SAFETY AND BIODISTRIBUTION OF SULFATED ARCHAEAL GLYCOLIPID ARCHAEOSOMES AS VACCINE ADJUVANTS

Bassel Akache, National Research Council Canada
Bassel.akache@nrc-cnrc.gc.ca
Felicity C. Stark, National Research Council Canada
Yimei Jia, National Research Council Canada
Umar Iqbal, National Research Council Canada
Lise Deschatelets, National Research Council Canada
Renu Dudani, National Research Council Canada
Blair Harrison, National Research Council Canada
Lakshmi Krishnan, National Research Council Canada
Michael J. McCluskie, National Research Council Canada

Key Words: Archaeosome, adjuvants, vaccine, safety , biodistribution, Sulfated archaeal glycolipids.

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.