

Catechol-O-

Methyltransferase

1. 1. 1. 1. 2. 1. 1

Association of the COMT Gene Polymorphism with the Risk of Endometriosis in Korean Women

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Objective: To investigate whether polymorphism of gene encoding COMT is associated with the risk of endometriosis in Korean women.

Methods: We investigated 136 patients with histopathologically confirmed endometriosis rAFS stage III/IV and 251 control group women who were surgically proven to have no endometriosis. Polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) of PCR products were done to determine each participant's COMT genotype.

Results: The distribution according to *NlaIII* genetic polymorphisms of COMT were as follows. COMT^{HH}, COMT^{HL}, and COMT^{LL} genotypes were 56.6% (77 women), 34.6% (47 women) and 8.8% (12 women) in the study group and 50.6% (127 women), 39.4% (99 women) and 10.0% (25 women) in the control group. There was no significant difference between the study group and the control group.

Conclusion: The results suggest that COMT genetic polymorphism may not be associated with the development of endometriosis in Korean women.

Key Words: Endometriosis, Genetic polymorphism, COMT, *NlaIII*

1940
 가 7~10% 가
 7 가 2
 75%

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 * 2003

3 가 , COMT가

가 .

가 , COMT

4 , (estrogen receptor, ER) COMT^L allele 가

5 Catechol-*O*-methyltransferase (COMT) 가

COMT isoform, 가 (soluble form, S-COMT) (membrane-bound form, MB-COMT) allele 가

19 22q encoding ,⁶ MB-COMT *N*-terminal 50 COMT^L allele

가 S- COMT ,²⁰ , Palmatier 1999 , 가

2 2-and 4-hydroxylated estrogens COMT ²¹ COMT

O-methylation COMT

NlaIII *NlaIII* , COMT 가

COMT (COMT^{LL}), (COMT^{HL}), (COMT^{HH}) , COMT methylation 60~75%⁸ , COMT exon 4

guanine alanine missense mutation 1. , MB-COMT 158 codon S-COMT

108 codon valine methionine 1996 9 2003 8 , COMT^L allele COMT^L가

COMT 가 3~4⁹ revised American Fertility Society catecholestrogen 가¹⁰ (rAFS, 1985) III IV 136

COMT

11,12 251

13 , 14 , 15 , 16 17

2.

genomic DNA QIA amp blood kit (QIAGEN Inc., USA)

DNA 260 nm 280 nm

1.7~1.9 . Catechol-0-methyltransferase (COMT)

primer 5'-TAC TGT GGC TAC TCA GCT GTG C-3'(F) 5'-GTG AAC GTG GTG TGA ACA CC-3'(R) . 0.1 µg genomic DNA 10 pmol/ml primers, 5 mmol/ml dNTP, 0.5 Units Taq polymerase (Takara rTaq), 200 mmol/ml Tris-HCl (pH 8.3), 500 mmol/ml KCl 30 mmol/ml MgCl₂ 20 µl PCR 가 94 5 , 94 30 denaturation, 56 30 annealing, 72 30 extension 35 72 7 elonga- tion . (Polymerase Chain Reaction) DNA *NlaIII* (New England Biolabs Inc.) (Restriction Fragment Length Polymorphism) . 10U/µl incubation 40 mmol/ml Tris-HCl (pH 8.3), 100 mmol/ml KCl, 20 mmol/ml MgCl₂, DTT 2 mmol/ml (pH 7.9) 37 3 incubation . PCR ethidium bromide가 2.8% 가 UV . 114 bp band allele *NlaIII* restri-

ction site가 homozygous HH
96 bp 18 bp band *NlaIII* restriction site가 allele homozygous (L/L) .
114 bp 96 bp, 18 bp band가 *NlaIII* restriction site가 allele heterozygous (H/L) .

3.

SPSS version 11.0
x² test logistic regression
analysis , p 0.05

31.7 (18~
41) , 33.1 (22~42)
. COMT

NlaIII PCR-RFLP
Fig. 1
, COMT^{HH} 204 (52.7%), COMT^{HL}
146 (37.7%), COMT^{LL} 37 (9.6%)

(Table 1).^{20,22,23} , COMT
NlaIII HH 가 , HL, LL
LL 10% .
(56.6%), 47 (34.6%), 12 (8.8%) , COMT
Nla 가

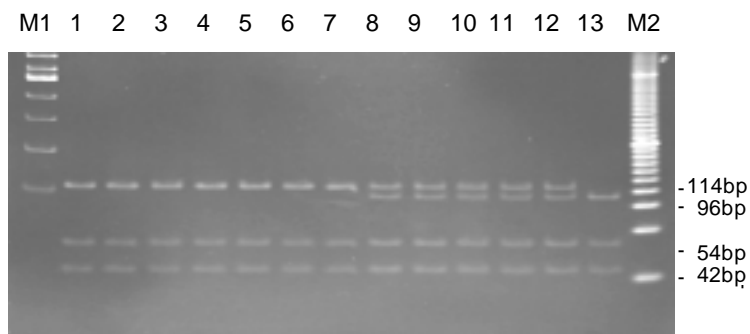


Figure 1. Electrophoresis of the products of PCR. for COMT *NlaIII*. individuals homozygous for the COMT *NlaIII* polymorphism (lanes 13, LL), heterozygous for the polymorphism (lanes 8-12, HL) and without polymorphism (lanes 1-7, HH). M1 = 100bp DNA marker, M2 = 20bp DNA marker

Table 1. Comparison of the distribution of genotyping for COMT *NlaIII*

	Lee (2004) Korean (n=387)	Park (2002) ²² Korean (n=206)	Yim (2001) ²⁰ Korean (n=326)	Wu (2003) ²³ Chinese (n=377)
HH	204 (52.7%)	124 (60.2%)	182 (55.8%)	203 (53.8%)
HL	146 (37.7%)	67 (12.5%)	125 (38.4%)	145 (38.5%)
LL	37 (9.6%)	15 (7.3%)	19 (5.8%)	29 (7.7%)
HL, LL	183 (47.3%)	82 (39.8%)	144 (44.2%)	174 (46.2%)

Table 2. The distribution of genotyping for COMT *NlaIII*

Polymorphism	Case (n=136)	Control (n=251)	Total (n=387)	Odds ratio	95% of confidence interval	P
COMT						
HH	77 (56.6%)	127 (50.6%)	204 (52.7%)	1		
HL	47 (34.6%)	99 (39.4%)	146 (37.7%)	1.305	0.832-2.046	0.258
LL	12 (8.8%)	25 (10.0%)	37 (9.6%)	1.263	0.600-2.659	0.394
Polymorphism	Case (n=136)	Control (n=251)	Tota (n=387)	Odds ratio	95% of confidence interval	P
COMT						
HH	77 (56.6%)	127 (50.6%)	204 (52.7%)	1		
HL, LL	59 (43.4%)	124 (49.4%)	183 (47.3%)	0.809	0.532-1.230	0.838

43.4% (59) , 49.4% ,
 (124) . COMT^L allele
 odds ratio
 0.809 (95% CI, 0.532~1.230) , 가
 COMT *NlaIII* 가²⁴
 가 (Table 2). CYP17,
 CYP19 17 -hydroxysteroid dehydrogenase (17 -
 HSD) 가
 가 가 CYPs
 2-hydroxylation
^{25,26}
 CYP1A2, 3A3 3A4
 CYP1A1
 가 ,
 4-hydroxylation
 CYP1B1^{25,26}

, 4-hydroxyestradiol 2-hydroxyestradiol

^{36,37}

²⁷ 2-, 4-hydroxylated estrogen COMT
O-methylation ^{25,28}
2-hydroxyestradiol

³⁸ N-acetyltransferase-2 (NAT-2)

O-methylation ²⁹

⁴⁰

, CYP1A1, CYP1B1, COMT

가

estrogen receptor

³⁰⁻³³

, COMT

COMT

COMT

가

가 ³⁴
가

COMT

가

가

가 ³⁵

가

가 ³⁰
, GST (Glutathione S-transferase)

GSTM1, GSTT1, GSTP1

GSTM1 GSTT1

CYP1A1 *MspI*

, CYP1A1 (*MspI*)

mutant allele GSTM1

GSTT1

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