HUMAN IN VITRO MODELING OF VACCINE ADJUVANTS FOR GLOBAL OPEN ACCESS

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Abstract

Adjuvants enhance vaccine immunogenicity, but their mechanism of action is incompletely understood. This hampers rapid applicability for pandemic vaccines. We characterized cellular and molecular activity of soluble, oil-in-water (OIW), and liposomal (LS) adjuvant formulations, including those developed for global open access. LS co-formulation of MPL (monophosphoryl lipid A) and QS-21 (*Quillaja saponaria*), comparable to licensed adjuvant system AS-01, was most potent in promoting dendritic cell maturation and differentiation, producing Th1-polarizing cytokines, and activating antigen-specific CD4⁺ and CD8⁺ T cells.

Background

Vaccination is a successful and cost-effective public health intervention that prevents millions of deaths every year. Adjuvanted vaccines reduce number of immunization doses, increasing availability for global supply. Major barrier to development of low-cost vaccines is restricted access to adjuvant formulations due to protection by intellectual property laws that limits research and impairs global access of vaccines.

Methods

- Four human *in vitro* platforms:

1. Whole blood assay (magnitude of immune activation and specificity towards distinct cell types)

2. Human tissue construct assay (fate of activated innate immune cells)

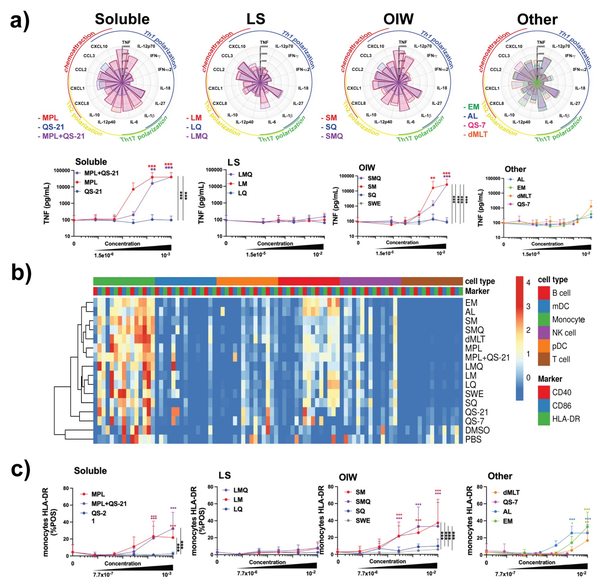
3. Monocyte-derived dendritic cell assay (differentiation of T-helper subsets)

4. Dendritic cell-T cell interface assay (antigen processing and presentation, and activation of CD4⁺ and CD8⁺ T cells)

- Cytokine multiplex: cytokine profiles of supernatants
- Flow cytometry: cell subpopulation identification and characterization (analyzed with FlowJo)
- Statistical analyses: GraphPad Prism (dose-response curves – ANOVA, Dunnett's method, Tukey's method; synergy calculation – Loewe method)

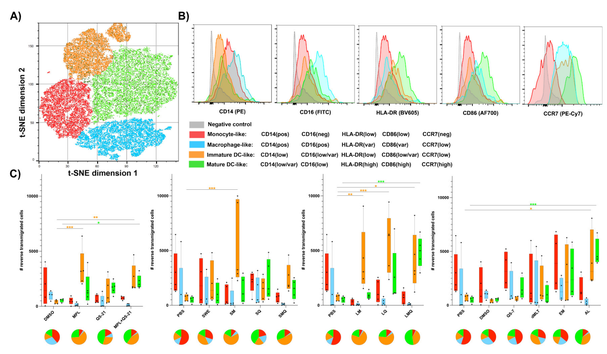
Results

1. Whole blood assay



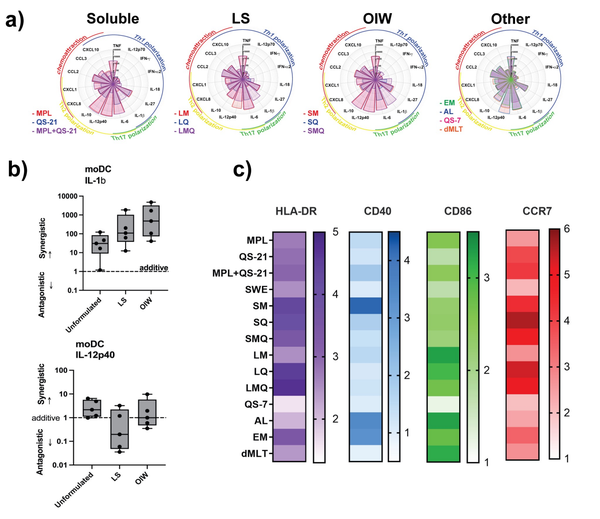
LS formulation attenuates reactogenicity potential of MPL

2. Human tissue construct assay



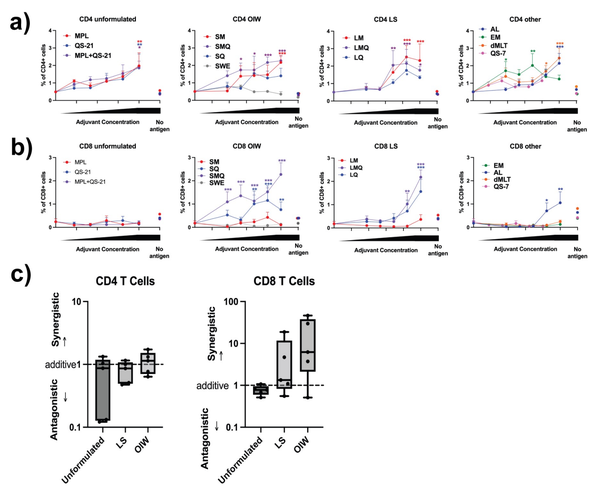
LS formulations drive monocyte differentiation to mature dendritic cell-like fate

3. Monocyte-derived dendritic cell assay



LS formulations induce Th1-polarizing cytokine response

4. Dendritic cell-T cell interface assay



MPL+QS-21 LS and OIW formulations synergistically induce CD8⁺ T cell response

Conclusion

Insight into mechanism of action of adjuvanted vaccine formulations provided by human *in vitro* modeling may advance public health by accelerating development of affordable and scalable vaccine adjuvants tailored to vulnerable populations.

References

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