

Non-Coding RNAs (microRNAs, lncRNAs, circRNAs) in Adenomyosis: A Systematic Review of Mechanistic and Translational Evidence.

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ABSTRACT

Adenomyosis (AM) is a hormonally responsive uterine disorder defined by ectopic endometrial tissue within the myometrium, causing pain, abnormal bleeding, and subfertility. Non-coding RNAs (ncRNAs)-including microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs)-are post-transcriptional regulators implicated also in uterine remodeling. We systematically reviewed original studies evaluating ncRNAs in AM using human samples, in vitro and animal models, or bioinformatic approaches. Data sources included PubMed and Google Scholar (inception up to 10 August 2025). Forty-one studies were included and synthesized across mechanistic, diagnostic, and translational domains. miRNAs (n = 31) were the most studied subclass, followed by lncRNAs (n = 10) and circRNAs (n = 5). Recurrent miRNAs such as miR-10b and miR-30c-5p (downregulated, inhibitory) and miR-145 (upregulated, promotive) regulate epithelial invasion, epithelial-mesenchymal transition, and cytoskeletal remodeling via PI3K-AKT/MAPK and Talin1 signaling. The let-7a/LIN28B axis governed estrogen-sensitive proliferation in the junctional zone, while miR-21 exhibited compartment-specific roles in decidualization and ectopic cell survival. Extracellular-vesicle (EV)-borne miRNAs (e.g., miR-92a-3p, miR-25-3p, miR-4669) contributed to immune polarization and show early diagnostic potential. lncRNAs and circRNAs acted via chromatin modifiers and ceRNA networks. Most findings remain at the discovery stage. Convergent dysregulation was observed in key signaling pathways, including JAK-STAT, Wnt/ β -catenin, and Hippo-YAP. ncRNAs regulate critical axes of invasion, proliferation, immune modulation, and hormonal response in AM. Targets with preliminary causal support-miR-10b/ZEB1, let-7a/LIN28B, and miR-145/Talin1-warrant further validation. Circulating miRNAs-especially in EVs-offer promise for non-invasive diagnosis.