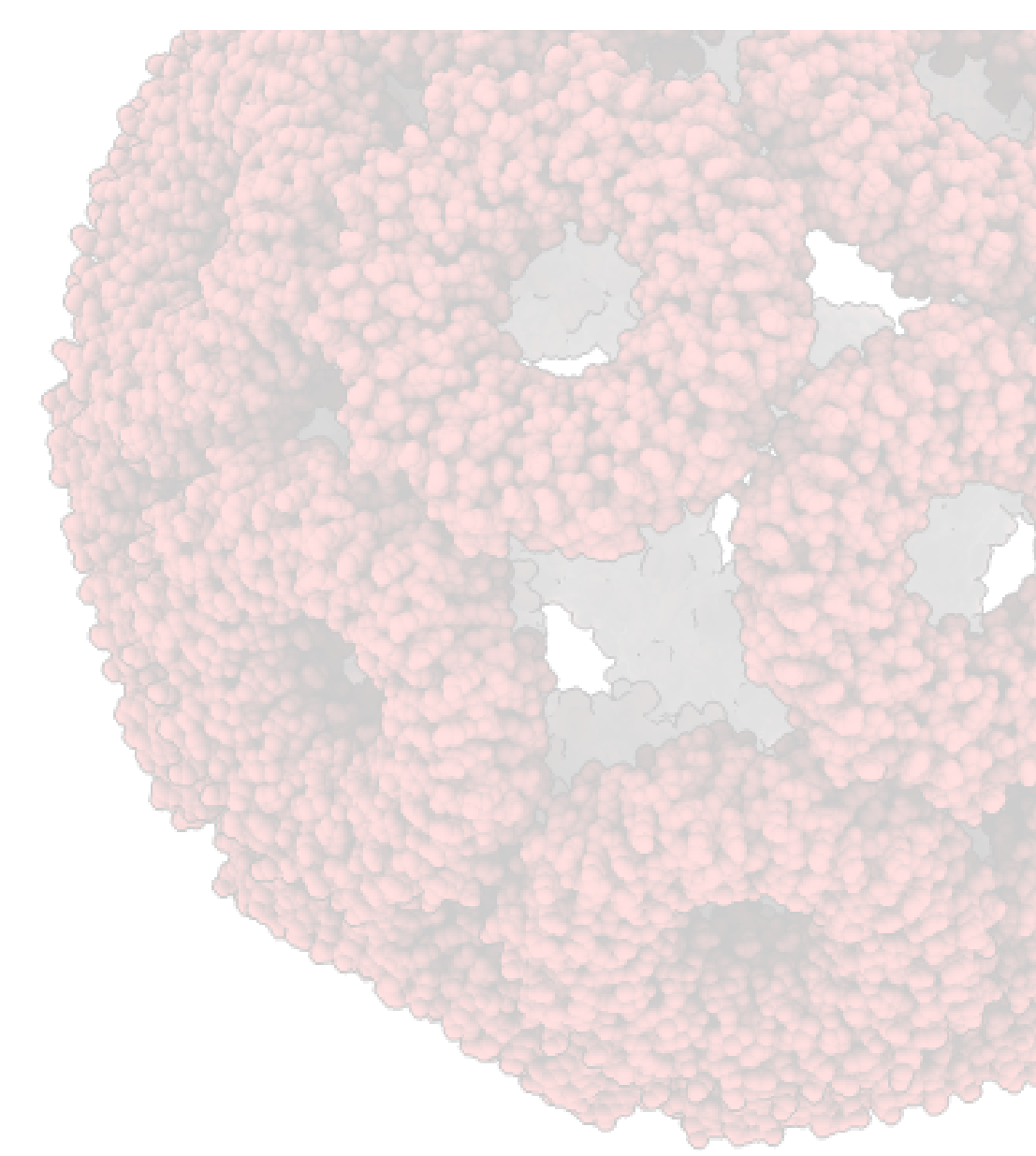




A novel, synthetic VLP platform for vaccine development

Authors: Izabela Stupka¹, Sylwia Świątek¹, Szymon Gaweł¹, Ivan Campeotto², Janet Daly³, Monika Jakubowska⁴, Agnieszka Dąbrowska⁴, Krzysztof Pyrc⁴, Jonathan G. Heddle¹

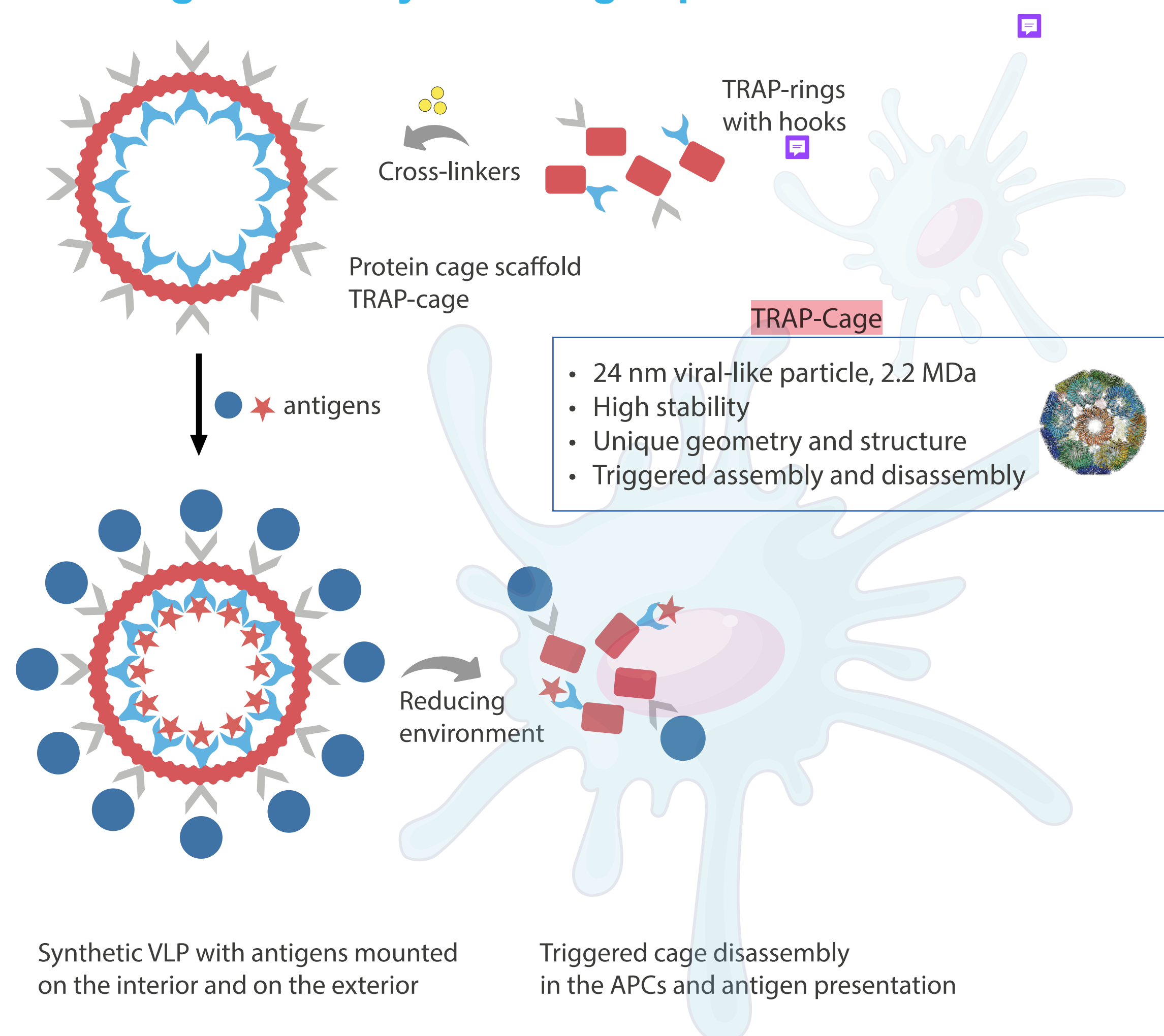
¹ nCage Therapeutics, Krakow, Poland, ² School of Bioscience, Division of Microbiology, Brewing and Biotechnology, University of Nottingham, Nottingham, UK, ³ School of Veterinary Medicine and Science, University of Nottingham, Nottingham, UK, ⁴ Malopolska Centre of Biotechnology, Jagiellonian University, Krakow, Poland

Protein cages are nano-scale biological structures which provide compartmentalization and perform essential functions in living systems. Taking inspiration from nature, non-infectious virus-like particles (VLPs) have been designed and demonstrated to be valuable in various biotechnological applications, including vaccine development.

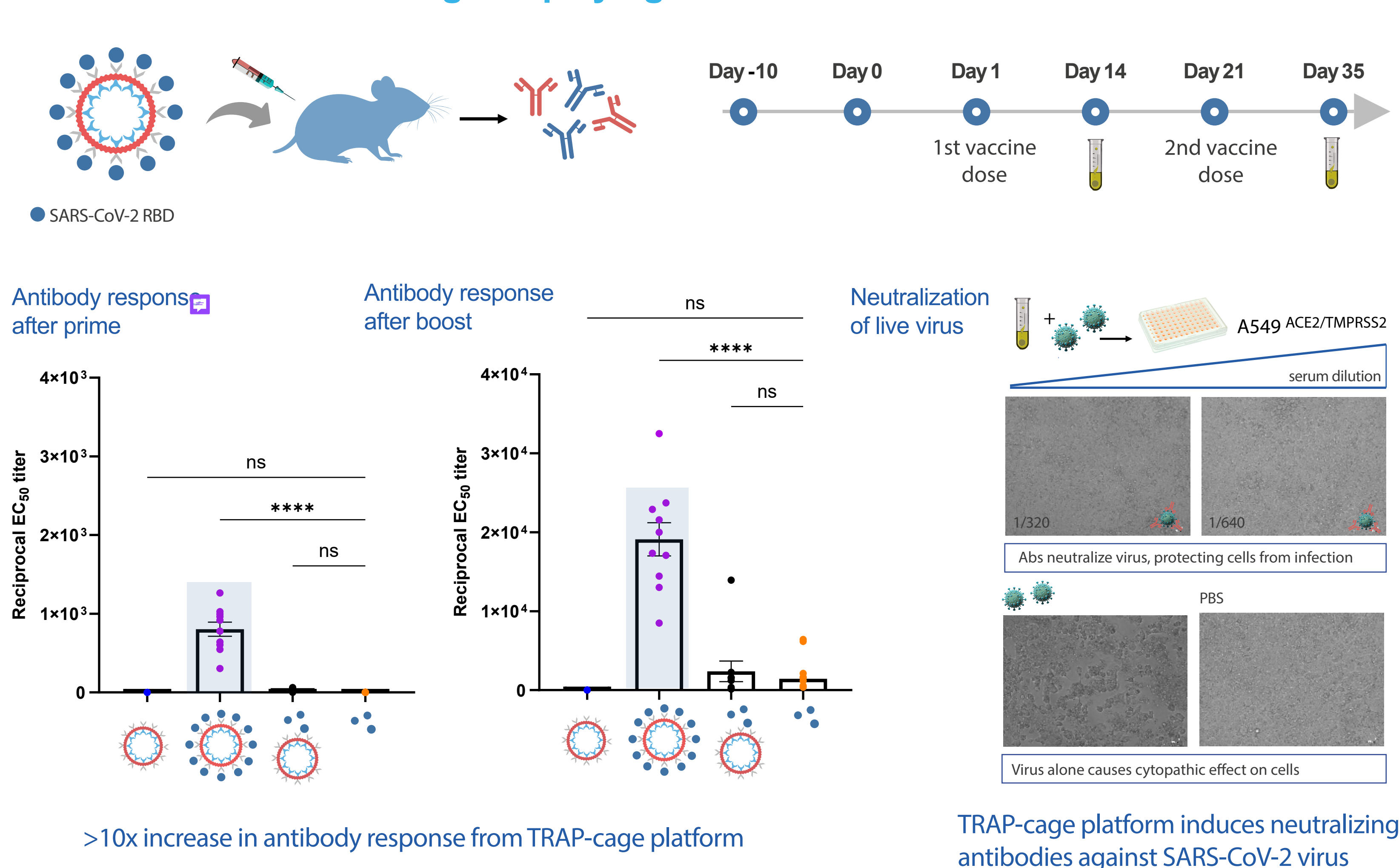
nCage Therapeutics have developed a non-viral, novel synthetic VLP constructed from a ring-shaped protein – trp-RNA binding attenuation protein (TRAP)^{1,2}. Among many potential applications, we are exploring TRAP-cage as a vaccine platform. TRAP-cages are unique in being able to deliver internal cargo (such as peptides) to antigen presenting cells.

We have successfully demonstrated the assembly of a TRAP-cage displaying multiple copies of the SARS-CoV-2 receptor binding domain (RBD) on its outer surface, which resulted in a strong antibody response in mice and effective neutralization of the live virus. Further, we have also showed an increased B cell and T cell response in mice after vaccination with TRAP-cage displaying SARS-CoV-2-RBDs and simultaneously multiple copies of viral peptides, conjugated to the inside of the cage.

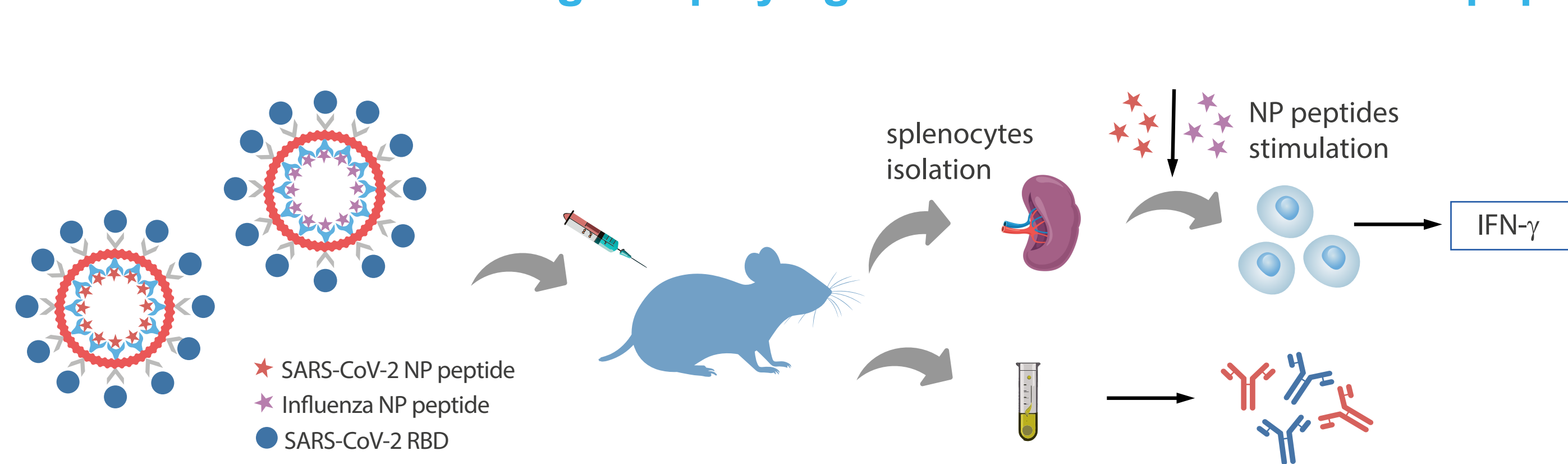
TRAP-cage assembly and antigen presentation



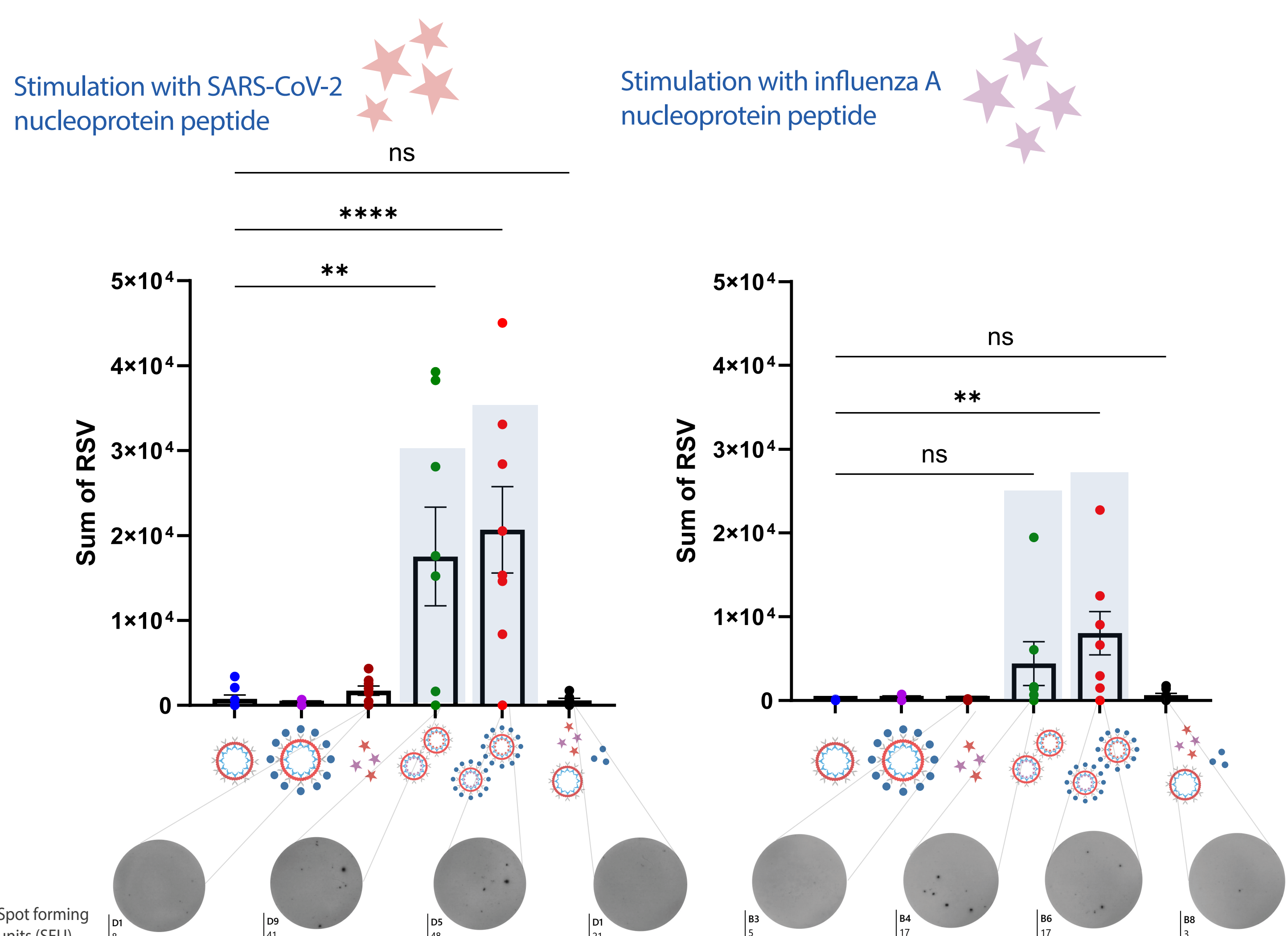
Vaccination with TRAP-cage displaying SARS-CoV-2-RBD



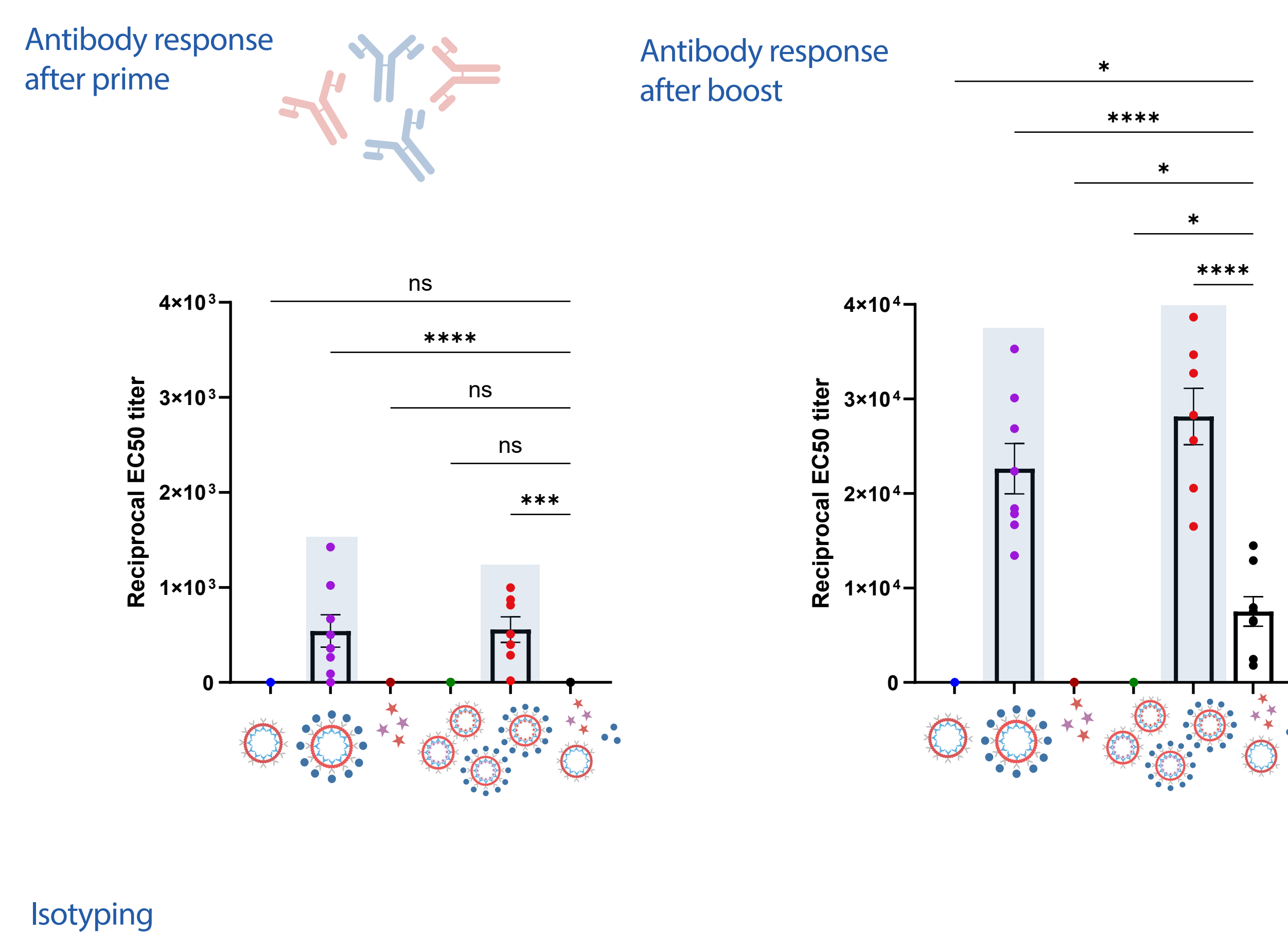
Vaccination with TRAP-cage displaying SARS-CoV-2 RBD and viral peptides in combination



Cell-mediated response - ELISpot assay



Humoral response



Isotyping

Conclusion

- TRAP-cage can be used as a synthetic virus-like particle mimicking the shape and structure of a virus
- nCage has demonstrated the potential of our vaccine platform in animal models showing up to ten fold increase in efficacy versus soluble antigen as well as induction of neutralizing antibodies
- TRAP-cage loading with viral peptides induces T cell response and production of IFN- γ after immunization in mice
- Full potential of TRAP-cage modifications and combination of different loading strategies can result in obtaining lasting immunity with the potential of triggering humoral as well as cell-mediated responses

¹ Malay A., et al. *Nature*, 2019

² Stupka I., et al. *Sci. Adv.*, 2022

