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Multiancestry Biobank GWAS Uncovers 27 New Endometriosis Risk Loci and 314 Candidate Genes

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Endometriosis -- a chronic, estrogen -dependent inflammatory condition in which tissue resembling the uterine lining grows outside the uterus -- affects roughly 10% of reproductive-age women worldwide, yet its molecular roots and diagnostic delays remain formidable clinical challenges. In a landmark study published in Nature Genetics on November 20, 2026, Lindsay A. Guare, Shefali Setia-Verma, and an international consortium within the Global Biobank Meta-analysis Initiative (GBMI) reported the most ancestrally diverse genetic investigation of endometriosis to date. Analyzing genomic and electronic health record (EHR) data from more than one million female participants across 14 biobanks , the team identified 58 genomic risk regions associated with the disease -- including 27 previously unreported loci -- and prioritized 314 candidate genes through integrative multi-omics.

Crucially, 32% of participants in the meta-analysis were of non-European ancestry, directly addressing a longstanding bias in gynecological genomics . Previous genome -wide association studies (GWAS), such as the major 2023 synthesis by Rahmioglu et al., relied overwhelmingly on European and East Asian cohorts, leaving African and Admixed-American populations severely underrepresented.

Expanding Discovery Through Multiancestry Biobank Inclusion

To overcome historical under-ascertainment in electronic health records -- where endometriosis is frequently under-coded or misclassified -- the investigators paired diagnostic billing codes with targeted surgical and imaging procedure codes. Across the resulting multiancestry dataset, the team uncovered genome-wide significant signals unique to African and Admixed-American populations , including distinct risk loci at chromosomal regions 1q42.13, 2p13.3, and 20q13.2 that are rare or absent in European-ancestry cohorts.

Because linkage disequilibrium blocks differ across global populations, multiancestry fine-mapping also sharpens the spatial resolution of shared risk regions, narrowing broad statistical peaks down to smaller sets of likely causal variants. This cross-ancestry approach ensures that future polygenic risk scores and diagnostic biomarkers will generalize more equitably across diverse clinical populations rather than amplifying Eurocentric bias.

| Study Dimension | | 2026 Multiancestry GBMI Analysis (Guare et al.) |

| Cohort Scale & Biobanks | | >1,000,000 female participants across 14 global biobanks |

| Ancestral Diversity | | ~32% non-European ancestry (including African & Admixed-American cohorts) |

| Genomic Risk Regions | | 58 total loci identified, including 27 previously unreported regions |

| Ancestry-Specific Signals | | Distinct loci at 1q42.13, 2p13.3, and 20q13.2 in African & Admixed-American groups |

| Multi-Omic Prioritization | | 314 candidate genes linked via transcriptomic, proteomic, methylomic & splice-omic layers |

| Systemic Pleiotropy | | Genetic correlations mapped across >130 pain, metabolic, vascular & psychiatric traits |

Integrating Multi-Omics to Pinpoint 314 Candidate Genes

Identifying a statistically significant single-nucleotide polymorphism (SNP) in non-coding DNA does not by itself reveal which gene is perturbed or in which tissue it acts. To bridge the gap from statistical association to biological mechanism, Guare and colleagues integrated GWAS summary statistics with four orthogonal molecular data layers: gene expression (transcriptomics), protein abundance (proteomics), DNA methylation (methylomics), and alternative RNA splicing (splice-omics), contextualized across relevant reproductive and immune cell types.

This multi-omic convergence prioritized 314 candidate genes clustering within four interconnected biological pathways: immune regulation and chronic inflammation , steroid hormone signaling , cellular differentiation and proliferation , and extracellular matrix / tissue remodeling . Together, these pathways help explain how ectopic endometrial-like lesions evade immune clearance, establish vascularized implants in the peritoneal cavity, and remodel surrounding pelvic tissues.

Systemic Pleiotropy Beyond the Reproductive Tract

Clinicians have long observed that patients with endometriosis experience disproportionately high rates of non-pelvic comorbidities. By testing genetic correlations across more than 130 health traits, the 2026 study demonstrates that many of these clinical overlaps reflect shared genetic architecture rather than purely secondary consequences of chronic pelvic pain.

Significant genetic correlations emerged between endometriosis and central pain syndromes (including migraine), cardiometabolic risk factors, and mental health or sleep traits such as anxiety and insomnia. Framing endometriosis as a multi-system inflammatory and neuroendocrine disorder -- rather than a strictly localized gynecological condition -- aligns with emerging clinical care models that pair hormonal or surgical management with systemic pain and metabolic screening.

Toward Non-Invasive Diagnostics and Drug Repurposing

Today, definitive diagnosis of endometriosis often requires invasive laparoscopy, contributing to average diagnostic delays of seven to ten years. Mapping 314 candidate genes and circulating proteomic signatures lays quantitative groundwork for non-invasive blood or biomarker panels that could stratify high-risk patients far earlier in their clinical course.

Equally promising is computational drug repurposing : because many of the newly implicated immune, vascular, and tissue-remodeling targets already have approved or investigational compounds in rheumatology, oncology , and metabolic medicine, cross-referencing multi-omic gene lists against pharmacological databases offers an

accelerated path toward non-hormonal therapies for patients who cannot tolerate standard estrogen-suppressive regimens.

References & Primary Sources

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