

## 정신과의 분자생물학 적용\*

최 인 근\*\*†

## Molecular Application in Psychiatry\*

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## ABSTRACT

The development of molecular biology has brought many changes in psychiatry. Molecular biology makes us possible to know the cause of mental disorders that provide the way to prevent the disorders, and to develop various accurate diagnostic and treatment methods for mental disorders. The author discusses the concept, cause, and treatment of mental disorders in the aspect of molecular biology. Importing the methods of molecular biology into psychiatry, we can anticipate to get a number of the goals of psychiatric genetics, including identification of specific susceptibility genes, clarification of the pathophysiological processes whereby these genes lead to symptoms, establishment of epigenetic factors that interact with these genes to produce disease, validation of nosological boundaries that more closely reflect the actions of these genes, and development of effective preventive and therapeutic interventions based on genetic counseling, gene therapy, and modification of permissive or protective environmental influences. In addition to their capacity to accelerate the discovery of new molecules participating in the nervous system's response to disease or to self-administered drugs, molecular biological strategies can also be used to determine how critical a particular gene product may be in mediating a cellular event with behavioral importance. Molecular biology probably enables us discover the environmental factors of mental disorders and allow rational drug design and gene therapies for mental disorders, by isolation of gene products that facilitate a basic understanding of the pathogenesis of these disorders. A specific genetic linkage may suggest a novel class of drugs that has not yet been tried. With respect to gene therapy, the hypothetical method would use a gene delivery system, most likely a modified virus, to insert a functional copy of a mutant gene into those brain cells that require the gene for normal function.

**KEY WORDS** : Molecular biology · Psychiatry · Implication · Mental disorder · Etiology · Treatment.

서 론(Before molecular psychiatry)

(pa-

가 . ttern) . 가

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가 ( ) 가 , DNA RNA mRNA 가 mRNA mRNA ( ) . 1980 DNA (Restriction Fragment Length Polymorphisms ; RFLPs) 가 가 가 가 RFLPs 50% dinucleotide (microsatellite marker)가 . 가

(McGuffin 2000). 1. Animal models of human disorders (homologous) 가 genome . 85% 가 genome transgenic . Transgenic 가 (Faraone 1999).

genome 6 가 가 , variable number of tandem repeats(VNTRs) tandemly repeated DNA ( ) (Knowles 1999). 가 PCR clone (McGuffin 2000).

ob leptin leptin (Kaplan & Sadock 1998).

Alzheimer 21 APP (McGuffin 2000). (Faraone 1999). Southern blotting DNA oligonucleotide (hybridization) DNA PCR (McGuffin 2000).

Calcium - calmodulin kinase II(CaMKII) . CaMKII 가 5 - HT<sub>1B</sub> 가 가 5 - HT<sub>1C</sub> 가 (MAO<sub>B</sub>)가 B barrel 가 fosB가 (Kaplan & Sadock 1998).

가 (Coyle & Hyman 1999). mRNA RNA Northern blotting ISHH(In situ hybridization histochemistry)

### 정신 장애의 분자생물학적 원인

50% , Tourette 99%,

70% . Tourette  
 10% 가 가 . ,  
 Tourette D<sub>2</sub> ,  
 가 (hydroxylase)  
 (Kaplan & Sadock 1998).

Alzheimer Alzheimer  
 CYP2D6 가  
 가 (Faraone 1999).  
 (retinoblastoma) 13  
 (RB1)가

hit)  
 '가  
 (stem cell)가  
 가 (Cooper 1996).  
 1. 정신분열병  
 5, 6, 8, 22 가  
 (Knowles 1999).  
 15 가  
 (HLA) DRB1\*04  
 가  
 (Kaplan & Sadock 1998).  
 (heterogeneity) 가 5  
 D5S393 pairwise lod 3.04  
 6 HLA (telomeric)  
 D6S296 lod 3.51  
 8 , 13 , 22  
 가 (ETD) P50 (auditoryevoked)  
 D6S271 15q13 - 14  
 3.51, 5.3 lod (Knowles  
 1999).

2. 기분(정동) 장애  
 Amish 11p15  
 가 RFLP DNA 가  
 Xq28  
 lod 가 7.52 - 9.17 가  
 Xq24 - q27.1  
 18, 21q, 4p, 12q 가

가 가  
 (genetic anticipation) (Kno-  
 wles 1999).

3. 불안 장애  
 가  
 (Knowles 1999).  
 (transporter) (Ka-  
 plan & Sadock 1998), Catechol - O -  
 methyltransferase(COMT)  
 (Knowles 1999).

4. 알코올리즘  
 D<sub>2</sub>  
 (DRD<sub>2</sub>) Taq A1 가  
 (Knowles  
 1999).

5. 자살과 충동적 행동  
 가  
 (tryptophan hydroxylase ; TPH)  
 (intron) 가 가  
 , " L " ,  
 5 - HIAA TPH  
 Brunner 's (X - linked  
 ) 가 A(MAO<sub>A</sub>) 936  
 가 MAO<sub>A</sub>  
 (Knowles 1999).

6. 성격 장애와 양적 행동 특성(Quantitative behavioral traits)  
 Novelty seeking 가 D<sub>4</sub> (DRD<sub>4</sub>)  
 3 exon 7 . DRD<sub>4</sub>  
 가 novelty seeking 3 4%  
 , novelty seeking 40% 가  
 DRD<sub>4</sub> 가 novelty see -  
 king 10% . Harm avoidance

8p21 - 23, 21q21 - 22.1, 11 20  
가

### 정신 장애의 분자생물학적 치료

(Knowles 1999).

#### 7. Alzheimer 질병 등 Alzheimer

. Alzheimer  
10% , 90%  
가 Alzheimer (FAD) PS1, PS2, APP  
. 14 가  
presenilin 1(PS1) 40 50  
70 80% , 1  
presenilin 2(PS2) 50  
20 30% , 2 3%  
21 ( APP)  
50 (Kaplan &

Sadock 1998). 가 가  
(APP) (amy -  
loid) (Knowles 1999).  
Alzheimer

19q13.2  
APOE Alzheimer  
(Knowles 1999).  
tau apo (apolipoprotein E)  
, 19 apo  
가 가 2 tau , /  
4 4/ 4 가

60 Alzheimer  
10 50% (Kaplan & Sa -  
dock 1998). Alzheimer APOE  
4 0.50 0.16  
. 4 FAD Gi  
7 9 (Knowles 1999).

Alzheimer PS1 in -  
tron 가 , 1 - anti -  
chymotrypsin APOE  
Alzheimer ,  
Alzheimer 70% cytochrome c  
CO1 CO2 가  
(Knowles 1999). , Alzheimer  
50% (Kaplan & Sadock

1998).  
Williams LIM kinase - 1  
(Kaplan & Sadock 1998).

“ - ”  
(Cooper 1996). 가,  
(Kaplan & Sadock 1998).

#### 1. 항정신병 약물

- adrenergic adenylyate cyclase  
cyclic AMP , norepinephrine  
cyclic AMP  
- adrenergic propranolol cyclic AMP  
, phenothiazine  
cyclic AMP  
, phenothiazines  
, haloperidol cyclic AMP  
(Coyle & Hyman 1999).

가  
adenylyate  
cyclase D<sub>1</sub> ,  
D<sub>2</sub> . D<sub>2</sub>  
adenylyate cyclase K<sup>+</sup>  
. D<sub>2</sub>

D<sub>3</sub>, D<sub>4</sub>  
clozapine D<sub>2</sub>  
D<sub>4</sub> . Clozapine  
D<sub>2</sub> clozapine  
D<sub>2</sub>  
“ ”  
(Coyle & Hyman 1999).  
clozapine  
HLA B38, DR4 DQW3  
(Knowles 1999).  
가 가

결 론(After molecular psychiatry)

(Coyle & Hyman 1999).

2. 항우울제

nortriptyline  
 . MAO phenelzine (epigenetic)  
 N - acetyl - transf - (permissive)  
 erase (Knowles 1999).  
 가 - ad - (Knowles 1999).  
 renergic 가 . - adrenergic  
 cyclic AMP kinase  
 kinase 가 - 가 (Cooper 1996).  
 가 noradrenergic  
 kinase 가 (Knowles 1999).  
 (linkage)  
 2 - adrenergic 5 - HT<sub>2</sub>  
 (Coyle & Hyman 1999).

3. 리티움

G - (Kaplan & Sadock 1998).  
 inositol inositol phosphatase  
 inositol phosphatidylinositol biphosp - 중심 단어 :  
 hate(PIP<sub>2</sub>) , PIP<sub>2</sub>  
 phosphatidylinositol 가 G -  
 adenylylate cyclase  
 (Coyle & Hyman 1999).

4. 항불안제

Benzodiazepines GABA<sub>A</sub> GABA  
 가 Cl<sup>-</sup> . Barbitu -  
 rates ethanol GABA<sub>A</sub> GABA  
 가 Cl<sup>-</sup> , barbi -  
 turates ethanol GABA가 Cl<sup>-</sup>  
 ethanol  
 glutamate  
 ethanol  
 (Coyle & Hyman 1999).

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