

In vivo versus *in vitro* metabolomics profiling of vaginal lactobacilli for probiotic use

D E O'Hanlon

Johns Hopkins University, USA

Vaginal microbiotas dominated by lactobacilli are associated with reduced reproductive tract disease, including sexually transmitted infections. Lactobacilli that produce hydrogen peroxide (H_2O_2) h_2o_2 under specific experimental conditions confer greater protection, compared to lactobacilli that do not produce H_2O_2 under the same conditions. H_2O_2 production is a generally used criterion in selecting lactobacilli for probiotic use.

However, the vaginal environment precludes significant *in vivo* production or accumulation of H_2O_2 . H_2O_2 -production is therefore an experimental metabolomics marker of protective lactobacilli, rather than a direct mechanism of *in vivo* protection. We investigated the metabolomic-profiles of vaginal lactobacilli *in vivo* and under different *in vitro* conditions. We compiled *in vivo* metabolomic-profiles by measuring metabolites (H_2O_2 , lactate, acetate and hydrogen ions) in freshly collected cervicovaginal fluid samples maintained under physiological conditions. We isolated the lactobacilli from the samples and measured metabolites under various *in vitro* conditions. *In vivo*, and in conditions consistent with those *in vivo*, H_2O_2 -production was trivial or undetectable (\sim μ M) and lactate production was high (1%). Under typical 'experimental' conditions, however, H_2O_2 -production was 1000-fold higher and lactate production was 10-fold lower. We found a general correlation of high H_2O_2 -production under experimental conditions with high growth rate and high lactate-production under *in vivo* conditions. However, the correlation is not perfect: the lactobacilli strain with the highest growth rate and lactate-production did not have the highest H_2O_2 -production. We believe that H_2O_2 -production under experimental conditions is a spurious criterion for selecting probiotic strains, and should be replaced by growth rate and lactate-production under physiological conditions.

eohanlon@jhu.edu