



APC-Targeted Vaccines Deliver Ag-specific Tolerance in Mouse Models of Autoimmunity

Louise Bjerkan

Discovery Project Leader, Senior Scientist

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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 pipeline de-risked through strong durability and survival data

- ◆ Lead asset VB10.16 focused on high-unmet need indications, including locally advanced cervical cancer and r/m head and neck cancer



Strategic partnerships with top tier US biopharma companies²

- ◆ Personalized cancer vaccine in partnership with Genentech
- ◆ Multiprogram (oncology and infectious diseases) collaboration with Regeneron

Genentech
A Member of the Roche Group

REGENERON



Autoimmune diseases constitute a potential new therapeutic vertical in high-unmet need indications (e.g., MS, T1D)



Well-capitalized with a cash position of \$136.5m at June 30, 2024

1. Note: Genentech has an exclusive license to VB10.NEO. Collaboration and license to 5 programs with Regeneron. Collaboration and license with Adaptive Biotechnologies on SARS-CoV-2 T cell vaccine. Roche supplies atezolizumab. Merck (MSD) supplies pembrolizumab

Top-tier collaborations for cancer and infectious disease vaccines valued potentially more than \$1.64 billion plus royalties

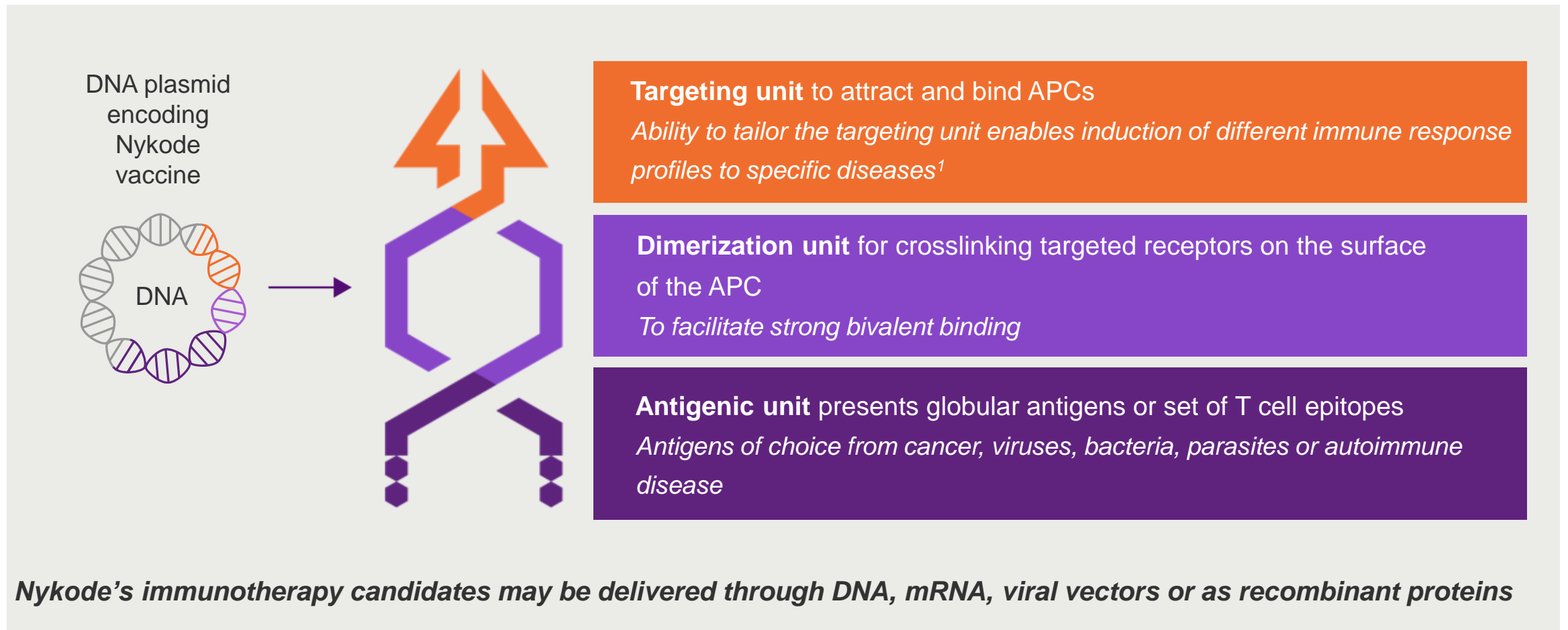
Partner	Collaboration	Terms	Clinical Development
REGENERON	Multi-target license and collaboration agreement to develop 3 oncology and 2 novel infectious disease programs	<p>\$925M~</p> <ul style="list-style-type: none"> ◆ \$30M upfront ◆ \$20M equity investment ◆ Potentially more than \$875M in milestone payments ◆ Tiered high single-digit to low double-digit royalties 	<p>Regeneron to develop and potentially commercialize products</p> <p>Nykode to supply technology and product supply through Phase 1 trials</p>
Genentech <i>A Member of the Roche Group</i>	Worldwide, exclusive license and collaboration agreement to develop VB10.NEO, Nykode’s individualized neoantigen cancer vaccine	<p>\$715M~</p> <ul style="list-style-type: none"> ◆ \$200M upfront/near term ◆ \$515M in potential payments and milestones ◆ Tiered low double-digit royalties 	<p>Nykode to conduct clinical trials through Phase 1b</p> <p>Genentech to subsequently conduct clinical, regulatory, manufacturing and commercialization activities</p>

Broad pipeline targeting early to late-stage cancer treatment

	Asset	Indication	Rights	Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Catalyst
Oncology								
Off-the-shelf	VB10.16	HPV16+ cervical cancer	1				C-02	Publication of final data
		HPV16+ head and neck cancer	2			C-03		Dose level recommendation (2H 2024)
		HPV16+ locally advanced cervical cancer	2					C-05
	Regeneron programs	Undisclosed	3					
Individualized	VB10.NEO	Incurable locally advanced and metastatic tumors	4				N-02	
Infectious Disease								
	Regeneron programs	Undisclosed	3					
Autoimmune								
	Internal	Undisclosed						Update in Q4

1. Wholly-owned by Nykode. Roche supplies atezolizumab; 2. Wholly-owned by Nykode. Merck (MSD) supplies pembrolizumab; 3. Collaboration with Regeneron; 4. Genentech has an exclusive license to VB10.NEO.

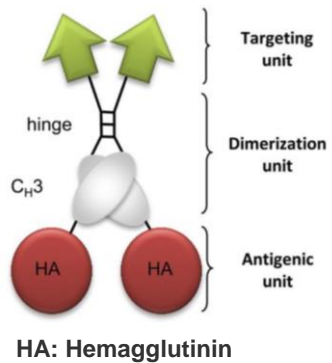
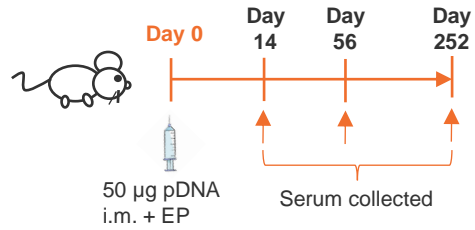
Nykode's proprietary technology platform allows APC-targeting to direct immune responses



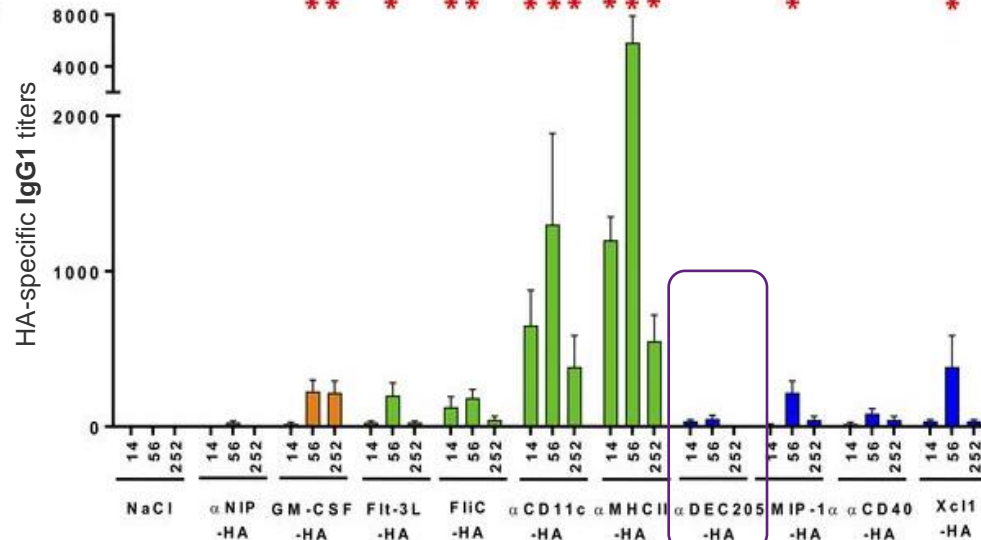


Autoimmune diseases: strong pre-clinical data

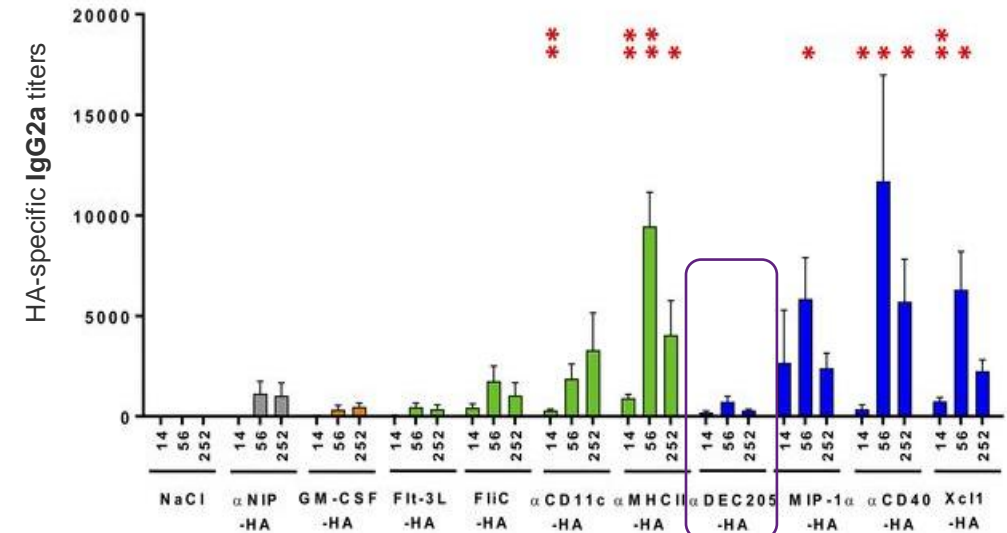
Differential immune responses (Antibodies) by targeting distinct receptors on APCs*



IgG1 titers



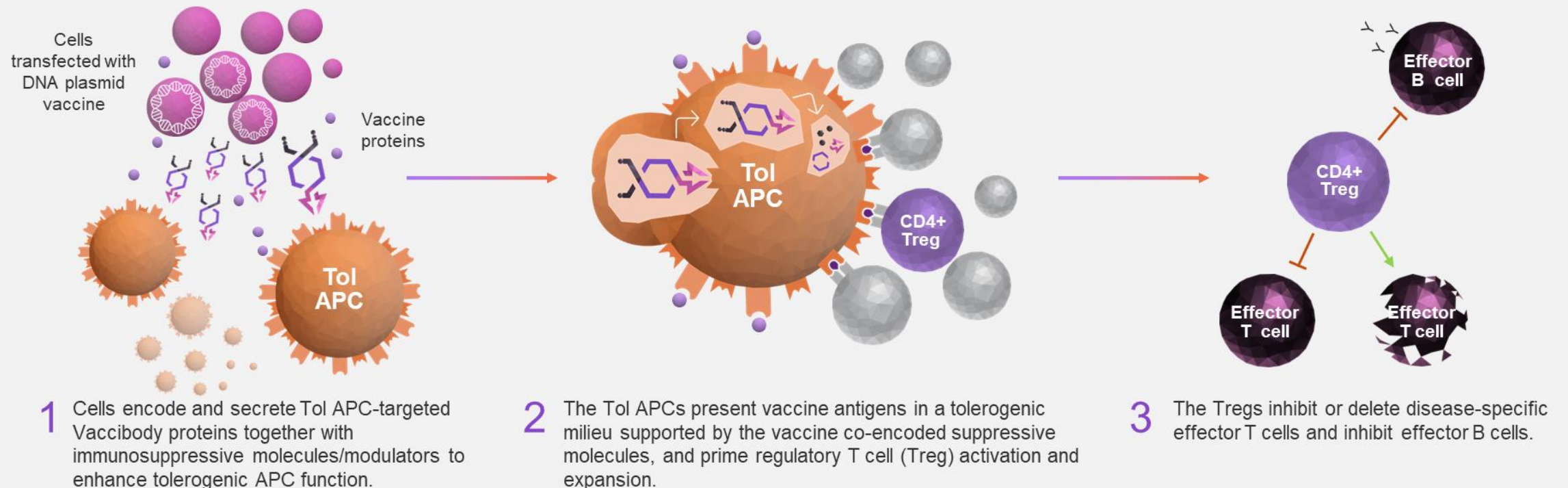
IgG2a titers



* 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.

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

MECHANISM OF ACTION – TOLERANCE INDUCTION (INVERSE VACCINATION)



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

Vector encoding
Nykode vaccine



+ / -



Module 1: Multiple targeting units¹ for receptors on tolerizing APCs identified including natural ligands and other targeting molecules

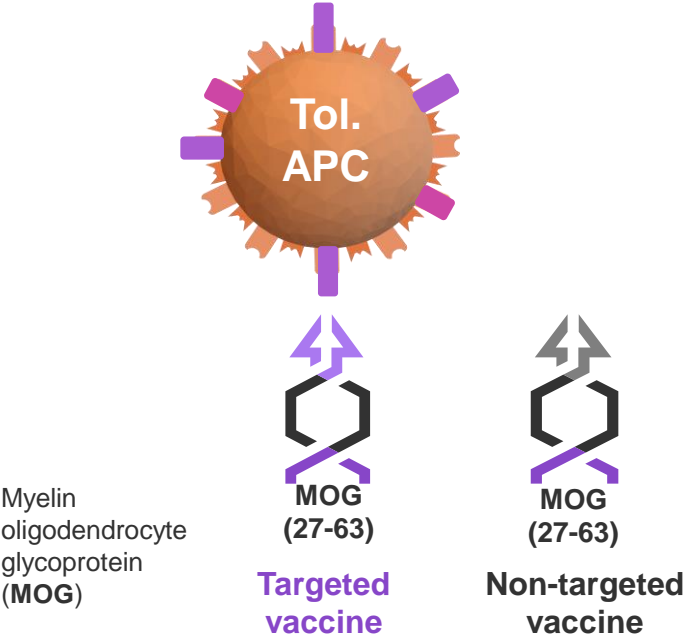
Module 2: Dimerization unit To facilitate strong bivalent interaction

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

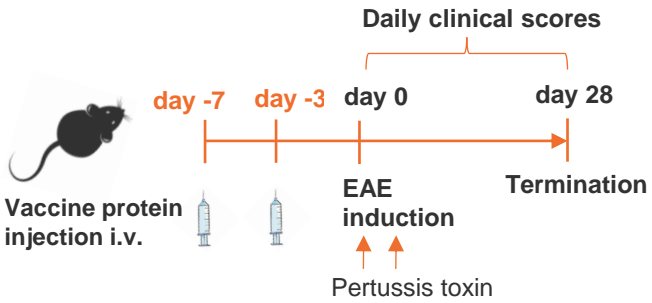
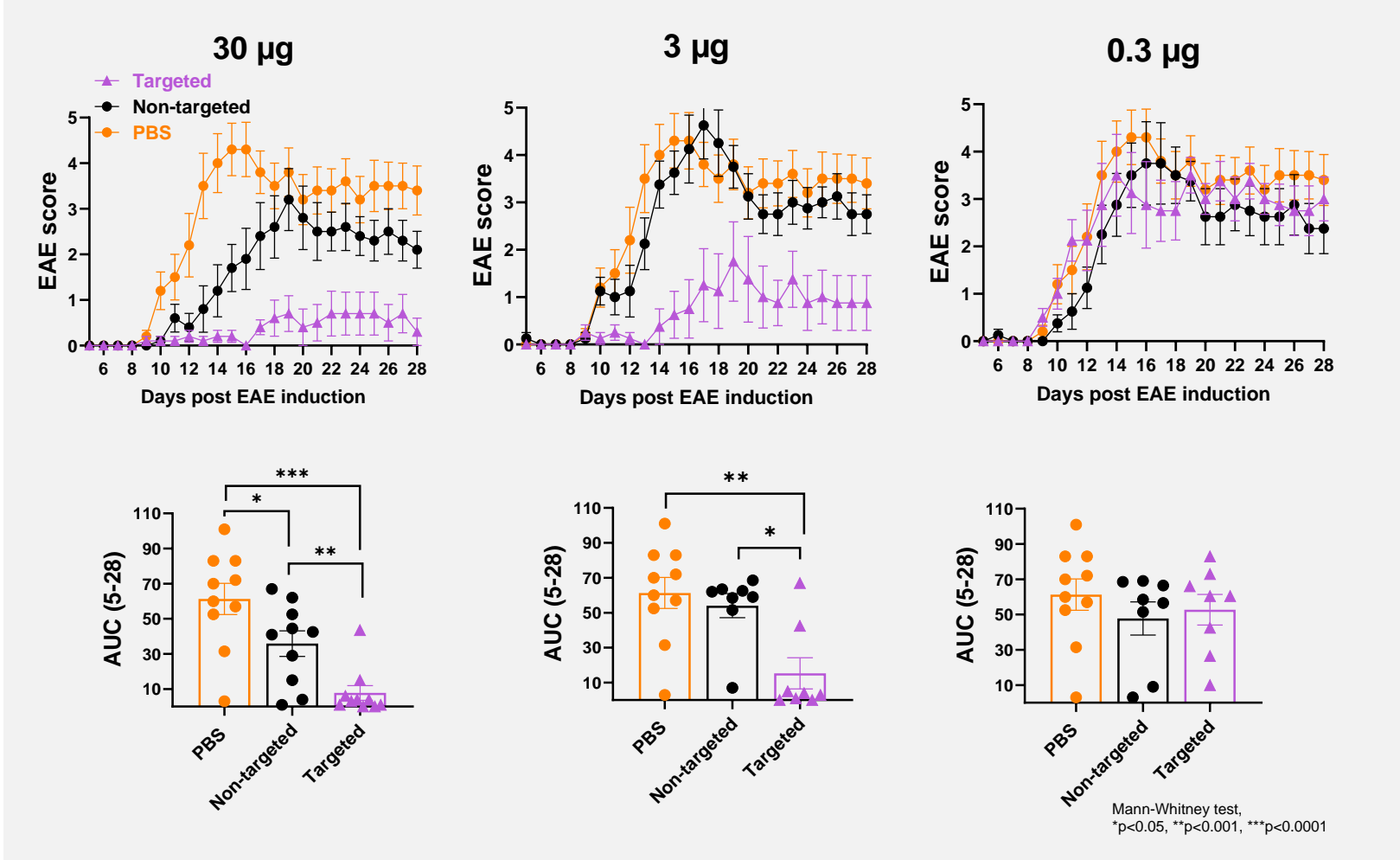
Module 4: Cytokines or modulators playing key roles in mediating anti-inflammatory immune responses

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

APC targeting is required for effective disease protection

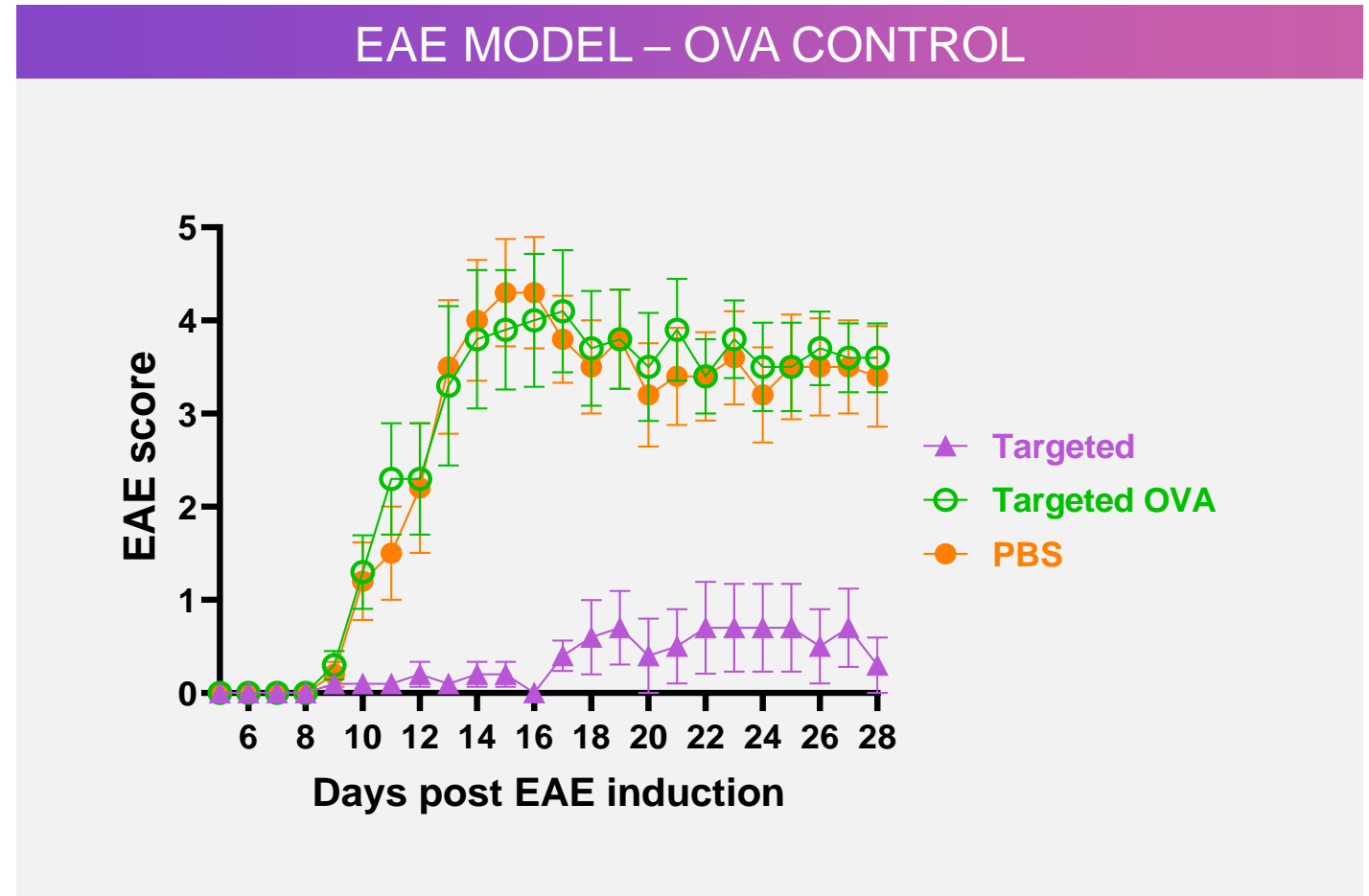
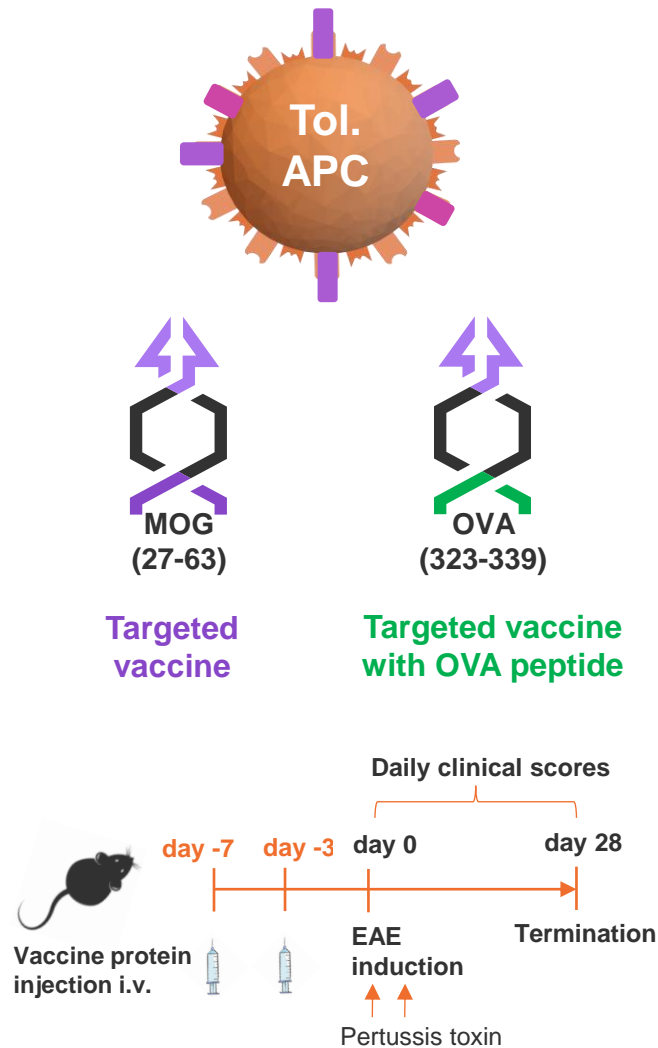


EAE MODEL – PREVENTIVE THERAPY



Experimental autoimmune encephalomyelitis (EAE)

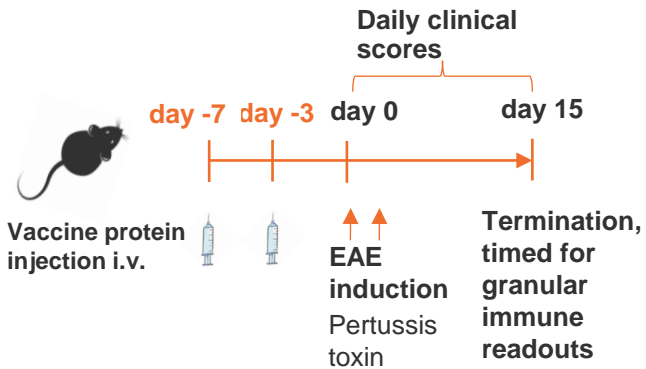
Nykode vaccine delivers Ag-specific suppression of EAE



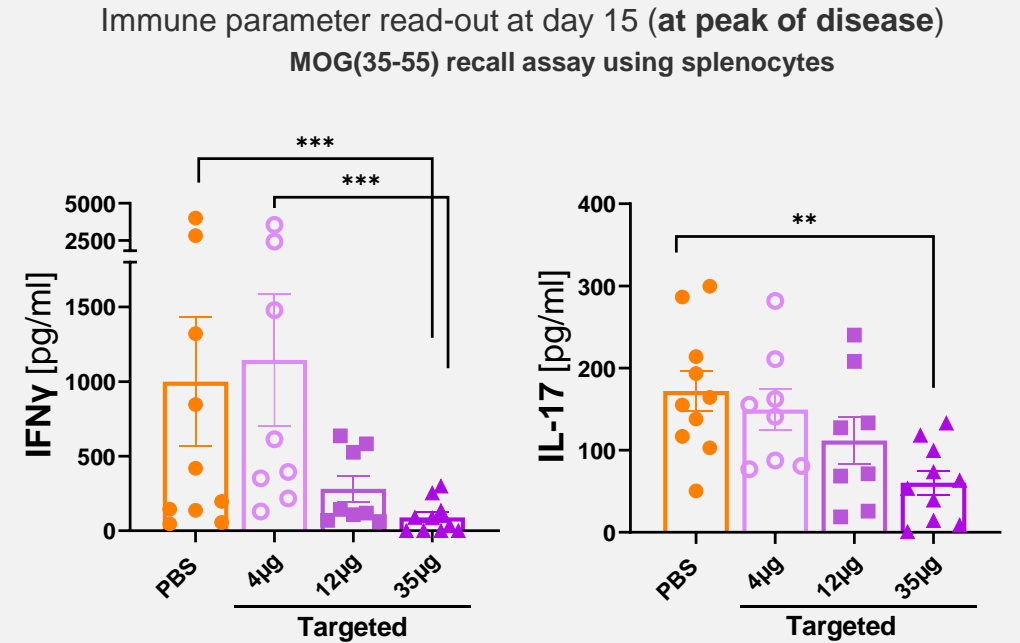
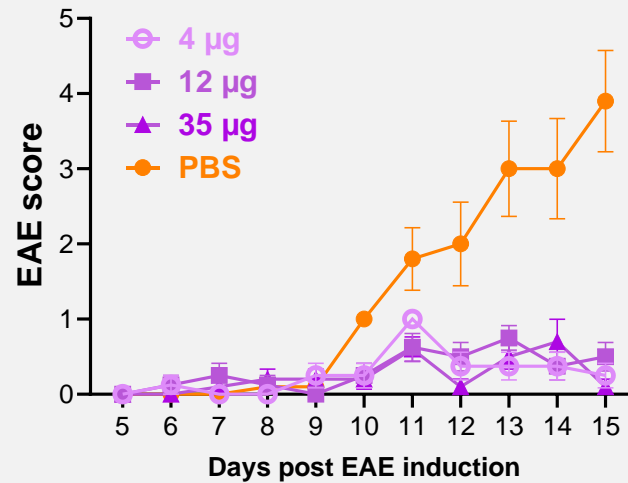
Nykode vaccine delivers dose-dependent effect on antigen-specific disease-associated cytokine-release



Targeted vaccine

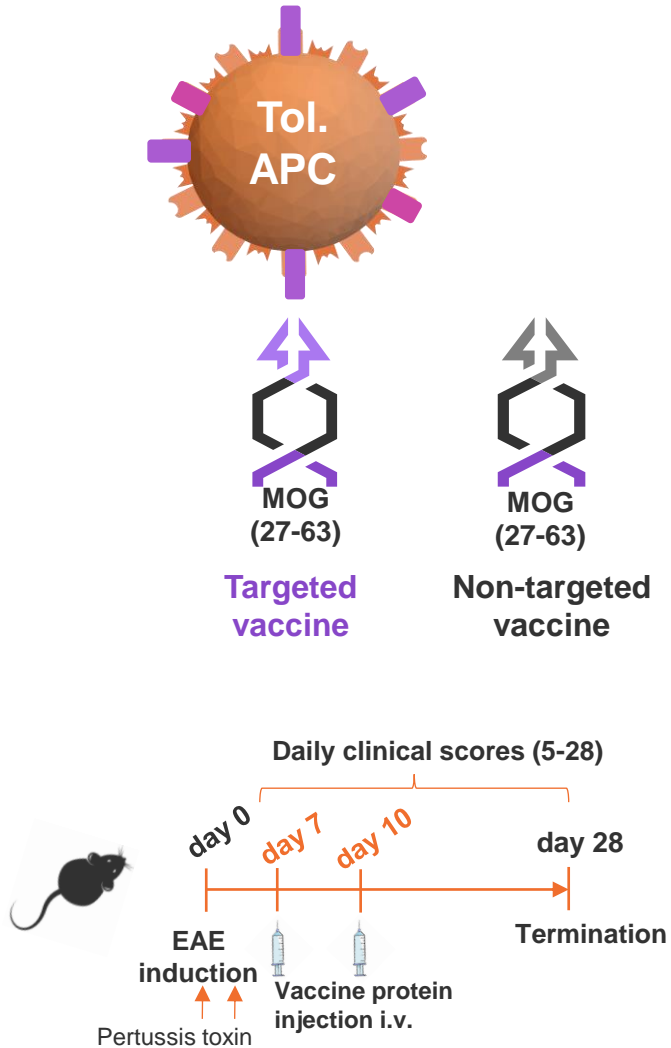


EAE MODEL – IMMUNE PARAMETER READ OUT

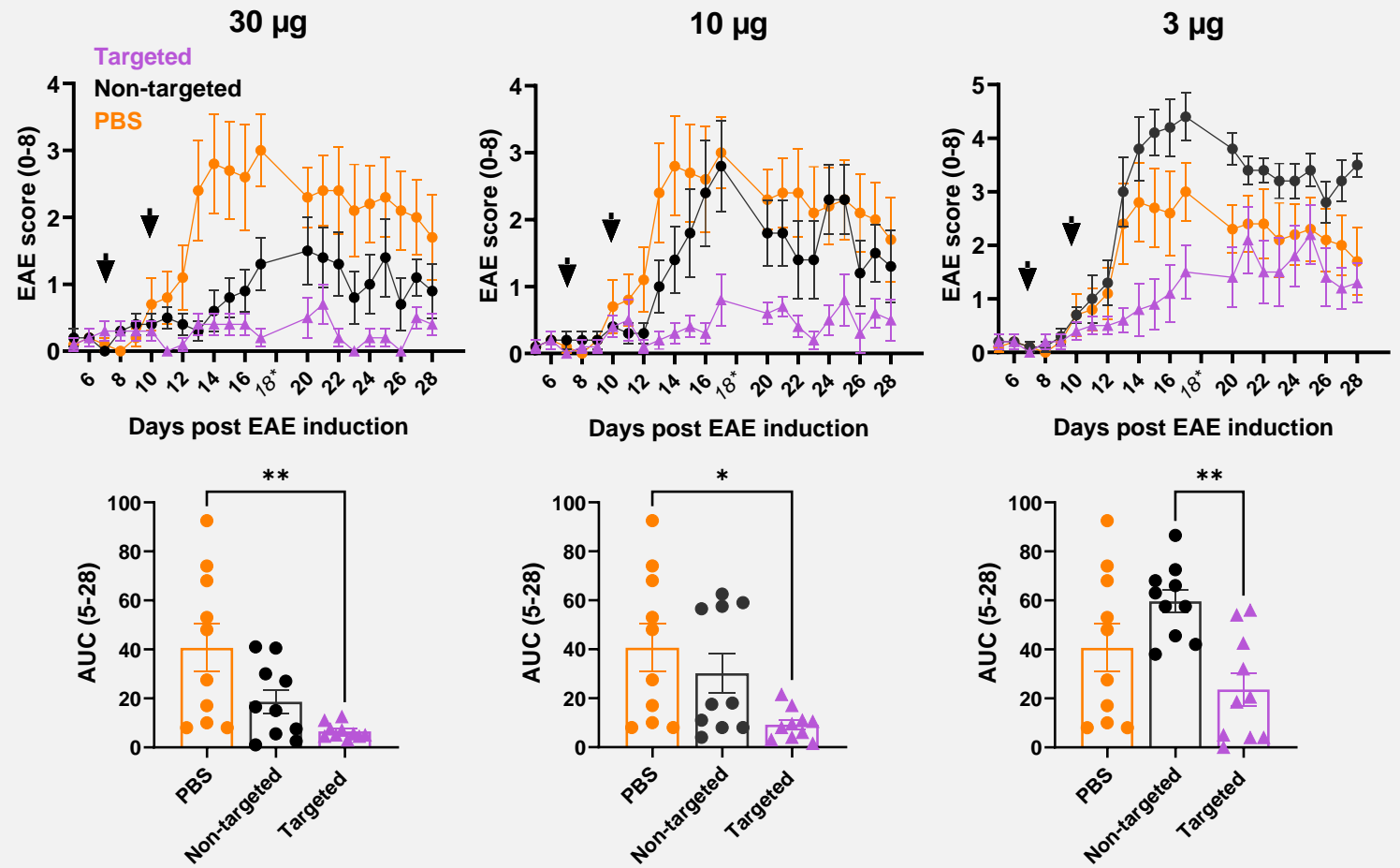


Mann-Whitney test, **P < 0.01, ***P < 0.001.

APC targeting is required for effective early therapy of EAE disease

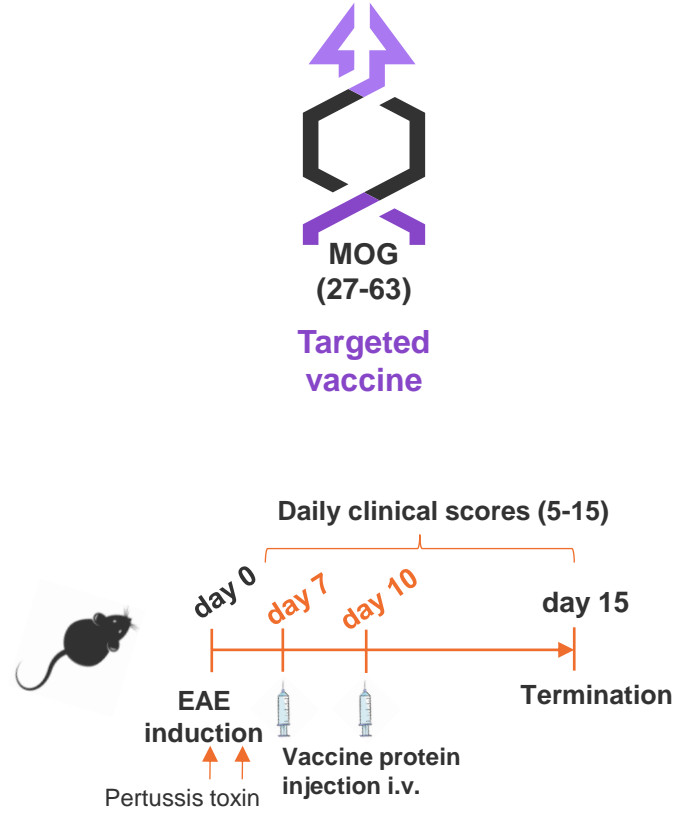


EAE MODEL – EARLY THERAPEUTIC DELIVERY



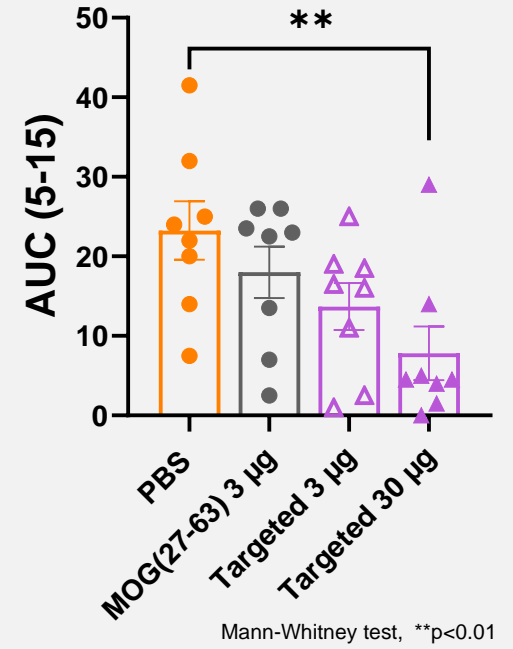
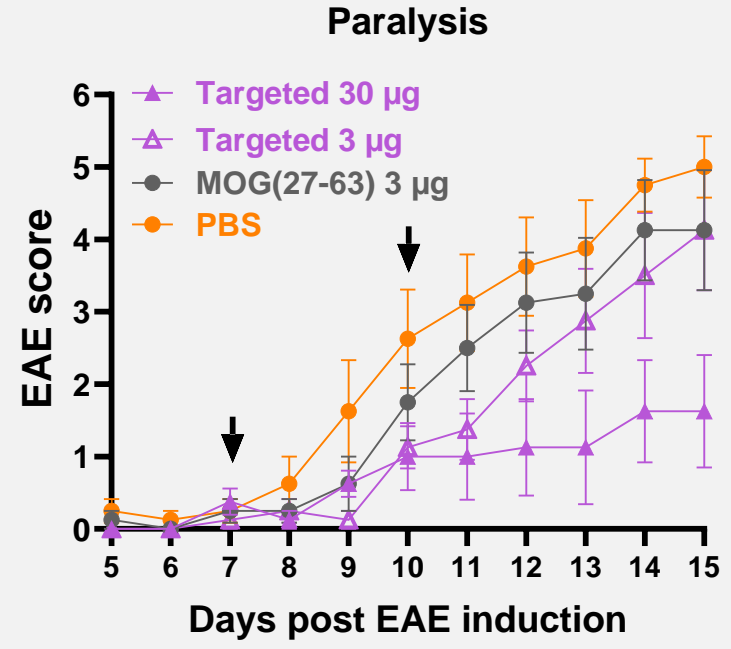
One-way ANOVA, multiple comparisons test, *p<0.05, **p<0.01

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

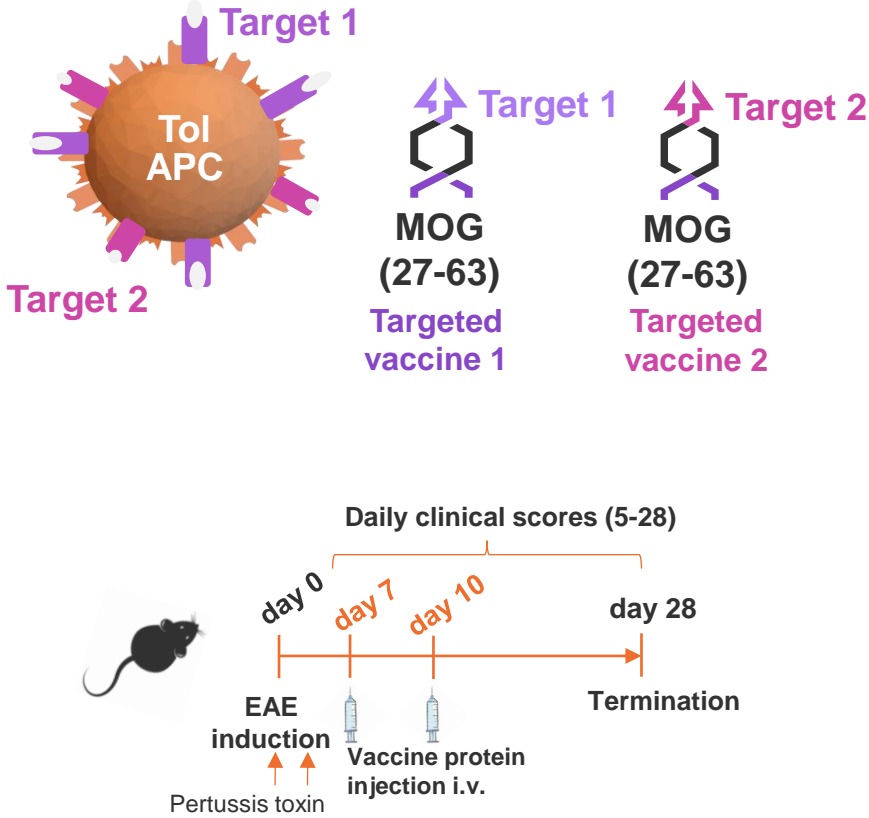


➤ Targeted vaccine 30 µg dose is equimolar to the MOG(27-63) 3 µg dose

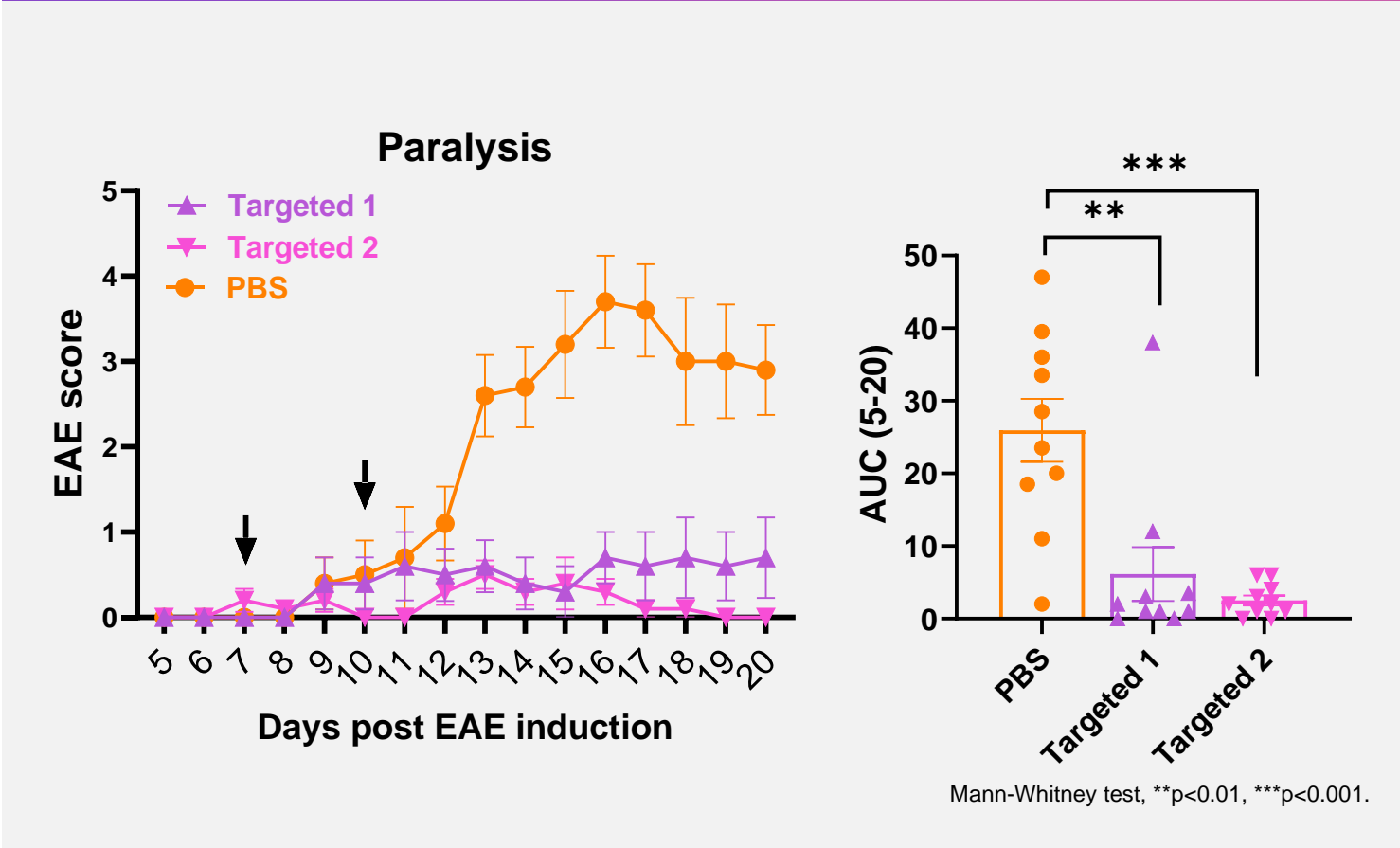
EAE MODEL – EARLY THERAPEUTIC DELIVERY



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



EAE MODEL – EARLY THERAPEUTIC DELIVERY

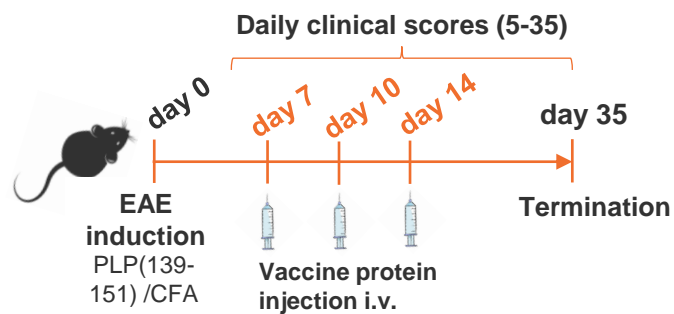


Early therapeutic treatment with Nykode vaccine alleviates disease progression in relapsing-remitting EAE

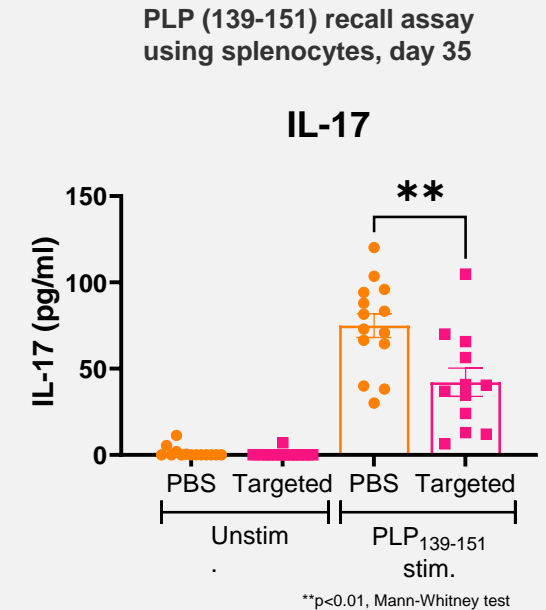
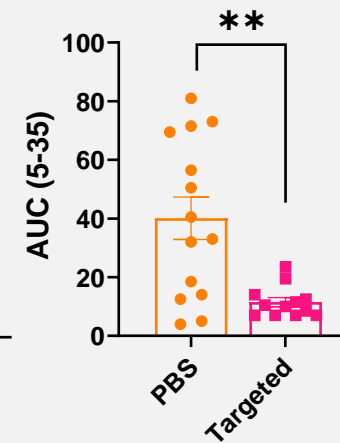
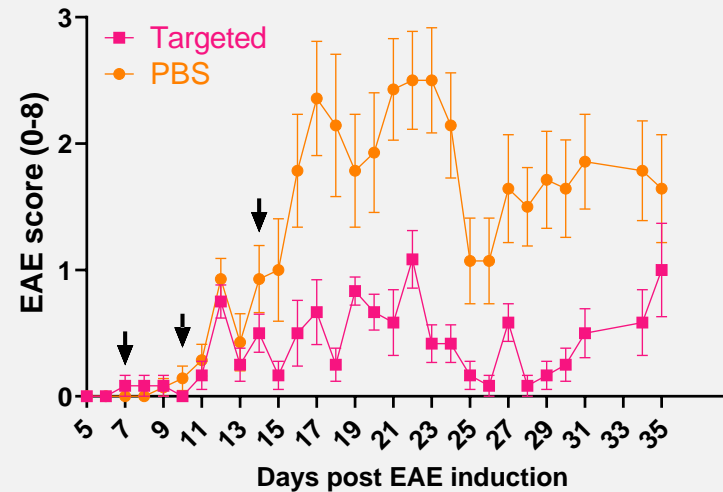


Proteolipid protein
PLP(139-151)

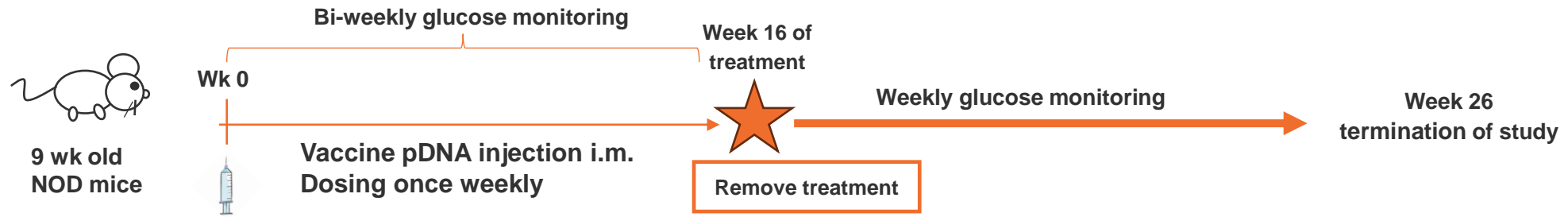
Targeted
vaccine



RELAPSING-REMITTING EAE MODEL – EARLY THERAPEUTIC DELIVERY



Nykode DNA vaccination targeting APCs show durable effect in NOD mice



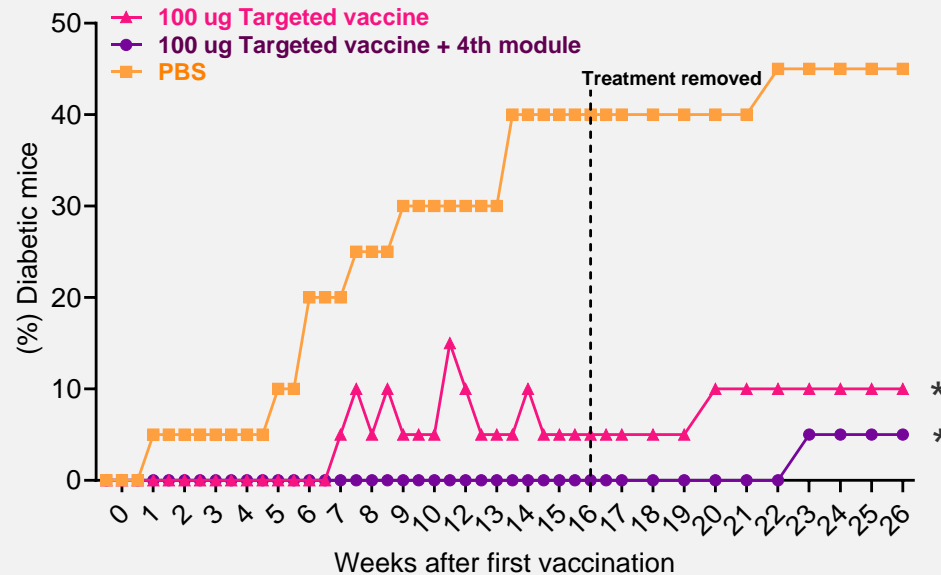
NOD DIABETES MODEL

Targeted vaccine

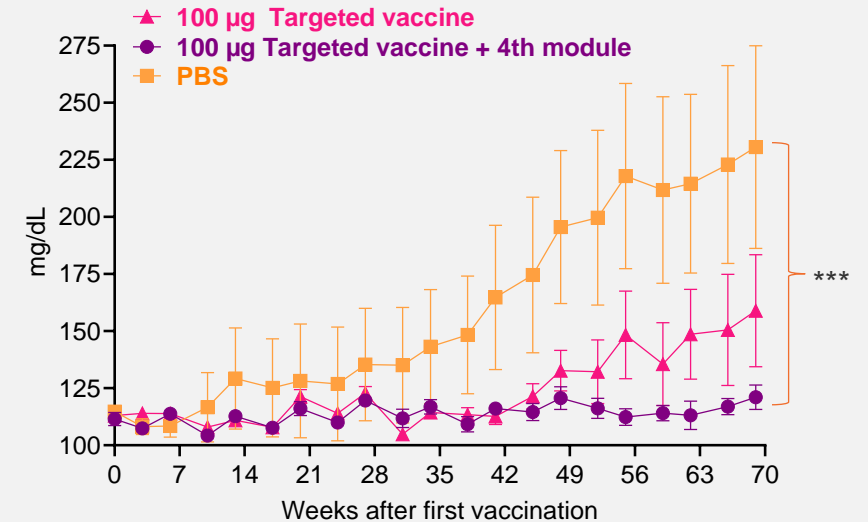


Diabetes antigen: PPI

Incidence of Diabetes



Blood glucose levels



Advancements highlight unique benefits of Nykode's APC-targeted vaccine platform in autoimmunity

Nykode's inverse vaccine demonstrate:

Disease Protection

Dose-dependent effects in both prophylactic and therapeutic contexts; in chronic and relapsing-remitting EAE models, and effect in T1D NOD model.

APC targeting MoA

Effects driven by Nykode's selective APC receptor targeting, antigen-specific and associated with reduction of disease-relevant cytokines.

Versatile Format

Potent tolerizing responses were reproducible with different targeting units, delivered with either protein or pDNA as modality.

Results support potency and versatility of Nykode's APC-targeted platform

Thank you to the team!

Proteins and Immunobiology

Joel B. Heim
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Emmanuelle Benard
Aleksandra Urban
Birthe Saberniak
Stine Granum

Cellular and Molecular Biology

Linn Guro Olsen
Ruixia Huang
Audun Bersaas

In Silico and AI Department

Amine Namouchi

Tolerance RTA

Louise Bjerkan
Anthony Ravussin
Christina Bartholdy
Henrik Søndergaard

CSO and BD

Agnete Fredriksen
Lev Kogon



UNLOCKING THE FUTURE OF MEDICINE

Contact:

Lev Kogon

Head of Business Development

Lkogon@nykode.com