A comprehensive screening study in endometriosis reveals miR-193b-5p as a novel regulatory marker

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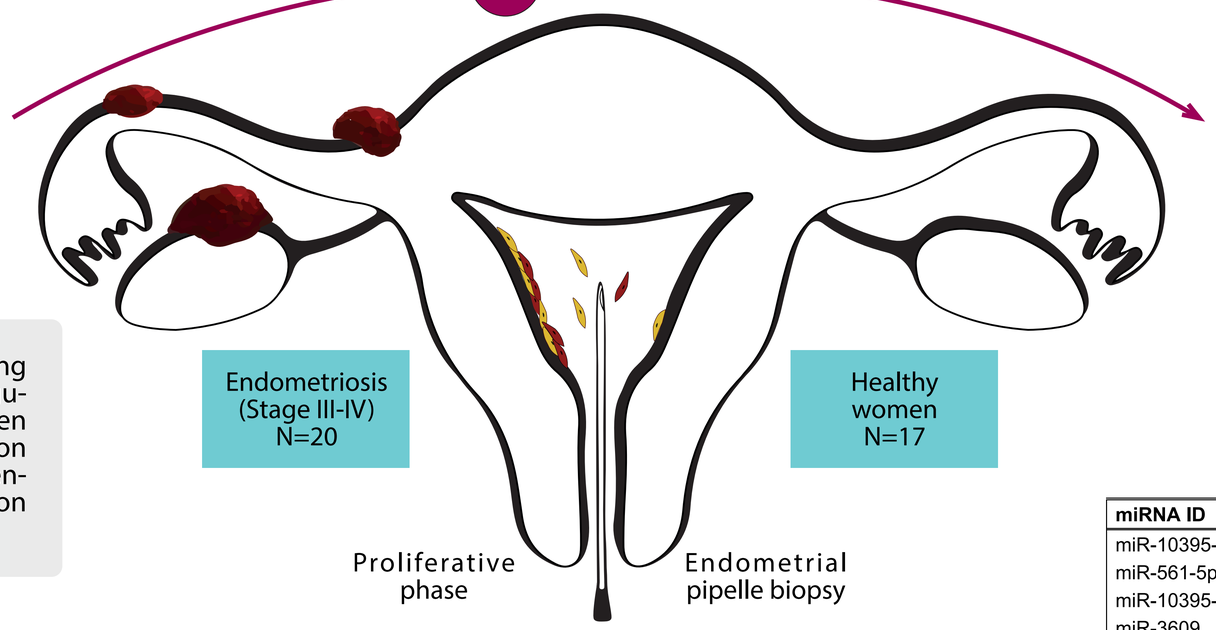
1 Introduction & Aim

The role of endometrial microRNAs in the pathogenesis of endometriosis is largely unknown. Our aim was to screen for dysregulated endometrial microRNAs in women with endometriosis and explore their function in-vitro.

2 Material



3 Methods

Dysregulated miRNAs were identified with small RNA sequencing and subsequent bioinformatic analyses. Target genes and pathways for the miRNAs were predicted using miRTarBase and gProfiler. A functional in-vitro study on migration was performed on selected miRNAs using a transwell migration assay on miRNA mimic transfected endometriotic 12Z cells.

4 Results

In total 15 miRNAs were dysregulated in women with endometriosis compared to controls (Table 1). We identified 23 enriched pathways related to endometriosis for the predicted miRNA target genes (Figure 1a). Target genes of miR-193b-5p, the top down miRNA, were enriched in focal adhesion and adherens junction signaling (Figure 1b). A marked decrease in cell migration from 901 cells per field to 488 cells (p-value 0.0021) was observed after 12Z cell mimic transfection of this miRNA (Figure 2). Thus, a down-regulation would cause an increase in migration.

miRNA ID	Fold change	
miR-10395-3p	2,4	↑
miR-561-5p	3,8	↑
miR-10395-5p	4,4	↑
miR-3609	4,2	↑
let-7d-3p	2,2	↑
miR-4497	4,9	↑
miR-7704	2,0	↑
miR-18b-5p	2,6	↑
miR-19a-3p	2,9	↑
miR-21-3p	2,0	↑
miR-374b-5p	3,6	↑
miR-136-5p	2,3	↑
miR-4516	3,5	↑
miR-193b-5p	-2,5	↓
miR-374c-3p	-3,2	↓
miR-320b	-2,0	↓

Table 1. Dysregulated miRNAs in women with endometriosis. Cut-off: fold change of -2< or >2 and adjusted p-value <0,05.

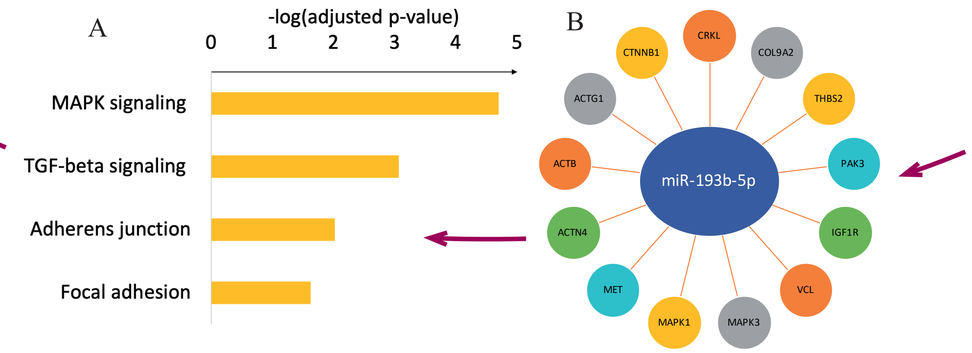


Figure 1. A) Selected significantly enriched KEGG biological pathways. B) Predicted target genes for miR-193b-5p enriched in focal adhesion and adherens junction signaling.

5 Conclusion

Our large screening dataset based on sequencing demonstrates that several microRNAs are dysregulated in the proliferative endometrium of women with endometriosis. Specifically, down-regulation of miR-193b-5p may increase cell migration of endometrial cells and thus could have an impact on the pathogenesis of the disease.

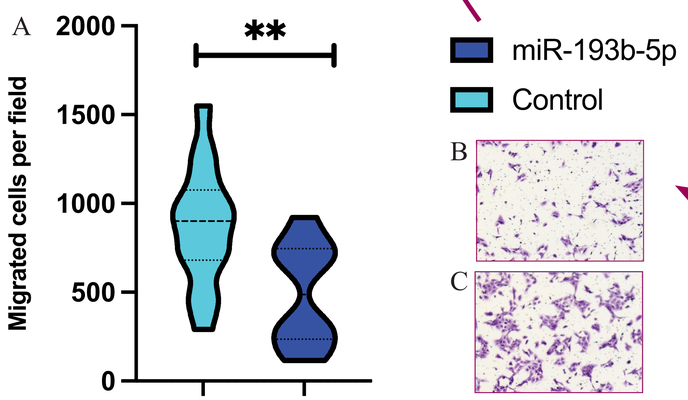


Figure 2. A) 12Z cell migration after miR-193b-5p mimic transfection compared to controls B-C) 5X images of the transwell membranes with the migrated mimic transfected cells (B) and control cells (C).

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