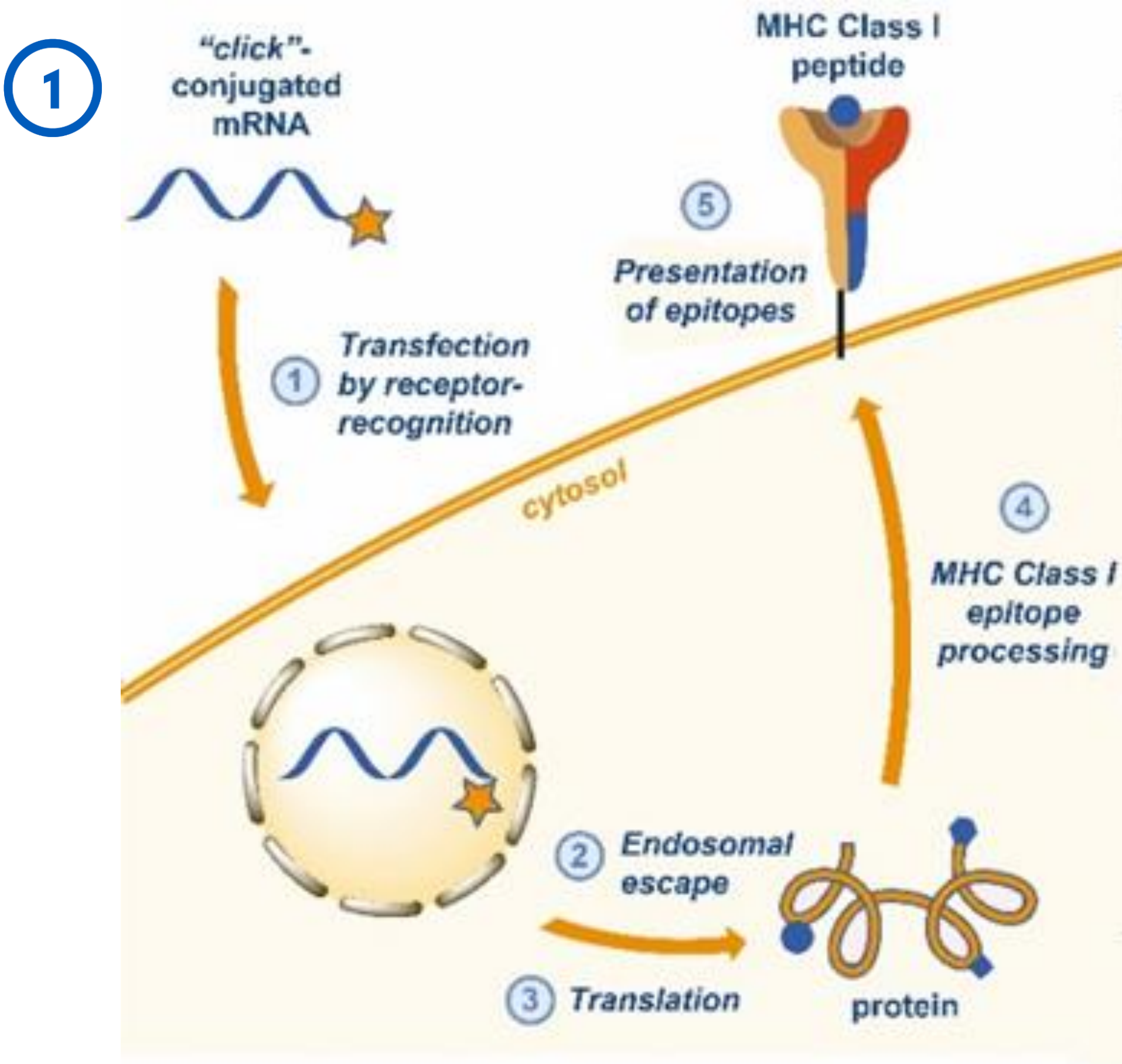


P. 72. Modified mRNA SARS-CoV-2 Vaccine Development for Targeted Delivery

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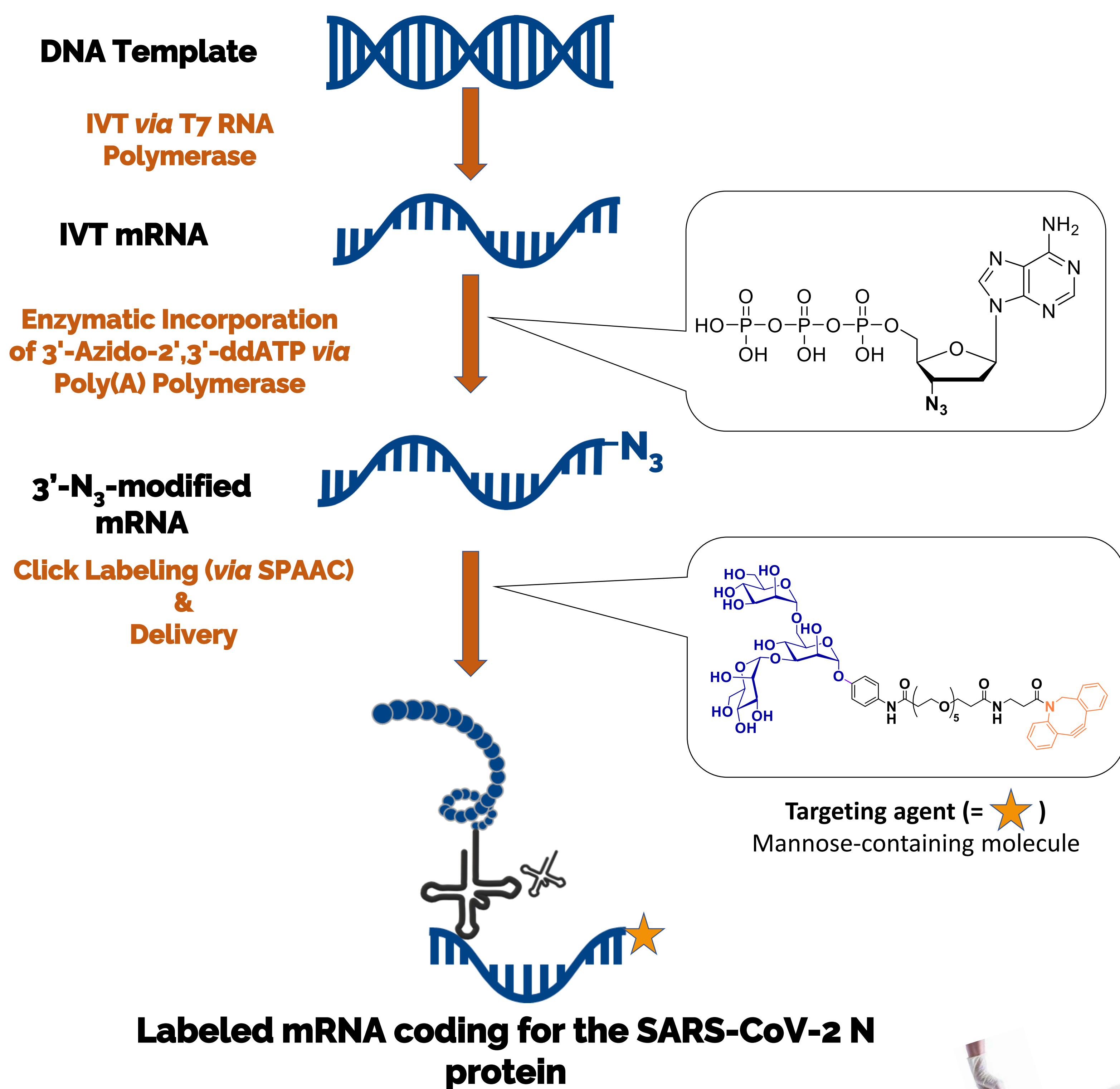
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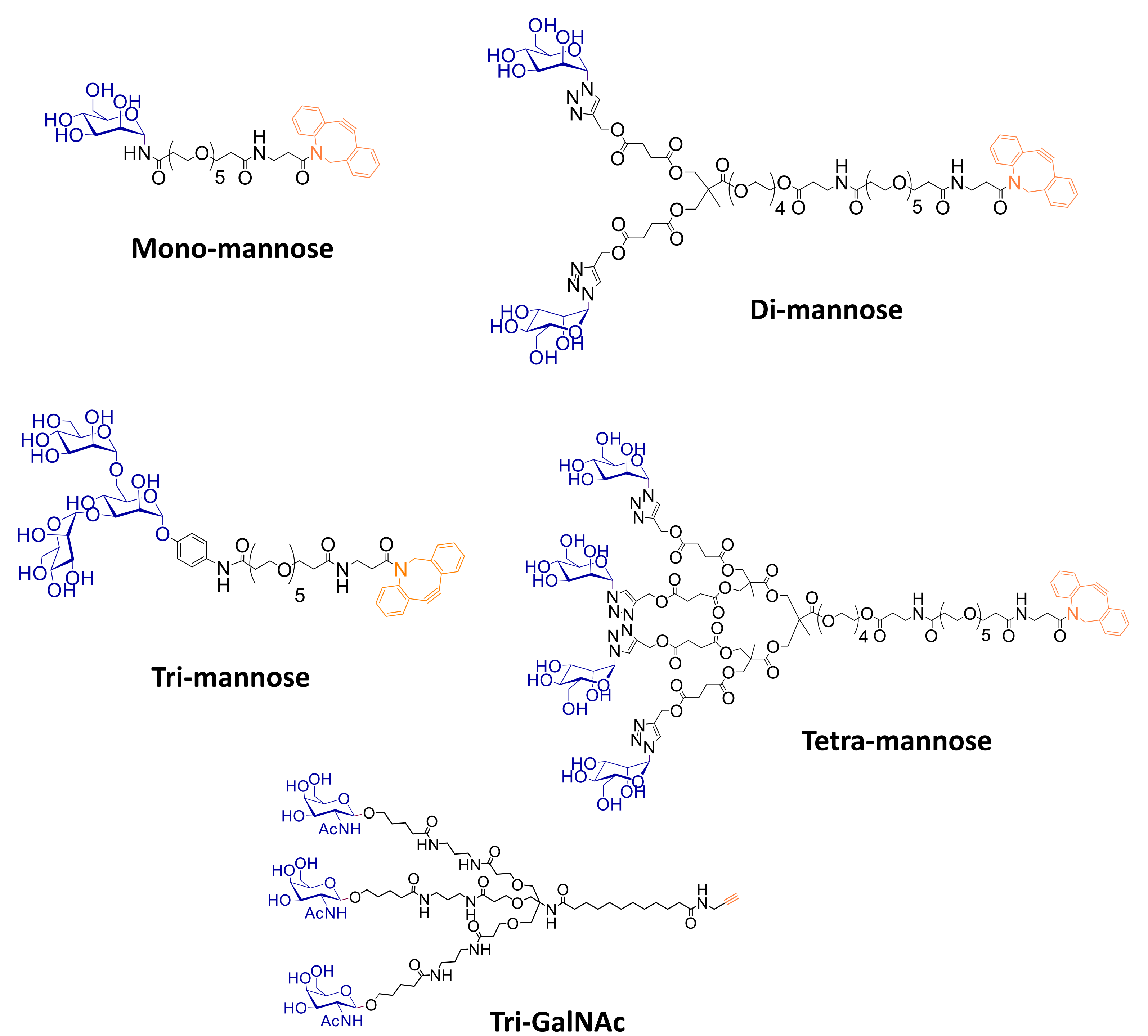
Introduction

The use of mRNA in therapeutics presents an enormous potential, especially in vaccination, cancer therapies and genetic diseases treatment. Cellular delivery methods, however, remain as one of the major limitations of these therapeutics.^{1,2} The aim of this project is to develop an mRNA delivery system to target immunocompetent cells, in particular macrophages or dendritic cells (DCs). We therefore propose a method based on chemically-modified mRNA *via* click chemistry with mannose- and GalNAc-containing molecules (targeting agents) to target C-type lectin receptors, which are highly expressed in DCs and play an important role in endocytosis mediation. Our approach, at baseclick GmbH, was applied towards the development of a candidate mRNA-based vaccine against SARS-CoV-2.

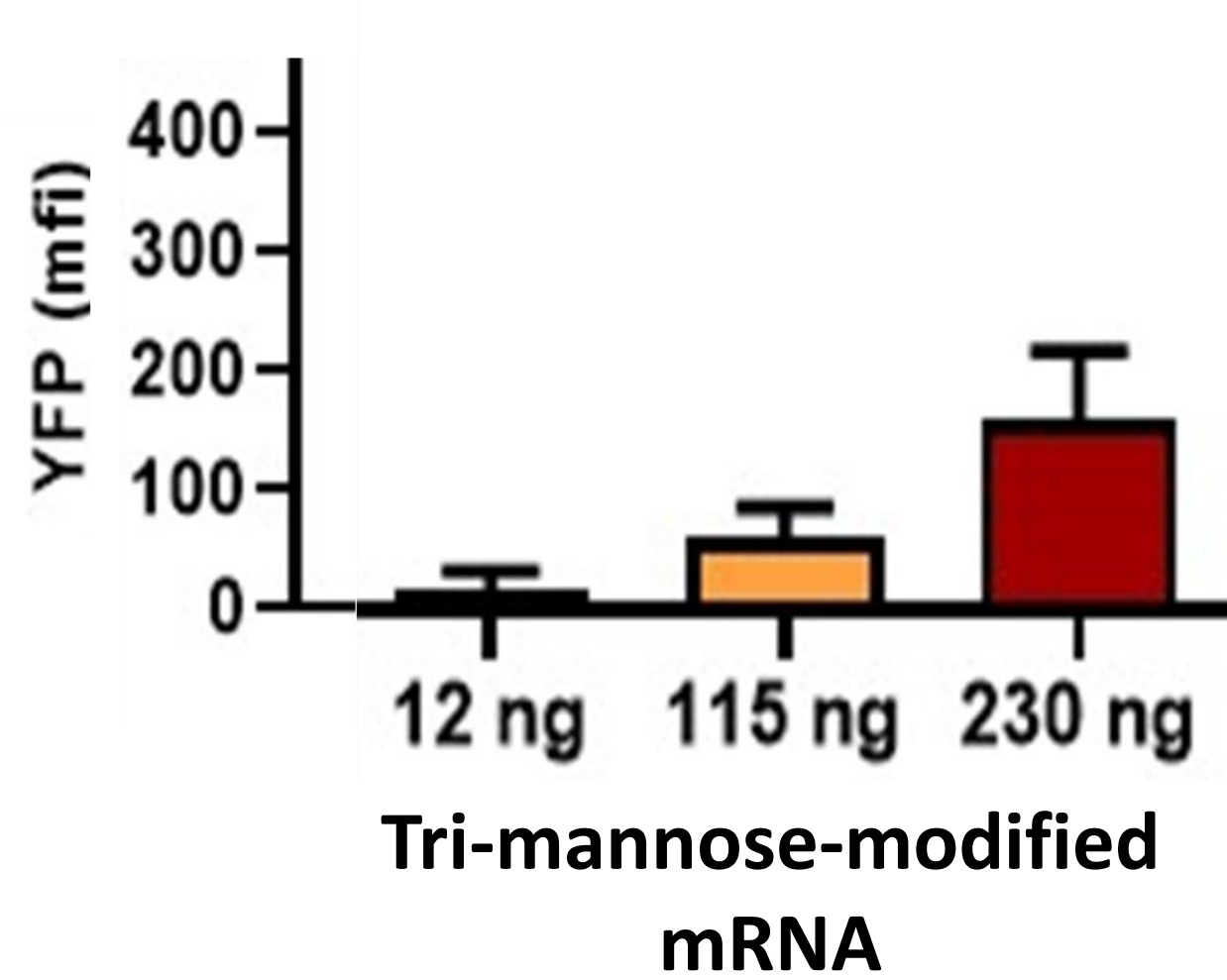
2 Technology



3 Synthesized Potential Targeting Agents



4 Chemically modified mRNA expression in DCs

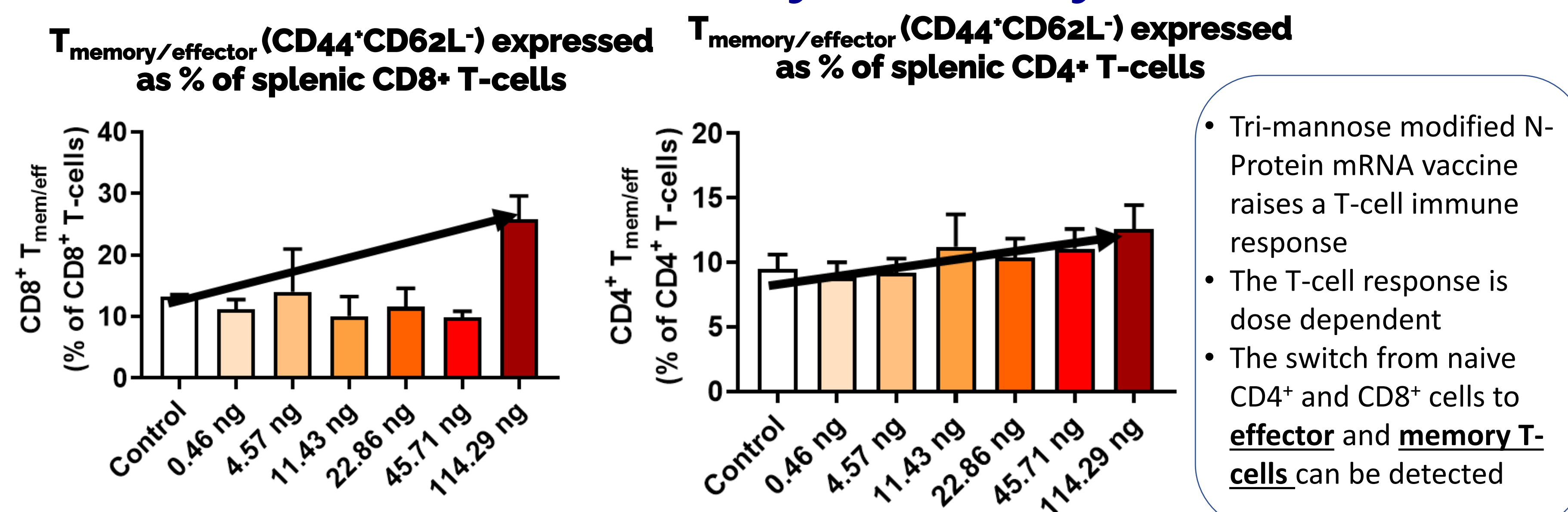


- YFP fluorescence is detected in dendritic cells in mice*, 48h after intramuscular injection with tri-mannose-modified YFP-mRNA.
- The expression of the YFP-protein increases in a dose dependent manner.

*YFP expression detection in DCs from the lymph knot adjacent to injection side

Figure 1: YFP expression in dendritic cells and macrophages in lymph nodes adjacent to injection site.

5 T-Cell activation by chemically modified mRNA



- Tri-mannose modified N-Protein mRNA vaccine raises a T-cell immune response
- The T-cell response is dose dependent
- The switch from naive CD4⁺ and CD8⁺ cells to **effector** and **memory T-cells** can be detected

Figure 2: FACS analysis of T-cell population in spleen of BCV-193N vaccinated mice (n=3).

References: (1) Mol. Ther. 2019, 27 (4), 710–728. (2) Expert Opin. Drug Deliv. 2008, 5 (6), 703–724.

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