

Original Research

Received 04 June 2026

Revised 16 July 2026

Accepted 31 July 2026

Natural Resources for Human
Health 2026, Vol. 6 (13s): 1118–1126

KEYWORDS:

Severe Endometriosis; Associated
Infertility; heterogeneity.

Severe Endometriosis Associated Infertility: An Integrated Transcriptomic and Bioinformatics Analysis of Molecular Biomarkers and Dysregulated Pathways

Sher Muhammad ¹, Ziauddin ², Sobia Naseem Siddiqui ³,
Ibtesam Mazahir ^{4*}, Amsa Fatima ⁵, Dr Kanwal Huma ⁶,
Sadaf Sultana ⁷

¹ Advanced Research Centre, European University of Lefke, Northern Cyprus, TR-10 Mersin, Turkey

² CASVAB, university of Balochistan Quetta

³ Department of Gynecology & Obstetrics, Shaukat Omar Memorial Hospital (Fauji Foundation), Karachi, Pakistan

^{4*} 1st Affiliation: Faculty of Communication Arts, Chulalongkorn University, Bangkok, Thailand

2nd Affiliation: Mohammad Ali Jinnah University, Karachi

⁵ Affiliation with Institution: University Institute of Diet and Nutritional Sciences, Faculty of Allied health sciences The University of Lahore

⁶ Assistant professor Biochemistry, at Rawalpindi medical university

⁷ M. Phil, University Institute of Biochemistry and Biotechnology, PMAS Arid Agricultural University Rawalpindi

Corresponding Author: Ibtesam Mazahir ^{4*}

sher1325@hotmail.com ¹, zia-quetta@hotmail.com ², sddqsobia@gmail.com

³ibtesam.mazahir@gmail.com ^{4*}, amsa.fatima92@gmail.com ⁵,

kanwal.huma@rmur.edu.pk ⁶, sadafsultana902@gmail.com ⁷

ABSTRACT: Background: Infertility is a highly significant problem in women with severe endometriosis and the molecular characteristics of infertile versus fertile women with advanced endometriosis have not been fully characterized.

Methods: We reanalyzed the whole normalized Series Matrix (36 secretory-phase endometrial samples; four balanced groups, n=9 per group) from GSE120103. The quality control consisted of sample-distribution assessment, the principal component analysis (PCA) and sample-correlation analysis. The main difference between the two groups was between infertile and fertile women with grade IV endometriosis of the ovary. Probe-level Welch tests with Benjamini-Hochberg false discovery rate (FDR) control were supplemented by a four group specificity analysis that compared infertility effects between disease-free women and stage IV disease. Published gene level limma, weighted gene co-expression network analysis, protein-interaction and enrichment results were used only as supplied external gene level benchmarks as the supplied "Series Matrix" does not include the GPL6480 probe to gene annotation table.

Results: 37,823 Agilent probe rows were left after discarding 91 control-style rows. Neuron 15,988 probes met FDR < 0.05 and a mean-expression difference of ≥ 1 (13,361 probes were higher; 2,627 probes were lower). Disease-free infertility had 8,156 probes with the same sensitivity requirement, while 3,064 of them had the same association with

stage IV, with 12,924 probes for stage IV showing a higher association with disease-free infertility. The first and second principal components (PCs) of the 5,000 most variable probes accounted for 65.7% and 11.9% of the variance, respectively, and exhibited significant heterogeneity with several stage IV infertile samples having distributions that were significantly shifted. Gene-level analyses of the same cohort published previously identified 1,990 genes as differentially expressed and suggested that the pathways of G protein-coupled receptor (GPCR), cyclic-nucleotide, cell-cycle/DNA-replication and metabolism were associated.

Conclusions: GSE120103 has a high and technically mixed signal of infertility. The 4-group analysis provides evidence of probe-level disease-context specificity; however, there is caution needed for interpretation due to wide differences in differential signal and sample heterogeneity. Before the translation, gene-level annotation, independent confirmation in severe endometriosis and experimental verification are required. Journal of Clinical Endocrinology & Metabolism, Epigenetics & Therapeutics, and Endocrinology, Diabetes & Metabolism are the primary journals where research on endometriosis is published. The main journals associated with endometriosis research are Journal of Clinical Endocrinology & Metabolism, Epigenetics & Therapeutics, Endocrinology, Diabetes & Metabolism.

1. INTRODUCTION

Endometriosis is a chronic gynecological disorder characterized by endometrial-like tissue outside the uterine cavity and is frequently associated with infertility. Its reproductive effects are multifactorial and may involve pelvic anatomy, inflammation, ovarian function, endocrine signaling, gamete or embryo transport, and impaired eutopic endometrial receptivity [1,2]. The eutopic endometrium is particularly relevant because implantation depends on coordinated hormonal responsiveness, immune tolerance, stromal remodeling, vascular adaptation and embryo-maternal signaling [12,13]. Transcriptomic profiling can therefore reveal coordinated disturbances that are difficult to infer from single-gene studies. GSE120103 provides an unusually useful four-group design: disease-free fertile women, fertile women with stage IV ovarian endometriosis, disease-free infertile women and infertile women with stage IV ovarian endometriosis, with nine samples in each group [3,4]. This permits infertility-associated expression changes in severe disease to be compared directly with infertility-related changes occurring without endometriosis. Previous analyses of this cohort have reported co-expression modules, G protein-coupled receptor (GPCR)-related signaling, cyclic-nucleotide pathways, cell-cycle processes and candidate hub transcripts [5,6]. More recent endometrial transcriptomic and single-cell studies emphasize that endometriosis is molecularly heterogeneous across epithelial, stromal and immune compartments and that receptivity-associated alterations are often modest, context dependent and sensitive to tissue composition [16-20]. The present study therefore emphasizes effect stability, four-group specificity and technical heterogeneity rather than treating statistical significance alone as evidence of a clinically useful biomarker.

2. MATERIALS AND METHODS

2.1 Data source and study population

The complete GSE120103 Series Matrix was analyzed. It contains 37,914 rows across 36 secretory-phase endometrial samples profiled on GPL6480 (Agilent-014850 Whole Human Genome Microarray 4x44K G4112F). The four clinical groups contain nine samples each [3,4]. The group definitions and sample counts are summarized in Table 1.

Group	Endometriosis	Fertility status	n
1A	Absent	Fertile	9
2A	Stage IV ovarian endometriosis	Fertile	9
1B	Absent	Infertile	9
2B	Stage IV ovarian endometriosis	Infertile	9

Table 1. Clinical grouping of GSE120103.

2.2 Probe filtering and quality control

The official GPL6480 platform annotation provides a separate field, called CONTROL_TYPE, to distinguish control features from biological probes. That annotation field in the provided Series Matrix was not embedded. A total of 91 rows with identifiers that do not start with “A_” were omitted from the matrix-level sensitivity analysis as non-standard/control-associated rows, leaving 37,823 probe rows. This filter was based on an identifier and is only shown for the processed-matrix sensitivity analysis and should not be used as an alternative to annotation-based control filtering. Sample-level means, medians, standard deviations and interquartile ranges were analyzed. The distributions of expression levels are plotted at the sample level for all 36 profiles in Figure 1. The 5,000 probes that had the greatest across-sample variance were selected for PCA (Figure 2), while the 5,000 probes were used to calculate a Pearson sample-correlation matrix (Figure 3). The processed Series Matrix was not technically and biologically sufficient to distinguish the technical and biological sources of heterogeneity, which is why all samples were kept.

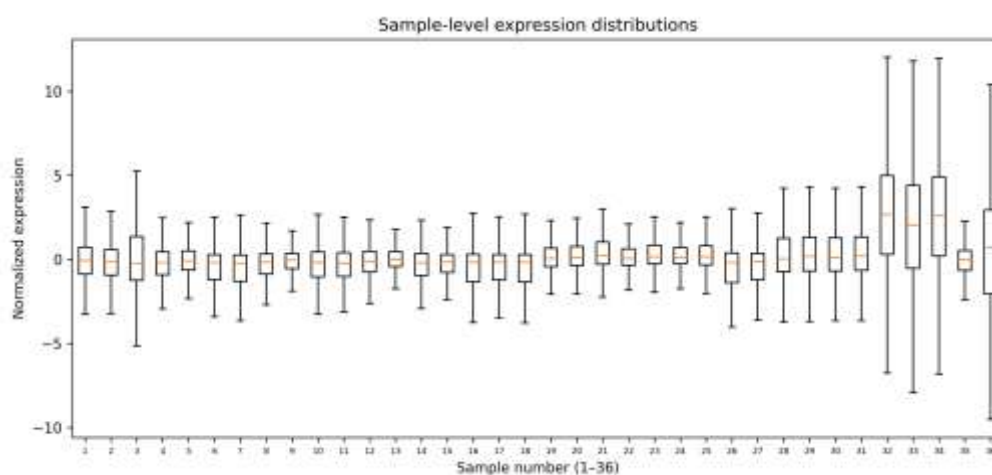


Figure 1. Sample-level distributions across the 36 normalized GSE120103 expression profiles. Samples 32–34 and 36 show visibly broader and/or shifted distributions and are treated as potential influential observations rather than automatically excluded.

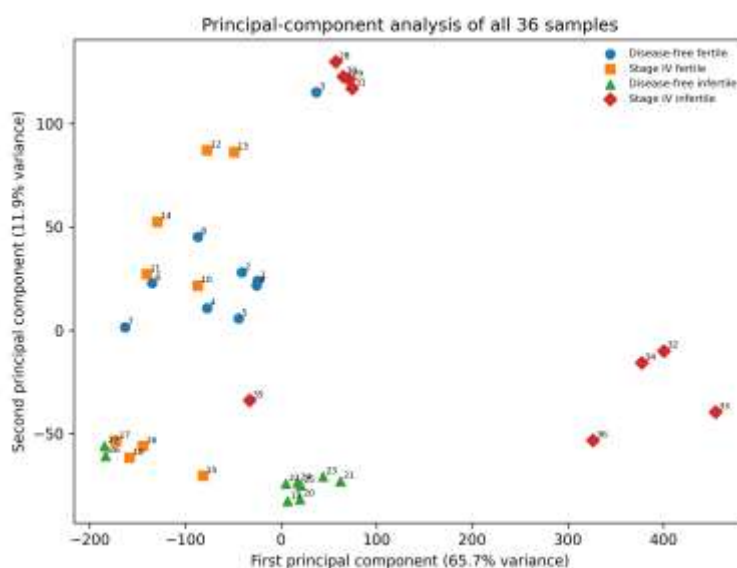


Figure 2. Principal-component analysis of all 36 samples using the 5,000 most variable retained probes. The plot demonstrates strong global structure and substantial within-group heterogeneity.

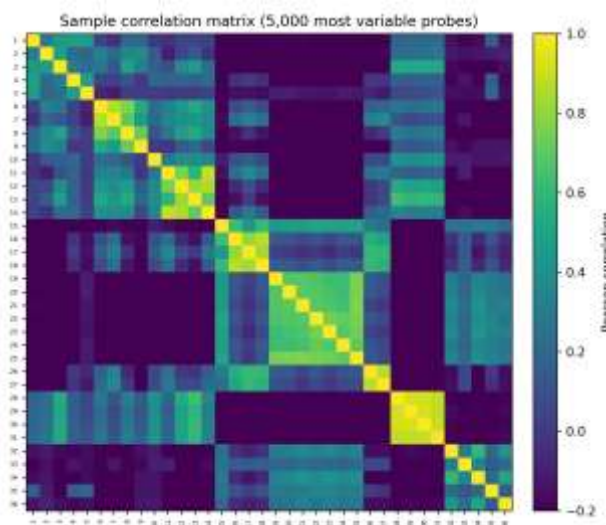


Figure 3. Sample-correlation matrix based on the 5,000 most variable retained probes. The matrix is used as a quality-control diagnostic rather than evidence of a biological subgroup.

2.3 Primary stage IV infertility contrast

They compared nine infertile women to nine fertile women who had stage IV ovarian endometriosis. A two-sample t-test was used for each probe and p values were adjusted using the Benjamini-Hochberg procedure [8]. A false discovery rate of less than 0.05 and an absolute difference between the two group means of at least 1 normalized expression unit was defined as a sensitivity signal. Since the provided values are in the form of a Series Matrix, and the platform annotation table is not included in that file, effect sizes are given as mean-expression differences and are not base-2 logarithmic fold changes.

2.4 Four-group disease-context specificity analysis

Disease-free infertile women and disease-free fertile women were treated in the same way. Stage IV signals were defined as those that also had the same false-discovery-rate and effect-size criteria in the disease-free infertility cohort. The two factor linear model including endometriosis and infertility status and their interaction was also fitted probe-wise to assess the context effect. These estimates of interaction were not considered to be valid biomarkers but were merely sensitivity evidence. The interaction analysis was not used as a definitive biomarker screen, but rather as a general determinant of the structure of the expression in each group; the results were interpreted in the light of the sample distributions, PCA and sample correlations.

2.5 Gene-level interpretation and enrichment

Probe-to-gene annotation fields are available in the GPL6480 platform record, such as GENE_SYMBOL and CONTROL_TYPE. This processed Series Matrix does not include the platform field, but rather includes probe identifiers and normalized expression values. The original analyses for this study are thus presented at the probe level. Those published gene-level analyses are only for biological comparison purposes and are clearly labelled "external" evidence; they are not presented as new results from this re-analysis.

2.6 Reproducibility

Original results were used to calculate all matrix level statistics presented in the supplied GSE120103 Series Matrix. It employed a deterministic filter, fixed group membership based on the metadata of the GEO, variance-ranked features to perform PCA and correlation analysis, welch testing, false-discovery-rate control using the Benjamini-Hochberg method and a two-factor linear model. The reported estimates were not affected by any random seed used for the analysis as it was not done through random resampling.

3. RESULTS

3.1 Dataset and quality-control findings

There were 37,914 rows and 36 samples in the matrix, with 91 control-style rows removed, leaving 37,823 rows. The expression distributions of several stage IV infertile samples, particularly 32–34 and 36 depicted in Figure 1, showed broader or shifted distributions. The first principal component captured 65.7% of the variance and the second principal component captured 11.9% (Figure 2) of the variance of 5,000 most variable probes by principal component analysis. The profile-sample correlation matrix shown in Figure 3 also indicates high structure between the profiles. The composite quality control results suggest that the overall differential signal requires consideration of significant sample-level variation.

3.2 Stage IV infertility-associated probe signal

Before applying an effect size threshold, 16,208 probes had a false discovery rate (FDR) < 0.05 in the stage IV comparison. After filter expression to get an absolute mean-expression difference of at least 1, this number was decreased to 15,988 probes, of which 13,361 were significantly more expressed in infertile women, while 2,627 were more expressed in fertile women. There were 13,452 probes remaining at an absolute difference of at least 2. The distribution of the effect size and adjusted significance value is shown in Figure 4. The width of this signal along with the different distributions and PCA structure observed in several samples suggests that biological difference might also exist in conjunction with normalization, batch, or influential-sample effects. This is therefore an interpretation of the sensitivity at the probe level, not a discovery set at the gene level.

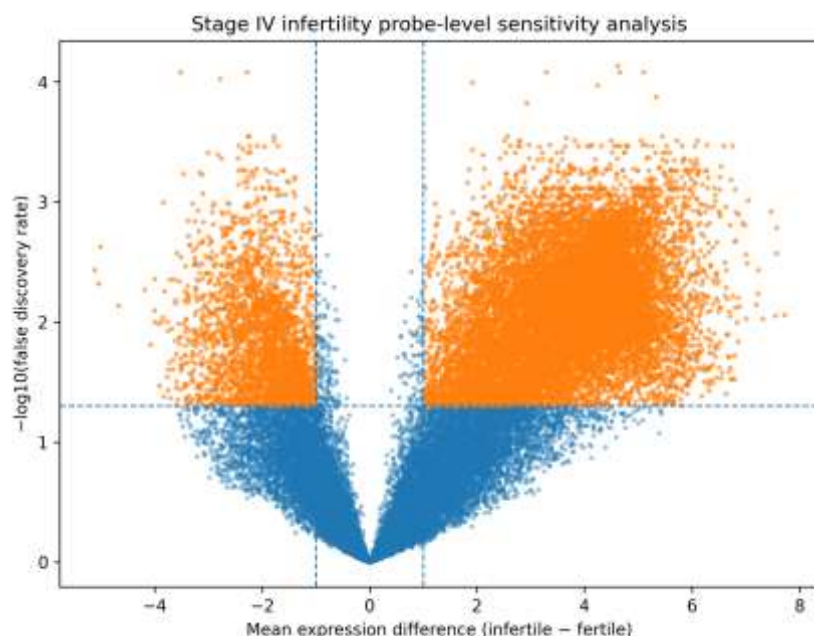


Figure 4. Probe-level volcano representation of the stage IV infertile-versus-fertile sensitivity analysis. Dashed vertical lines mark an absolute mean-expression difference of 1; the horizontal line marks false discovery rate = 0.05.

3.3 Four-group specificity analysis

Infertility (disease free) resulted in 8,156 probes with a false discovery rate < 0.05 and an absolute mean-expression difference of ≥ 1 , of which 4,891 were higher and 3,265 were lower. There were 15,988 stage IV signals, of which 3,064 had also been disease-free and 12,924 did not. The effect of infertility is compared to that observed with and without endometriosis in figure 5. There were 17,255 probes with the two factor interaction sensitivity analysis that passed the false discovery rate test at $p < 0.05$, of which 17,200 showed an absolute interaction effect of 1 or more. The large numbers suggest that there was a high degree of group structure within the processed matrix, and thus that apparent disease-context specificity should be interpreted with caution.

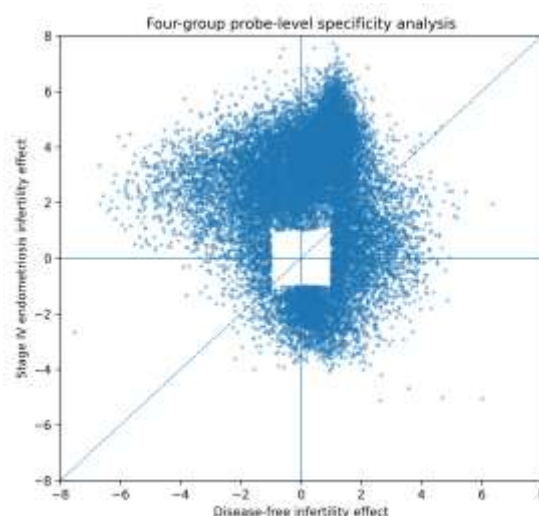


Figure 5. Four-group specificity analysis. Each point represents a probe meeting the stage IV and/or disease-free infertility sensitivity criterion. The x-axis is the infertility effect without endometriosis; the y-axis is the infertility effect in stage IV disease.

3.4 Published gene-level benchmark and pathway evidence

The same stage IV comparison was analyzed at the gene level using linear models for microarray data, which resulted in 1,990 differentially expressed genes and a protein-interaction network of 1,174 nodes and 12,150 edges [5]. Weighted gene co-expression network analysis (WGCNA) was used to integrate with the 20 hub mRNAs and nine hub lncRNAs [5] were identified. A separate public analysis was performed using a different analysis pipeline, which reported 3,149 differentially expressed genes [6]. Special attention is given to selected published hub genes and their reported effect estimates, showing the impact of preprocessing and analytical decisions on the discovery of genes at this level in this small cohort (Table 2).

Gene	Direction	Functional context	Published log2 fold change	Published FDR
ADCY6	Down	Adenylate cyclase / cAMP signaling	-4.323	1.62×10 ⁻¹³
FSTL3	Down	TGF-β/activin-related regulation	-6.060	1.09×10 ⁻¹²
ADCY1	Up	Adenylate cyclase / cAMP signaling	+4.540	8.07×10 ⁻¹²
CASR	Up	Calcium-sensing GPCR	+4.155	7.0×10 ⁻⁹
CCKAR	Up	Peptide-hormone GPCR	+5.338	3.77×10 ⁻¹²
CFTR	Up	Ion transport / epithelial function	+6.436	1.21×10 ⁻¹³
CRH	Up	Stress/endocrine signaling	+4.785	1.38×10 ⁻¹¹
GLP1R	Up	Metabolic GPCR signaling	+6.073	4.19×10 ⁻¹³
GPR55	Up	GPCR signaling	+4.930	9.49×10 ⁻¹²
GPRC6A	Up	Class C GPCR / nutrient sensing	+4.304	4.51×10 ⁻¹²

Table 2. Selected hub mRNAs reported by Wu et al. [5]. Values are published gene-level benchmarks and are not presented as newly estimated statistics.

Enrichment results published by different groups come together around the following pathways: G protein-coupled receptor signaling, cyclic-nucleotide signaling, estrogen-related regulation, autophagy, programs of cell-cycle and DNA-replication, and metabolic pathways [5,6]. These pathways and their biological hallmarks are biologically relevant to endometrial signaling and receptivity. In this study, this is treated as an external, gene level evidence, instead of being new enrichment results.

3.5 Biomarker validation evidence

A public data set that included the directly comparable combination of severe endometriosis, fertility phenotype, and eutopic endometrium, and sampling context was not identified. As an indirect validation dataset, Wu et al. selected GSE26787, where the fertility status was known but the status of endometriosis was unknown [5]. There were eight differentially expressed hub mRNAs from the overlapping infertility-related dataset, while five of the reported endometriosis-associated-infertility-specific hub mRNAs were not. These observations provide some signals of infertility, but these findings are not independent validation of any specific biomarker of endometriosis.

4. DISCUSSION

In the enlarged analysis, GSE120103 is interpreted in an important manner. There is a clear structure in the data that has a strong link to the infertility, however there is also a great amount of heterogeneity seen at the sample level. Several samples exhibited a shifted distribution and weak PCA structure and broad probe-level significance, such that statistical significance is not enough to prioritize biomarker.

The four-group design is still a strong one. An interpretation of the data possible only if the infertility effect in stage IV is compared directly with the infertility effect in disease-free women is a separation of the generic infertility-associated expression from signals that are more context dependent. In the current sensitivity analysis, few of the stage IV significant probes were stage IV in disease-free infertility. The number of interactions is very high, however, which suggests that technical structure may play a role in apparent disease-context specificity. Thus, there is a need for gene-level annotation and raw-data-aware modelling beforehand to define individual candidates as endometriosis specific.

A biologically coherent framework for interpretation is found in the published gene-level literature. Wu et al. found GPCR-centered co-expression and interaction networks and reported 1,990 DEGs [5] while Li et al. reported a larger set of DEGs, and focused on amino-acid metabolism, cyclic guanosine monophosphate dependent protein kinase, and cyclic adenosine monophosphate (cAMP) signaling. The disagreement in the number of differentially expressed genes is informative in and of itself because it shows that the processing, annotation, and statistical decisions do make a difference in discovering genes that are differentially expressed in this small cohort. The G protein coupled receptors and cyclic-nucleotide signaling are potential mechanistic themes as endometrial cells are able to integrate multiple endocrine, paracrine, inflammatory and metabolic signals through receptor-mediated pathways.

The second-messenger signaling is positioned at the center of the reported network as indicated by published hub genes such as ADCY1, ADCY6, CASR, CCKAR, GPR55 and GLP1R [5]. Other connections with cyclic remodeling, stress responses and implantation competence include estrogen signaling, autophagy, cell-cycle control, and DNA replication.

4.1 Positioning against contemporary transcriptomic evidence

The signal level of the probe should be read in the context of the broader endometrial transcriptomic evidence in GSE120103. A meta-analysis of 8 studies of mid-secretory transcriptomics from 2022 (125 women) showed no single transcript to survive strict multiple testing correction although chemotaxis, Locomotion and Immune/defence pathways were still enriched [16].

This, combined with the present results, indicates that the very wide signal seen here is not necessarily a reflection of thousands of universally stable infertility markers and further underscores the need for technically sensitive analyses and independent replication and annotation-complete modeling. Recent single-cell studies also reveal the presence of transcriptional abnormalities in endometriosis are found in separate populations of epithelial, stromal, immune and microenvironmental cells [17-19].

In 2023, over 370,000 cells were profiled and the authors showed that the transcription of cells changes in a tissue- and cell-type-specific manner [17] and in 2024, an integrated Human Endometrial Cell Atlas of 313,527 cells from 63 women was created, independently validating cell states with over 312,000 nuclei [19]. This cell-type resolution highlights the high sensitivity of whole-endometrium microarrays to potentially exhibit large aggregate changes, as changes in cell-state abundance and cell-state composition can simultaneously occur alongside changes in within-cell transcriptional regulation. The evidence of interpretation in the context of fertility is also limited. The altered hormonal signaling, immune regulation, decidualization, and endometrial receptivity are supported by contemporary studies and mechanistic research, however, the results are not consistent across clinical and transcriptomic studies [20-22].

Specifically, there is experimental evidence of defective decidualization in endometriosis associated with impaired bone morphogenetic protein/transforming growth factor beta (BMP/TGF- β) signaling [21], and meta-analysis of transcriptomics scores suggests that differences in endometrial receptivity may be small, but real [16]. The current findings are thus best regarded as a disease-context signal generating analysis, rather than a diagnostic panel that could be ready for use. Recent integrative biomarker studies have integrated differential expression, co-expression network, and machine learning analysis with single-cell localization to examine in detail the overlap between endometriosis and implantation failure [23].

This type of work facilitates multi-layer prioritization, but it also points to a key translational need: candidate genes must be replicated across cohorts and must still contain discriminatory information when the generic infertility and cell-composition effects are taken into account. The four-group structure of GSE120103 is useful for this purpose, but is not definitely validated due to the small sample size and heterogeneity of the processed-matrices. The current results support the use of a different approach for the selection of candidates for the development of biomarkers, rather than just true change or false discovery rate. The following criteria should be satisfied for a candidate to pass the probe-to-gene annotation: a gene-level effect should be stable, disease context specificity, a coherent pathway or network, and replication in an independent cohort. A lack of a truly matched external severe-endometriosis infertility cohort continues to be the main validation gap. There are a number of cautions to be taken. One of the first reasons is because only 9 participants are present in each group. Secondly, the data is microarray-based and the uploaded processed matrix is highly heterogeneous.

Third, the probe-to-gene fields (gene-symbol) in the official GPL6480 platform record do exist but the annotation table was not included in the series matrix provided, so the probe-to-gene remapping was not fabricated and published gene-level results are clearly distinct from newly calculated probe-level results. Fourth, whole-endometrium expression might involve cell-composition differences, which was highlighted by recent single-cell atlases [17-19]. Fifth, observational expression data cannot prove causality. The limitations do not preclude clinical claims but they do not reduce the value of the data for hypothesis generation.

5. CONCLUSION

The strong and heterogeneous endometrial expression pattern found in GSE120103 was later identified as being linked to infertility in stage IV endometriosis by reanalysis. The separation in the four-group comparison and the complete-matrix quality control indicated that the effects of infertility differed by context of endometriosis, with probe level effects differing from the unusually broad differential signal requiring caution, as technical structure and influential samples may be responsible for the observed separation. Here, published gene level studies of the same cohort implicate GPCR and cyclic-nucleotide signaling, hormonal regulation, cell-cycle and DNA-replication processes, and metabolism as comparative biological evidence, not as new findings. Before any candidate transcript can be considered a validated biomarker, independent cohorts with matched severe-endometriosis and fertility phenotypes are needed.

REFERENCES

- [1] Zondervan KT, Becker CM, Missmer SA. Endometriosis. *N Engl J Med.* 2020;382:1244–1256. doi:10.1056/NEJMra1810764.
- [2] Saunders PTK, Horne AW. Endometriosis: etiology, pathobiology, and therapeutic prospects. *Cell.* 2021;184:2807–2824. doi:10.1016/j.cell.2021.04.041.
- [3] Bhat MA, Sharma JB, Roy KK, Sengupta J, Ghosh D. Genomic evidence of Y chromosome microchimerism in the endometrium during endometriosis and in cases of infertility. *Reprod Biol Endocrinol.* 2019;17:22. doi:10.1186/s12958-019-0465-z.
- [4] NCBI Gene Expression Omnibus. GSE120103 and GPL6480: Agilent-014850 Whole Human Genome Microarray 4×44K G4112F. National Center for Biotechnology Information.
- [5] Wu J, Xia X, Hu Y, Fang X, Orsulic S. Identification of infertility-associated topologically important genes using weighted co-expression network analysis. *Front Genet.* 2021;12:580190. doi:10.3389/fgene.2021.580190.
- [6] Li X, Guo L, Zhang W, et al. Identification of potential molecular mechanism related to infertile endometriosis. *Front Vet Sci.* 2022;9:845709. doi:10.3389/fvets.2022.845709.
- [7] Ritchie ME, Phipson B, Wu D, et al. limma powers differential expression analyses for RNA-sequencing and microarray studies. *Nucleic Acids Res.* 2015;43:e47. doi:10.1093/nar/gkv007.
- [8] Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc Series B.* 1995;57:289–300.

- [9] Langfelder P, Horvath S. WGCNA: an R package for weighted correlation network analysis. *BMC Bioinformatics*. 2008;9:559. doi:10.1186/1471-2105-9-559.
- [10] Szklarczyk D, Kirsch R, Koutrouli M, et al. The STRING database in 2023: protein–protein association networks and functional enrichment analyses. *Nucleic Acids Res*. 2023;51:D638–D646. doi:10.1093/nar/gkac1000.
- [11] Subramanian A, Tamayo P, Mootha VK, et al. Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proc Natl Acad Sci USA*. 2005;102:15545–15550. doi:10.1073/pnas.0506580102.
- [12] Lessey BA, Kim JJ. Endometrial receptivity in the eutopic endometrium of women with endometriosis. *Fertil Steril*. 2017;108:19–27. doi:10.1016/j.fertnstert.2017.05.031.
- [13] Kao LC, Germeyer A, Tulac S, et al. Expression profiling of endometrium from women with endometriosis reveals candidate genes for disease-based implantation failure and infertility. *Endocrinology*. 2003;144:2870–2881. doi:10.1210/en.2003-0043.
- [14] Zhou Y, Zhou B, Pache L, et al. Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. *Nat Commun*. 2019;10:1523. doi:10.1038/s41467-019-09234-6.
- [15] Johnson WE, Li C, Rabinovic A. Adjusting batch effects in microarray expression data using empirical Bayes methods. *Biostatistics*. 2007;8:118–127. doi:10.1093/biostatistics/kxj037.
- [16] Vargas E, García-Moreno E, Aghajanova L, et al. The mid-secretory endometrial transcriptomic landscape in endometriosis: a meta-analysis. *Hum Reprod Open*. 2022;2022(2):hoac016. doi:10.1093/hropen/hoac016.
- [17] Fonseca MAS, Haro M, Wright KN, et al. Single-cell transcriptomic analysis of endometriosis. *Nat Genet*. 2023;55(2):255–267. doi:10.1038/s41588-022-01254-1.
- [18] Tan Y, Flynn WF, Sivajothi S, et al. Single-cell analysis of endometriosis reveals a coordinated transcriptional programme driving immunotolerance and angiogenesis across eutopic and ectopic tissues. *Nat Cell Biol*. 2022;24(8):1306–1318. doi:10.1038/s41556-022-00961-5.
- [19] Marečková M, Garcia-Alonso L, Moullet M, et al. An integrated single-cell reference atlas of the human endometrium. *Nat Genet*. 2024;56(9):1925–1937. doi:10.1038/s41588-024-01873-w.
- [20] Racca A, et al. Endometrial receptivity in women with endometriosis. *Best Pract Res Clin Obstet Gynaecol*. 2024;102438. doi:10.1016/j.bpobgyn.2023.102438.
- [21] Liao Z, Tang S, Jiang P, et al. Impaired bone morphogenetic protein signaling pathways disrupt decidualization in endometriosis. *Commun Biol*. 2024;7:227. doi:10.1038/s42003-024-05898-z.
- [22] Ou Y, Wang H, Zhou C, et al. Endometriosis-associated infertility: multi-omics insights into pathogenesis and precision therapeutics. *Front Endocrinol (Lausanne)*. 2025;16:1613334. doi:10.3389/fendo.2025.1613334.
- [23] Li H, Zhu C, Gu Y, et al. Shared diagnostic biomarkers and underlying mechanisms between endometriosis and recurrent implantation failure. *Front Endocrinol (Lausanne)*. 2025;16:1490746. doi:10.3389/fendo.2025.1490746.
- [24] Liu S, Li X, Gu Z, et al. Single-cell and spatial transcriptomic profiling revealed niche interactions sustaining growth of endometriotic lesions. *Cell Genom*. 2025;5(1):100737. doi:10.1016/j.xgen.2024.100737.