nCage

A breakthrough platform with a potential to revolutionize vaccines and cancer treatment

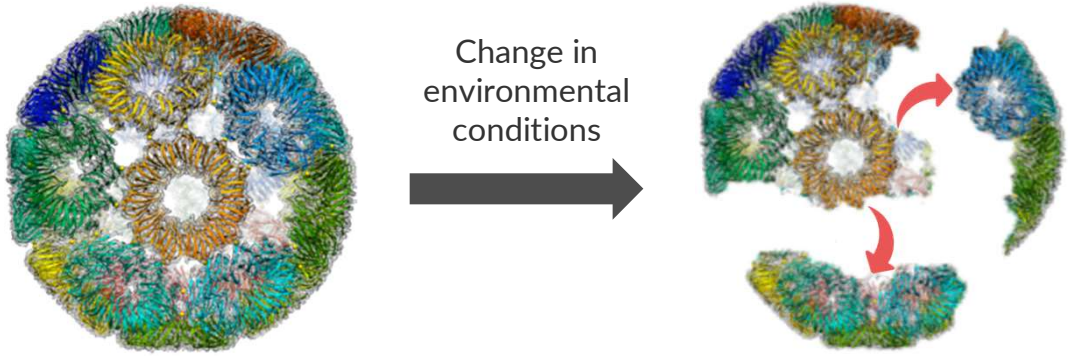
Prague Bio 2024

nCage Therapeutics S.A.

TRAP-CAGE TECHNOLOGY

Unique aspect of nCage technology – programmable opening of TRAP-cages

A unique aspect of nCage technology – **TRAP-cages can be programmed to open and close in certain environmental conditions,** such as the reducing conditions inside of a cell. This allows for **delivery of a cargo**.



Improved targeting

Protein cages are adaptable allowing for delivery to different areas of the body and targeted delivery into the interior of cells.

Programmable opening of protein cages allows for development of:

- **Next generation vaccines**
- **Drug delivery system (DDS)**

TRAP-CAGE TECHNOLOGY

nCage solution mimics the structure of a virus supporting vaccine development

Typical virus

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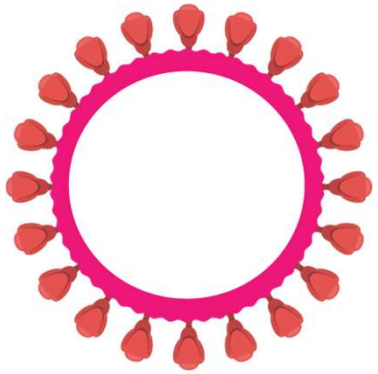
Synthetic virus-like particle (VLP)

Variants have been tested by nCage and its competition



Resembles the exterior of a virus and can be used as vaccines

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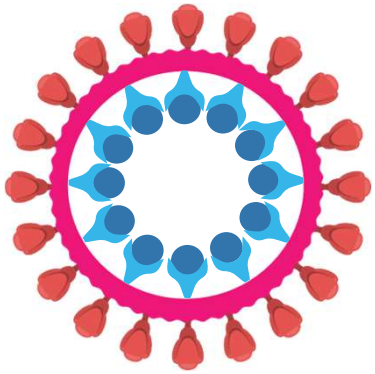
TRAP-cage

A specific synthetic VLP developed by nCage



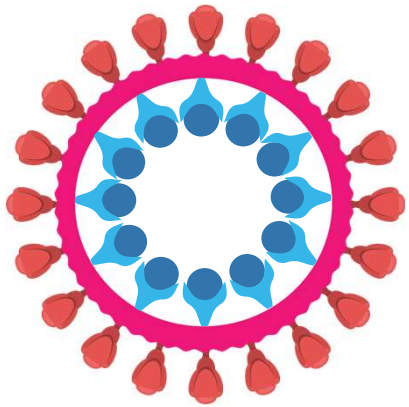
nCage's solution has programmable opening and closing that supports drug delivery, and improved vaccine designs

A Virus-like structure allows for best in class vaccines, and a drug delivery system (DDS) that has scope for greater efficacy than current approaches

TRAP-CAGE TECHNOLOGY

TRAP-cage – a proprietary protein scaffold for the development of novel vaccines

TRAP-cage – nCage's proprietary synthetic virus-like particle (VLP)



TRAP-cage

Synthetic VLP developed by nCage

Synthetic virus-like particles (VLPs) are artificially designed molecules based on protein cages, closely resembling viruses.

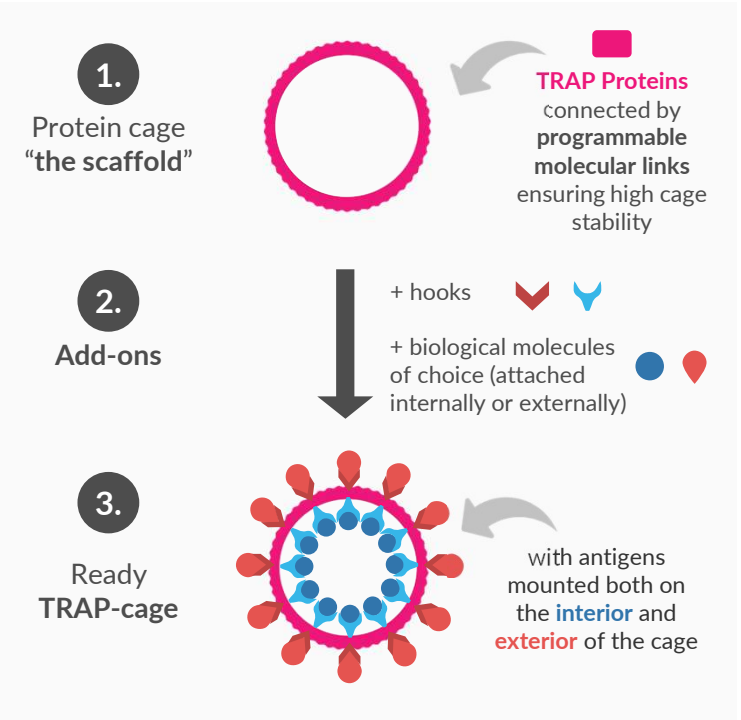
TRAP-cage – a specific synthetic VLP made by nCage

- **multiple copies** of protein components designed to form stable, hollow protein shapes
- platform **based on the bacterial TRAP protein**
- resemblance to synthetic viral particles, but no nucleic material)
- outside of cages used to mount repeating arrays of antigens for use as **combination vaccines**
- repeating arrays of antigens **producing a stronger and more robust immune response**

TRAP-cage can:

- display biological material **on their surface**
- transport molecular cargoes **into the interior of the cell**.

How does nCage make TRAP-cages?



TRAP-cages have huge potential as either **artificial and programmable viral vaccines**, or a **targeted drug delivery system (DDS)**, and provide nCage the ability to compete in a multi-billion dollar market with superior technology.

SYNTHETIC VLP VACCINES

Synthetic VLPs have clear competitive advantages versus current vaccines

	Viral Particles	Recombinant Protein	Viral Vectors	mRNA	Naturally occurring Virus-like Particles (VLPs)	Synthetic VLPs
Illustration						
Description	Inactivated viral particles	Adjuvanted protein subunit vaccine	Replication-incompetent viral vector vaccines that cause cells within the body to express antigen	Antigen encoded on genetic material and expressed by the body	Few cases where soluble antigen naturally forms a particle structure	Artificially designed and manufactured VLPs, applicable to all viruses
Pros	• Many examples of successful viral vaccine developments using this methodology	• Easy storage and transport • Strong efficacy in clinical trials	• Low cost • Easy manufacturing	• Strong efficacy in clinical trials (and real world) • Allows for 'programmable' vaccines	• Very good vaccines • Strong and durable responses • Considered best vaccines on the market	• Strong efficacy • Low side effects • Easy manufacturing • Easy storage and transport
Cons	• Supply issues due to scale-up problems • Safety concerns due to incomplete virus inactivation	• Not as fast to develop as competitive technologies	• Question marks regarding the safety of adenovirus vaccines • Lower efficacy	• Complicated distribution due to cold storage supply • Side effect after multiple boosters	• Only successful for HPV and HepB • **To date, most viral antigens do not form a VLP structure**	• New technology – only one vaccine approved to date
Big Pharma players in the area	GSK	novavax sanofi	Johnson & Johnson AstraZeneca	BIONTECH moderna	GSK MSD	

SYNTHETIC VLP VACCINES

In vivo study confirming nCage's ability to produce effective respiratory vaccines

Study design

Mice used in the experiment

50 mice

- **10 mice** – PBS/Addavax (control group)
- **10 mice** – TRAP-cage/Addavax
- **10 mice** – TRAP-cage-RBD/Addavax
- **10 mice** – RBD/Addavax
- **10 mice** – TRAP-cage + unconjugated RBD/Addavax

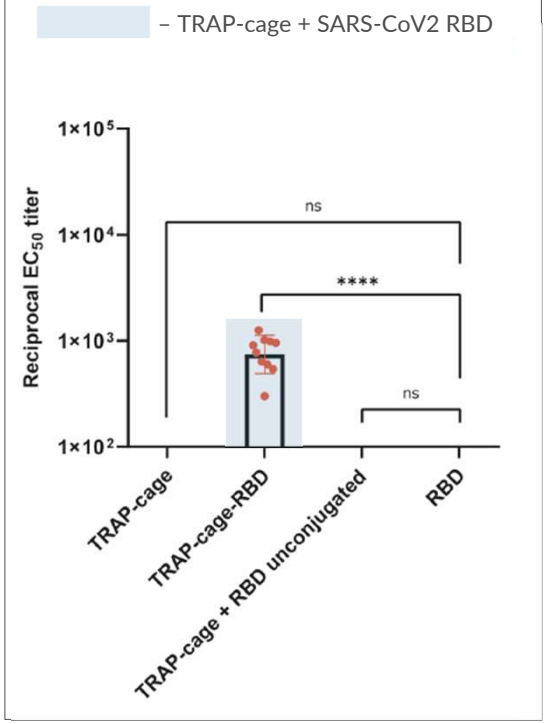
Key time points

25th May 2023 – 10th July 2023

Day -10	Day 0	Day 1	Day 14	Day 21	Day 35
mice arrived	1st vaccine dose	1st blood sample	2nd blood sample	2nd vaccine dose	final blood sample

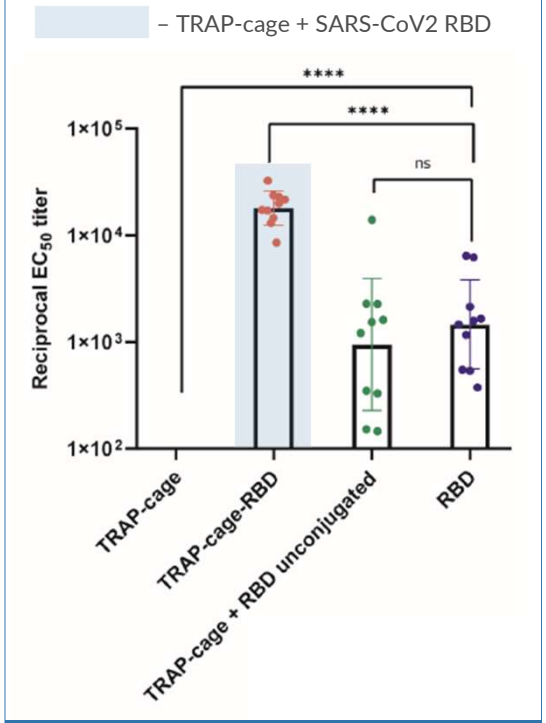
Results

Antibody response after 1st dose



ns – statistically not significant
**** - statistically significant, p<0.0001

Antibody response after 2nd dose



>10x increase in antibody response from TRAP-cage platform

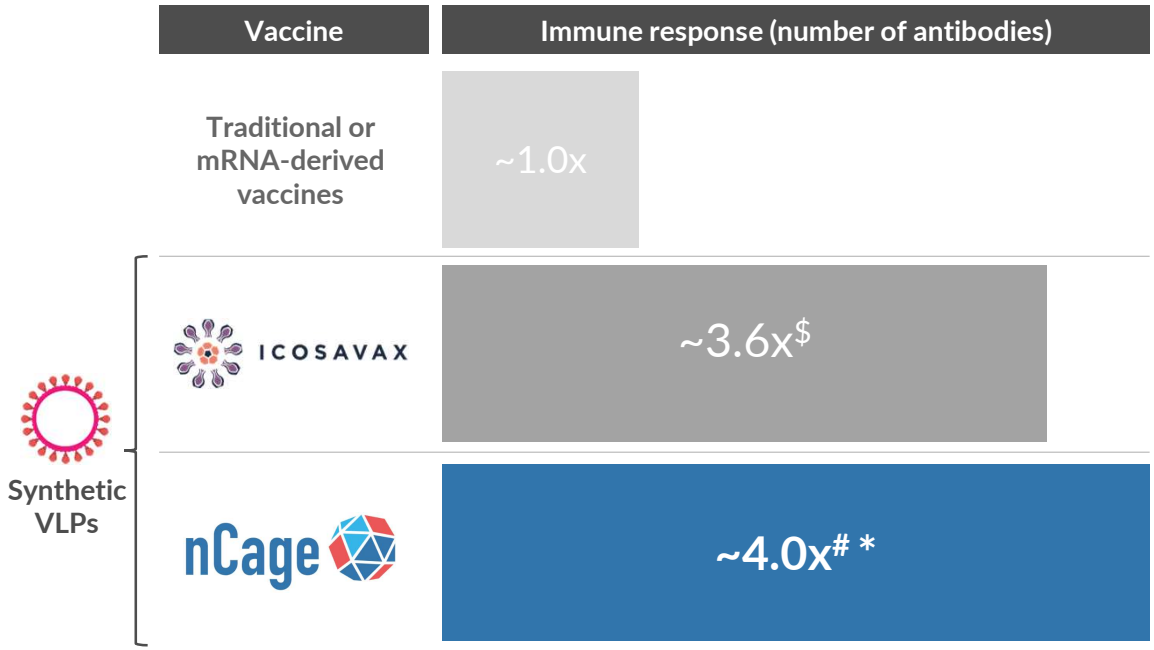
SYNTHETIC VLP VACCINES

Significant competitive edge over the NASDAQ-listed synthetic VLP developer

Multiple advantages of nCage's TRAP-cages over Icosavax's protein cages

	nCage	ICOSAVAX
Hyper Stable	✓	✓
Can Display External Antigens	✓	✓
Folded Antigen Display	✓	✓
Programmable Disassembly	✓	✗
Triggerable Disassembly	✓	✗
Plug and Play Platform	✓	✗
Internal Cargo	✓	✗
Display of Oligomeric Antigen	✓	✓
Cell Delivery	✓	✗

TRAP-cage triggers superior immune response compared to traditional vaccine types and synthetic VLP vaccine market leader



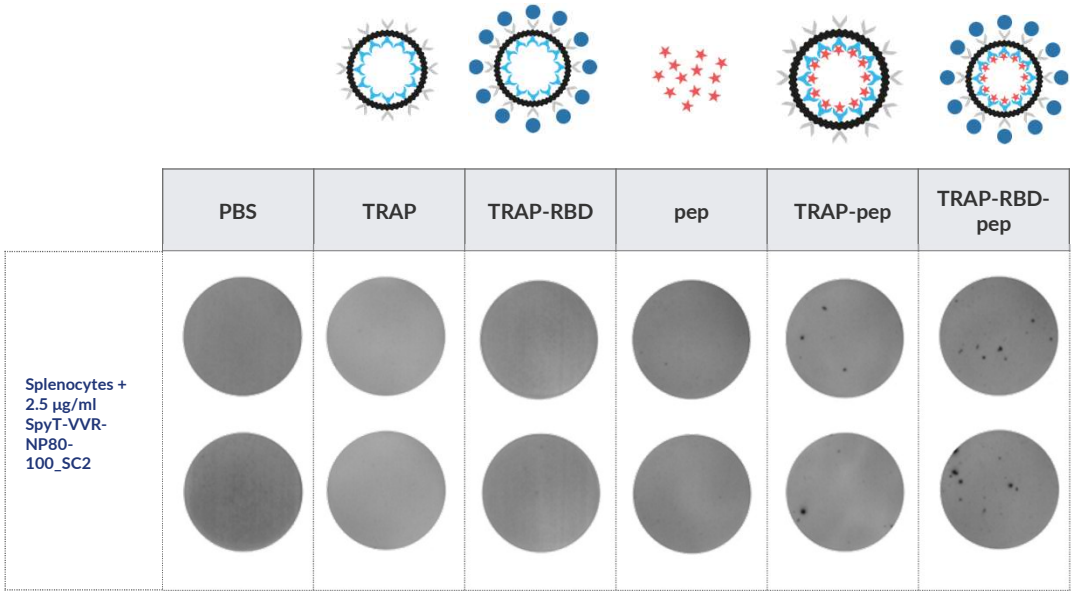
Mounted antigen source: $ovalbumin, #RSV

** nCage's in vivo experiment conducted in 2022 in collaboration with MSD*
Source: Data on File Merck Sharp & Dohme, nCage Therapeutics, Figure 4 C, Marcandalli et al. Cell 176, (2019): 1420- 1431

SYNTHETIC VLP VACCINES

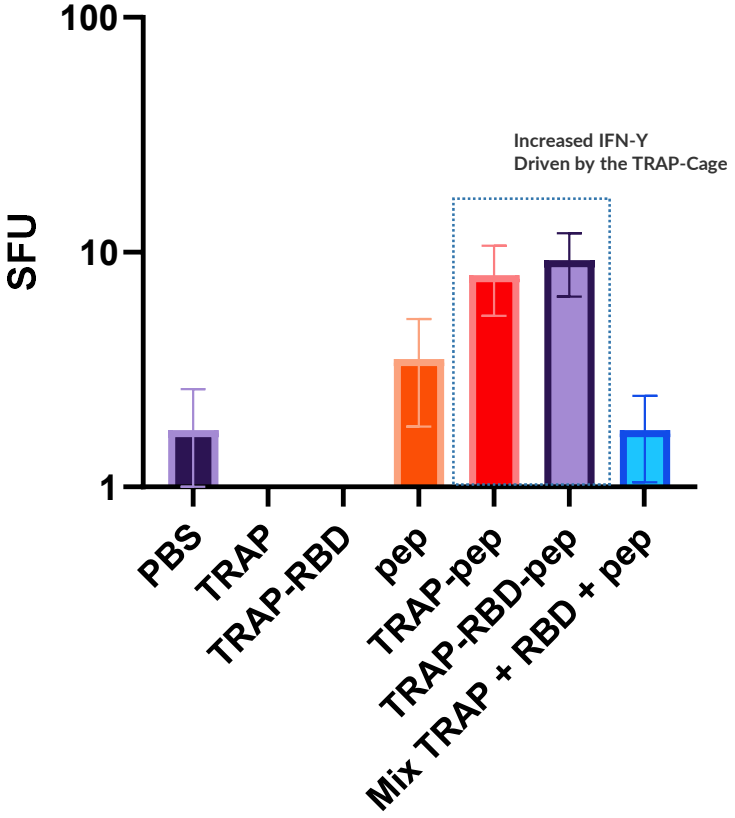
Demonstration of efficacy over Icosavax

- T Cell response is measured by the production of IFN-Y (a marker of anti viral T cell activity)
- Spleens were extracted from mice inoculated with different prototype vaccines
- Splenocytes were exposed to peptide antigen and IFN-Y response was measured using a fluorescent assay



- SARs-CoV2 RBD
- SARs-CoV2 NP Peptide

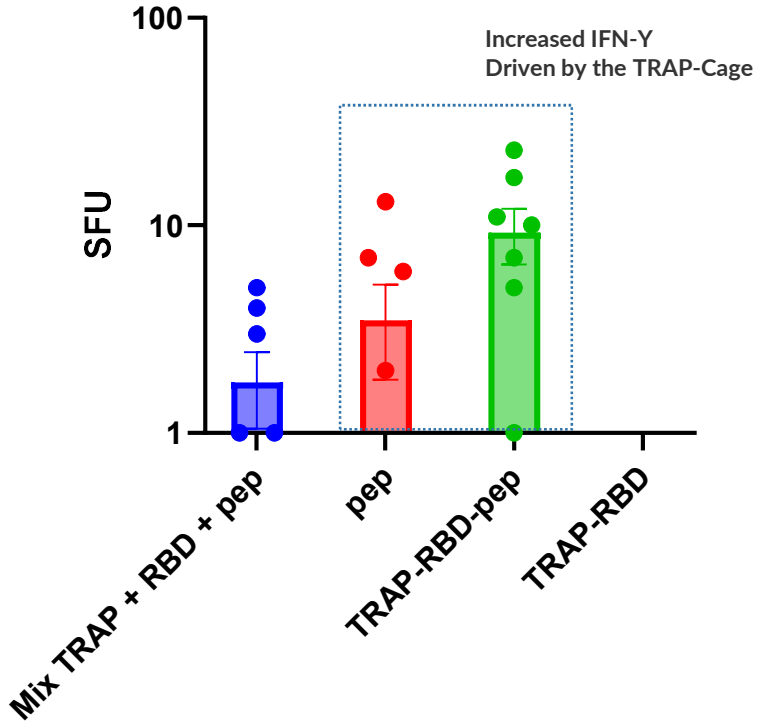
T-Cell Response Driven by the TRAP-Cage



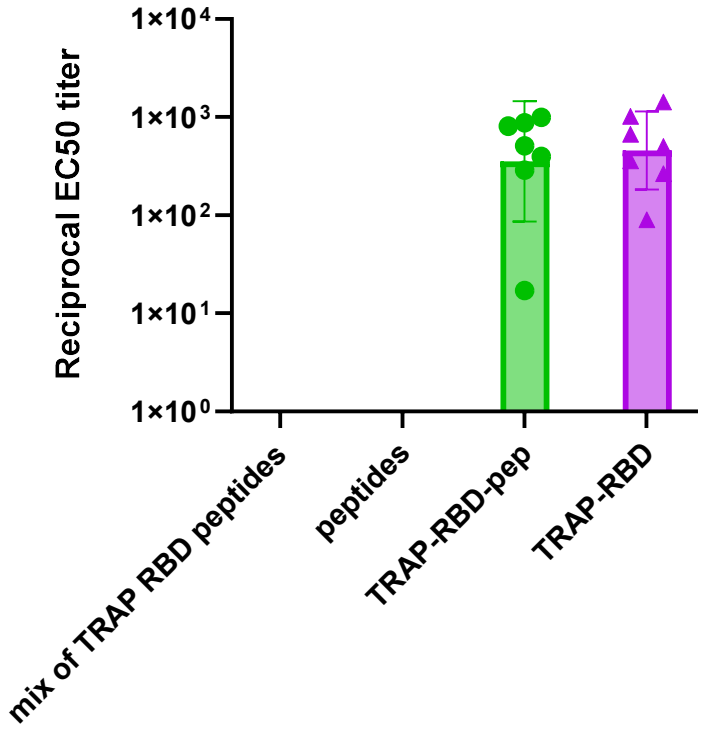
TRAP CAGE VACCINES

T-Cell and B-Cell Response

T-Cell Response



One-Dose Antibody Response



Logarithmic scale

SYNTHETIC VLP VACCINES

Two nCage's combo vaccine candidates with potential to become best-in-class

Vaccine projects developed in collaboration with two major British academic centers

Product	Stage of development	Rationale for market entry	Phase I start date	Academic partner
Combo RSV/hMPV Vaccine	Antigen Production	• There are currently no vaccines for hMPV • RSV vaccines are yet to be trialed in large populations and limited options for patients	2025	THE UNIVERSITY of EDINBURGH
Combo Covid/Flu Vaccine	Selection of Antigens	• Elderly patients are recommended to have both Covid and Flu boosters • No combo option available	2026	The University of Nottingham

