The user wants me to translate a Chinese academic paper title: "子宫内膜异位症的多组学研究进展后印本" Let me break this down: - 子宫内膜异位症 = endometriosis (a medical condition) - 的 = possessive particle - 多组学 = multi-omics / multi-omics studies - 研究 = research / studies - 进展 = advances / progress - 后印本 = postprint So···

Authors: The user has provided a single name: "杨泊娇". This is a Chinese name. The task is to translate it from Simplified Chinese to English with the highest accuracy and academic tone, following the critical requirements and output rules provided.

Let me analyze the requirements:

1. The input is just a name: "杨泊娇"
2. I need to translate this to English
3. The context is academic/scientific translation
4. I must preserve LaTeX commands, citation commands, and tags - but there are none in this input
5. I must maintain academic tone and formal scientific writing style
6. I must use precise technical terminology from the glossary - but the glossary doesn't cover names
7. I must preserve section structure and paragraph organization - but there's just a name
8. I must translate all content completely - don't omit information

For Chinese names in academic contexts, the standard practice is: - Use Pinyin transliteration - Family name first, given name second (maintaining Chinese order) - Capitalize the first letter of each part - No hyphenation unless the name itself contains it

"杨泊娇" would be transliterated as "Yang Bojiao" in academic contexts.

However, I need to check if there are any tags. The user just provided the name without any tags. The instructions say I must preserve tags if they exist. Since they don't exist, I should just provide the translation.

But wait - the instructions are very specific about the format. They say "Return ONLY the translated text for the given input" and mention the tags. Let me re-read the instructions carefully.

The instructions say: - "PRESERVE ALL ···paragraph wrapper tags EXACTLY" - "Maintain exact count and IDs of ···tags" - "Never remove or modify ···tags"

Since the input "杨泊娇"doesn't have any tags, I should just output the translated name without any tags. The instructions about tags are conditional - they apply when tags are present. When they' re not present, I just translate the content.

The name "杨泊娇" is a Chinese personal name. In academic translation: - 杨 (Yáng) is a common Chinese surname - 泊娇 (Bójiāo, The user has provided a single word "师伟" which is a Chinese name. This is not a scientific paper or academic text with LaTeX commands, citations, or tags. The instruction is to translate from Simplified Chinese to English with academic tone, but this is just a name.

Looking at the glossary provided: - 机器学习 => machine learning - 深度学习 => deep learning

But "师伟" is not in the glossary. It' s a proper name. In academic contexts, Chinese names are typically transliterated using Pinyin. "师伟" would be "Shi Wei" (surname first, then given name).

However, the user might be testing the system or this could be a fragment. The instructions say: - "Return ONLY the translated text for the given input (no explanations, no quotes, no headings you invent)." - "Preserve ALL ···paragraph wrapper tags EXACTLY" - "Preserve ALL LaTeX commands and placeholders exactly"

Since there are no tags, no LaTeX, no citations, and just a single name, the most appropriate translation is the Pinyin transliteration "Shi Wei" .

But wait - the user might have intended to provide more text and this is just a fragment. However, I must work with what was given. The instructions are very specific about preserving tags and structure, but there are none here.

Let me consider if "师伟"could be something else: - 师 (shī) = teacher/master/expert - 伟 (wěi) = great/magnificent

But as a compound, it' s almost certainly a name. In academic contexts, we would transliterate it as "Shi Wei" .

The instructions say "Translate from Simplified Chinese to English" . A name is not really "translated" but transliterated. The standard academic practice is to use Pinyin.

Given the strict output rules, I should just provide the transliteration without any additional text. The simplest and most accurate response is:

Shi Wei

But let me double-check the instructions again. They mention: - "Preserve ALL ···paragraph wrapper tags EXACTLY" - "Keep one output paragraph per input paragraph; do not merge or split paragraphs."

Since there' s no paragraph tag in the input, I shouldn' t add one. The input is just "师伟" on its own.

The, Shi Wei

Date: 2025-12-25T11:58:19+00:00

Abstract

The user wants me to translate a Chinese academic text about endometriosis (EMs) into English. Let me break down the requirements:

1. **CRITICAL REQUIREMENTS:**
   - Preserve ALL LaTeX commands and placeholders exactly
   - Preserve ALL citation commands ([**?**], **??**, (**??**), etc.) exactly
   - **PRESERVE ALL ···paragraph wrapper tags EXACTLY**
   - Maintain academic tone and formal scientific writing style
   - Use precise technical terminology - obey the glossary strictly
   - Preserve section structure and paragraph organization
   - Translate all content completely - do not omit any information
2. **OUTPUT RULES:**
   - Return ONLY the translated text (no explanations, no quotes, no headings)
   - Keep one output paragraph per input paragraph
   - **Maintain exact count and IDs of ···tags**
   - Do NOT add Markdown formatting unless present in source
   - Preserve original line breaks when meaningful
3. **FORMATTING GUIDELINES:**
   - Keep mathematical expressions in original LaTeX format
   - Preserve equation numbers and references
   - Maintain proper academic paragraph structure
   - Use formal scientific language
4. **Glossary:**
   - 机器学习 => machine learning
   - 深度学习 => deep learning

Looking at the input text:

子宫内膜异位症（EMs）是一种常见的妇科疾病，全球受累女性超过1.7亿例，严重影响患者的身心健康及

This appears to be a single paragraph. However, the user hasn' t provided any tags in this input. Let me re-read the instructions carefully.

The user says: "Translate from Simplified Chinese to English with the highest accuracy and academic tone."

The input is just plain text without any tags. But the instructions say "PRESERVE ALL ···paragraph wrapper tags EXACTLY" . This is a bit confusing. Let me check if the user might have forgotten to include the tags, or if I should add them.

Looking at the "OUTPUT RULES" section

Full Text

Advances in Multi-omics Research on Endometriosis

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Abstract

Endometriosis (EMs) is a common gynecological disorder affecting over 170 million women worldwide, significantly impairing both physical and mental health as well as quality of life. Conventional diagnostic approaches, characterized by low sensitivity, invasiveness, and substantial diagnostic delays, pose major challenges in clinical management. In recent years, rapid advances in multi-omics technologies have provided new perspectives for elucidating the complex pathophysiology of EMs. This review summarizes specific diagnostic and therapeutic targets identified through multi-omics approaches and outlines molecular networks to facilitate the discovery of novel non-invasive diagnostic tools, offering new insights for overcoming diagnostic delays and advancing precision treatment pathways for EMs.

Keywords: Endometriosis; Multi-omics; Review; Molecular subtyping; Therapy

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Endometriosis (EMs) is a condition characterized by the growth of endometrial tissue outside the uterine cavity, causing symptoms such as dysmenorrhea, pelvic pain, and infertility. Its etiology is complex, involving multiple interacting factors including genetics, immunity, endocrine function, and environmental influences. Currently, the primary non-invasive biomarkers used clinically for diagnosing EMs are carbohydrate antigen CA125 and anti-endometrial antibodies. However, CA125 has limited specificity and sensitivity, while anti-endometrial antibodies show low sensitivity, resulting in a lack of reliable biomarkers for EMs diagnosis. Moreover, diagnosis still relies on invasive laparoscopic surgery,

leading to an average diagnostic delay of 7–10 years and a misdiagnosis rate of 60%–70% [1].

The rapid advancement of high-throughput sequencing technologies has opened multidimensional perspectives for EMs research through genomics, epigenomics, transcriptomics, proteomics, metabolomics, and microbiomics. These approaches enable systematic analysis of the dynamic molecular interaction networks within the lesion microenvironment through disease screening, precise phenotyping, prognostic stratification, and targeted therapy. However, single-omics approaches provide insufficient understanding of EMs pathological mechanisms, and each omics layer has its own strengths and limitations. To achieve multi-dimensional, multi-level coordinated regulation from "gene to epigenetics to treatment," it is necessary to integrate multiple omics layers to compensate for individual shortcomings, identify high-specificity biomarkers, discover key therapeutic targets, construct personalized medicine pathways, and propel EMs diagnosis and treatment toward precision and dynamic monitoring.

[Figure 1: see original paper]

1 Genomics

Genetic factors play a crucial role in EMs development, with approximately 50% of patients having a family history, and malignant transformation tendencies associated with abnormal expression of multiple genes. Genomics, as the genetic blueprint of disease, can identify hereditary and malignant predispositions at the gene level. The SAPKOTA team identified five novel EMs risk loci through cross-ethnic meta-analysis: fibronectin 1 (FN1), coiled-coil domain containing 170 (CCDC170), estrogen receptor 1 (ESR1), spectrin repeat containing nuclear envelope protein 1 (SYNE1), and follicle-stimulating hormone subunit beta (FSHB). These loci participate in EMs pathogenesis by regulating steroid hormone synthesis and immune microenvironment remodeling [2]. Additionally, insulin-like growth factor 1 (IGF1) was identified as a hub gene in EMs through transcriptional pathways that stimulate overexpression of estrogen receptor β (ERβ) and aromatase, with its isoform-specific expression patterns effectively distinguishing deep infiltrating endometriosis (DIE) from ovarian EMs alone [3]. In terms of immune regulation, the palmitoylation-related genes vaccinia-related kinase 1 (VRK1), polypeptide N-acetylgalactosaminyltransferase 12 (GALNT12), and RecQ-mediated genome instability protein 1 (RMI1) provide novel insights for clinical diagnosis and disease monitoring through their immunoprotective effects [4]. THOMAS et al. [5] identified neuropeptide S receptor 1 (NPSR1) as a non-hormonal therapeutic target for EMs with increased correlation to stage III/IV disease through genetic analysis and validation. Meanwhile, abnormal overexpression of estrogen-responsive gene growth regulation by estrogen in breast cancer 1 (GREB1) and SYNE1 is directly associated with follicular development disorders and luteal insufficiency, serving as molecular markers for evaluating EMs-related infertility [6]. A recent

large-scale GWAS study discovered 42 new risk loci, demonstrating significant correlations between EMs and chronic pain and inflammatory conditions, providing molecular markers for early screening and high-risk population intervention [7].

Furthermore, characteristic copy number variations (CNVs) exist in ectopic endometrial tissues of EMs patients. ROBERT et al. [8] used exome sequencing and targeted sequencing to identify phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA), Kirsten rat sarcoma viral oncogene homolog (KRAS), and AT-rich interaction domain 1A (ARID1A) as early markers of malignant transformation in EMs that may drive oncogenic events. Among these, KRAS mutations are the most common driver alterations in EMs, with activation increasing the risk of endometrioid carcinoma [9], while ARID1A mutations occurring at 30%–50% frequency in ovarian endometrioid adenocarcinoma and clear cell carcinoma highlight its potential as a malignant transformation warning marker [10].

Through weighted gene co-expression network analysis (WGCNA) and machine learning models, GENG et al. [11] screened AE binding protein 1 (AEBP1), homeobox B6 (HOXB6), Kruppel-like factor 2 (KLF2), and RAR-related orphan receptor B (RORB) as core genes that may serve as potential biomarkers for EMs and targets for commonly used drugs goserelin and dienogest, with KLF2 and HOXB6 showing higher potential value. JIANG et al. [12] validated a LASSO diagnostic model based on machine learning, selecting chemokine ligand 12 (CXCL12), platelet-derived growth factor receptor-like (PDGFRL), angiotensin II receptor type 1 (AGTR1), prostaglandin E receptor 3 (PTGER3), and sphingosine-1-phosphate receptor 1 (S1PR1) as a diagnostic marker panel, providing new strategies for targeted EMs therapy.

Genomic research has also opened new avenues for non-hormonal treatments. For example, NPSR1 inhibitor development offers new options for alleviating EMs-related inflammation and pain [5]. Bonnie' s team utilized an AI platform integrating GWAS data with single-cell atlases to discover novel therapeutic targets including guanylate binding protein 2 (GBP2), hematopoietic cell kinase (HCK), and integrin subunit beta 2 (ITGB2), confirming that ITGB2 antagonist Lifitegrast effectively inhibits lesion growth [13]. Additionally, screening of potential drug targets such as catenin beta 1 (CTNNB1) and protein tyrosine phosphatase non-receptor type 7 (PTPN7) lays a theoretical foundation for precision therapy [14] and provides complementary mechanisms to bridge the "genotype-phenotype" gap together with epigenetics.

However, several limitations of genomics research must be noted. First, genomic data primarily reflect static genetic variations and cannot fully capture complex features such as hormonal fluctuations and dynamic changes in the immune microenvironment during EMs development. Second, the heterogeneity of gene mutations demands higher-resolution analytical techniques, such as single-cell multi-omics or spatial transcriptomics, to decipher cell-cell interaction mechanisms at the ectopic endometrial-stromal interface. Future studies must

integrate proteomics and metabolomics to reveal the temporal characteristics and spatial heterogeneity of EMs pathogenesis.

2 Epigenetics

Epigenetic regulation influences disease progression through non-genetic sequence modifications, offering reversible and environmentally sensitive approaches for EMs diagnosis and treatment. DNA methylation is the most characteristic epigenetic modification in EMs, with DNA methyltransferases (DNMTs) precisely regulating gene expression through CpG island methylation [15]. Abnormal expression of DNMT1, DNMT3A, and DNMT3B in ectopic endometrium of EMs patients leads to methylation imbalance of key genes [16]. For instance, promoter hypermethylation of HOXA10 inhibits its expression, directly impairing endometrial receptivity and representing a core mechanism of EMs-related infertility [17]. Additionally, GSTM1 hypomethylation promotes ectopic lesion proliferation by inhibiting apoptosis [18], while abnormal methylation of steroidogenic factor 1 (SF-1) activates steroidogenic acute regulatory protein (StAR) and cytochrome P450 family 19 subfamily A member 1 (CYP19A1), promoting local estrogen synthesis and accelerating disease progression through GATA binding protein 6 (GATA-6)-mediated inflammatory responses [19]. Simultaneously, high expression of ERβ (ESR2 gene) and methylation silencing of progesterone receptor (PR) exacerbate estrogen-dependent lesion growth and progesterone resistance, providing molecular explanations for hormonal therapy resistance in EMs [20].

Histone acetylation is primarily regulated by histone acetyltransferases (HATs) and histone deacetylases (HDACs). HDAC1 overexpression aggravates inflammatory responses through the lncRNA HOTAIR-mediated epigenetic axis [21], and synergizes with HDAC2 to suppress tumor suppressor genes such as hepatocyte nuclear factor 4α (HNF4α) and ARID1A, promoting ectopic endometrial invasion. Conversely, HDAC3 downregulation leads to abnormal collagen deposition, interfering with endometrial receptivity [22]. Additionally, class III HDAC Sirtuin 1 (SIRT1) and its corepressor BCL6 have been identified as potential biomarkers for EMs. Abnormally high SIRT1 expression in EMs patients not only promotes disease progression but may also worsen conditions by facilitating ovarian cancer transformation [23].

Histone methylation modifications occur primarily at arginine or lysine residues in the N-termini of H3 and H4. Among these, methylation at H3K4 (including H3K4me2 and H3K4me3) is an important epigenetic mark for gene transcriptional activation. Enrichment of H3K4me2 at promoters of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) genes drives expression and secretion of these inflammatory factors [24], while H3K4me3 exacerbates estrogen signaling abnormalities by regulating ERβ expression [25]. In contrast, H3K27me3 modification promotes disease progression through epigenetic silencing mechanisms, and H3K27ac modification levels can reflect chromatin openness states, with abnormalities potentially serving as novel diagnostic markers for EMs [26].

Furthermore, elevated H3K27me3 levels mediated by histone methyltransferase EZH2 in ectopic endometrium enhance lesion invasiveness by upregulating EMT key factors such as Slug and Snail [27].

The reversibility of epigenetic modifications provides new directions for targeted drug therapy. Studies show that DNMT inhibitor 5-Aza-2'-deoxycytidine (AZA) can reverse HOXA10 methylation, improving endometrial function and fertility outcomes [28]. HDAC inhibitors (vorinostat, trichostatin A, romidepsin, etc.) suppress ectopic lesion proliferation by restoring histone acetylation [22]. Additionally, SIRT1 inhibitor EX-527 restores decidualization capacity in mouse endometrium and significantly inhibits growth and invasion of ectopic lesions, suggesting therapeutic potential [29]. Preclinical studies confirm that EZH2 targeting agents targeting the H3K27me3-mediated EMT pathway reduce lesion invasiveness [27]. Moreover, multi-level interventions combining H3K4me2 inflammatory axis and H3K27me3 epithelial-mesenchymal transition (EMT) pathway targeting can synergistically overcome hormonal therapy resistance and reduce recurrence risk.

Compared with the static DNA sequences of genomics, epigenetic marks exhibit spatiotemporal specificity, more closely reflecting real-time functional regulation changes and providing upstream explanations for transcriptional abnormalities. Additionally, epigenetics offers new tools for precision diagnosis and treatment. However, epigenetic-targeted drugs suffer from non-specificity defects that may cause severe off-target effects and adverse reactions, necessitating integration with other omics technologies to improve accuracy. As single-cell epigenomics advances specific marker screening and novel epigenetic tool development, the transition from broad-spectrum inhibition to lesion-specific regulation becomes possible.

3 Transcriptomics

Transcriptomics focuses on quantifying and analyzing gene expression activity, revealing EMs syndrome differentiation, therapeutic efficacy evaluation, and personalized treatment applications through dynamic network analysis. Non-coding RNAs (ncRNAs) not only drive key pathological pathways (such as angiogenesis, EMT, and immune escape) but also exhibit tissue-specific expression and circulating stability, making them highly promising diagnostic markers and therapeutic targets.

3.1 ncRNA

The miR-200 family, including miR-200b, miR-141, and miR-200c, shows significant dysregulation in EMs, regulating angiogenesis, proliferation/invasion, and EMT to inhibit disease progression, with plasma stability making them promising early non-invasive diagnostic markers [30]. Notably, miR-125b-5p currently demonstrates the highest specificity and sensitivity as a single diagnostic biomarker for EMs [31]. Combining other significantly differentially expressed

potential markers such as miR-150-5p, miR-342-3p, miR-451a, miR-3613-5p, and let-7b can construct multi-dimensional diagnostic models [32]. Additionally, expression levels of miR-199a and miR-122 significantly correlate with disease stage, with dynamic changes distinguishing mild (stages I/II) from severe (stages III/IV) EMs [33]. Furthermore, miR-297 reduces endometrial receptivity by inhibiting PR expression in endometrial stromal cells (ESCs), while specific inhibitors can reverse PR suppression effects, improving decidualization defects and enhancing fertility potential [34].

Long non-coding RNAs (lncRNAs) are non-coding RNAs longer than 200 nt that regulate EMs pathological processes through multiple mechanisms. XU et al. [35] found that LNC-MALAT1 promotes NLRP3 expression through "sponging" miR-141-3p, inducing fibrosis, while enhancing erastin-induced ferroptosis through the miR-145-5p/muc1 pathway, suggesting its potential as a targeted intervention target [36]. Additionally, LncRNA NEAT1 is highly expressed in ectopic lesions; knockdown inhibits ESC proliferation and migration while promoting apoptosis through targeting miR-124-3p, and combined detection with miR-124-3p constitutes a potential diagnostic marker for EMs-related infertility [37]. Lnc-PVT1 combined with hypoxia-inducible factor 1α (HIF-1α) detection can reflect R-AFS stage progression, providing new indicators for early diagnosis and staging assessment [38]. Lnc-H19 inhibits TH17 differentiation and ESC proliferation through the miR-342-3p/IER3 pathway [39], and its high expression is confirmed as an independent prognostic factor for EMs recurrence, potentially serving as a recurrence prediction marker [40].

Circular RNAs (circRNAs) have attracted attention in EMs research due to their structural stability and tissue-specific expression. Studies confirm that circATRNL1 is significantly upregulated in patient serum, positively correlating with clinical stage and driving EMs progression through promoting cell proliferation, invasion, and EMT, demonstrating dual value for diagnosis and prognosis assessment [41]. In vivo experiments show that hsa_{{{circ}}*{{0063526}}} *suppresses lesion growth by regulating miR-141-5p, suggesting its potential as both biomarker and therapeutic target [42]. Mechanistically, circ*{0061140} enhances cell migration and invasion through the miR-140-3p-Notch2 axis, mimicking tumor-like pro-invasive effects [43]; circ_{0007331} acts as a miR-200c-3p sponge, indirectly regulating HIF-1α function, and circ_{0007331} knockdown inhibits EMs development by downregulating HIF-1α expression [44]. Additionally, Circ_{0075503} inhibits E2-induced migration and invasion of ectopic endometrial cells through the miR-15a-5p/KLF12 axis, providing novel intervention strategies for hormone-dependent EMs.

3.2 Single-cell and Spatial Transcriptomics

Single-cell sequencing precisely resolves cellular heterogeneity in EMs ectopic lesions. First, fibroblasts from ectopic lesions show high genetic homology with eutopic endometrium, with synchronized evolution of their motility trajectories and pathogenic gene profiles confirming the eutopic endometrial origin theory

of EMs stromal cells. Notably, fibroblasts from ovarian and peritoneal EMs exhibit different pathogenic gene profiles (e.g., specific high StAR expression), supporting their existence as independent disease subtypes [45]. Additionally, the immune microenvironment of EMs lesions shows characteristic immune imbalance with M2 macrophage polarization, NK cell exhaustion, and T cell functional suppression [46], while dendritic cells expressing MRC1/VSIG4 promote lesion colonization through mediating immune escape, and CCL19+ perivascular cells drive pro-angiogenic phenotypes through SNCG signals, collectively forming an immune-tolerant microenvironment [47]. Recent digital droplet ELISA (ddELISA) technology based on SiO2 nanoparticles has achieved femtomolar detection of inflammatory markers such as osteopontin (OPN) and IL-6 in menstrual blood, with ultra-high sensitivity and non-invasive sample characteristics providing tools for early EMs screening [48].

Spatial transcriptomic analysis reveals cell-cell interaction networks in EMs lesions at three-dimensional spatial scales. Studies show ovarian stromal cells (OSC) divide into profibrotic (OSCb) and proinflammatory (OSCa) subpopulations, with OSCb forming fibrotic ring structures around epithelial-like cells (EnS) while OSCa establishes immune barriers through CXCL12-macrophage interactions, collaboratively maintaining lesion immune evasion [49]. Additionally, ectopic endometrial stromal cells trigger cascading inflammatory responses and abnormal cell proliferation by aberrantly activating WNT5A signaling to transmit "proliferation instructions" to surrounding ovarian stromal cells, a mechanism confirmed as the "initiation switch" for EMs lesion growth. Moreover, spatial colocalization deficiency of decidualization key genes DKK1 and interleukin-15 (IL15) impairs endometrial receptivity and causes progesterone resistance, providing molecular explanations for clinical drug resistance phenomena [49].

Transcriptomics bridges genomic variation and proteomic function by deeply analyzing transcriptional dynamics, revealing phenotype-molecular mechanism associations suitable for screening key differentially expressed genes and signaling pathways to enable disease subtyping and targeted therapy. However, cellular heterogeneity or lack of spatial information requires supplementation with single-cell and spatial transcriptomics. Additionally, due to translational regulation and post-translational modifications, mRNA levels cannot directly reflect protein abundance and functional status, necessitating proteomics validation and establishing dynamic feedback networks through "miRNA-mRNA-protein" regulatory axes to advance precision diagnosis and treatment frameworks.

4 Proteomics

Proteomics focuses on protein expression differences—the terminal products of genes—to gain molecular-level insights into key pathological mechanisms including cell adhesion, invasion, metastasis, and inflammatory immunity in EMs patients, while uncovering multi-level diagnostic markers. The recently developed Olink ultra-sensitive proteomics technology enables parallel detection of 1,763

proteins per sample, identifying novel protein candidate biomarkers for early non-invasive diagnosis [50]. Studies show that cell adhesion-related proteins such as CD44, fibrinogen-α, and FN1 are abnormally expressed in serum and lesion tissues of EMs patients, potentially correlating with lesion metastasis and high recurrence rates [51], while intercellular adhesion molecule 1 (ICAM-1) shows diagnostic potential by mediating inflammatory and immune responses. Additionally, molecules including the annexin family (Annexin A2/A4), apolipoprotein A1 (APOA1), and serpin family C member 1 (SERPINC1) provide biological basis for constructing novel molecular diagnostic systems [52]. Notably, coordinated upregulation of the complement system (C1S, C1QA, etc.) and tissue factor (TF) suggests a key role for complement-coagulation cascades in EMs microenvironment remodeling, offering new directions for targeted intervention strategies [53].

In diagnostic marker development, inflammatory factors IL-8 and MCP-1 have been incorporated into clinical auxiliary diagnostic systems [54], while IL-1α, IL-1β, and IL-6 demonstrate higher detection value in stage III/IV patients [55]. Additionally, combined detection of oxidative stress markers superoxide dismutase (SOD) and glutathione peroxidase (GPX) shows high sensitivity and specificity [56], and dominant expression of S100-A8 in peritoneal fluid is specific for early diagnosis of deep infiltrating EMs [57]. At the functional level, abnormal activation of osteopontin and urokinase-type plasminogen activator not only participates in invasion processes but may also serve as therapeutic targets [58]. Metabolism-related proteins such as FN1 and triosephosphate isomerase 1 (TPI1) regulate angiogenesis and immune responses, correlating closely with EMs-associated dysmenorrhea to form a dysmenorrhea-specific protein marker profile [59]. Meanwhile, abnormal expression of cytotoxic T lymphocyte-associated antigen 4 (CLTA-4) and programmed death-ligand 1 (PD-L1) provides new perspectives for mechanism analysis of infertility [60-61].

Proteomics directly detects protein expression levels and post-translational modifications, more directly reflecting cellular functional states. Compared with RNA, proteins are more stable and suitable for clinical detection, and more closely reflect biological phenotypes to reveal true molecular functional networks, making them ideal for precision drug development. However, proteomics suffers from low reproducibility and insufficient sample detection sensitivity and specificity. Additionally, transformation of biomarkers to clinical research lacks large-sample multicenter validation. Future directions include deepening mechanistic research through organoid models and spatial proteomics technology, while establishing standardized biobanks and interdisciplinary translational medicine platforms to accelerate translation from basic discovery to clinical application [62].

5 Metabolomics

Metabolites are the end products of gene, transcription, and protein activities. Metabolomics provides deeper insights into complex molecular mecha-

nisms through systematic analysis of dynamic metabolic changes in body fluids (plasma, urine, peritoneal fluid, etc.) of EMs patients. For diagnostic markers, metabolic models constructed from β-hydroxybutyrate, glutamine, and tryptophan have demonstrated high diagnostic accuracy [63], while altered amino acid profiles including alanine, leucine, and lysine also serve as non-invasive diagnostic bases [64]. Notably, urinary taurine participates in EMs pathological processes by regulating oxidative stress, with similar patterns to malignancies, while combined detection of octenyl acid and sphingosine-1-phosphate further enhances diagnostic efficacy [65].

EMs patients exhibit characteristic lipid metabolism abnormalities, commonly showing elevated levels of low-density lipoprotein (LDL), non-high-density lipoprotein (non-HDL), triglycerides (TG), and total cholesterol (TC). This dyslipidemia synergizes with chronic inflammation to exacerbate vascular damage and increase cardiovascular risk [66]. At the molecular level, ceramide/sphingolipid metabolic pathway dysregulation [67] and abnormalities in phosphatidylethanolamine (Lysope) and omega-3 arachidonic acid levels suggest critical roles for lipid remodeling in lesion formation [68]. More clinically valuable is the finding that elevated sphingomyelin and phosphatidylcholine combined with decreased phosphatidylserine constitute a diagnostic biomarker triad for EMs [69]. For ovarian EMs, combined detection of phosphatidylcholine (PC) 36:2 to PCae 34:2 ratio with SMOH 16:1 enables molecular subtyping to guide personalized treatment [70].

At the energy metabolism level, EMs patients exhibit typical "Warburg effect" characterized by enhanced glycolytic pathways. Overexpression of specific genes (HIF-1, TGF-β, LDHA, PDK1, PDH, and SOD) leads to lactate accumulation, while mitochondrial dysfunction causes abnormal accumulation of tricarboxylic acid cycle intermediates (citrate, α-ketoglutarate), and elevated reactive oxygen species levels trigger DNA oxidative damage, forming a vicious cycle [71]. Clinical studies also found that elevated fasting insulin levels exacerbate fertility disorders by disrupting energy supply in follicular microenvironments, providing new predictive indicators for EMs-related infertility [72].

Current findings reveal the molecular basis of EMs from a metabolic perspective, offering new directions for developing targeted intervention strategies. Metabolomics directly reflects physiological and pathological states with sensitive dynamic responses, making it suitable for rapid clinical screening. However, its functional interpretation is unclear, making it difficult to map metabolic changes directly to specific molecular mechanisms, and detection of low-abundance metabolites is challenging, preventing comprehensive metabolite coverage. Therefore, cross-omics integration can construct mechanistic chains of transcriptional regulation-protein modification-metabolic pathways, and future research should conduct full-cycle dynamic monitoring and spatial metabolic mapping of key EMs metabolites.

6 Microbiomics

In recent years, microbiomics research in EMs has gained attention due to its non-invasive nature and diagnostic potential. Targeted microbiota diagnosis and treatment strategies break through traditional dependence on histopathology, providing a novel dimension for early diagnosis and treatment of EMs.

6.1 Relationship Between EMs and Gut Microbiota

Studies show that EMs patients have significantly reduced gut microbiota α-diversity with increased Firmicutes/Bacteroidetes ratio [73]. Among these, dominant genera such as *Prevotella* activate the β-glucuronidase system to convert conjugated estrogen into active free forms, creating a hormonal microenvironment that promotes lesion growth [74]. Notably, stage III/IV patients show increased abundance of Enterobacteriaceae (*Escherichia coli*, *Shigella*) [75], which not only exacerbates loss of α-diversity but also releases neuroactive metabolites such as glutamate that can further amplify estrogen synthesis pathways through the hypothalamic-pituitary-ovarian (HPO) axis. Based on characteristic gut microbiota alterations, diagnostic models with clinical potential have been established, with *Ruminococcus* and *Pseudomonas* serving as specific biomarkers for gut and pelvic cavity. Gut microbiota-based diagnostic models achieve 84% accuracy, significantly outperforming cervical mucus microbiota detection [76]. Additionally, microbiota-derived metabolites such as quinic acid, 4-hydroxyindole, and short-chain fatty acids (e.g., n-butyrate) can reduce inflammatory cell infiltration and inhibit lesion growth [77].

In targeted therapy, mouse experiments have confirmed that antibiotic treatment (e.g., metronidazole targeting *Bacteroides*) significantly reduces EMs lesion volume, and oral administration of feces from diseased mice can restore inflammatory environment and ectopic lesion growth capacity [78]. Furthermore, high-fat diets reduce *Bacteroides* and *Faecalibacterium* abundance, suggesting that dietary intervention or probiotic therapy may become potential treatment strategies for EMs [79]. Therefore, gut microbiota and their metabolites can regulate the inflammatory-hormonal environment of EMs ectopic lesions to inhibit growth, providing important basis for novel diagnosis and treatment strategies.

6.2 Reproductive Tract Microbiota Imbalance

Reproductive tract microbiota imbalance also constitutes a critical link in EMs development. *Lactobacillus*, the core genus maintaining vaginal microbiota balance, is significantly reduced in reproductive tracts of EMs patients [80]. Meanwhile, accumulation of low-abundance genera including *Prevotella*, *Streptococcus*, *Bifidobacterium*, *Megasphaera*, and *Veillonella*, particularly *Enterobacter* and *Streptococcus*, are found in vaginal and cervical microbiota of EMs patients [81]. GUO et al. [82] identified *Faecalibacterium prausnitzii* as a key species crucial in EMs pathogenesis using tissue biopsy and rRNA sequencing, warranting in-depth investigation.

Furthermore, diagnostic model development based on microbiota characteristics has achieved important breakthroughs recently. Integrating abundance changes of marker genera such as *Anaerococcus* enables accurate prediction of EMs disease staging [83], while reproductive tract microbiota imbalance in EMs patients is specifically associated with complications such as infertility, revealing the application potential of vaginal or cervical microbiota in detecting common reproductive tract diseases [84]. From microbiota structure remodeling to metabolite interactions, these findings enable EMs diagnosis through microbiota characteristics and lay theoretical foundations for developing targeted therapies such as probiotic modulation and microbiota transplantation. A summary of different omics characteristics is presented in Table 1.

7 Multi-omics Integration Research

This review summarizes multi-omics research on EMs to achieve a leap from single-omics to systems biology, integrating multi-dimensional data including genomic variation, transcriptional regulatory networks, protein post-translational modifications, and metabolic pathways to reveal molecular cooperative mechanisms of immune escape, hormonal response, and fibrosis progression in the EMs lesion microenvironment. For example, integrated proteomics-metabolomics analysis can identify key enzymes or regulators locking glycolysis/oxidative phosphorylation imbalance, while spatial transcriptomics combined with single-cell sequencing can precisely capture phenotypic plasticity of endometrial stromal cells in ectopic microenvironments. These breakthroughs provide theoretical basis for developing cell-specific targeted therapeutic strategies. Although multi-omics technologies offer new ideas for developing diagnostic models and predictive scoring systems, integration of high-dimensional heterogeneous data still faces dual challenges of algorithm optimization and biological validation. AI and machine learning-driven multi-omics integration represents a breakthrough path for constructing EMs precision diagnosis and treatment systems, requiring extraction of molecular modules with clinical predictive value from massive data and establishment of standardized multi-omics data platforms, while attention must still be paid to high-quality dataset collection and clinical translation efficiency.

Traditional Chinese medicine modernization research provides unique perspectives for multi-omics integration. Taking *Lindera aggregata* and *Salvia miltiorrhiza* as examples, ZHU et al. [85] predicted anti-inflammatory targets through network pharmacology and molecular docking, confirming that active components (luteolin, quercetin, etc.) can precisely regulate the STAT3-PI3K/MAPK signaling axis to inhibit inflammasome activation and abnormal cell proliferation. More breakthroughly, pharmacological network construction identified 28 active components in Sanjie Zhentong Capsule targeting 52 EMs key targets including EGFR, MMP9, CYP3A4, and AKT1, inhibiting proliferation and oxidative stress of ectopic endometrial cells [86]. Traditional formulas such as Wenjing Decoction have also been shown through network pharmacology

to regulate 48 inflammation and endocrine-related targets including IL-6 and ESR1 to exert therapeutic effects [87], revealing the scientific essence of multi-target synergistic action of Chinese medicine formulas. This establishment of "component-target-pathway" multi-dimensional mapping models provides a new paradigm for precision therapy with traditional Chinese medicine.

In recent years, different omics technologies have profoundly analyzed the vicious cycle essence of interactions among genes, proteins, metabolites, and host microenvironment in EMs, providing new perspectives for breaking through traditional diagnosis and treatment bottlenecks. However, candidate biomarkers screened through massive omics technologies still face insufficient clinical translation rates. Therefore, a shift from single, scattered omics discoveries to systematic, standardized research paradigms is needed. Through preliminary cross-omics integration analysis, this review summarizes key molecular functional networks of EMs and analyzes their potential clinical translation benefits, hoping that future multi-omics data can cross-integrate with cutting-edge technologies. For example, *in vivo* molecular imaging technology can achieve dynamic visualization of lesions, AI-driven dynamic prediction models can quantify disease evolution risk for prospective intervention, and organoid-microbiome co-culture technology can provide platforms for personalized drug screening. Through interdisciplinary collaboration optimizing the "data-algorithm-clinical" three-level framework, a closed-loop diagnosis and treatment model from molecular subtyping to personalized therapy can be realized.

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