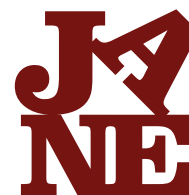


NextGen Jane

www.nextgenjane.com



Deep diving into menstrual cycle data to enhance women's health

How NextGen Jane's menstrual data platform is addressing some of the most prevalent unmet healthcare needs.

NextGen Jane (NGJ) is tackling a foundational challenge in women's health. Working with partners, the company is addressing the dearth of molecular data from reproductive tissues to accelerate diagnosis, develop companion diagnostics, and show how drug molecules affect female-born individuals.

Molecular data are critical to understanding disease etiology, diagnosis, and treatment. Yet, limited access to routine tissue sampling, the use of male animal models in basic research, and the suppression of the menstrual cycle in clinical trials has created a shortfall of evidence. The result is a lack of insights into the rapidly changing molecular signatures of the menstrual cycle and the effect of drugs on female biology.

Those factors, coupled to underinvestment in diagnostics for uterine diseases, are negatively affecting half the population. Interventions have specific effects on female biology, as was shown by the impact of COVID-19 vaccines on menstrual-cycle length, but researchers lack the tools to assess such differences in clinical trials. Equally, the lack of non-invasive tests means women can wait 10 years for an endometriosis diagnosis, often while suffering disabling pain, and hinders drug development.

"Physicians have blunt instruments for diagnosing and treating reproductive disorders. In endometriosis, you need laparoscopic surgery to diagnose the disease," Stephen Gire, CSO at NGJ, said. "With molecular tools, physicians could potentially diagnose and treat earlier; drug developers could find new targets, leading to more-refined therapeutics, and run more-efficient clinical trials."

Drug companies have needed a non-invasive diagnostic for at least 20 years

Stephen Palmer, Associate Professor and Director, lead discovery and development at Baylor College of Medicine

Enabling molecular characterization

NGJ has created a tampon-based solution to the problem. The shedding of the uterine lining provides an opportunity to analyze cellular and molecular signals. NGJ is seizing the opportunity with a platform that enables end-to-end analysis.

The platform features a scalable, at-home sample-collection system that supports non-invasive, routine, longitudinal data acquisition, for example by sending kits to patients before and after an intervention. NGJ

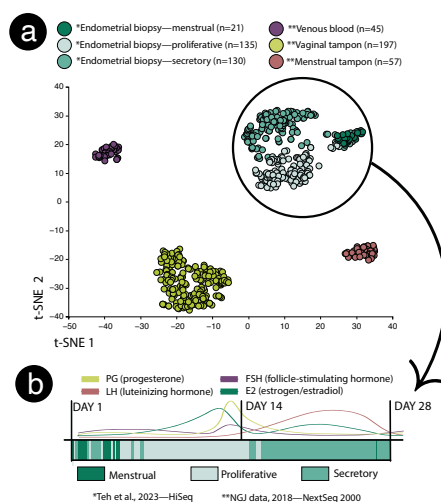


Fig. 1 | Comparative analysis of genetic data from shed and biopsy tissue samples. **a**, t-distributed stochastic neighbor embedding (t-SNE) plot of 52 genes that comprise uterine and vaginal gene modules developed by NextGen Jane (NGJ) using vaginal and menstrual samples collected throughout a 28-day cycle from 32 individuals. Plotted are data collected from NGJ for venous blood, vaginal fluid, and menstrual fluid (NGJ data) and endometrial biopsies¹. Reduced heterogeneity in samples collected during the menstrual phase of the cycle (biopsies and menstrual fluid). **b**, Hierarchical heat map (Pearson) of the endometrial biopsies for the same 52 genes in the NGJ modules. This demonstrates the wide variation (micropulsatility) in gene expression throughout the menstrual cycle due to rapid hormonal changes that can hinder reproducibility in tissue sampling.

has analyzed over 2,000 tampons from 335 patients to understand the menstrual kinetics, enabling it to build bioinformatic approaches to account for natural variability and better stratify the data.

Through this work, NGJ has made a patient-annotation system with clinical and self-reported features, and a molecular-phenotyping and classification tool to resolve the heterogeneity of menstrual effluence. The final piece is a novel taxonomic and hierarchical data structure to organize the complex, multi-day, multi-cycle menstrual data. The frequency and timing of sampling is critical to the platform (Fig. 1).

"Depending on the day you sample, you're going to see something very different because the patient is under this completely different hormonal cascade," NGJ's CEO Ridhi Tariyal said. "With a saliva

or venous blood-based test, you can't really ensure someone's giving you a sample on the same day of their cycle."

Endometrial biopsies have the same issue. The tampon-based solution inherently and passively avoids this problem. By analyzing menstrual effluence, NGJ ensures samples are taken at the same time in the cycle, thereby addressing the variability that affects tests of saliva, venous blood, and tissue.

Deploying the platform

NGJ chose endometriosis as its first indication. The lack of a non-invasive test for the condition is delaying diagnosis and drug development, as Stephen Palmer, associate professor and director, lead discovery and development at Baylor College of Medicine, explained.

"You have to do a laparoscopy before any treatment to see what kind of disease burden there is. Then you treat for six months or so and perform another laparoscopy to see if the treatment was successful. Surgeons say, 'Why should I open up this patient and not take out the lesions?'," Palmer said. "Drug companies have needed a non-invasive diagnostic for at least 20 years."

NGJ could meet the need. By analyzing messenger RNA (mRNA) and microRNA (miRNA) from people with and without endometriosis, the company has created a classifier to identify those who have the condition. Early data suggest the non-invasive test can differentiate between subtypes of endometriosis.

As NGJ has worked to understand endometriosis, it has generated insights into autoimmune disease and aging. The platform and foundational knowledge base of molecular gynecologic health have positioned NGJ to help partners develop women's health drugs, show how molecules affect female-born bodies, create companion diagnostics, and increase the number of people who get a clear, early diagnosis.

The foundations to support those breakthroughs are now in place. The next step is for organizations that want to include uterine-response data in women's health projects to partner with NGJ and start to tackle perhaps the most widespread, persistent unmet need in healthcare.

1. Teh, W. T. et al. *Nat. Commun.* **14**, 6222 (2023). <https://doi.org/10.1038/s41467-023-41979-z>

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