

S-9 [16:10-16:40]

Diagnosis of Alzheimer's disease
through measurement of anti-beta
amyloid antibody in patient's serum

Dr. Young Ho Kim
(*Digitalbiotech, Inc.*)

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Diagnosis of Alzheimer's disease through measurement of anti-beta amyloid antibody in patient's serum

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Abstract

Amyloid beta (A β) is believed one of the major pathogens of Alzheimer's disease (AD), and the reduction of A β is considered a primary therapeutic target. Immunization with A β can reduce A β burden and pathological features in transgenic AD model mouse. This means anti-A β autoantibodies may have a role in AD pathology. Recent findings suggest anti-A β autoantibodies level decrease in AD patients. The early detection of AD is important for treatment of this disease. However, diagnosis on AD has only been possible through limited methods such as neuropsychological examination or MRI. To investigate whether it was possible to detect the presence and different levels of naturally occurring anti-A β autoantibodies in the plasma of patients with AD and age-matched controls. An advanced ELISA was performed to detect levels of naturally occurring anti-A β autoantibodies in the plasma. The level of anti-A β auto-antibodies from patients with idiopathic Parkinson's disease or stroke and from normal controls were compared to that of AD patients. Our results showed a significantly lower anti-A β autoantibodies level in AD compared to those with other neurological diseases or control. The level of anti-A β autoantibodies in the serum may be used to diagnose the presence of AD.

Diagnosis of Alzheimer's disease through measurement of anti-A β autoantibodies in serum

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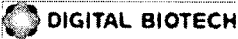


Unmet needs of Alzheimer's disease

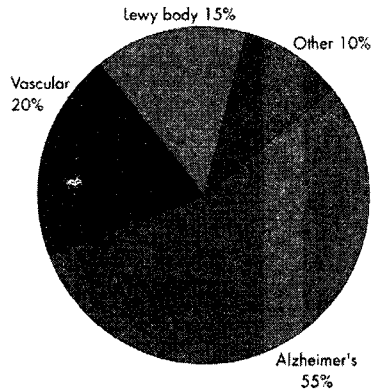
- Increase AD patients with high age society
- no curable medicine ever developed

Disease	no. of patients	medical expenses/year
Alzheimer's	5,000,000	100 billion dollar
Parkinson	1,000,000	5 - 10 billion dollar
stroke	3,000,000	50 billion dollar
spinal injury	500,000	5 billion dollar
schizophrenia	1,500,000	40 billion dollar

(ref: NIH, Voluntary Organization, 1990, 1997, USA; NINDS Congressional Report 2001)



Dementia and Alzheimer's disease



No. of AD patients

USA	4M
World	1.5M

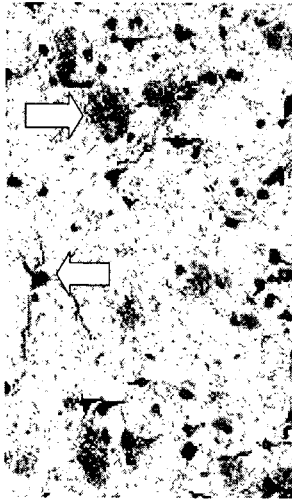
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Genes associated with Alzheimer's disease

Disease Onset	Gene Product	Chromosome
Early	Amyloid precursor protein (APP)	21
	Presenilin 1 (PS1)	14
	Presenilin 2 (PS2)	1
Late	Apolipoprotein E	19
	LDL receptor-related protein (LRP)	12
	α_2 -Macroglobulin (α_2 M)	12
	FE65	11
	Chromosome 12 gene product distinct from LRP and α_2 M	12
	Chromosomal loci	10

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Neuropathology of AD



❖ Neuritic plaques
beta amyloid

❖ Neurofibrillary tangles
tau protein



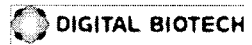
Clinical diagnosis of AD

Imaging from
MRI



normal

Alzheimer



Clinical diagnosis of AD

Biological markers

blood / CSF

Molecular diagnosis - APP, PS1, PS2, ApoE e4.

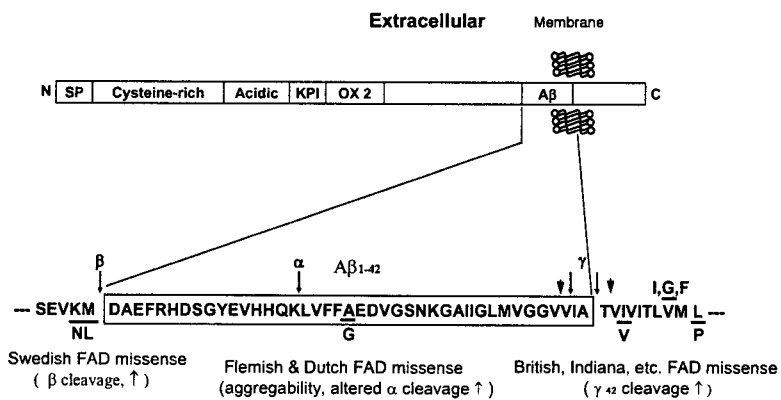
Blood test - beta amyloid, Tau protein.

CSF test - beta amyloid, Tau protein, Neuronal thread protein

Others - skin amyloid, Tropicamide, Olfactory biopsy

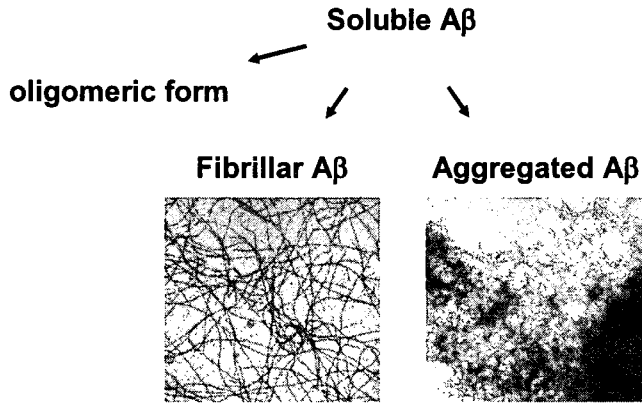


Schematic structure of APP



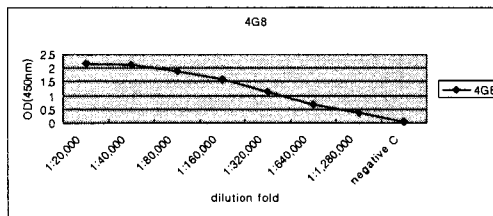
Beta amyloid as causative reagent for AD

Different forms of A β

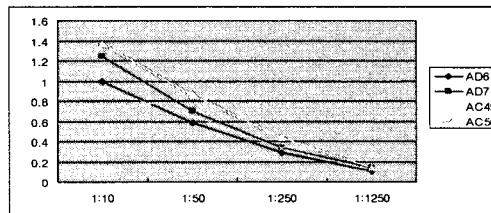


Development of an advanced ELISA test

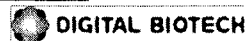
Determination of standard material (comparison mouse Mab vs. human serum)



<mouse monoclonal>

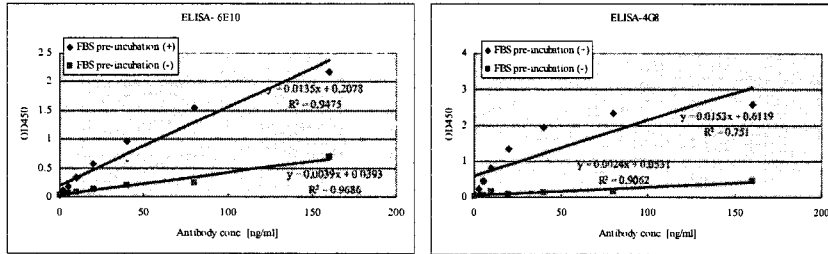


<human serum>



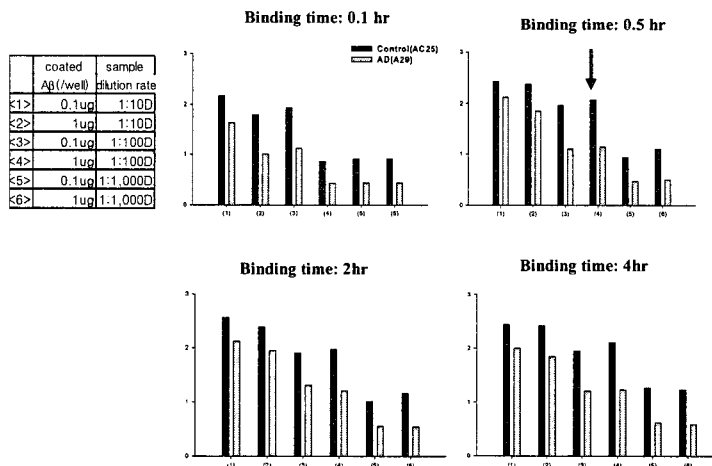
Development of an advanced ELISA test

Determination of standard material



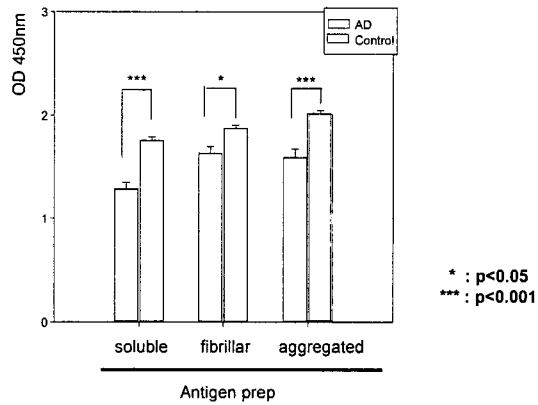
Development of an advanced ELISA test

Determination of incubation time and coating concentration



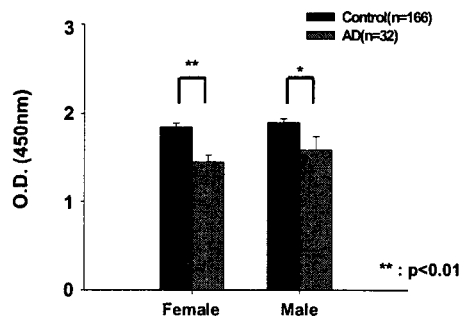
**Anti-A β autoantibodies in the serum of AD patients
recognized different forms of A β**


AD patients vs. Control



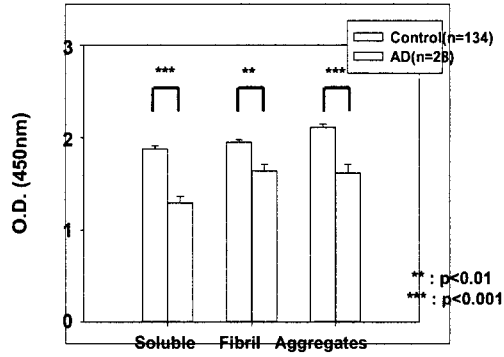
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Female vs. Male in AD patients



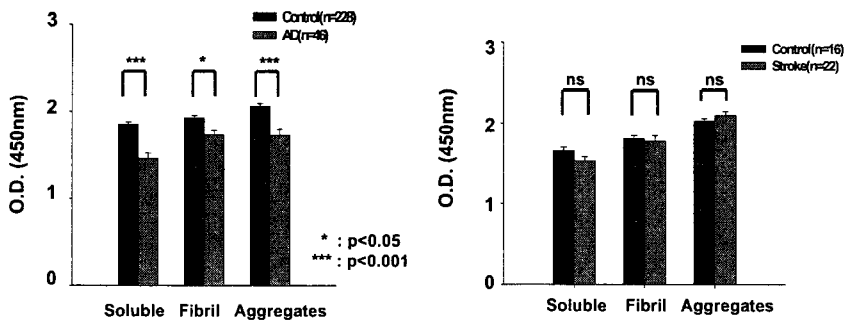
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61~80 year old group



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Anti-Ab antibodies in serums of AD and Stroke patients

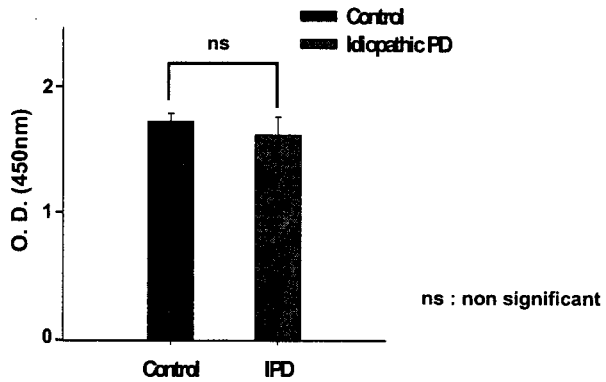


Ns: not significant

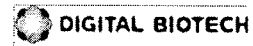
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Idiopathic Parkinson's Disease vs. Control

(IPD n=11, control n=28)



* Idiopathic Parkinson's Disease : the most common form of Parkinsonism, a group of movement disorders that have similar features and symptoms.



Results of Clinical Field Test

Results	AD samples (272)		Normal samples (478)	
	positive	negative	positive	negative
No. of samples	226	46	167	311
analysis	sensitivity		specificity	
	226/272*100= 83.1%		311/478*100= 65.1%	



Development of diagnostic ELISA kit for Alzheimer's disease



Digitalbiotech, Inc. cooperate with Standard Diagnostic, Inc.



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