ABSTRACT

INHIBITION OF NEISSERIA GONORRHOEAE EPITHELIAL CELL INTERACTIONS BY VAGINAL LACTOBACILLUS SPECIES

By

Rachel R. Spurbeck

Urogenital infections, including the sexually transmitted disease gonorrhea, are one of the main reasons women visit the doctor in the United States. One potential approach to the treatment or prevention of vaginally acquired infections is through the use of beneficial microbes known as probiotics. Most probiotic research, in both the gastrointestinal and vaginal tracts, has focused on species from the genus Lactobacillus since this genus is a member of the indigenous microbiota that is associated with health. The presence of Lactobacillus species in the vaginal tract has been correlated with a reduced risk of acquiring sexually transmitted infections upon exposure, and therefore has the potential for development as a vaginal probiotic. In this work Lactobacillus jensenii, one of the most common species of lactobacilli in the healthy human vaginal tract, was found to inhibit the interaction of Neisseria gonorrhoeae with epithelial cells at the levels of adherence and invasion. This inhibition was not due to direct killing of the pathogen or co-aggregation, as has been suggested in the case of uropathogens. Further characterization of the inhibition of adherence mediated by L. jensenii determined that the inhibition was independent of an epithelial cell response and due to Lactobacillus surface-associated proteins. By characterizing a cell-free preparation of released surface components from L. jensenii, it was shown that one of the surface associated inhibitory proteins was an enolase. The

surface bound enolase inhibits gonococcal adherence to epithelial cells when produced recombinantly in E. coli and purified as a C-terminal His6-tagged protein, and retains enolase activity. Finally, it was determined that the substrate-binding site of the enzyme, but not the enolase activity, is necessary for inhibition of gonococcal adherence. The discovery of a protein from a commensal organism of the healthy human vaginal tract that inhibits gonococcal adherence is significant, and may lead to the production of new therapeutics to treat and prevent the sexually transmitted disease, gonorrhea, as well as other vaginally acquired infections.