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**mir-126 rs4636297 and TGF β RI rs334348 functional gene variants are associated with susceptibility to endometriosis and its severity**

Neda Sepahi¹, Leila Kohan¹², Athar Rasekh Jahromi³, Yahya Daneshbod⁴, and Elahe Nimi Hoveidi¹

¹Department of Biology, Islamic Azad University, Arsanjan Branch, Arsanjan, Iran, ²Young Researchers and Elite Club, Islamic Azad University, Arsanjan Branch, Arsanjan, Iran, ³Department of Obstetrics and Gynecology, Jahrom University of Medical Sciences, Jahrom, Iran, and ⁴Department of Molecular Pathology, Shiraz Molecular Pathology Research Center, Daneshbod Lab, Shiraz, Iran

**Abstract**

microRNAs (miRNAs) are negative regulators in a variety of cellular processes that occur in endometriosis. Therefore, functional polymorphisms in miRNA and miRNA binding sites may affect gene expression and contribute to susceptibility of endometriosis. In this study, we evaluated the association of two miRNA related polymorphisms, mir-126 rs4636297 and TGF β RI rs334348, with endometriosis risk and its severity. This case-control study was done on 157 endometriosis patients and 252 healthy women as a control group. Tetra amplification refractory mutation system-polymerase chain reaction (tetra-ARMS PCR) was designed to determine the polymorphisms. Our finding showed significant differences in genotype frequency of mir-126 rs4636297 between the groups (χ² = 6.26, p = 0.044). A significant protection against endometriosis was found for mir-126 rs4636297 in allele (G versus A allele: OR = 0.695, 95% CI = 0.519-0.931, p = 0.015) and genotype (GG versus AA genotype: OR = 0.451, 95% CI = 0.233-0.873, p = 0.018). Significant association was also observed between the A allele and severity of endometriosis (OR = 0.478, 95% CI = 0.297-0.768, p = 0.002). Moreover, we found a significant association between AA genotype with the risk of endometriosis (OR = 0.493, 95% CI = 0.250-0.970, p = 0.041) and its severity (OR = 0.240, 95% CI = 0.065-0.883, p = 0.032) regarding
TGF β RI rs334348 polymorphism. These findings suggest that, for the first time, mir-126 rs4636297 and TGF β RI rs334348 polymorphisms may influence individual’s susceptibility to endometriosis and its severity.

Keywords
Endometriosis, mir-126, polymorphism, severity, TGF-β RI

mir-126 rs4636297 and TGF β RI rs334348 功能基因变异与子宫内膜异位症易感性及其严重程度相关

Neda Sepahi1, Leila Kohan1,2, Athar Rasekh Jahromi3, Yahya Daneshbod4, and Elahe Nimi Hoveidi1

1Department of Biology, Islamic Azad University, Arsanjan Branch, Arsanjan, Iran, 2Young Researchers and Elite Club, Islamic Azad University, Arsanjan Branch, Arsanjan, Iran, 3Department of Obstetrics and Gynecology, Jahrom University of Medical Sciences, Jahrom, Iran, and 4Department of Molecular Pathology, Shiraz Molecular Pathology Research Center, Daneshbod Lab, Shiraz, Iran

摘要
微小 RNAs (miRNAs) 是子宫内膜异位症发生过程中各种细胞进程的负调控因子。因此，miRNA 和 miRNA 结合位点的功能多态性可能影响基因表达，并增加子宫内膜异位症的易感性。本研究中，我们评估了两种多态性相关的 miRNA，即 mir-126 rs4636297 和 TGF β RI rs334348，与子宫内膜异位症风险及其严重程度的关联性。该病例对照试验研究了157例内异症患者和252名健康女性作为对照组。多态性检测采用四引物扩增受阻突变体系-多聚酶链式反应 (tetra-ARMS PCR)。我们的研究显示两组 mir-126 rs4636297 的基因型频率有显著差异 ($\chi^2=6.26$, $p=0.044$)。mir-126 rs4636297 的等位基因 (等位基因 G vs A: OR=0.695, 95% CI=0.519-0.931, $p=0.015$) 和基因型 (基因型 GG vs AA: OR=0.451, 95% CI=0.233-0.873, $p=0.018$) 被发现对内异症有显著的保护作用。等位基因 A 与内异症的严重性有显著相关性 (OR=0.478, 95% CI=0.297-0.768, $p=0.002$)。此外，关于 TGF β RI rs334348 的多态性，我们发现基因型 AA 与内异症风险 (OR=0.493, 95% CI=0.250-0.970, $p=0.041$) 及其严重性 (OR=0.240, 95% CI=0.065-0.883, $p=0.032$) 有显著相关性。这些发现提示，mir-126 rs4636297 和 TGF β RI rs334348 的多态性可能影响内异症的个体易感性及其严重性。

关键词
内异症，mir-126，多态性，严重性，TGF-β RI