260e Engineering Bacterial Outer Membrane Vesicles for DNA Vaccine Delivery

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The therapeutic promise of DNA vaccines lies in their ability to elicit both cell-mediated and antibody-mediated immune responses. These vaccines, which carry genes encoding protein antigens, have had limited success due in large part to the chemical and physical barriers to gene delivery. Gram negative bacteria (e.g., *E. coli*) are able to deliver plasmids and proteins to other bacteria as well as to mammalian cells through vesicles derived from their outer membrane. These outer membrane vesicles (OMVs) are approximately 100-150 nm in diameter and contain protein and plasmid products that originate from the bacterial periplasm. Through recombinant DNA technology, both the surface properties and luminal contents of OMVs may be modified to improve their ability to serve as DNA vaccine vehicles. We have engineered OMVs to alter their ability to interact with mammalian cell membranes and enter cells by endocytosis. Additionally, we have successfully incorporated marker gene plasmid DNA (pCMV-luc) into the OMV lumen. This work harnesses the intrinsic transformation capability of bacterial outer membrane vesicles for use in DNA vaccine delivery.