Molecular Biology Research Communications 2026;15(2):131-132 DOI:10.22099/mbrc.2025.55165.2254

Letter to Editor MBRC Open Access

Observations and points of interest regarding bioinformatics predictions of miRNA targeting syncytin genes in endometriosis and miscarriage

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Dear Editor,

We read with great interest the recent published article entitled "Prediction of microRNAs affecting the syncytin-1 (HERV-W) and syncytin-2 (HERV-FRD) genes regulation in endometriosis and miscarriage" by Gholami-Barzoki et al. [1]. This study addresses an emerging and biologically significant topic at the intersection of retroviral-derived placental genes, reproductive pathologies, and bioinformatics-driven miRNA discovery. The investigation contributes important preliminary insights into the potential regulatory miRNAs influencing Syncytin-1 and Syncytin-2, which are central to trophoblast fusion and placental development.

A notable strength of this work is the systematic integration of multiple prediction platforms-TargetScan, DIANA microT-CDS, miRDB, and miRWalk. By employing a consensus-based approach and weighting miRNAs predicted across several tools, the authors increase the reliability of computational predictions, which is essential given the variability among algorithms. The study also provides a comprehensive description of bioinformatics workflows, including seed pairing, conservation metrics, and context++ scoring, which enhances methodological transparency and reproducibility [1].

Another important contribution is the focus on HERV-derived Syncytin genes, which remain understudied in the context of endometriosis and miscarriage despite their well-established regulatory roles in trophoblast biology. The identification of miR-509-3p and miR-625-5p as shared candidates across platforms provides a valuable starting point for downstream functional investigations. The authors effectively contextualize these findings within the broader miRNA literature related to endometrial remodeling, EMT, trophoblast invasion, and recurrent pregnancy loss, thus highlighting the clinical significance of their predictions.

Despite its contributions, the study presents several limitations intrinsic to in silico research that merit consideration. The most important limitation is the absence of experimental validation. Although integrative prediction increases confidence, miRNA–mRNA interactions are highly context-dependent and require functional assays, such as luciferase reporter analysis, AGO-CLIP datasets, or miRNA overexpression/knockdown in trophoblast or endometrial cells to confirm specificity and regulatory impact. Without validation, it remains uncertain whether the identified miRNAs truly regulate Syncytin-1 or Syncytin-2 in biological systems.

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pISSN 2322-181X eISSN 2345-2005

Additionally, the study does not incorporate expression datasets or publicly available transcriptomic resources that could provide supportive evidence of miRNA dysregulation in endometriosis or miscarriage tissues. Integrating expression profiles with prediction algorithms would strengthen the biological relevance of candidate miRNAs.

Another limitation is the lack of structural or evolutionary analysis of Syncytin 3′ UTRs and coding regions. Since HERV-derived loci differ in conservation and regulatory architecture across human populations, UTR variability could influence miRNA binding site predictions [2]. A comparative genomics approach or haplotype-based analysis would have provided valuable context.

Finally, the study does not explore pathway-level implications of the predicted miRNAs. Given that both endometriosis and miscarriage involve complex interactions among decidualization, inflammation, EMT, and angiogenesis, enrichment analysis could have helped identify shared regulatory networks or revealed whether the predicted miRNAs converge on relevant biological pathways.

Overall, this article provides a thoughtful and methodologically sound computational framework for identifying candidate miRNAs that may regulate Syncytin-1 and Syncytin-2 in reproductive disorders. However, the conclusions should be interpreted cautiously until validated experimentally. Future work integrating expression data, functional assays, and pathway analysis will be essential for translating these predictions into clinically meaningful biomarkers or therapeutic targets.

Conflict of Interest: None

REFERENCES

1. Gholami-Barzoki M, Shatizadeh-Malekshahi S, Shayestehpour M, Soltanghoraee H. Prediction of microRNAs affecting the syncytin-1 (HERV-W) and syncytin-2 (HERV-FRD) genes regulation in endometriosis and miscarriage. Mol Biol Res Commun 2026;15:63-70.
2. She J, Du M, Xu Z, Jin Y, Li Y, Zhang D, Tao C, Chen J, Wang J, Yang E. The landscape of hervRNAs transcribed from human endogenous retroviruses across human body sites. Genome Biol 2022;23:231.