines Are Influenced by Specificity for APC Surface Molecules. *Immunohorizons*. 2018 Jan 18;2(1):38-53.

Strong in-house AI/ML capabilities applied for optimal vaccine design across therapeutic areas

D-KODE

AI guided vaccine design

- *Proprietary state-of-the-art protein AI models*
- *Built on experience from clinically studied vaccines*
- *Iterative learning from growing proprietary data sets including 1000+ vaccine designs across therapeutic areas*

Integrity
Expression
Secretion

NeoSELECT

Identification of patient-specific neoepitopes

Advanced AI/ML platform built on the proprietary data

- *Validated in two clinical trials*
- *Successful personalized vaccine design for > 100 patients across multiple indications*
- *Vaccine induced neoantigen immune response in 91 % of evaluable patients*
- *Integration with multi-biopsy data and liquid biopsies to account for cancer heterogeneity*
- *Multiple neoantigen classes including frameshift neoantigens*

sharedSELECT

Identification of shared antigens for off-the-shelf vaccines

Maximum coverage proprietary algorithm

- *Applicable to multiple disease areas: Infectious disease, Oncology, Tolerance*
- *Includes dark antigen discovery*
- *Successfully designed and validated multiepitopes vaccines*

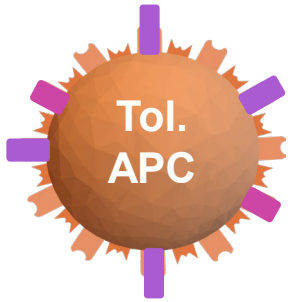
Immune Tolerance

AI guided inverse vaccines design

Building on experience in oncology

- *AI driven structure modelling for platform development and vaccine design*
- *In-house multiomics analysis driving design of platform and APC-targeting units to induce tolerance*
- *MHCII presentation predictions & sequence conservation analysis to apply in tolerance inducing antigen selection*
- *Uniquely positioned to pivot into personalized tolerance vaccines based on proprietary NeoSelect experience*

APC targeting is required for effective disease protection



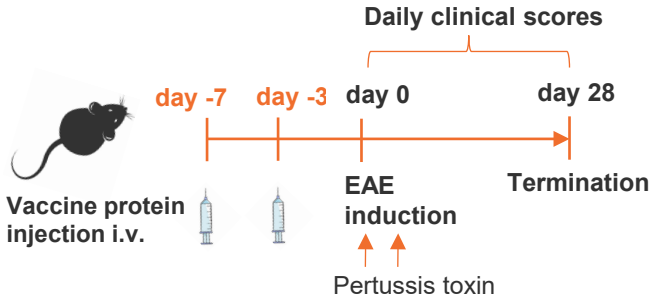
Myelin oligodendrocyte glycoprotein (**MOG**)

MOG (27-63)

Targeted Vaccine 1

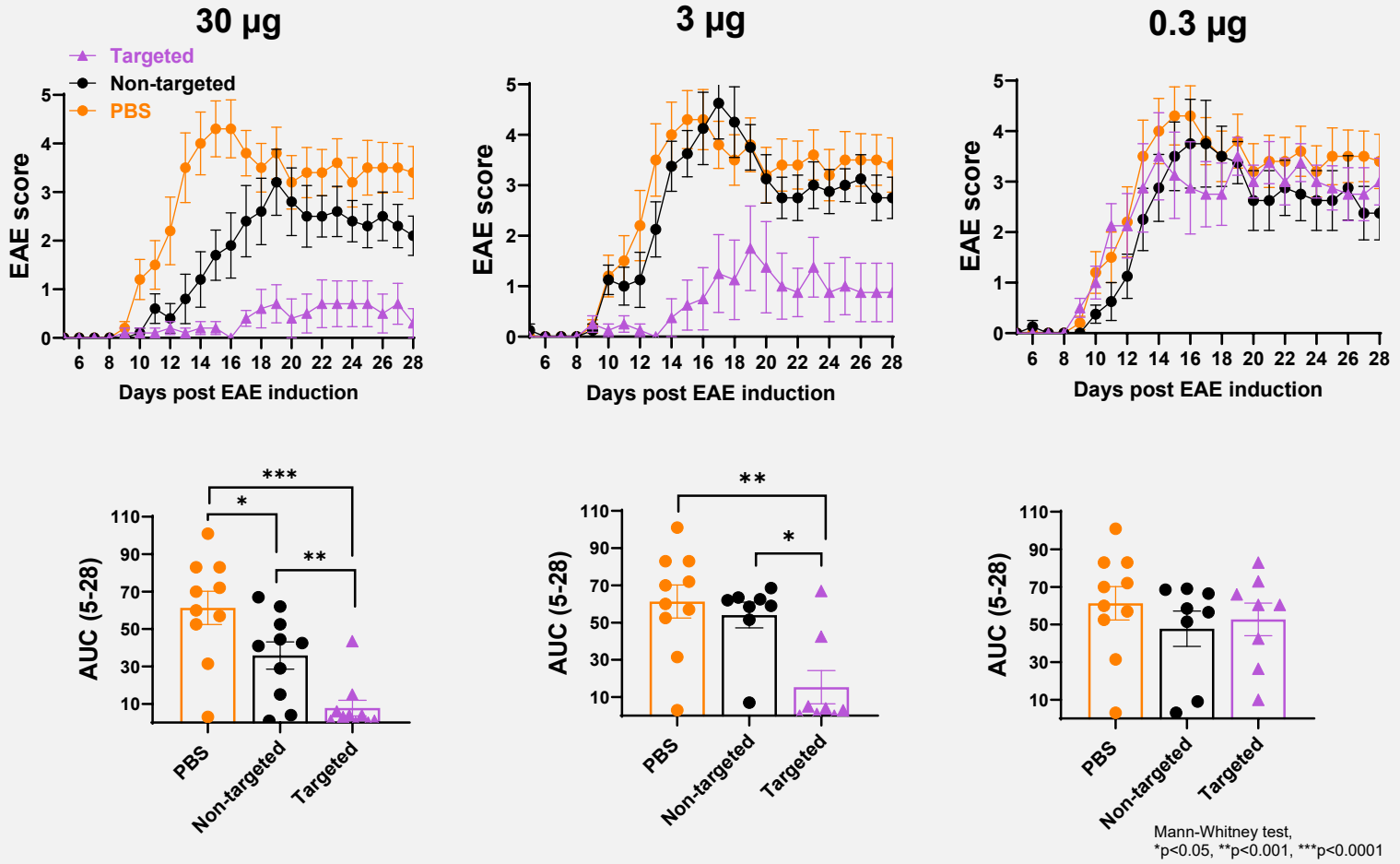
MOG (27-63)

Non-targeted vaccine

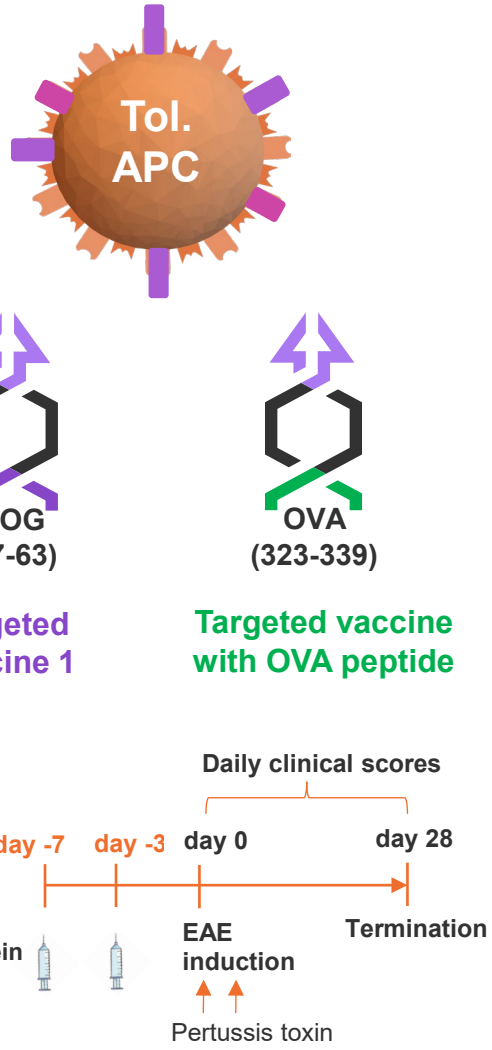


Experimental autoimmune encephalomyelitis (**EAE**)

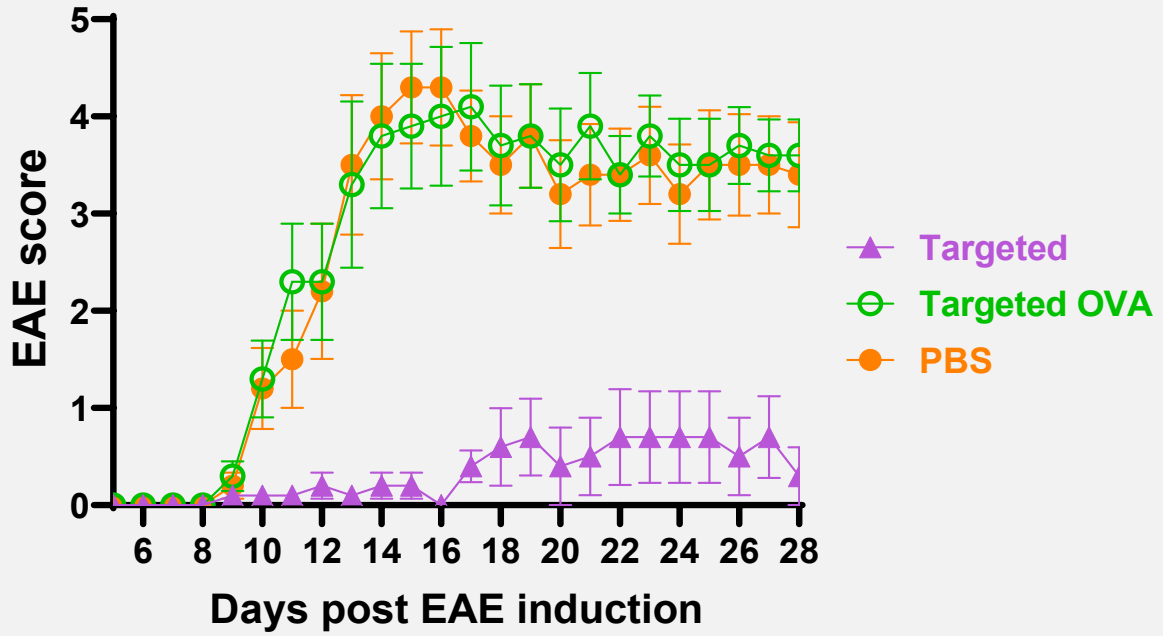
EAE MODEL – PREVENTIVE THERAPY



Nykode vaccine delivers Ag-specific suppression of EAE



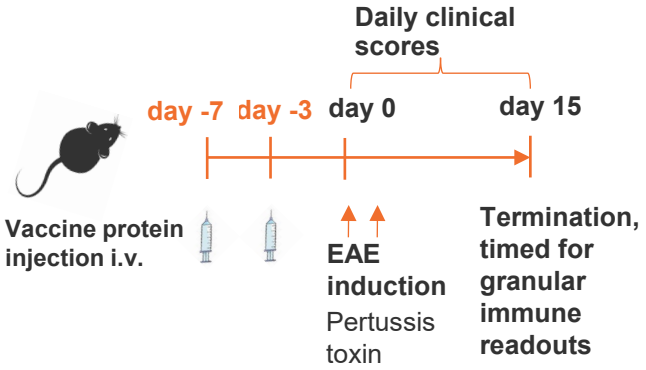
EAE MODEL – OVA CONTROL



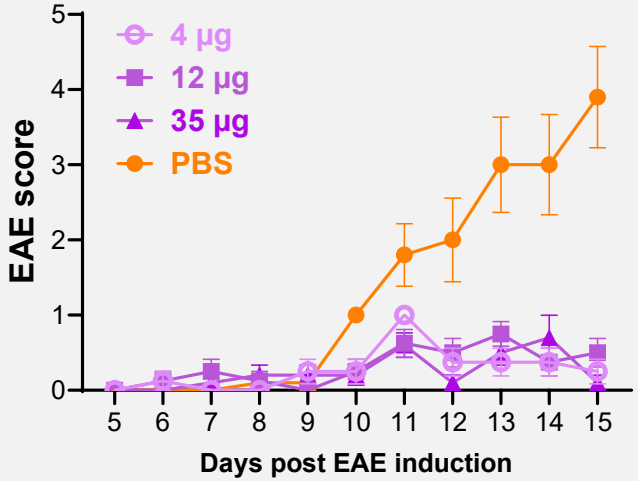
Nykode vaccine delivers dose-dependent effect on antigen-specific disease-associated cytokine-release

MOG
(27-63)

Targeted
Vaccine 1

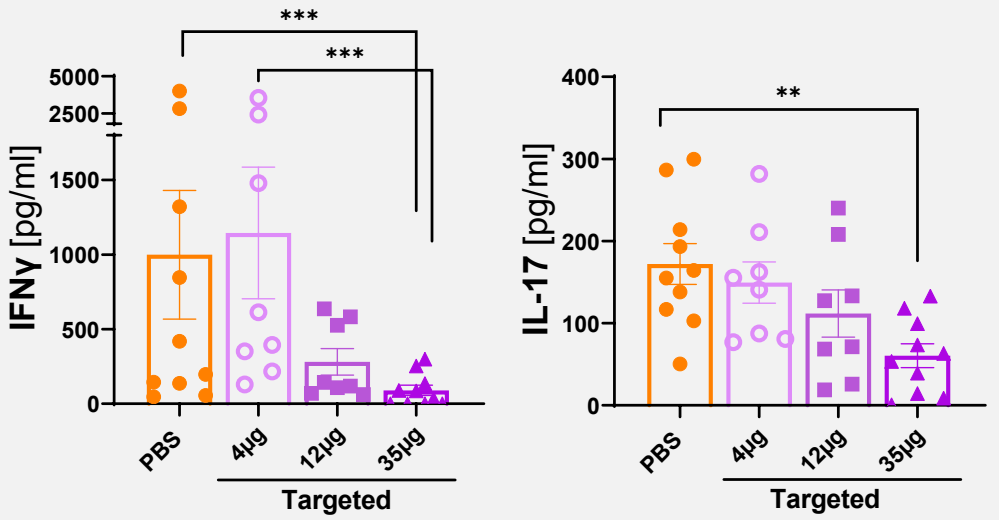


EAE MODEL – IMMUNE PARAMETER READ OUT



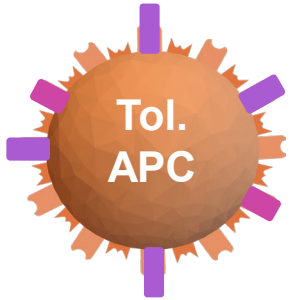
Immune parameter read-out at day 15 (**at peak of disease**)

MOG(35-55) recall assay using splenocytes



Mann-Whitney test, **P < 0.01, ***P < 0.001.

APC targeting is required for effective early therapy of EAE disease

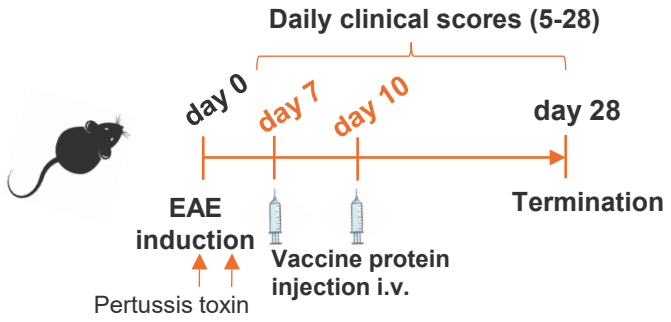


MOG (27-63)

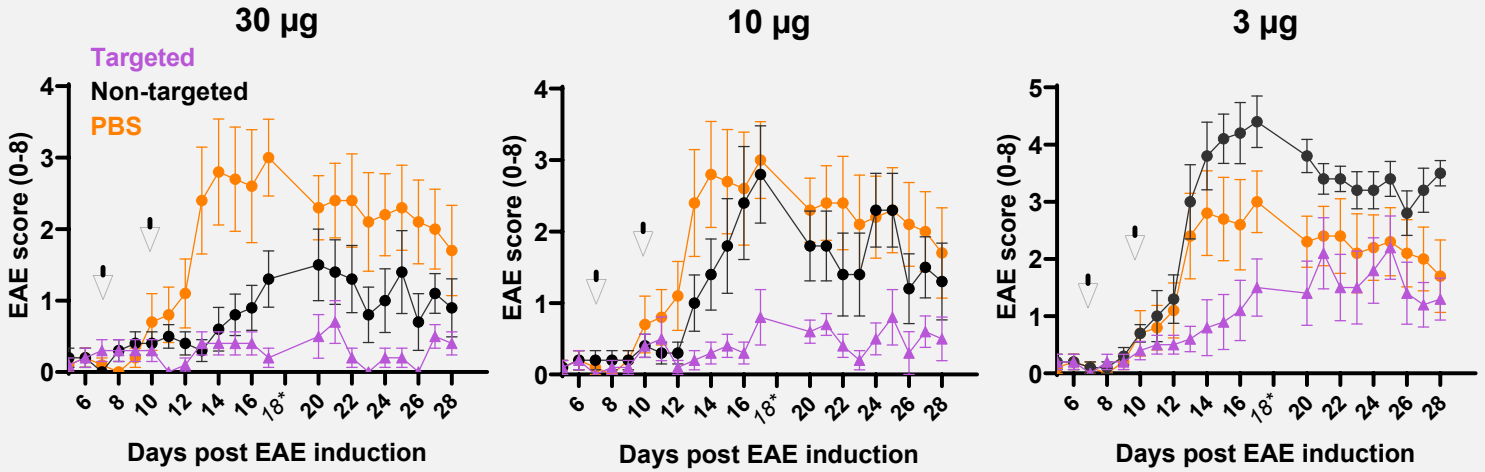
Targeted Vaccine 1

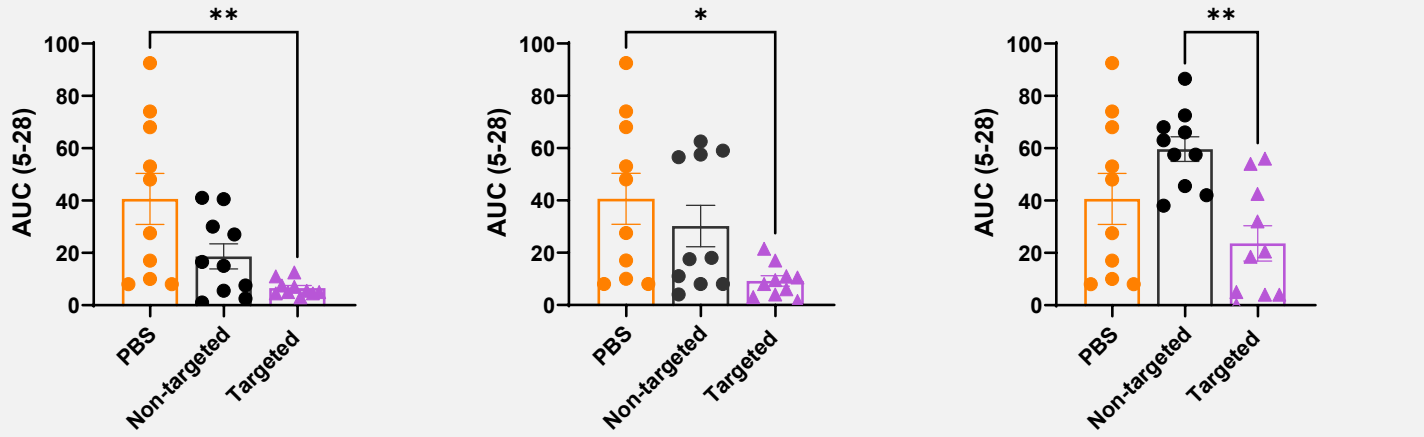
MOG (27-63)

Non-targeted vaccine



EAE MODEL – EARLY THERAPEUTIC DELIVERY



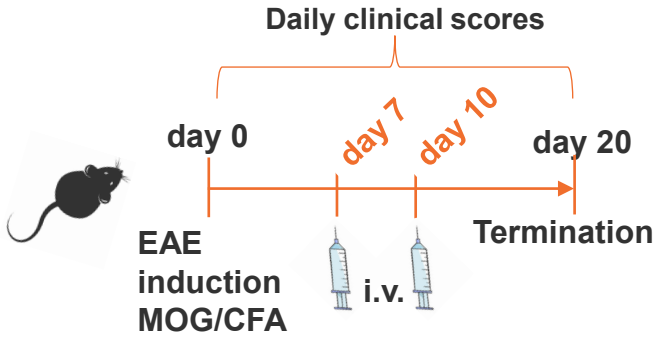


One-way ANOVA, multiple comparisons test, *p<0.05, **p<0.01

Nykode vaccine deliver early therapeutic disease protection, in contrast to equimolar dose of antigen peptide alone

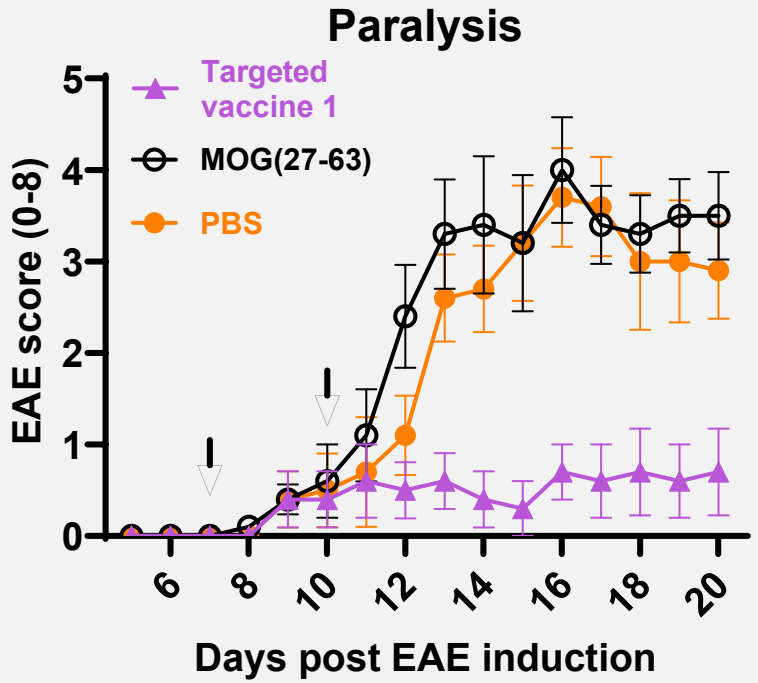
MOG
(27-63)

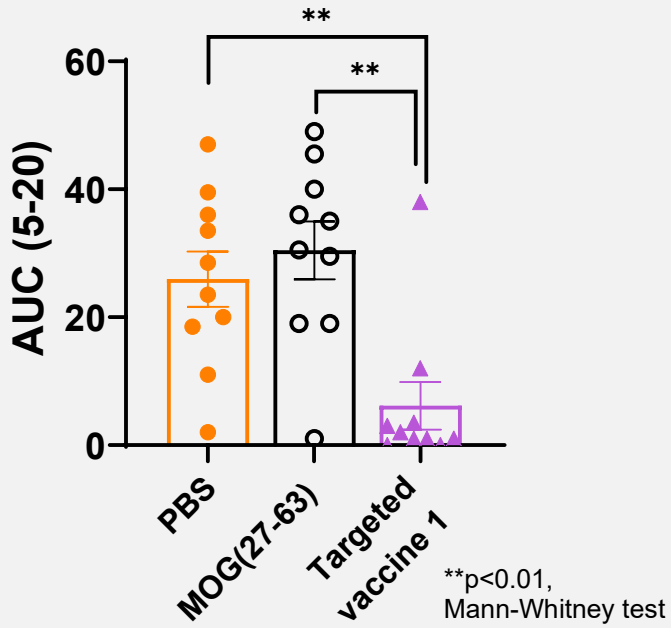
Targeted Vaccine 1



- **Targeted vaccine 30 µg** dose is equimolar to the **MOG(27-63) 3 µg** dose

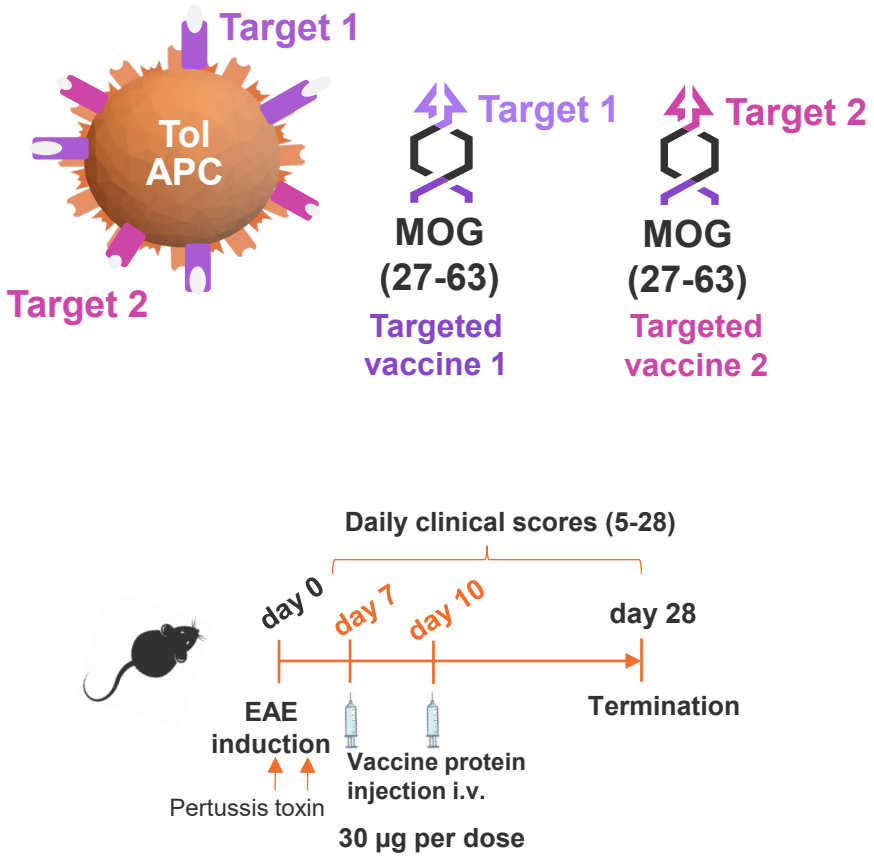
EAE MODEL – EARLY THERAPEUTIC DELIVERY



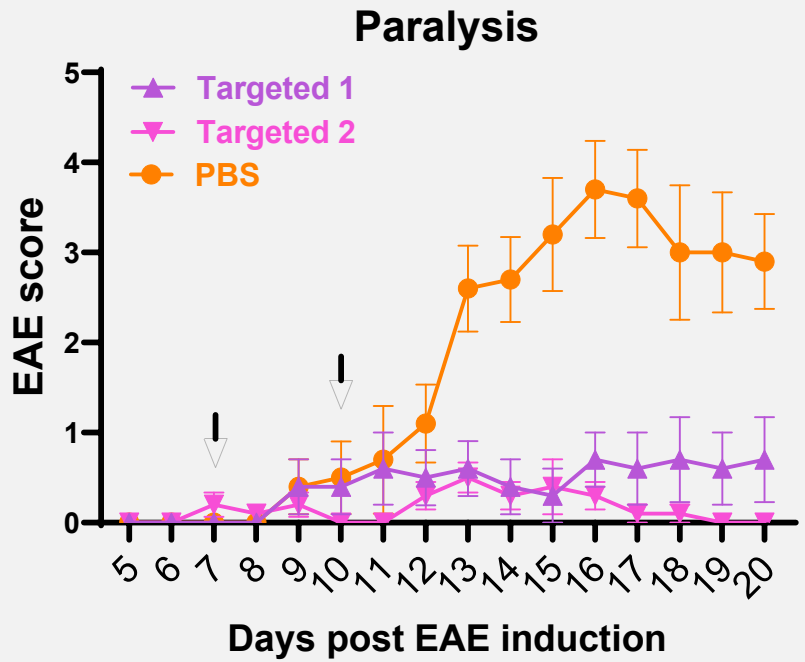


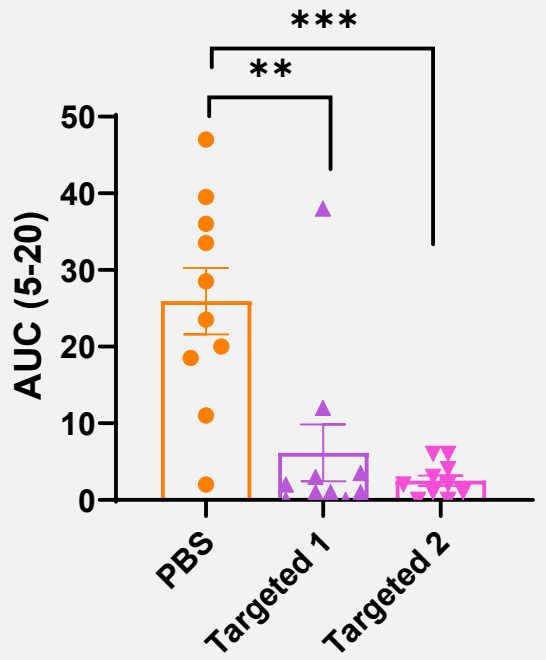
**p<0.01,
Mann-Whitney test

Nykode vaccine targeting different receptors on APCs is effective as early therapeutic in EAE



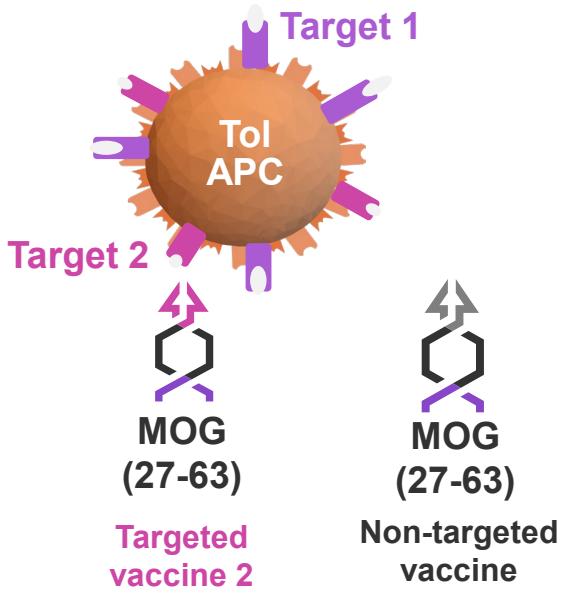
EAE MODEL – EARLY THERAPEUTIC DELIVERY

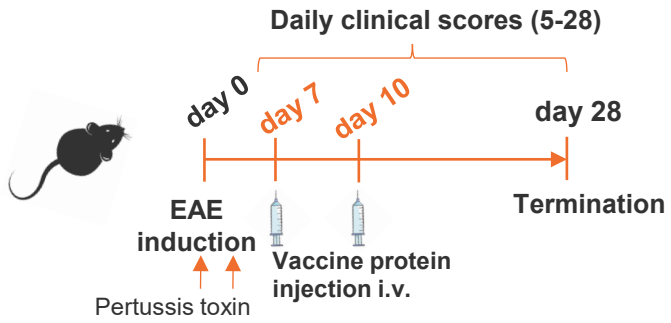




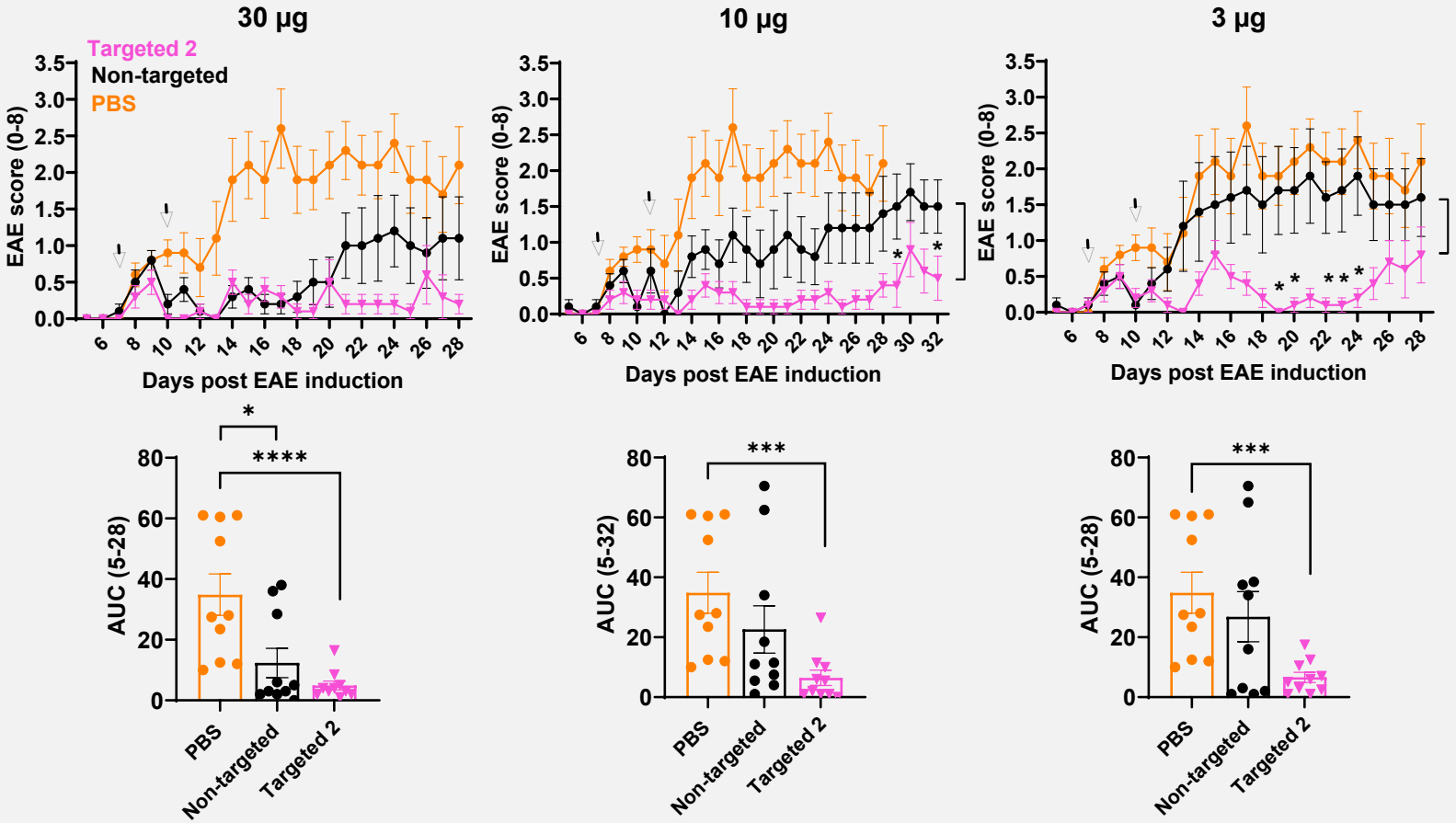
Mann-Whitney test, **p<0.01, ***p<0.001.

APC targeting is required for potent and prolonged effect of vaccine to second target as early therapy in EAE





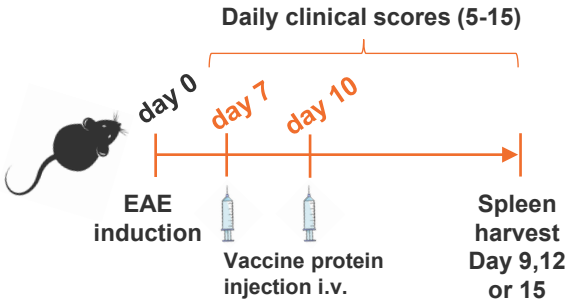
EAE MODEL – EARLY THERAPEUTIC DELIVERY



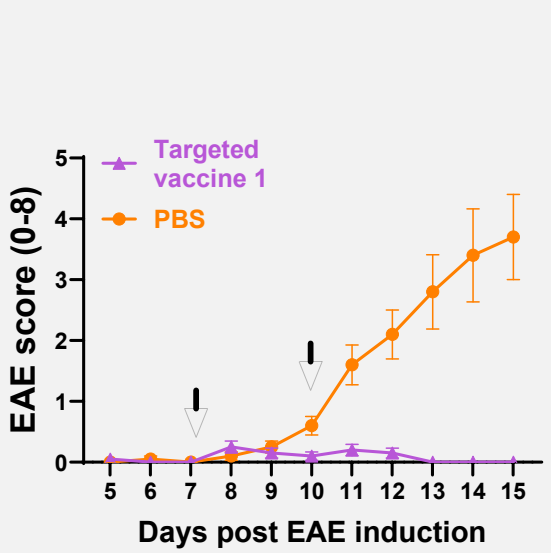
Nykode vaccine reduce Ag-specific effector T cell responses and increases frequency of T cells with immune inhibitor

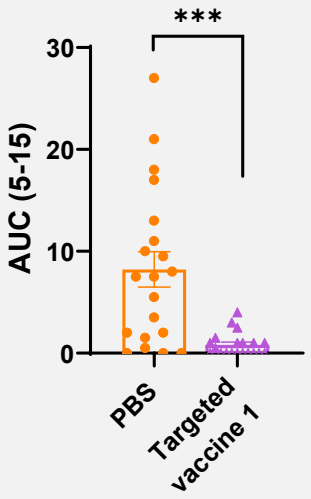
MOG
(27-63)

Targeted Vaccine 1

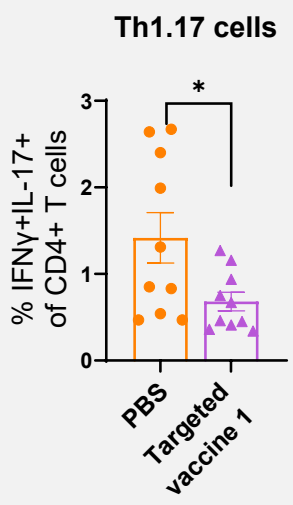


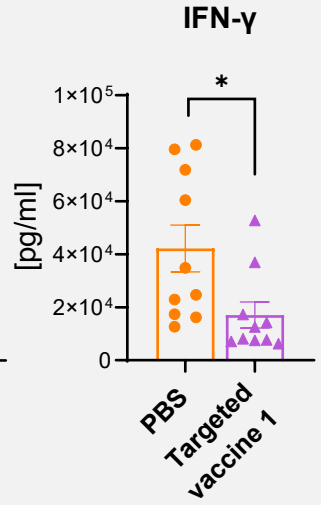
EAE MODEL – EARLY THERAPEUTIC DELIVERY

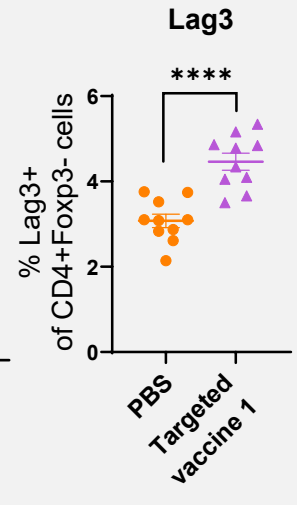




Day 12 post EAE induction:
MOG-recall Splenocytes

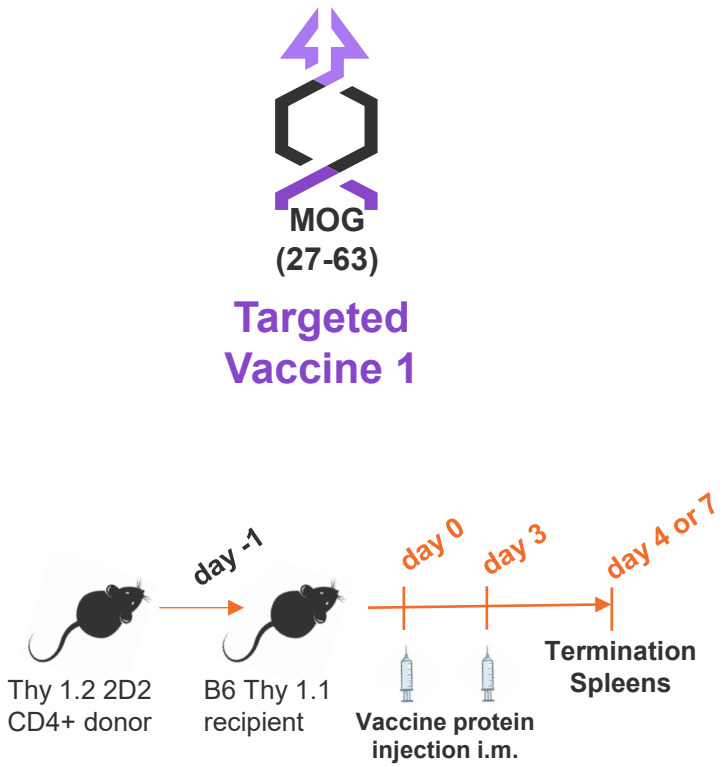




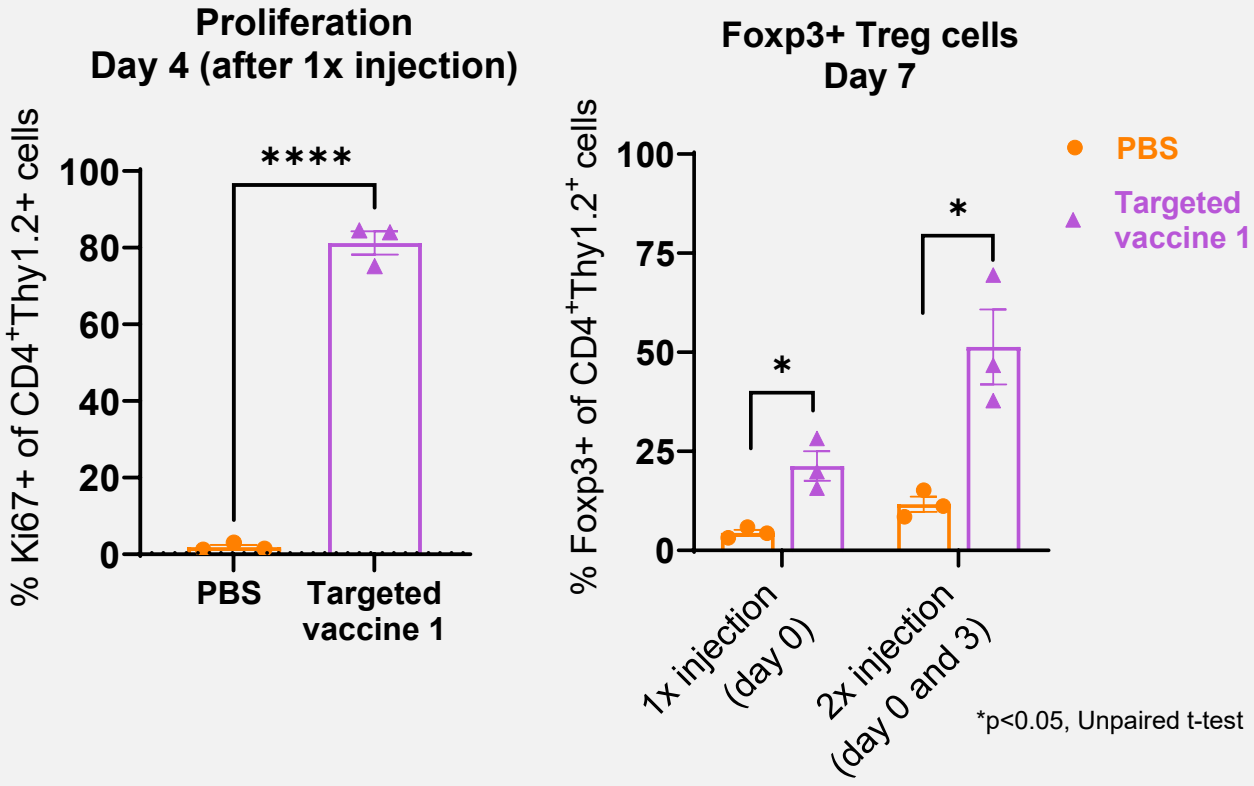


*p<0.05, ***p<0.001, ****p<0.0001, Unpaired t-test

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



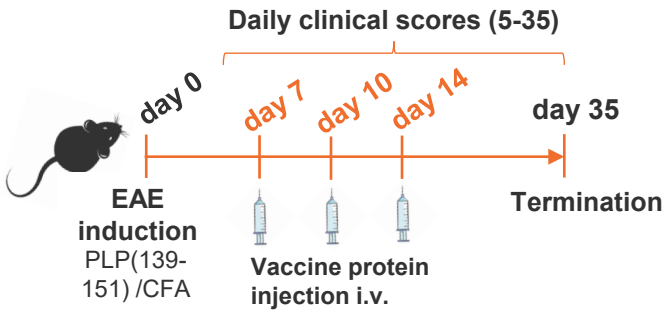
ADOPTIVE TRANSFER OF MOG-SPECIFIC CD4+ T CELLS



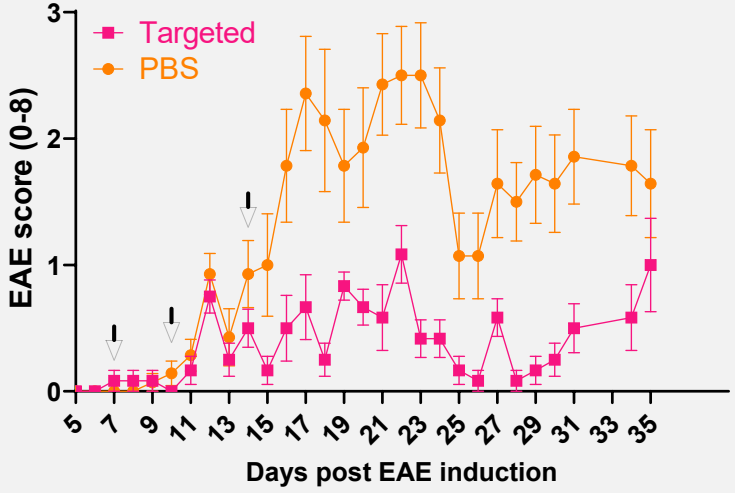
Early therapeutic treatment with Nykode vaccine alleviates disease progression in relapsing-remitting EAE

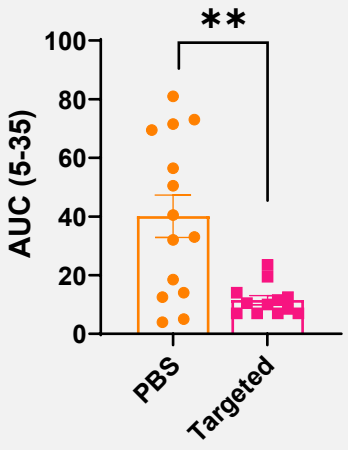
Proteolipid protein
PLP(139-151)

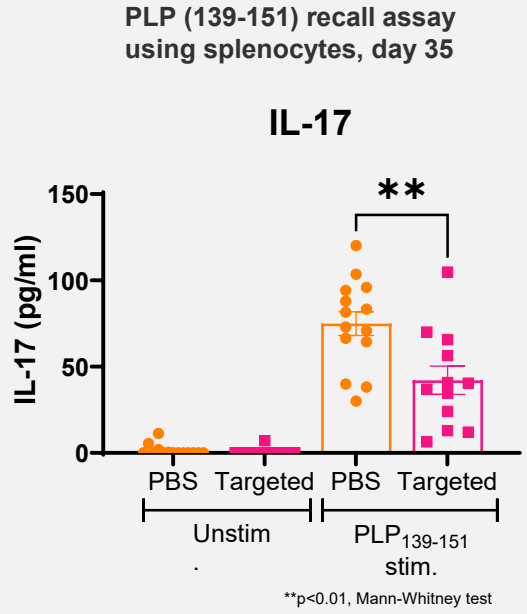
Targeted
Vaccine 1



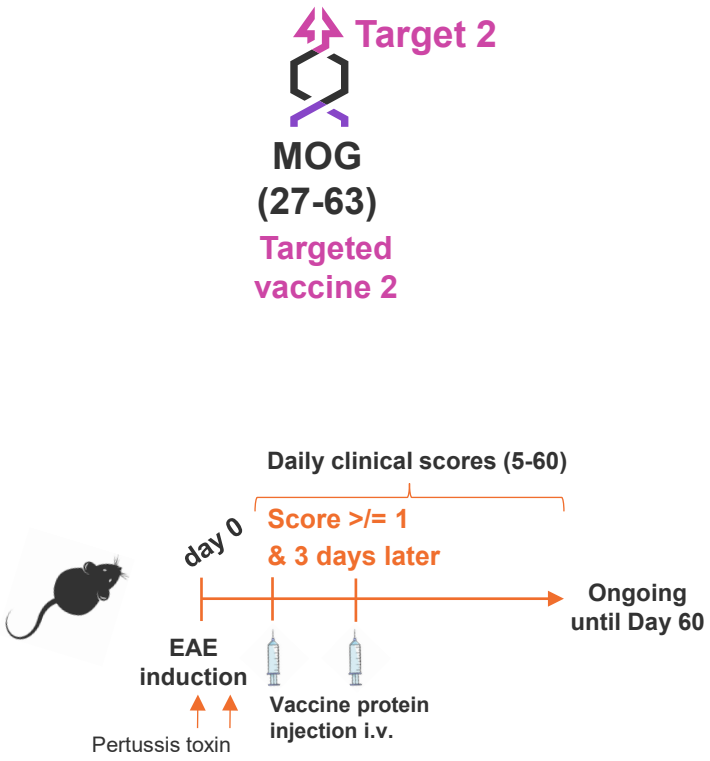
RELAPSING-REMITTING EAE MODEL – EARLY THERAPEUTIC DELIVERY



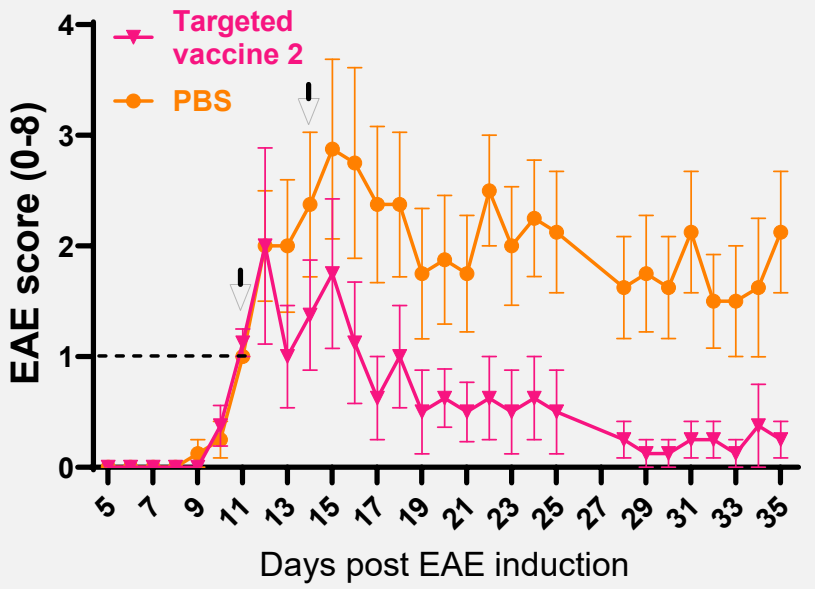


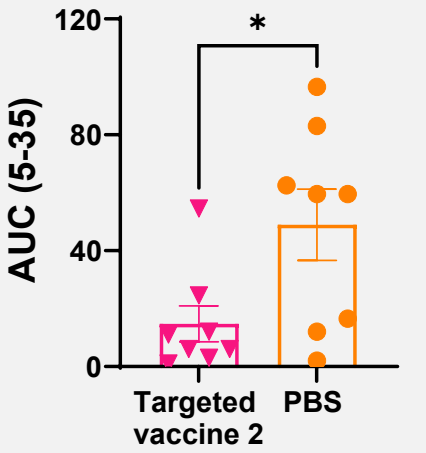


Nykode vaccine significantly ameliorates EAE disease in symptomatic mice



LATER THERAPEUTIC TREATMENT – EAE MODEL



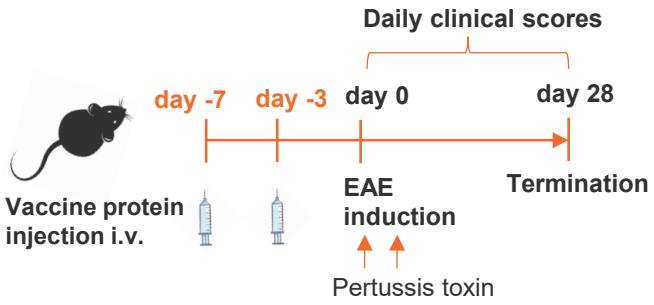


*p<0.05, Mann-Whitney test

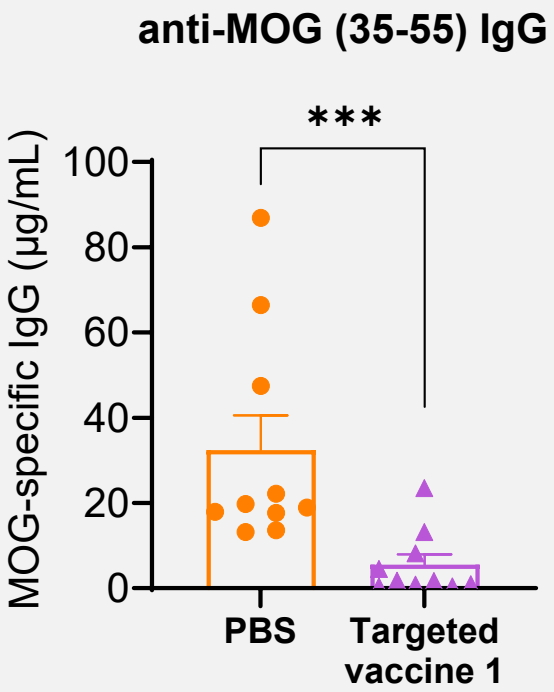
APC targeting can also impact humoral immune responses

MOG
(27-63)

Targeted
Vaccine 1



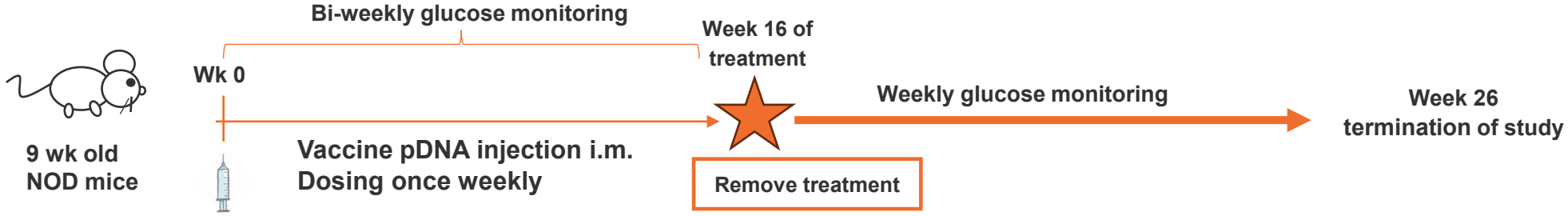
EAE MODEL – AUTOANTIBODY READ OUT



***p<0.001, Mann-Whitney test

- **Auto-antibodies play an important role in immune diseases**
- **Treatment induced reduction of MOG-specific IgG auto-antibodies in EAE**

Nykode DNA vaccination targeting APCs show durable effect in NOD mice

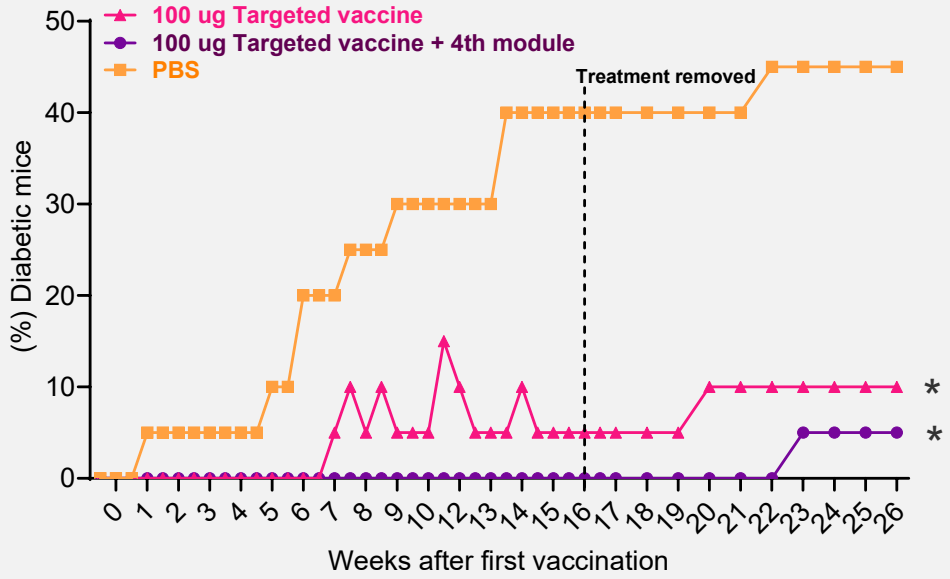


NOD DIABETES MODEL

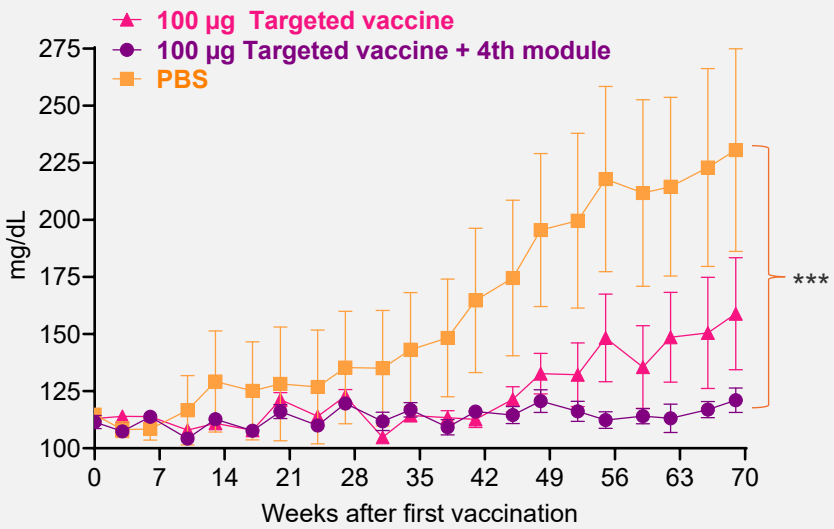
Targeted vaccine

Diabetes antigen: PPI

Incidence of Diabetes



Blood glucose levels



PPI antigen alone is not protective in this model. Grönholm J et al.,2017, Pagni PP et al (2022), Pham MN et al, 2016, Daniel C et al. 2011

The ideal inverse vaccine platform

Antigen-specific down-regulation of immune responses	Ag-specific T cell efficacy and effector T cell cytokine downregulation
Affecting all major components of the immune system	Downregulate Ag-specific IgG and effector T cells, upregulating regulatory T cells
Differentiated and versatile MoA allowing adaptation to specific disease	APC-targeting essential for efficacy and durability. Binds specific receptors on mouse and human APCs (from hPBMCs). Panel of APC-targeting units characterized for differentiated immune-modulating effect
Long-lasting efficacy both in early stage and late stage disease	Preventive and therapeutic efficacy in EAE and T1D. Durable efficacy (d30+ in EAE)
Bystander suppression capacity	Relapsing-remitting (RR) EAE model established. APC-targeted PLP vaccine effective in RR-EAE as early therapy. Ag-specific cytokine downregulation part of vaccine effect
Flexibility to incorporate different antigens coupled with AI solutions for optimal design	Relapsing-remitting (RR) EAE model established. APC-targeted PLP vaccine effective in RR-EAE as early therapy. Ag-specific cytokine downregulation part of vaccine effect

UNLOCKING THE FUTURE OF MEDICINE