



CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG RESEARCH HOURS

EXECUTIVE SUMMARY 9/27/2024 U-RIG RESEARCH HOUR

Goal: Facilitate knowledge exchange and spur collaborations in the urobiome and adjacent fields

U-RIG RESEARCH HOUR

FEAT: NICOLE DE NISCO, PHD

**FATTY ACID AUXOTROPHY AS A DEFINING METABOLIC
ADAPTATION OF UROGENITAL LACTOBACILLI**

9/27/24 [3-4PM EDT] (2PM CT | 12PM PT)



Overview of Lactobacillus Species and Their Importance

- Reviewed metabolic requirements of Lactobacillus species in the urinary microbiome.
- Lactobacillus predominance is linked to urogenital health, supported by studies and estrogen hormone therapy.
- The complexity of Lactobacillus was discussed, with a mention of a 2020 taxonomic note separating the genus into new genera.

Taxonomic Changes and Their Implications

- Dr. De Nisco detailed the new genera within the Lactobacillus family, such as LactoCaseibacillus and Limosilactobacillus and explained the importance of these taxonomic changes in understanding phenotypic differences between different genera and species.
- Urogenital lactobacilli were discussed, with a focus on Lactobacillus crispatus, Lactobacillus jensenii, and Lactobacillus gasseri.
- Dr. De Nisco noted the development of family or genus-level probes to identify these species within samples.

Growth Media and Metabolic Requirements of Lactobacillus

- Dr. De Nisco discussed the use of MRS media for growing Lactobacilli, noting its undefined nature.
- Her lab started removing components to understand the metabolic requirements for growth.
- Tween 80 (polysorbate 80) was found to be essential for the growth of urogenital Lactobacillus species.
- The structure of Tween 80 and its potential role in fulfilling the oxytroph for fatty acids is explored.

Development of Chemically Defined Media

- **Her lab developed a chemically defined media to test the hypothesis that Tween 80 provides oleic acid.**
- Oleic acid was found to improve growth in chemically defined media, supporting the hypothesis.
- Growth experiments with different Lactobacillus species confirmed the requirement for oleic acid.
- The lab also tested the growth of LactoCaseibacillus and Lactiplantibacillus, which do not require oleic acid.

Fatty Acid Biosynthesis and Gene Synteny Analysis

- Dr. De Nisco's lab used gene synteny analysis to determine if the fab operon for fatty acid biosynthesis is conserved in urogenital Lactobacillus species.
- Analysis showed that non-urogenital Lactobacilli have the fab operon synteny; urogenital Lactobacilli lack it.
- **This led to the hypothesis that urogenital Lactobacillus species cannot perform de novo fatty acid biosynthesis.**
- Metabolic tracing analysis was conducted to further test this hypothesis.

Metabolic Tracing and Fatty Acid Incorporation

- Dr. De Nisco's lab used C-13 labeled glucose to trace the incorporation of fatty acids into phospholipids.
- *Lactobacillus rhamnosus* and *Lactobacillus crispatus* were used as representatives of Lactocaseibacilli and urogenital Lactobacilli, respectively.
- **Lactobacillus crispatus could not incorporate C-13 into its fatty acids, supporting the hypothesis.**
- The lab also tested the incorporation of oleic acid and its trans isomers, confirming the ability to use both forms.

Utilization of Host Lipids and Future Directions

- The lab isolated lipids from bladder epithelial cells and fed them to *Lactobacillus crispatus* and gasseri.
- **Results showed that these lipids stimulated growth, indicating potential use of host lipids as fatty acid sources.**
- Dr. De Nisco discussed the importance of understanding the nutritional requirements of urogenital Lactobacilli for probiotic approaches.
- The lab plans to further optimize the extraction and identification of host lipids to understand their incorporation.

Recent publications by Dr. De Nisco:

1. Dalvi, H., & De Nisco, N. J. (2024). The evolving world of the urinary microbiome. *Current opinion in urology*, 10.1097/MOU.0000000000001222. Advance online publication. <https://doi-org.ezproxy.library.wisc.edu/10.1097/MOU.0000000000001222>
2. Gadhvi, J. G., Kenney, P. R. M., Lutz, K. C., Khan, F., Li, Q., Zimmern, P. E., & De Nisco, N. J. (2024). Bladder-resident bacteria associated with increased risk of recurrence after electrofulguration in women with antibiotic-recalcitrant urinary tract infection. *medRxiv : the preprint server for health sciences*, 2024.07.03.24309902. <https://doi-org.ezproxy.library.wisc.edu/10.1101/2024.07.03.24309902>
3. Johnson, A. O., Shipman, B. M., Hunt, B. C., Learman, B. S., Brauer, A. L., Zhou, S. P., Hageman Blair, R., De Nisco, N. J., & Armbruster, C. E. (2024). Function and contribution of two putative *Enterococcus faecalis* glycosaminoglycan degrading enzymes to bacteremia and catheter-associated urinary tract infection. *Infection and immunity*, 92(7), e0019924. <https://doi-org.ezproxy.library.wisc.edu/10.1128/iai.00199-24>
4. Johnson, A. O., Shipman, B. M., Hunt, B. C., Learman, B. S., Brauer, A. L., Zhou, S. P., Blair, R. H., De Nisco, N. J., & Armbruster, C. E. (2024). Function and contribution of two putative *Enterococcus faecalis* glycosaminoglycan degrading enzymes to bacteremia and catheter-associated urinary tract infection. *bioRxiv : the preprint server for biology*, 2024.05.08.593205. <https://doi-org.ezproxy.library.wisc.edu/10.1101/2024.05.08.593205>
5. Zimmern, P. E., De Nisco, N. J., & Prokesch, B. C. (2024). Electrofulguration for Women With Uncomplicated Recurrent Urinary Tract Infections and Chronic Cystitis: Time for Trials!. *The Journal of urology*, 212(1), 220–222. <https://doi-org.ezproxy.library.wisc.edu/10.1097/JU.0000000000003943>
6. Ebrahimzadeh, T., Basu, U., Lutz, K. C., Gadhvi, J., Komarovskiy, J. V., Li, Q., Zimmern, P. E., & De Nisco, N. J. (2024). Inflammatory markers for improved recurrent UTI diagnosis in postmenopausal women. *Life science alliance*, 7(4), e202302323. <https://doi-org.ezproxy.library.wisc.edu/10.26508/lsa.202302323>
7. Sawant, N. V., Chang, S. S., Pandit, K. A., Khekare, P., Warner, W. R., Zimmern, P. E., & De Nisco, N. J. (2024). Vesix cetylpyridinium chloride is rapidly bactericidal and reduces uropathogenic *Escherichia coli* bladder epithelial cell invasion *in vitro*. *Microbiology spectrum*, 12(3), e0271223. <https://doi-org.ezproxy.library.wisc.edu/10.1128/spectrum.02712-23>
8. Nguyen, V. H., Sharon, B. M., Shipman, B. M., Zimmern, P. E., & De Nisco, N. J. (2024). Complete genomes of *Limosilactobacillus portuensis* and *Limosilactobacillus vaginalis* isolated from the urine of postmenopausal women. *Microbiology resource announcements*, 13(1), e0088323. <https://doi-org.ezproxy.library.wisc.edu/10.1128/MRA.00883-23>
9. Sharon, B. M., Arute, A. P., Nguyen, A., Tiwari, S., Reddy Bonthushu, S. S., Hulyalkar, N. V., Neugent, M. L., Palacios Araya, D., Dillon, N. A., Zimmern, P. E., Palmer, K. L., & De Nisco, N. J. (2023). Genetic and functional enrichments associated with *Enterococcus faecalis* isolated from the urinary tract. *mBio*, 14(6), e0251523. <https://doi-org.ezproxy.library.wisc.edu/10.1128/mbio.02515-23>
10. Zimmern, P., & DeNisco, N. (2023). Letter to the Editor: Long-term efficacy of complete trigonal electrofulguration for women with recurrent urinary tract infections by Leopoldo Ribeiro-Filho et al. *Neurourology and urodynamics*, 42(8), 1861–1862. <https://doi-org.ezproxy.library.wisc.edu/10.1002/nau.25268>
11. Sharon, B. M., Hulyalkar, N. V., Zimmern, P. E., Palmer, K. L., & De Nisco, N. J. (2023). Inter-species diversity and functional genomic analyses of closed genome assemblies of clinically isolated, megaplasmid-containing *Enterococcus raffinosus* Er676 and ATCC49464. *Access microbiology*, 5(6), acmi000508.v3. <https://doi-org.ezproxy.library.wisc.edu/10.1099/acmi.0.000508.v3>
12. Hagge, L. M., Shahrivarkevishahi, A., Al-Kharji, N. M., Chen, Z., Brohlin, O. R., Trashi, I., Tumas, A., C Herbert, F., Adlooru, A. V., Lee, H., Firouzi, H. R., Cornelius, S. A., De Nisco, N. J., & Gassensmith, J. J. (2023). Intracellular delivery of virus-like particles using a sheddable linker. *Journal of materials chemistry. B*, 11(30), 7126–7133. <https://doi-org.ezproxy.library.wisc.edu/10.1039/d3tb00696d>
13. Sharon, B. M., Arute, A. P., Nguyen, A., Tiwari, S., Bonthushu, S. S. R., Hulyalkar, N. V., Neugent, M. L., Araya, D. P., Dillon, N. A., Zimmern, P. E., Palmer, K. L., & De Nisco, N. J. (2023). Functional and genetic adaptations contributing to *Enterococcus faecalis* persistence in the female urinary tract. *bioRxiv : the preprint server for biology*, 2023.05.18.541374. <https://doi-org.ezproxy.library.wisc.edu/10.1101/2023.05.18.541374>
14. Trashi, I., Durbacz, M. Z., Trashi, O., Wijesundara, Y. H., Ehrman, R. N., Chiev, A. C., Darwin, C. B., Herbert, F. C., Gadhvi, J., De Nisco, N. J., Nielsen, S. O., & Gassensmith, J. J. (2023). Self-assembly of a fluorescent virus-like particle for imaging in tissues with high autofluorescence. *Journal of materials chemistry. B*, 11(20), 4445–4452. <https://doi-org.ezproxy.library.wisc.edu/10.1039/d3tb00469d>
15. Colbert, J. F., Kirsch, J. M., Erzen, C. L., Langouët-Astrié, C. J., Thompson, G. E., McMurtry, S. A., Kofonow, J. M., Robertson, C. E., Kovacs, E. J., Sullivan, R. C., Hippensteel, J. A., Sawant, N. V., De Nisco, N. J., McCollister, B. D., Schwartz, R. S., Horswill, A. R., Frank, D. N., Duerkop, B. A., & Schmidt, E. P. (2023). Aging-Associated Augmentation of Gut Microbiome Virulence Capability Drives Sepsis Severity. *mBio*, 14(3), e0005223. <https://doi-org.ezproxy.library.wisc.edu/10.1128/mbio.00052-23>
16. Neugent, M. L., Hulyalkar, N. V., Kumar, A., Xing, C., Zimmern, P. E., Shulaev, V., & De Nisco, N. J. (2023). Urinary Glycosaminoglycans Are Associated with Recurrent UTI and Urobiome Ecology in Postmenopausal Women. *ACS infectious diseases*, 9(4), 1022–1032. <https://doi-org.ezproxy.library.wisc.edu/10.1021/acsinfectdis.3c00027>
17. Neugent, M. L., Hulyalkar, N. V., Kumar, A., Xing, C., Zimmern, P. E., Shulaev, V., & De Nisco, N. J. (2023). Urinary Glycosaminoglycans are Associated with Recurrent UTI and Urobiome Ecology in Postmenopausal Women. *bioRxiv : the preprint server for biology*, 2023.01.11.523678. <https://doi-org.ezproxy.library.wisc.edu/10.1101/2023.01.11.523678>
18. Colbert, J. F., Kirsch, J. M., Erzen, C. L., Langouët-Astrié, C. J., Thompson, G. E., McMurtry, S. A., Kofonow, J. M., Robertson, C. E., Kovacs, E. J., Sullivan, R. C., Hippensteel, J. A., Sawant, N. V., De Nisco, N. J., McCollister, B. D., Schwartz, R. S., Horswill, A. R., Frank, D. N., Duerkop, B. A., & Schmidt, E. P. (2023). Aging-associated augmentation of gut microbiome virulence capability drives sepsis severity. *bioRxiv : the preprint server for biology*, 2023.01.10.523523. <https://doi-org.ezproxy.library.wisc.edu/10.1101/2023.01.10.523523>
19. Zimmern, P. E., Sawant, N. V., Chang, S. S., Warner, R. W., & De Nisco, N. J. (2023). Intravesical Vesix as a Last Resort Therapy in Women With Antibiotic-Refractory Recurrent Urinary Tract Infections Contemplating Bladder Removal: A Preliminary Report. *The Annals of pharmacotherapy*, 57(3), 350–351. <https://doi-org.ezproxy.library.wisc.edu/10.1177/1060028022112111>