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GENETICS

Association of *WNT4* polymorphisms with endometriosis in infertile patients

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Abstract
Purpose Recently, several genome-wide association studies have demonstrated an association between endometriosis and markers located in or near to *WNT4* gene. In order to assess the validity of the findings, we conducted a replication case–control study in a Brazilian population.
Methods Genetic association study comprising 400 infertile women with endometriosis and 400 fertile women as controls. TaqMan allelic discrimination technique was used to investigate the relationship between endometriosis and four single-nucleotide polymorphisms (rs16826658, rs3820282, rs2235529, and rs7521902) in *WNT4* gene. Genotype distribution, allele frequency, and haplotype analysis of the *WNT4* polymorphisms were performed. A p value <0.05 was considered significant.
Results The results revealed a significant association of rs16826658 (p=7e-04) and rs3820282 (p=0.048) single-nucleotide polymorphisms (SNPs) on *WNT4* gene with endometriosis-related infertility, while rs2235529 and rs7521902 SNPs showed no difference between cases and controls.
Conclusions Our results suggested that rs16826658 and rs3820282 polymorphisms on *WNT4* gene might be involved in the pathogenesis of endometriosis in the infertile women studied. Analysis of *WNT4* genetic variants might help to identify patients at high risk for disease development.

Keywords Endometriosis · *WNT4* gene · Polymorphism · Infertility

Capsule Analysis of *WNT4* gene identified rs16826658 and rs3820282 polymorphisms involved in the pathogenesis of endometriosis in Brazilian infertile women.

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Introduction

WNT family is a large group of secreted glycoproteins encoded by 19 distinct genes involved in the WNT signaling pathway [1]. WNT-mediated signal transduction pathways direct the specific activation of sets of genes regulating several cellular responses such as cell growth, differentiation, movement, migration, polarity, cell survival, and immune response [2].

A member of the WNT family, encoded by *WNT* located on chromosome 1p36.23-p35.1 (OMIM#603490), WNT is classified as a noncanonical protein [3] that plays an important role on the development of the female reproductive tract [4] and steroidogenesis [5]. According to Jordan et al. (2001) [6], WNT4 is the first signaling molecule which affects the cascade of events that culminates in sex determination, through local secretion of growth factors.