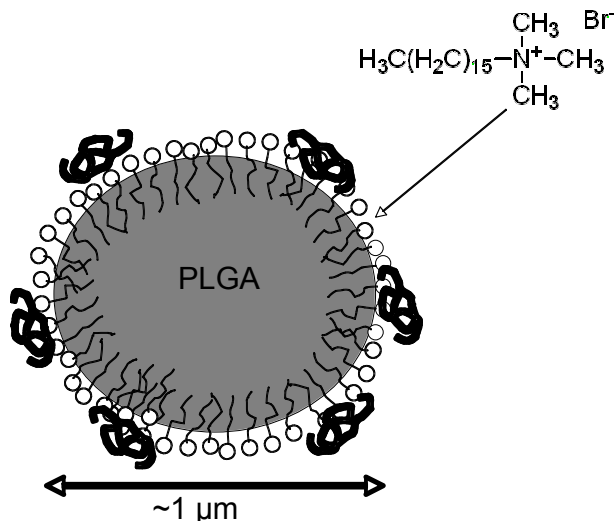


Uploaded on the MIT server are 4 journal articles related to the problem of oral vaccination:

1. Neutra and Kozlowski, 'Mucosal vaccines: the promise and the challenge,' *Nat. Rev. Immunol.* **6** 148-158 (2006)
2. Keegan and Saltzman, 'Biomimetic design in microparticulate vaccines,' *Biomaterials* **24** 4435-4443 (2003)
3. Mutwiri et al., 'Microparticles for oral delivery of vaccines,' *Expert Opin. Drug Deliv.* **2**(5) 791-806 (2005)
4. Frey et al. 'Role of the glycocalyx in regulating access of microparticles to apical plasma membranes of intestinal epithelial cells: Implications for microbial attachment and oral vaccine targeting,' *Journal of Experimental Medicine* **184** 1045-1059 (1996)

Using these references as a starting point, we will critique a novel strategy for oral immunization against rotavirus, an intestinal pathogen, using a recombinant protein antigen. The immunization system is based upon poly(lactide-co-glycolide) microparticles surface-modified with a cationic surfactant, cetyltrimethylammonium bromide (CTAB), which is embedded in the polymer at the surface of the particles. The CTAB molecules provide a net positive surface charge, which allows the adsorption of the rotavirus protein antigen VP6. The particles have a mean diameter of  $\sim 1 \mu\text{m}$  and are intended to be delivered orally to provide protective mucosal immunity.



Write a 6-page analysis of this immunization strategy, using concepts from class, the references given above, and any other resources you choose from the primary literature. In your analysis answer the following questions in as much detail as possible:

1. What are the advantages and disadvantages to the proposed immunization strategy? What is the greatest strength of this approach, and the greatest weakness? Explain your answers.
2. Describe in as much detail as possible how you would modify this strategy to improve the success of this proposed immunization scheme. Identify materials/components you would use explicitly and explain their mechanism of action.
3. This strategy seeks to address a major need in vaccines, the development of suitable needle-free immunization methods. A second technological challenge for vaccination is the development of technologies to provide 'boosting' of the immune response from a single treatment, to avoid the need for repeated immunizations—this is especially of concern in developing countries, where families may have infrequent access to vaccination clinics and may only be able to receive treatment once per year. Propose an approach to modify this biomaterials strategy to allow a single oral dose from this immunization system to provide sequential exposure of the immune system to antigen in 3 week intervals 3-5 times. Provide as much detail to your concept as possible.

A strong analysis will be one that responds to the questions above with detailed answers and cites the primary literature where appropriate. Do not be afraid to be creative or implement ideas that are a synthesis of things you have learned in the course or read—you will not be penalized for proposing untested ideas if you explain your reasoning behind them. There is no required or minimum length for the bibliography.

Format: 6 pages (not including references), 1" margins, 12-point font, single-spaced or 1.5-line spacing. Include a bibliography of references from **primary journal articles** (no page limit).