INTERACTIONS OF COMMENSAL URINARY LACTOBACILLI WITH URINARY PATHOGENS

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INTRODUCTION

- Over 170 million cases of the urinary tract infections are registered annually around the world. Majority of the UTIs are caused by enteric bacteria (Escherichia coli, Klebsiella pneumoniae, Enterococcus faecalis). The standard treatment for UTIs is a course of antibiotics but the urinary pathogens are becoming increasingly resistant to antibiotics.
- It has become evident that diverse commensal bacteria inhabit the lower urinary tract. The composition of the urinary microflora correlates with several urological conditions, including urinary tract infections (UTIs).
- Lactobacilli are also found in human oral, intestinal and vaginal microenvironments and are often applied as probiotic for various health preservation due to their ability to inhibit growth of other bacteria.
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RESULTS

Collecting and characterizing a small repository of urinary commensal bacteria

- 64 isolates of urinary commensal microbes were collected from asymptomatic postmenopausal women using Enhanced Quantitative Urine Culture technique.
- There are 27 lactobacilli strains that belong to seven different species: L. gasseri, L. delbrueckii, L. rhamnosus, L. acidophilus, L. jensenii, L. iners, L. crispatus.
- There are also 14 strains of classic urinary pathogens such as E. coli, K. pneumoniae, K. oxytoca, and E. faecalis.
- Draft genomes of L. gasseri S1, S2, S3, K. pneumoniae S8, L. delbrueckii S9 were established. Lactobacilli genomes range from 1.7 to 1.8 Mb and found to be closely related to vaginally isolated strains. K. pneumoniae S8 strains contain several antibiotic resistance genes.

Inhibition tests with model uropathogens and resistant clinical isolates

- We tested first two urinary lactobacilli strains from two different species in well-diffusion inhibition assays against model uropathogenic strains of E. coli, K. pneumonia, and E. faecalis.
- Growth of the model uropathogenic E. coli (UPEC) strains CFT073, D57, UT189 and K. pneumoniae TOP52 is inhibited by urinary lactobacilli L. gasseri S1 and L. delbrueckii S9 while E. faecalis strains (OG1RF, JH2-2, V863 and MMH584) appear to be more resistant to these urinary lactobacilli.
- Well-diffusion tests showed that multidrug resistant clinical isolates of E. coli are being inhibited by the two tested lactobacilli strains as well.

Screening a broader range of urinary lactobacilli

- Another 18 strains of urinary lactobacilli were tested for their ability to inhibit the growth of UPEC CFT073 strain and most were shown to inhibit the uropathogen to varying degree.
- Preliminary quantification of the inhibition does not show strong indication of any particular lactobacilli species and thus careful genetic and phenotypic analysis of individual strains is warranted.

METHODS

- Growth optimization of urinary commensals in aerobic and anaerobic conditions.
- Whole genome sequencing using Illumina platform followed by de novo assembly by Unicyclic program.
- Well-diffusion inhibition assay to test interaction of lactobacilli with other bacteria.

RESULTS

Table 1. Collection of urinary commensals

- | Species          | No. of Strains |
- |------------------|---------------|
- | L. gasseri       | 6             |
- | L. delbrueckii   | 5             |
- | L. rhamnosus     | 1             |
- | L. acidophilus    | 1             |
- | L. jensenii      | 2             |
- | L. iners         | 1             |
- | L. crispatus     | 1             |

FUTURE DIRECTIONS

Establishing the mechanism of growth inhibition

- Genome analysis of S1 and S9 identifies several genes that encode protein toxins – bacteriocins.
- More functional and genetic studies are needed to show whether bacteriocin production is responsible for the observed inhibition of uropathogens.

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SUMMARY

- We collected a repository of commensal urinary bacteria containing 27 strains of urinary lactobacilli, and established draft genome sequences of several first isolates.
- Other urinary lactobacilli are capable of inhibiting uropathogenic E. coli growth to different extents.

REFERENCES