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Spray dried cubosomes as effective vaccine delivery system

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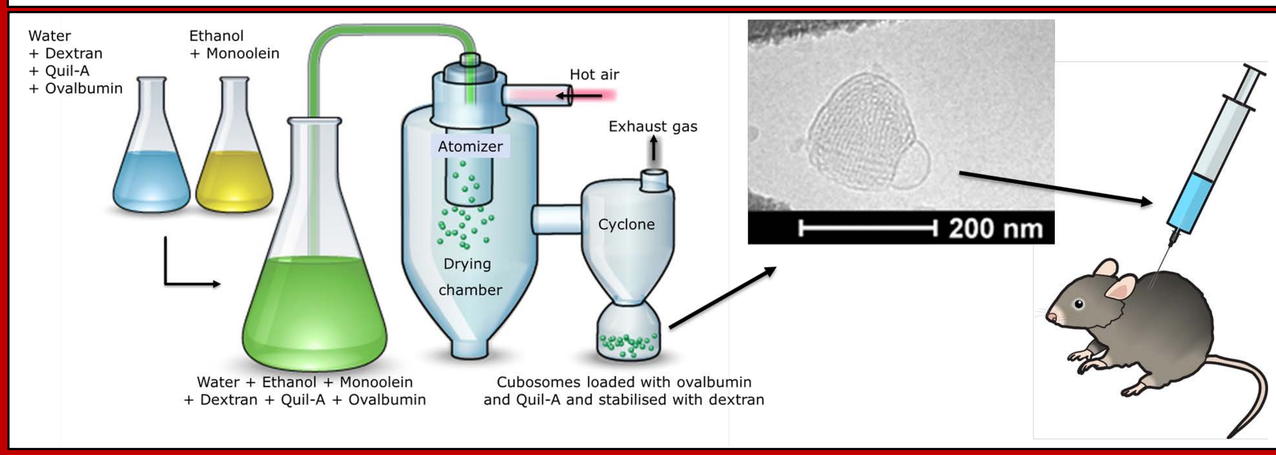
Aim

The aim of this study was to spray dry cubosomes with ovalbumin (OVA) as model antigen and Quil-A as adjuvant and investigate *in vitro* characteristics and *in vivo* immunogenicity following subcutaneous (s.c.) and oral administration to mice. Since oral vaccination with cubosomes had no effect, we applied microcontainers (MC) as oral delivery system, characterized the system *in vitro* and evaluated its oral immunogenicity *in vivo* as oral booster following s.c. injected primer and in an oral prime-boost setting.



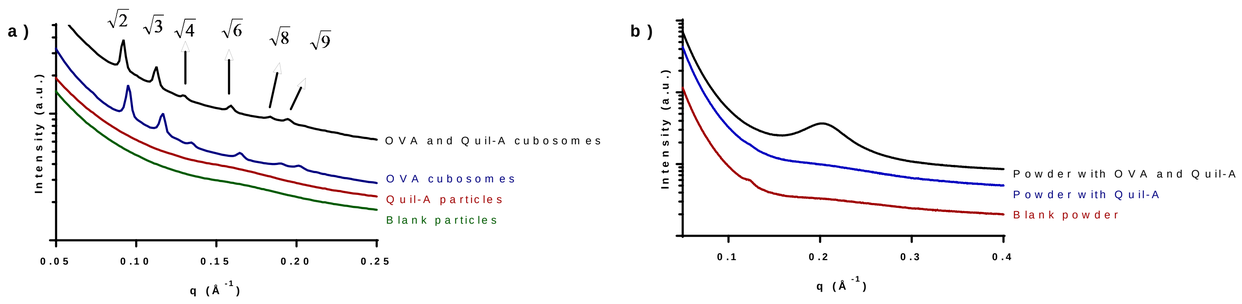


Figure 1: q vs intensity patterns obtained from SAXS measurements of a) dispersions in water of cubosomes with no Quil-A or OVA (blank), only Quil-A, only OVA, and OVA and Quil-A. b) Spray dried powders of monoolein and dextran with no Quil-A or OVA (blank), only Quil-A, and with OVA and Quil-A.

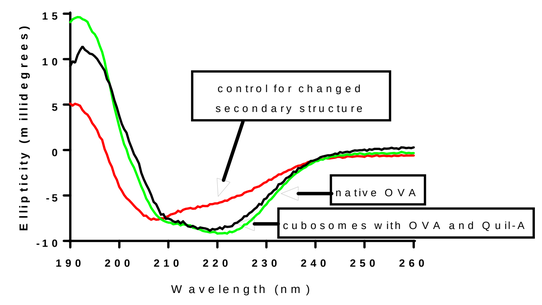


Figure 2. Representative circular dichroism spectra of spray dried cubosomes with OVA and Quil-A after secondary drying at 86°C for 24 h (concentration of OVA was 106 µg/mL).

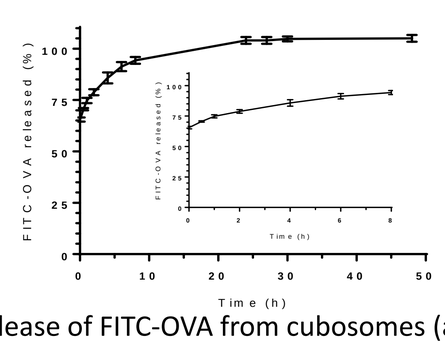


Figure 3. Release of FITC-OVA from cubosomes (also containing Quil-A) in 9.5 mM PBS at pH 7.3 and 37°C. The insert shows the release over the first 8 h. Data are expressed mean ± SD (n = 4).

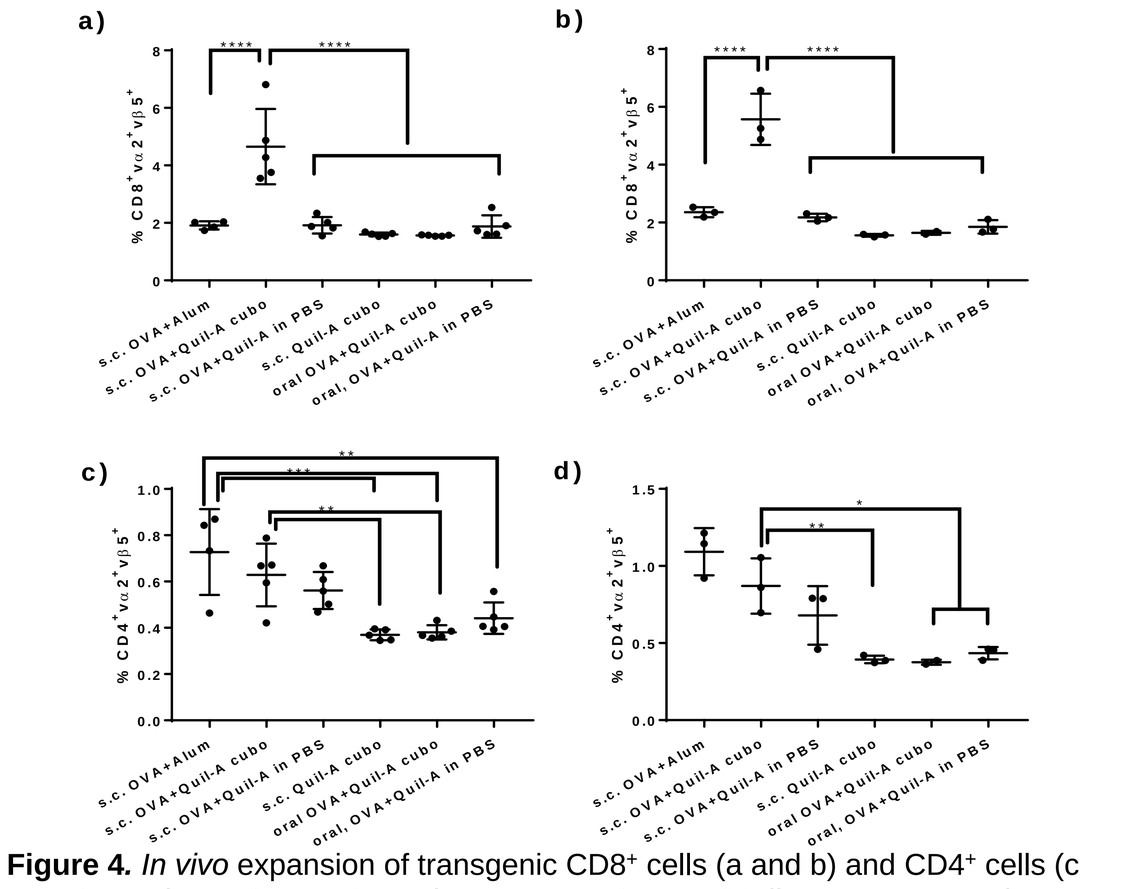


Figure 4. *In vivo* expansion of transgenic CD8⁺ cells (a and b) and CD4⁺ cells (c and d) in spleens (a and c) and lymph nodes (b and d) following s.c. or oral administration. Data in a and c are results from individual mice plus the mean and SD from a representative experiment of three independent experiments (n = 5 mice/experiment). Data in b and d are pooled data from 4-5 mice in each of three independent experiments. *p < 0.05, **p < 0.01, ***p < 0.001, **** p < 0.0001

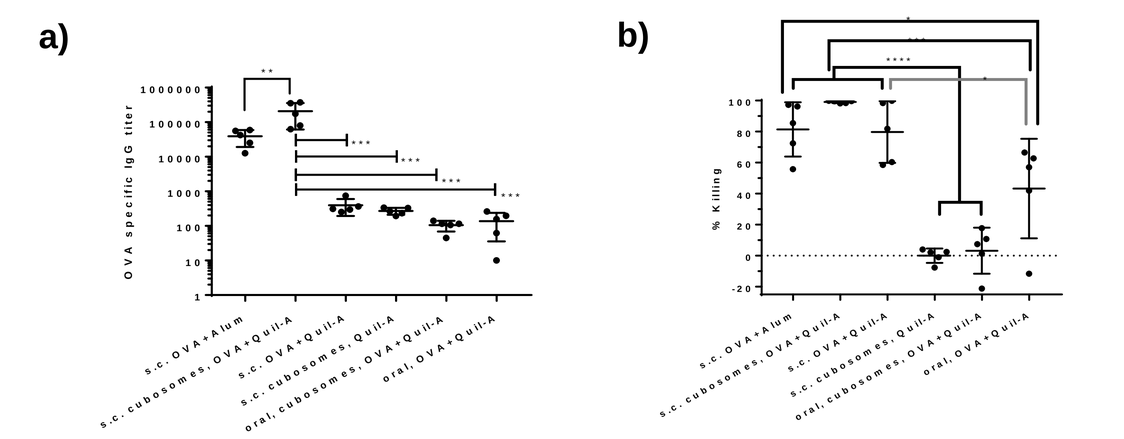
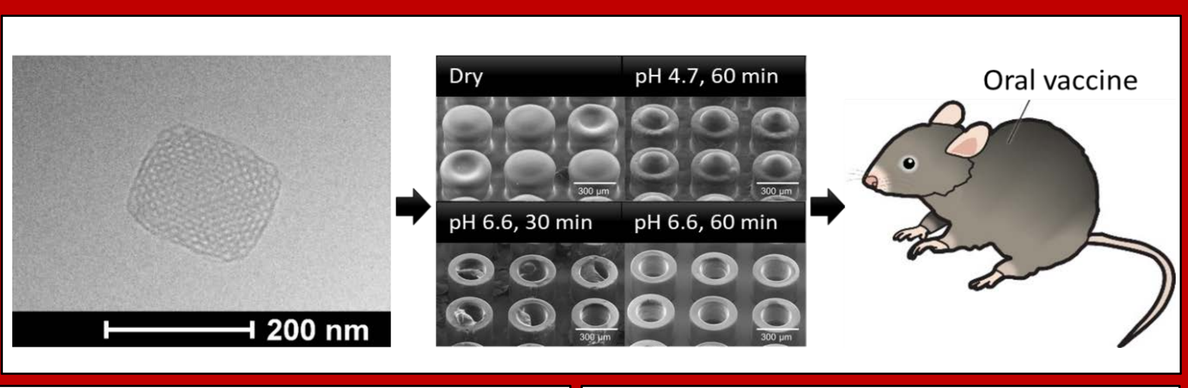


Figure 5. OVA specific serum IgG antibody titers (a) and target cell killing in spleens (b). Data shown are from individual mice from a representative experiment of 3 independent experiments (n = 5 mice/experiment). ** p < 0.01, *** p < 0.001, **** p < 0.0001



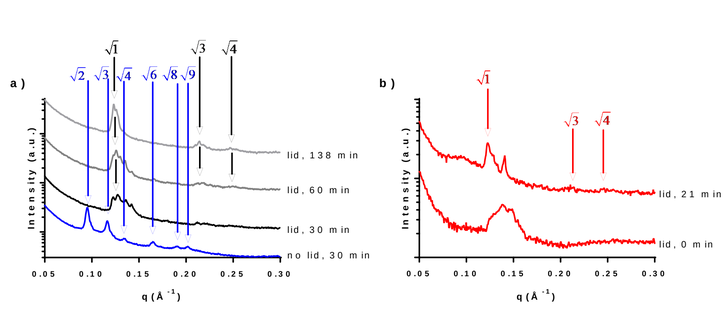


Figure 8. q vs. intensity patterns obtained from SAXS measurements of cubosomes with OVA and Quil-A released at 37°C from microcontainers with or without Eudragit L100-55 lids as indicated in PBS (a) and mouse intestinal medium (b).

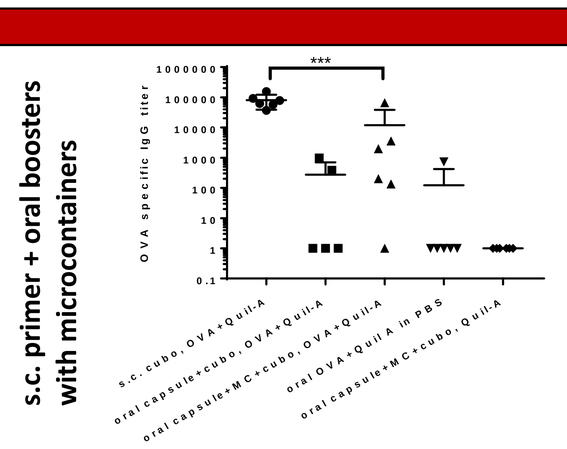


Figure 9. OVA specific serum IgG antibody titers from individual mice from a representative experiment of 3 independent experiments (n = 5 mice/experiment). *** p < 0.001

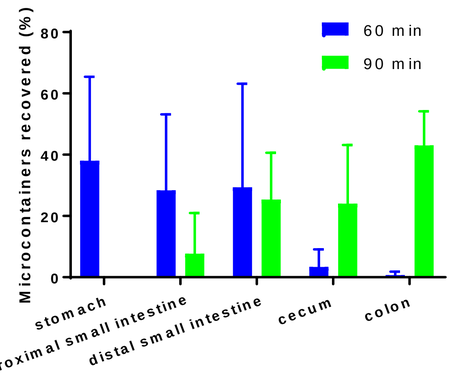


Figure 6. Microcontainers found in segments of the GI tract when sacrificing mice 60 or 90 min after oral gavage. Data are presented as mean±SD (n = 3).

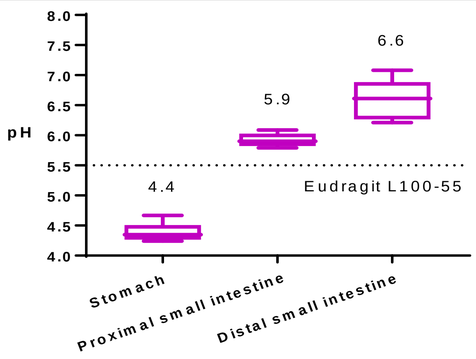


Figure 7. pH in the GI tract of mice at 37°. Whiskers on the boxplots indicate maximum and minimum (n = 5). Averages are written above each group.

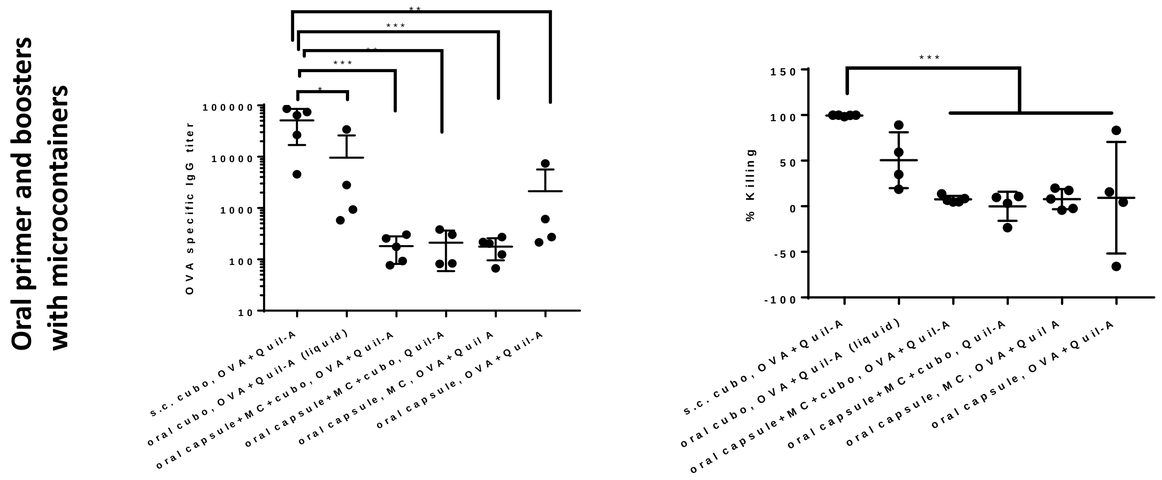


Figure 10. OVA specific serum IgG antibody titers (a) and target cell killing in spleens (b). Data shown are from individual mice from a representative experiment of 2 independent experiments (n = 5 mice/experiment). * p < 0.05, ** p < 0.01, *** p < 0.001

Conclusions

Cubosomes with OVA and Quil-A stimulate strong humoral and cellular immune responses after s.c. administration but not oral. MC protect cubosomes *in vitro* and release them in the small intestine. MCs improve immunogenicity *in vivo* of oral boosters but no effect is seen after oral primer and booster.

Acknowledgements

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