SELF-ADJUVANTING IMMUNIZATION BY RED BLOOD CELL OPSONIZATION IN VIVO

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Immunizations often require that the potency of immunogens be increased by adjuvants or by targeting to specific cells or receptors. Non-specific immune adjuvants are frequently used to enhance the immune response, but they can cause adverse effects. We are developing a strategy to potentiate immune responses by routing immunogens to the immune system via red blood cells (RBCs). In addition to transporting oxygen, RBCs also serve to collect foreign materials on their surface. RBCs bearing immune complexes on their surface (or opsonized) are removed from the circulation by the reticuloendothelial system, and their bound materials are presented to the immune system very effectively. We designed a generic delivery vehicle that couples to immunogens and homes them to the RBC surface. The delivery vehicle is a fusion protein consisting of an antibody fragment that recognizes a RBC surface epitope, and streptavidin, a biotin-binding protein. Biotinylated immunogens combine with the fusion protein ex vivo. Using influenza peptide M2e, we immunized mice and measured an IgG response that was 2,000-fold greater in the presence of the fusion protein than peptide alone or adsorbed onto alum. These results validate the technology in vivo and indicate the utility of this immune augmentation strategy for the generation of monoclonal and polyclonal antibodies. Furthermore, RBC opsonization in vivo is a promising technology with dose-sparing and immune enhancing properties that will be useful in prophylactic and therapeutic vaccines against infectious pathogens and other conditions amenable to vaccine intervention.