SAFETY AND BIODISTRIBUTION OF SULFATED ARCHAEOAL GLYCOLIPID ARCHAEOSOMES AS VACCINE ADJUVANTS

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Archaeosomes are liposomes comprised of ether lipids derived from various archaea which, as adjuvants, can induce robust, long-lasting humoral and cell-mediated immune responses to entrapped antigens. Traditional total polar lipid (TPL) archaeosome formulations are relatively complex and semi-synthetic archaeosomes involve many synthetic steps to arrive at the final desired glycolipid composition. We have developed a novel archaeosome formulation comprising a sulfated saccharide group covalently linked to the free sn-1 hydroxyl backbone of an archaeal core lipid (sulfated S-lactosylarchaeol, SLA) mixed with uncharged glycolipid (lactosylarchaeol, LA). This new class of adjuvants can be easily synthesized and retains strong immunostimulatory activity for induction of cell-mediated immunity following systemic immunization. Herein, we demonstrate the safety of SLA/LA archaeosomes following intramuscular injection to mice and evaluate the immunogenicity, in vivo distribution and cellular uptake of antigen (ovalbumin) encapsulated into SLA/LA archaeosomes. Overall, we have found that semi-synthetic sulfated glycolipid archaeosomes are a safe and effective novel class of adjuvants capable of inducing strong antigen-specific immune responses in mice and protection against subsequent B16 melanoma tumor challenge. A key step in their mechanism of action appears to be the recruitment of immune cells to the injection site and the subsequent trafficking of antigen to local draining lymph nodes. A better understanding of the safety and mechanism of action of novel adjuvants such as archaeosomes is a key step in their advancement into clinical use.