

**Original Article**

## Screening of Exons 4-9 Polymorphisms of *FTO* Gene in Endometrial and Ovarian Cancers

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### Abstract

Endometrial and ovarian tumours are almost mechanistically affected by reproductive hormones. Ovarian cancer may be explained as metastatic or synchronous primary ovarian cancer, and the specific diagnosis is a challenge. This study aimed to investigate the mutations in fat mass and obesity-associated (*FTO*) genes and investigated the association of these mutations with the risk of endometrial and ovarian cancers as well as with cancer grade and stage. Blood samples were collected from 48 endometrial and ovarian cancer cases and 48 healthy women. Genomic DNA was extracted, and PCR was done to amplify *FTO* exons 4-9. Sanger sequencing identified 6 different novel mutations submitted to DDBJ: p.W278G and p.G284G in exon 4, p.S318I and p.A324G in exon 5 and two mutations in intron 4. Other mutations were also detected in *FTO* gene sequencing results, rs112997407 in intron 3, rs62033438, rs62033439, rs8048254 and rs8046502 in intron 4. The novel p.W278G, p.S318I and p.A324G mutations were predicted to be damaging. We did not find a significant association for all variables with cancer risk or clinical stage and grade except for rs62033438 variants, which showed a significant association with cancer grade, especially AA genotype (OR= 15, 95% CI:1.32 -169.88, P= 0.03). In conclusion, the statistical analysis did not clarify whether *FTO* mutations are implicated in cancer. Further studies with more samples are recommended to provide a more accurate picture of the correlation between *FTO* mutations and endometrial and ovarian cancer susceptibility.

**Keywords:** Screening, *FTO*, Endometrial cancer, Ovarian cancer

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### 1. Introduction

Endometrial and ovarian tumours are almost mechanistically affected by reproductive hormones. Ovarian cancer may be explained as metastatic or synchronous primary ovarian cancer, and the specific diagnosis is a challenge (1). The study of genetic predisposition has become one of the priorities of scientific research interested in knowing the causes of cancer spread in the world in general and in Iraq in particular (2).

Fat mass and obesity-associated (*FTO*) gene is the first gene that has been proven to be associated with

obesity (3). *FTO* protein is an AlkB-like 2-oxoglutarate—dependent nucleic acid demethylase, 3-methyl thymidine and 3-methyl uracil in nuclear acids, which are its specified substrates (4). It favours single-stranded nuclear acids, hence methylated RNA instead of DNA. N6-methyladenosine in mRNA is the molecular target of *FTO* (5).

*FTO* was described as the first N 6 -methyladenosine (m6A) demethylase of eukaryotic messenger RNA (mRNA), and the roles of *FTO* in adipogenesis and tumorigenesis have been associated with its m6A demethylase activity (6). The functions of m6A