

Poster presentation

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P10-02. Toll-like receptor activation profiles of wild-type, recombinant, and mutant *Lactobacillus*: implications for vaccine design

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Background

Lactobacillus spp. are commensal bacteria that have long been utilized as probiotics and are generally regarded as safe for use in humans. We are currently investigating the use of *Lactobacillus* spp. as vaccine vectors for oral immunization against HIV infection. While some lactobacilli seem to induce oral tolerance, others induce an adaptive immune response. The differences in these responses may be due to activation of specific Toll-like receptors (TLR).

Methods

Using HEK293 cells engineered to express single TLRs, we determined the ability of mutant and wild-type *L. gasseri* and *L. acidophilus* to activate TLR1/2, TLR2/6, TLR2 (homodimer), TLR3, TLR4/MD2, TLR5, TLR7, TLR8 and TLR9.

Results

Our data show that *Lactobacillus* species primarily activate TLR 2/6, with additional, though lesser, activation of TLR1/2 and TLR2. Bacteria with mutations in mucus binding proteins tended to induce greater activation through TLR2/6 compared to wild-type bacteria. The TLR activation profile of *L. gasseri* genetically engineered to express feline immunodeficiency virus (FIV) gag protein did not differ from wild-type bacteria, however, *L. gasseri* expressing human immunodeficiency virus (HIV) gag protein showed a modest increase in TLR 2/6 activation. In order to expand the TLR activation profile, we transfected *L. gasseri* with a plasmid expressing *FliC*, the gene encoding bac-

terial Flagellin which activates TLR5. Indeed, this recombinant *L. gasseri* demonstrated strong activation of TLR5 and TLR2/6 as well as moderate activation through TLR1/2 and TLR2.

Conclusion

In conclusion, *Lactobacillus* species can be modified either by mutation of genes or addition of genes to modulate its TLR activation profile to enhance immunogenicity as a vaccine vector.

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