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Poster presentation

P11-18. Immunogenicity of *Lactobacillus gasseri*-FliC as an oral mucosal vaccine adjuvant for HIV

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Background

Transmission of HIV-1 across mucosal surfaces is the most prevalent mode of viral infection. Therefore, a successful vaccine must induce broad anti-viral immunity at the mucosal surface. In the present study, we investigated the immunogenicity of a novel *Lactobacillus gasseri* mucosal vaccine vector for use in oral delivery of HIV antigens. *L. gasseri* was genetically engineered to express *Salmonella* spp. flagellin (*L. gasseri*-FliC) – the agonist for Toll-like receptor 5 (TLR5) and a potent activator of innate immune cells.

Methods

To evaluate the potential adjuvant activity of our vector, we determined the ability of *L. gasseri*-FliC to induce myeloid dendritic cell (DC) activation as measured by phenotypic activation and cytokine production. Briefly, myeloid DCs were isolated and co-cultured with live *L. gasseri* (w.t.), *L. gasseri*-pTRK (empty plasmid), *L. gasseri*-FliC, and *Lactobacillus acidophilus*, as well as TLR agonists rFliC (TLR5) and rFLS-1 (TLR2/6). After 24 hours of co-culture, cytokine production was analyzed via a 27-plex Luminex assay and DC phenotype determined through flow cytometry.

Results

Each *Lactobacillus* treatment induced a unique response from the DCs regardless of strain, though different from purified TLR agonists alone. All treatment groups yielded higher surface concentrations of CD86 than CD80 amongst populations of $CD80^{+}CD86^{+}HLAII^{+}$ DCs, but only *L. acidophilus*, *L. gasseri*-FliC, and rFliC induced significant increases in the overall percent of DCs expressing co-stimulatory molecules. Elevated levels of cytokines IL10, IL1RA, IFNγ, IL6, TNFα, IL1β, GM-CSF, G-CSF, and chemokines IL8, MIP1α, MIP1β were produced by *Lactobacillus*-pulsed DCs. IL12, IL2 and IL15 were produced in minimal concentrations, with the IL10:IL12 ratio being 100-fold greater than that of TLR agonists alone.

Conclusion

These results suggest DC phenotypic maturation is significantly affected by *Lactobacillus* treatment and immunological recruitment is likely, but the functional significance of the mixed inflammatory and anti-inflammatory cytokine profile must be evaluated *in vivo* to include the immunological perspective of the mucosa.