

양극성 장애 환자에서 CTLA-4 유전자 다형성

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Polymorphism of CTLA-4 Gene in Patients with Bipolar Disorder

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ABSTRACT

Objective : Bipolar disorder is known to have strong genetic background and cellular immune activation. Based on the hypothesis that abnormalities of normal inhibitory control of T cell immunity can contribute to the pathophysiology of bipolar disorder, we investigated the relationship between the first exon at position +49(A/G) polymorphism of cytotoxic T lymphocyte antigen 4(CTLA4) gene and bipolar disorder.

Method : Among the Korean patients diagnosed as bipolar disorder according to DSM - , 90 patients without serious medical illness, neurologic illness, hormonal disorder, or concomitant mental illness were selected. The normal control group consisted of 149 age - and sex - matched subjects without current or past history of autoimmune diseases or mental disorder. DNA was extracted from whole blood and the exon 1 region of CTLA - 4 gene was amplified by polymerase chain reaction. Gene typing was performed using single strand conformation polymorphism.

Results : There were no significant differences in genotype frequencies of G/G, G/A, and A/A between the patients with bipolar disorder and the control group(48.9% vs 46.3%, 44.4% vs 39.6%, and 6.7% vs 14.1%, respectively). There were no significant differences in allelic frequencies of G and A between the patients with bipolar disorder and the control group(71.1% vs 66.1%, and 28.9% vs 33.9%, respectively).

Conclusion : This study did not show the association of exon 1 polymorphism of CTLA - 4 gene with bipolar disorder.

KEY WORDS : CTLA - 4 · Polymorphism · Bipolar disorder.

서 론

1% 6.5%

1-4)

*가

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가 가 alanine

가 ⁵⁾ , CTLA - 4
가

가 ⁶⁾ CTLA - 4 exon 1 +49

가 ⁷⁾⁸⁾ - 2
(soluble interleukin - 2 receptor : sIL - 2R) sIL -
6R 가 phytohemagglutinin

⁹⁾¹⁰⁾ Cytotoxic T lymphocyte antigen - 4(CTLA - 4)
T (cell
surface molecule) , (antigen - prese-
nting cell) B7 ¹¹⁾
CTLA - 4 B7 가 T
(negative signal) , ¹²⁾ T
CTLA - 4
T (negative regulation) T
(homeostasis) ¹³⁾¹⁴⁾ , CTLA - 4가 T

가
CTLA - 4
2q33 가 ¹⁵⁻¹⁸⁾
Graves ¹⁹⁾ ²⁰⁾²¹⁾
CTLA - 4
exon 1 +49(A/G)
가 (systemic ²²⁾²³⁾
lupus erythematosus)
exon 1 +49 A/G threonine

연구 대상 및 방법

1. 연구 대상

가
DSM - ²⁴⁾
1 90
149

2. CTLA-4 유전자 형질분석

1) DNA 추출

(Becton Dickin-
son Vacutainer System, USA) 10ml
Proteinase K가
DNA

2) Polymerase chain reaction(PCR)

CTLA - 4 exon 1 +49 A/G
2ul DNA 10X buffer
(500mM KCl, 100mM Tris - HC1 pH 8.3, 15mM
MgCl₂) 2ul, 20uM oligonucleotide primers(5' - GCT
CTA CTT CCT GAA GAC CT - 3' , 5' - AGT CTC
ACT CAC CTT TGC AG - 3') 2ul, 2mM dNTP
2ul, Taq DNA polymerase(5U/ul : Boehringer Man-
nheim, Germany) 0.2ul D/W 가
20ul Thermal cycler(Ge-
neAmp PCR System 9600, Perkin Elmer, Foster
City, USA) 94 4 , 94 45
(denaturation), 62 45

(annealing), 72 45 (elongation)
35

(power) 0.05

3) Single strand conformation polymorphism (SSCP)

13% (w=0.13)
(power=0.80) ²⁶⁾

PCR (single strand)
DNA 95 5 4
stop buffer(95% formamide : 10mM
NaOH : 0.25% bromophenol blue and 0.25% xylene
cyanol) , 14 4W
MDE™ gel(BioWhittaker Molecular Applications,
Rockland, NY, USA)
silver stain DNA (1).

결 과

($\chi^2=0.59$, p=
($\chi^2=2.03$, p=
0.74)
0.36) Hardy - Weinberg
가

3. 통계 분석

1) SAS/PC version 14.1%)(1).
6.0

CTLA - 4
G/G, G/A A/A 가
(48.9% 46.3%, 44.4% 39.6%, 6.7%

2) 0.05

CTLA - 4
G A 가 (,
71.1% 66.1%, 28.9% 33.9%)(1).

고 찰

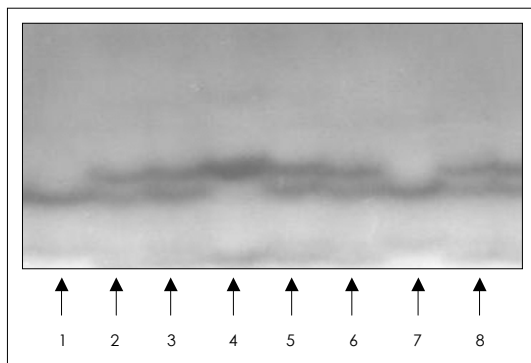


Fig. 1. The SSCP finding of the CTLA-4(A/G)dimorphism :
Lanes 1 and 7 : CTLA-4*G/G ; Lanes 2, 3, 5, 6 and
8 : CTLA-4*G/A ; Lane 4 : CTLA-4*A/A.

Table 1. Frequencies of the genotypes and alleles of the CTLA-4 gene

Group	Genotypes ^a			Alleles ^b	
	G/G n(%)	G/A n(%)	A/A n(%)	G n(%)	A n(%)
Patients (n=90)	44(48.9)	40(44.4)	6(6.7)	128(71.1)	52(28.9)
Controls (n=149)	69(46.3)	59(39.6)	21(14.1)	197(66.1)	101(33.9)

^a: $\chi^2=3.14$, d.f.=2, p=0.208
^b: $\chi^2=1.29$, d.f.=1, p=0.256

CTLA - 4 exon 3 3 - untranslated re-
gion 642 (AT)n ¹⁷⁾ exon
1 +49(A/G) ¹⁸⁾
(promoter) - 318(C/T) ¹⁶⁾
가
CTLA - 4 ²²⁾²³⁾ Grave's
disease, ¹⁹⁾ ²⁰⁾²¹⁾

CTLA - 4
CTLA - 4 exon 1(+49)
가
CTLA - 4 (as-
sociation) 가
CTLA - 4
CTLA - 4 ²⁷⁾²⁸⁾
CTLA - 4 ²⁷⁾

중심 단어 : CTLA - 4

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가
가
T
29)
CTLA - 4
가
가
가
30)
interferon -
(mitogenic) 31)
가
32)
(negative immune regulation)
가
CTLA - 4
가
가
(w=0.13)
(odds ratio) 1.83
(0.80)
13%
CTLA - 4 exon 1
가
CTLA - 4 exon 1

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