Dendritic mesoporous silica nanoparticles as self-adjuvants for peptide-based vaccine sustained delivery

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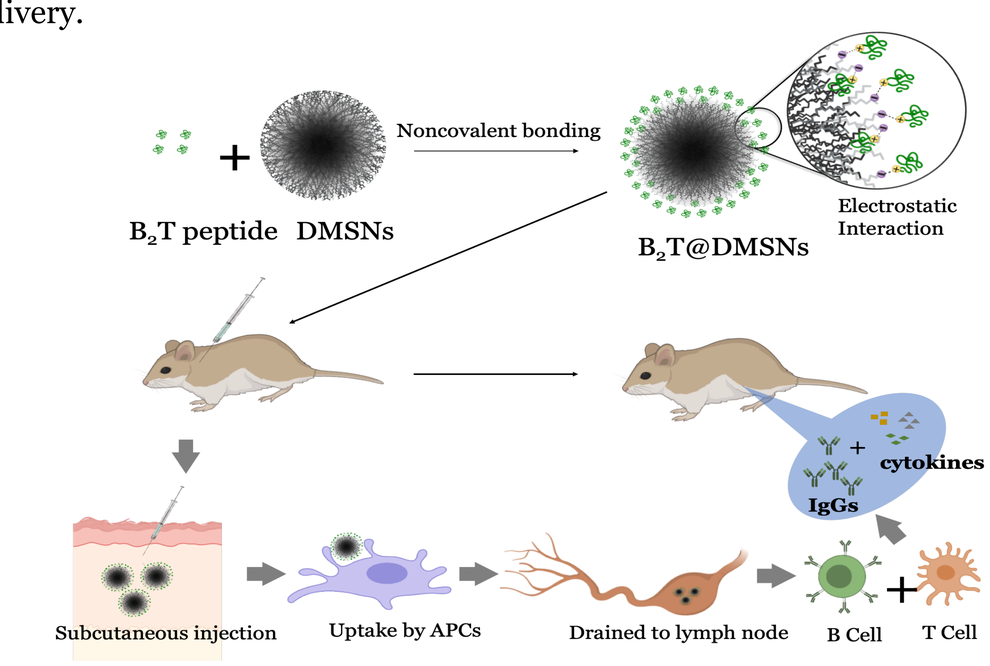
INTRODUCTION

Mesoporous silica nanoparticles have drawn increasing attention as promising candidates in vaccine delivery[1]. Previous studies for evaluating silica-based vaccine delivery systems concentrated largely on macromolecular antigens. In this study, dendritic mesoporous silica nanoparticles (DMSNs) were used to evaluate their effectiveness as delivery platforms for peptide-based subunit vaccines capable of inducing significant levels of protective response without co-injection of adjuvants. An earlier reported foot-and-mouth disease virus (FMDV) peptide vaccine prototype named B_2T[2,3] was employed as antigen model. Our nanoparticle-codelivery system (B_2T@DMSNs) efficiently loaded B_2T and showed long-time sustained release up to 930h in vitro. Besides, B_2T@DMSNs of different sizes were assessed for their in vitro cellular uptake as well as in vivo immunogenicity, eliciting specific immune responses in mice with high IgG production in a particle size-dependent manner. Our results portray DMSNs nanocarriers as an attractive platform for developing peptide-based vaccine delivery.



RESULTS

1.1 Characteristics of DMSNs

1.1.1 TEM images

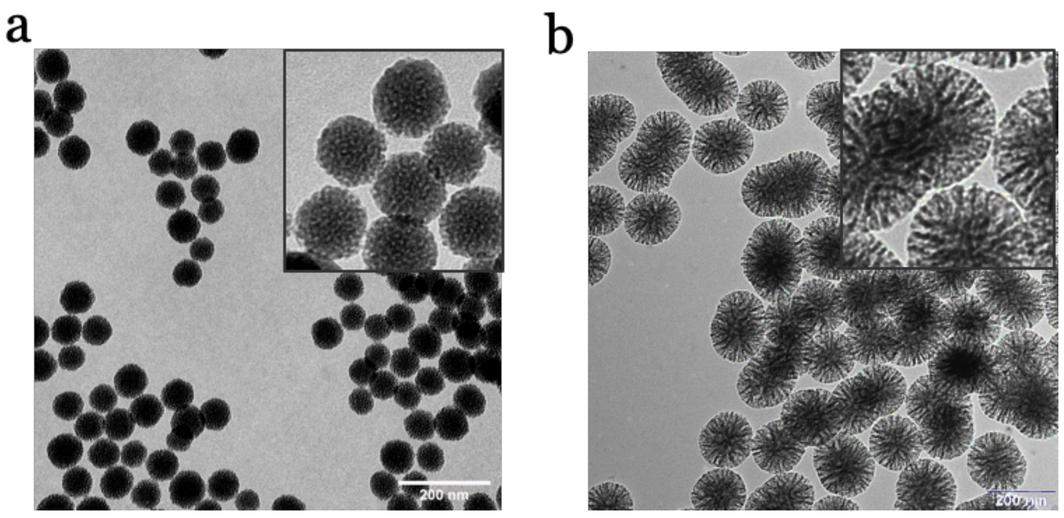


Figure 1. a) TEM image of DMSNs-57. b) TEM image of DMSNs-156.

1.1.2 DLS analysis results

Nanoparticle Type	Hydrodynamic Diameter (nm)	ζ-potential (mV)	Polydispersity Index (PDI)
DMSNs-57	75.1	-30.2	0.060
DMSNs-156	227.1	-37.1	0.061

1.2 B_2T sustained release profile in DPBS and BSA-DPBS

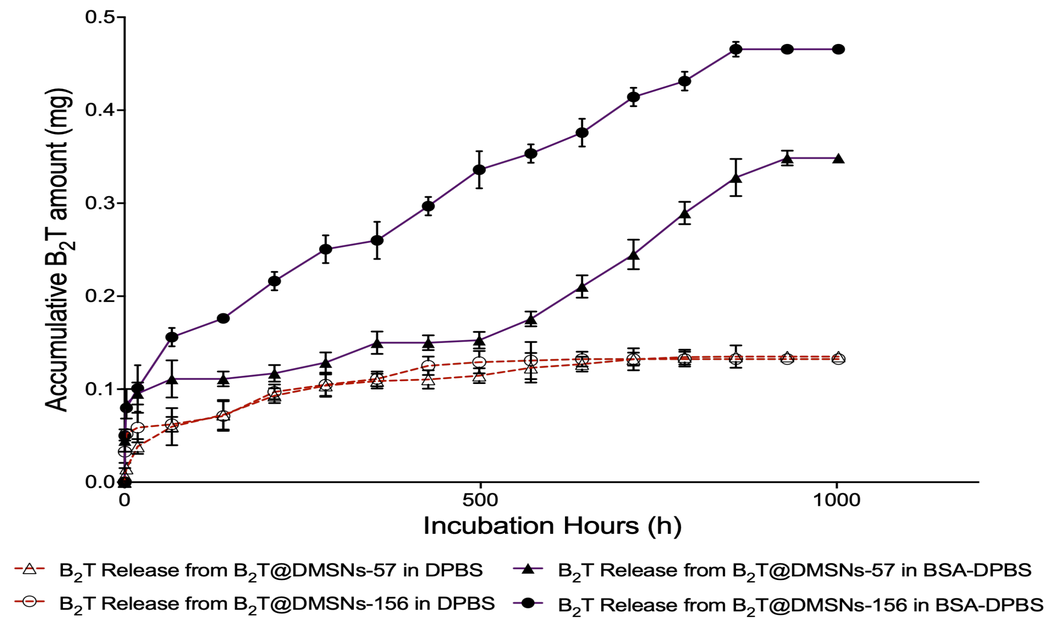


Figure 2. B_2T release profiles for B_2T@DMSNs-57 and for B_2T@DMSNs-156 in DPBS and BSA - DPBS.

1.3 Immunogenicity of B_2T@DMSNs in Mice: long-term response and particle-size effect

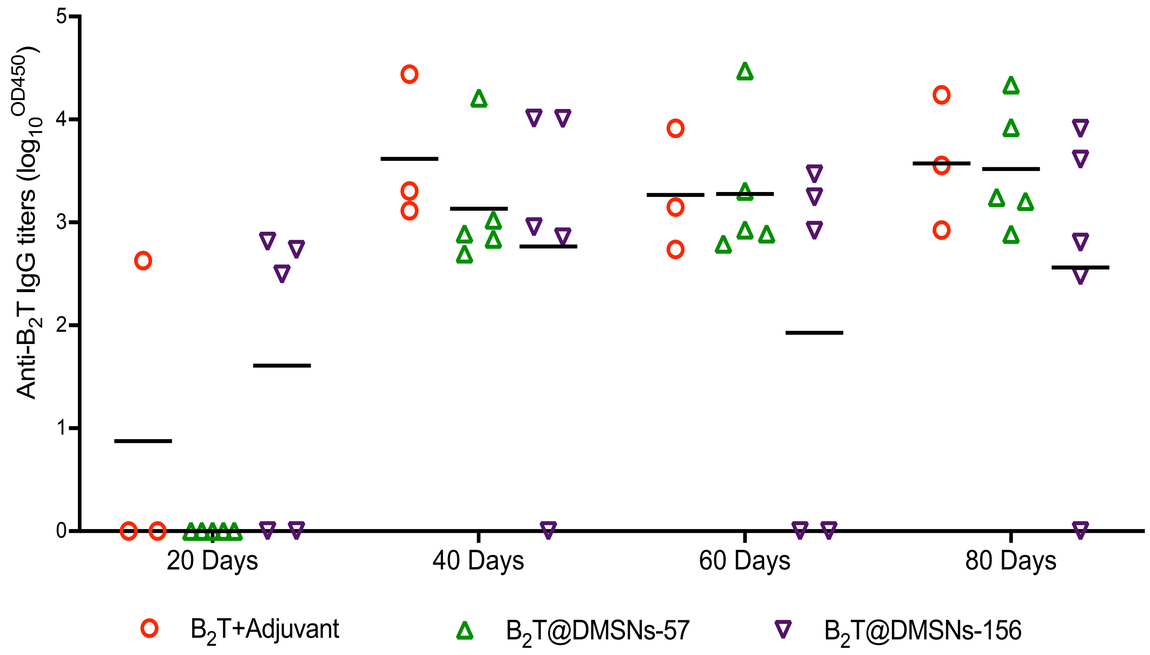


Figure 3. Results of Anti-B_2T IgG titers, measured by ELISA, from sera collected at days 20(pre-boost), 40, 60, and 80 in Swiss Mice immunized with B_2T+Adjuvant (red circle), B_2T@DMSNs-57 (green up triangle) and B_2T@DMSNs-156 (purple down triangle).

CONCLUSION

- From the TEM images, two sizes of dendritic mesoporous silica nanoparticles with excellent monodispersity and uniformity were displayed, their slightly larger sizes from DLS measurement than those measured by TEM are due to the surface hydration in aqueous solution. And both nanoparticles displayed negative charge.
- Both B_2T@DMSNs-57 and B_2T@DMSNs-156 codelivery systems showed sustained release properties in vitro, we also discovered that introducing BSA into DPBS indeed influenced the B_2T release, frankly, significantly promoted the release.
- Thought, the largest increase in anti-B_2T IgG titers after boost was recorded in mice given the B_2T emulsified in Montanide adjuvant (positive control group) and the other two groups vaccinated with DMSNs showed lower post-boosting titers. However, remarkably, in the case of B_2T@DMSNs-57 immunized animals, serum IgG titers kept increasing over the long assay timespan until reaching comparable IgG levels to the positive control group. These results suggest that DMSNs not only may help the antigen to be internalized by immune cells but also delay or slow down their *in vivo* release, finally leading to a long-lasting sustained immune response activation.

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ACKNOWLEDGEMENTS

This work was supported by China Scholarship Council (201694910800). (RYC-2012-10059, MDM-2014-0370-04, CTQ2013-45433-P[FEDER], MAT2016-75362-C3-2-R, AEI-SAF2015-73052-EXP) acknowledge the Ministry of Science, Innovation and Universities (MICINN) and AGAUR (2017 SGR 1054) for financial support. The Custom Antibody Service (CAbS, IQAC-CSIC, CIBER-BBN), is acknowledged for the assistance and support on animal experiments.