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## Development of Vaginal Lactobacilli for Mucosal Delivery of a Topical Microbicide, Cyanovirin-N (CV-N)

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### Background

Women are particularly at risk of HIV infection, therefore, female initiated strategies are essential to curtail the HIV/AIDS pandemic worldwide.

### Material and Methods

We developed a live topical microbicide, which is an H<sub>2</sub>O<sub>2</sub>-producing *Lactobacillus jensenii*, a natural component of the vaginal microflora, as a delivery vehicle for the potent HIV inhibitor, cyanovirin-N (CV-N).

### Results

The optimized CV-N expression cassette was stably integrated in single copy into the lactobacillus bacterial chromosome, and resolved from extraneous plasmid DNA and antibiotic resistance determinants. The *L. jensenii*-expressed CV-N dramatically decreased CCR5-trophic HIV<sub>BAL</sub> infectivity *in vitro*, with an IC<sub>50</sub> of 0.3 nM. Histological examination of CD1 mice, which were intra-vaginally inoculated with *L. jensenii* expressing CV-N, revealed that *L. jensenii* was associated with keratinized epithelium present during estrus or free in the vaginal lumen and secreted full-length CV-N *in vivo*.

### Conclusion

This live microbicide represents a major step towards developing inexpensive, durable protein-based microbicides to address the urgent need for female-controlled approaches to block the heterosexual transmission of HIV.