

## Researchers develop first catalogue of genes that comprise community of microbes in vaginal microbiome

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University of Maryland School of Medicine's (UMSOM) Institute for Genome Sciences (IGS) researchers have created the first catalog of genes that comprise the community of microbes, which inhabit the human vagina. The catalog, called human vaginal non-redundant gene catalog (VIRGO), was recently released as a public resource that can be used by researchers to facilitate a more in-depth understanding of the role of vaginal microorganisms in women's health and to potentially develop future treatments for certain gynecologic conditions.

An IGS study describing the development of VIRGO and demonstrating its utility in research was published today in *Nature Communications*.

"The value of VIRGO is that it functions as both a central repository and a highly scalable tool for fast, accurate characterization of vaginal microbiomes," said study lead author Bing Ma, Ph.D., Research Associate in the Department of Microbiology and Immunology at the Institute for Genome Sciences (IGS) at UMSOM. "VIRGO is particularly useful for users with limited computational skills, who want to analyze a large volume of sequencing data and with access to limited computing infrastructure."

The community of microbes (microbiota) that inhabit the human vagina play critical roles in health and diseases, but current knowledge of the genetic and functional diversity of microbiomes is still limited. Scientists know that optimal vaginal microbiomes are most often dominated by one or more species of Lactobacillus, including Lactobacillus crispatus, L. gasseri and L. jensenii. Research suggests that these beneficial



bacteria produce large amounts of lactic acid leading to an acidic environment that protects against harmful infections. Researchers are aiming to learn more, however, about how these bacteria contribute to a woman's health and disease.

VIRGO could facilitate that goal with close to 1 million genes in the catalogue, each annotated with the name of the bacterium that carries it and with its function, affording a composition and functional characterization of vaginal microbiomes. The researchers estimate that VIRGO contains over 95 percent of all the genes found in vaginal microbiomes. VIRGO is thus comprehensive and the study team showed it is applicable to populations from North America, Africa and Asia. Ultimately, VIRGO and its associated analytical framework will facilitate and standardize the analysis and interpretation of large metagenomic and meta-transcriptomics datasets. VIRGO and its associated files are freely available for free at this website.

The resource was constructed using a combination of metagenomes sequenced at IGS and urogenital bacterial isolate genomes in part downloaded from public repositories. Sequencing was performed through Maryland Genomics, which is part of the IGS and composed of the Genomic Resource Center (GRC), Informatic Resource Center (IRC) and the Microbiome Service Laboratory (MSL). Innovative analytical strategies were applied to develop VIRGO, leveraging the computational infrastructure and expertise of the IGS Microbiome group.

"VIRGO will facilitate the analysis of data now common to <u>microbiome</u> studies and provide comprehensive insight into microbial membership, function, and ecological perspective of the vaginal microbiome," said Michael France, Ph.D., Postdoctoral Fellow at the Institute for Genome Sciences (IGS) at UMSOM, and co-author on the study.



The team demonstrated the power of VIRGO in analyzing over 1,500 vaginal metagenomes. In doing so, the research team discovered that vaginal bacteria are more genetically diverse than originally thought, meaning that women each carry their own personalized version of these bacteria. More importantly, they found that optimal vaginal microbiota dominated by Lactobacillus species are actually made of several strains of the same species. Each strain brings a unique function to the community, and the combination of these strains is what define the strength of the protective properties of the optimal vaginal microbiota.

"This finding is a paradigm changing discovery, as it moves the field away from the idea that a single strain of Lactobacillus is responsible for an optimal microbiome," said Jacques Ravel, Ph.D., Professor of Microbiology and Immunology, Associate Director and Senior Scientist at the Institute for Genome Sciences (IGS) at UMSOM.

While the IGS researchers will continue to update and expand VIRGO, they will further their understanding of the role played by the vaginal microbiome in conditions such as bacterial vaginosis, sexually transmitted infections and adverse obstetrics outcomes including preterm birth. Their research is funded by the National Institute of Health (NIH), National Institute for Nursing Research (NINR), National Institute for Allergies and Infectious Diseases (NIAID), and the Bill and Melinda Gates Foundation.

"Important efforts are underway by UMSOM faculty to translate our growing understanding of human-associated microbial communities into clinical biomarkers and treatments," said UMSOM Dean E. Albert Reece, MD, Ph.D., MBA, who is also Executive Vice President for Medical Affairs, University of Maryland and the John Z. and Akiko K. Bowers Distinguished Professor. "This groundbreaking research provides powerful, publicly available tools to researchers who are addressing key health issues for women."



**More information:** Bing Ma et al, A comprehensive non-redundant gene catalog reveals extensive within-community intraspecies diversity in the human vagina, *Nature Communications* (2020). DOI: 10.1038/s41467-020-14677-3

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