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antibodies MDPI

A broad-spectrum SARS-CoV-2 immunization strategy targeting the highly conserved MPER of the Spike protein

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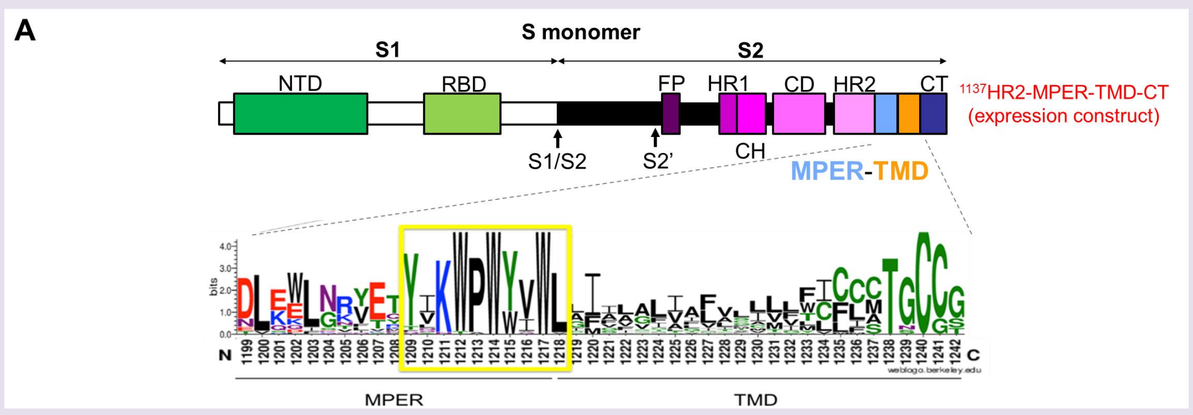
INTRODUCTION & AIM

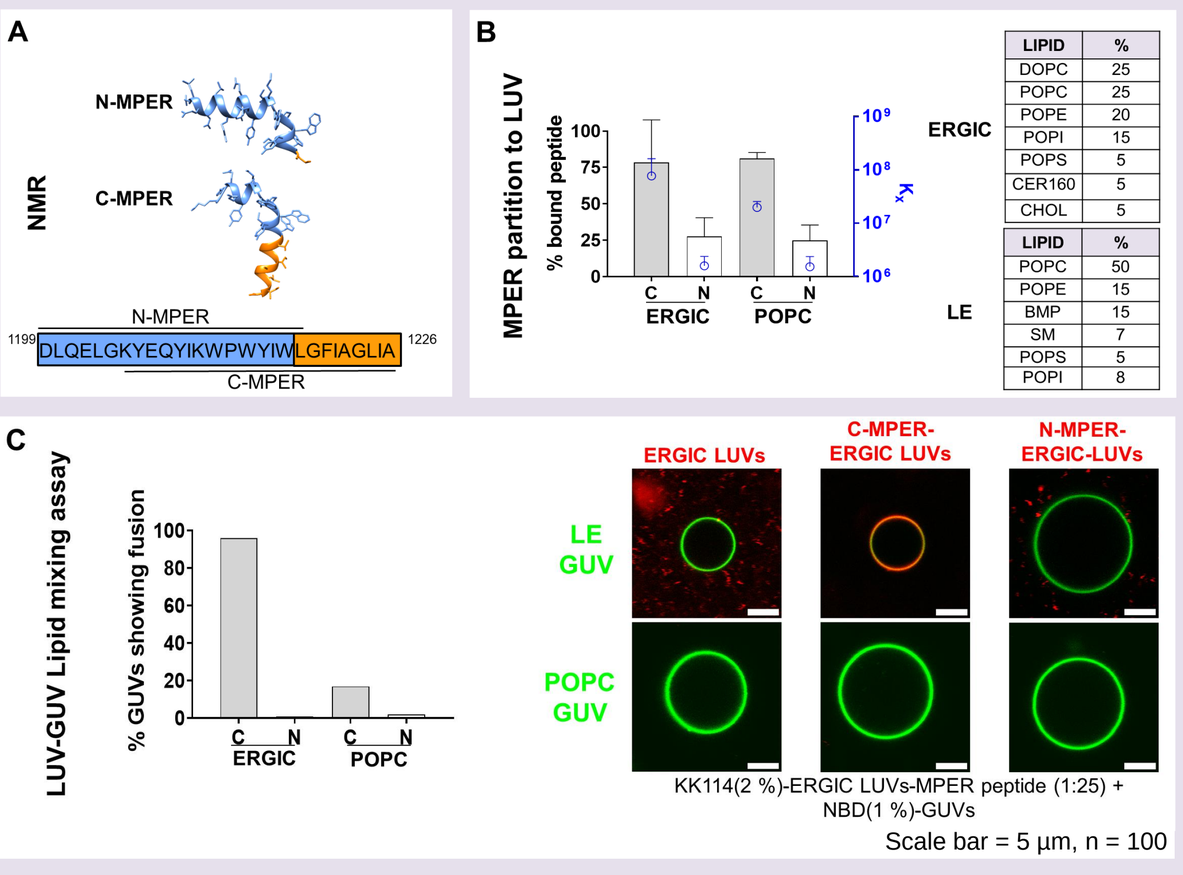
SARS-CoV-2 remains in circulation 5 years after the first cases of COVID-19 were reported, during which time several variants have been selected with mutations accumulating especially in the more accessible S1 subunit[1] of the Spike protein (S). Thus, current vaccine platforms have been updated to ensure effectiveness against the Omicron XBB.1.5 variant, highlighting the need for ongoing surveillance. To overcome this limitation, we analyzed in a SARS-CoV-2-infected human cohort the immunogenicity of the **highly conserved membrane-proximal external region (MPER)** of the S2 subunit. A portion of the patients, even if weakly, did elicit antibodies against the MPER. Additionally, we characterized its structure in a low-polarity environment and, also, showed its fusogenic potential. Considering the impact that lipid membranes may have on the structure of this region, we assessed its expression in eukaryotic cells. For that, we designed wild-type and modified[2] S2-derived DNA sequences including the MPER. The results obtained support the **feasibility of designing vaccines focused on the conserved MPER** region.

RESULTS & DISCUSSION

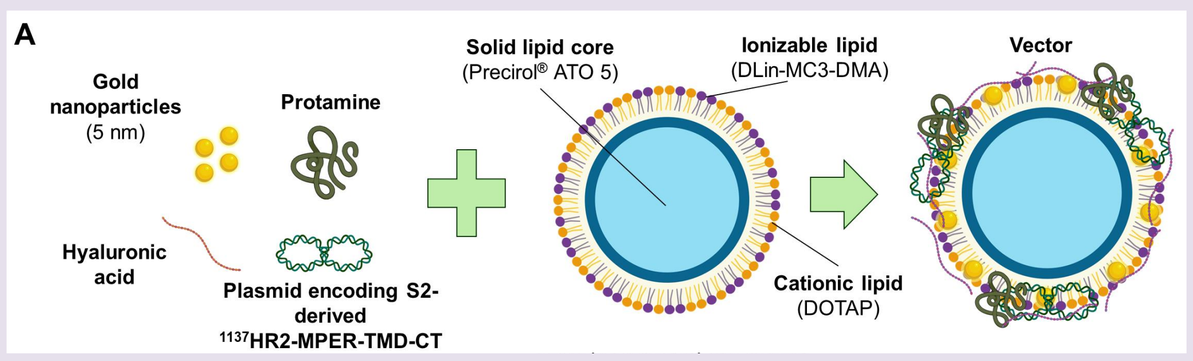
1 MPER is highly conserved and during natural infection elicits antibodies



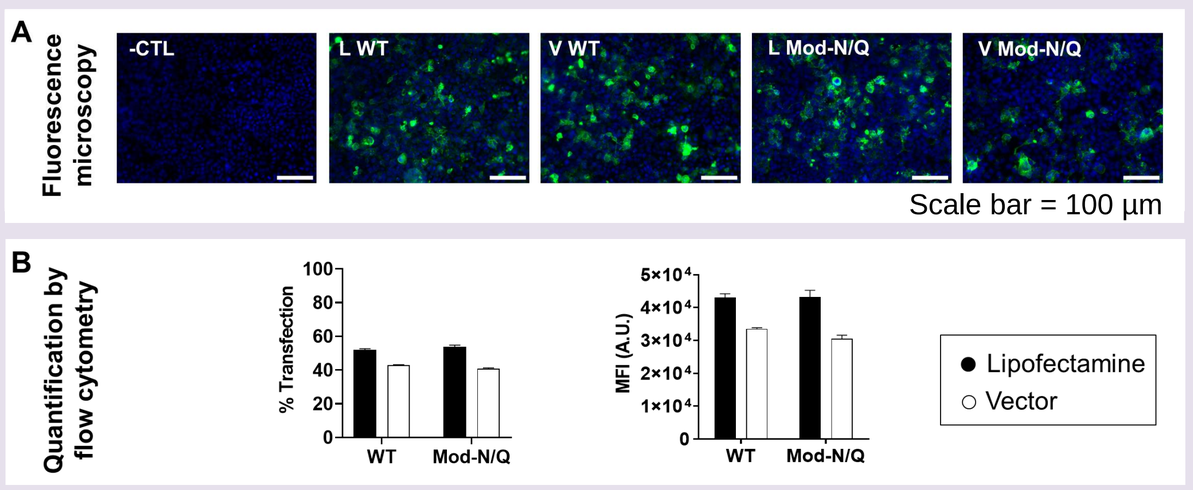
2 MPER consists of an α-helix and promotes fusion between lipid membranes relevant for viral infection



3 S2 construct optimization and characterization of solid lipid nanoparticle-based vectors



4 WT and Mod-N/Q constructs can be effectively expressed in HEK-293 cells



CONCLUSIONS

- The conserved MPER shows **fusogenic** activity, underlining its importance for infection
- SLN-based vectors delivering conserved regions achieve **high transfection** levels ***in vitro***
- Vaccination with a construct with MPER may be a feasible strategy to **inhibit viral entry**

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