Vaccine Adjuvant Activity of Conifer-derived Oil-in-Water Nanoemulsions

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Abstract: Next to aluminum salts, squalene nanoemulsions comprise the most widely employed class of adjuvants in approved vaccines. Despite their importance, the mechanisms of action of squalene nanoemulsions are not completely understood, nor are the structure/function requirements of the oil composition. In this study, we build on previous work that compared the adjuvant properties of nanoemulsions made with different classes of oil structures to squalene nanoemulsion. Here, we introduce conifer-derived polyprenol nanoemulsions as novel vaccine adjuvant compositions. In contrast with long-chain triglycerides that do not efficiently enhance an immune response, both polyprenols and squalene are comprised of multimeric isoprene units, which may represent an important structural property of oils in nanoemulsions with adjuvant properties. Oils were extracted from conifers and used to prepare oil-in-water nanoemulsions by microfluidization. Conifer-derived nanoemulsions were formulated with or without a synthetic TLR4 ligand and characterized regarding physicochemical and biological activity properties in comparison to squalene nanoemulsions. Emulsion droplet diameter stability was characterized by dynamic light scattering. Nanoemulsions were evaluated for in vitro biological activity using human whole blood, and in vivo biological activity in mouse, pig, and ferret models when combined with pandemic influenza vaccine antigens. Nanoemulsions comprised of conifer-derived polyprenol oils demonstrated long-term physical stability, stimulated cytokine production from human cells in vitro, and promoted antigen-specific immune responses in various animal models, particularly when formulated with the TLR4 ligand GLA. Conifer-derived nanoemulsions are compatible with inclusion of a synthetic TLR4 ligand and promote antigen-specific immune responses to pandemic influenza antigens in mouse, pig, and ferret models.

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