Seoul National University

Technology Overview

1. Background of Technology

1.1. Clinical implication of Tau modification in Alzheimer's disease

- Clinical association of Tau hyper-phosphorylation with Alzheimer's disease

: PHF(paired helical filament) with hyper-phosphorylated tau found in AD patients and Tauopathy

: Gsk and cdk5 kinase are responsible for Tau pathologic phosphorylation

- Clinical correlation of Tau aggregation with Alzheimer's disease

: Tau oligomer and aggregates found in AD patients and Tauopathy

1.2. Newly being developed but not successful yet

- Active initiation of Tau modification/aggregation pathology research

: Compared to amyloid, less effort has been done. But active researches increase (2008, 2009, ICAD)

- Recent initiation with High through-put screening for Tau aggregation modulator

: Development for cdk5 Inhibitors and screening of Tau aggregation blocker (2008, 2009 ICAD)

1.3. Limited screening assays and a few available targets for drug development

- A few targets, including GSK3b and cdk5/p25

: Most laboratories or Biotech Inc. are working on a few targets known in public domain for tauopathy, such as GSK3b and cdk5. There are not many targets for drug development.

-Competitive new targets needed

: More targets are required, including upstream of GSK or cdk5 for Tau modification and aggregation etc.

2. Description on Technology Applied

2.1. Unique establishment of modified-Tau cell-based assay for high contents screening

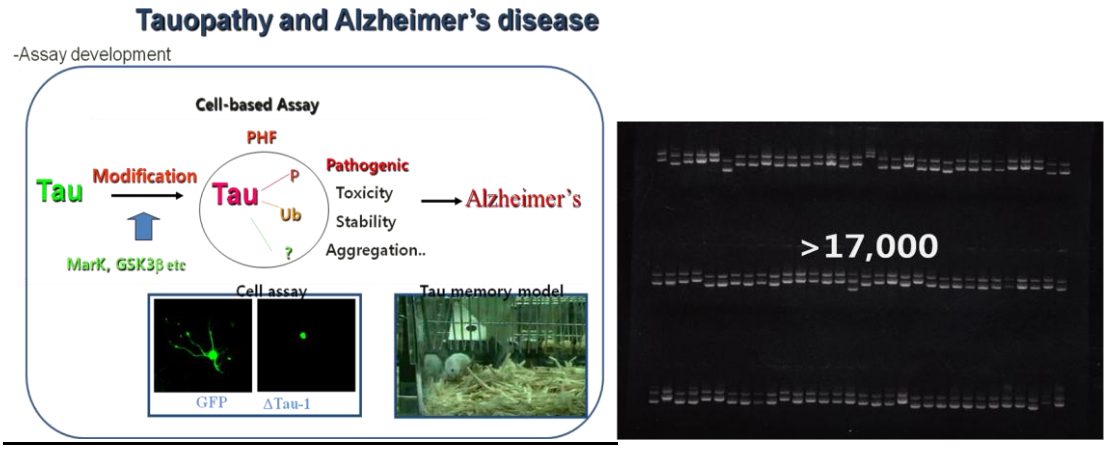
- We established Tau aggregation cell-based assay and prepared cDNA library for screening

: Most laboratories have used *in vitro* aggregation assays using purified Tau for compound screening because there is little available cell-based assay system. We established modified Tau-

based cell assay for tau aggregation. In contrast to other genome-wide screening, we collected human cDNA in a mammalian expression vector (>17,000) for gain-of-screening (Fig. 1).

-**Successful high-content screening for gain-of-function using cDNA**

: From high-content screening using cDNA (>4,000 cDNA), we successfully isolated new genes and pathways which regulate Tau aggregation and hyper-phosphorylation.



(Fig. 1) Tau cell-based assay (left) and cDNA libarary (right))

2.2. R receptor: Isolation of new pathway (genes) for Tau phosphorylation/aggregation

- In vitro characterization: Role of R receptor in Tau hyper-phosphorylation/aggregation

: Expression or knockdown of R receptor modulates Tau phosphorylation/aggregation in neuronal cells. In addition, R receptor affects neuronal cell's viability.

-**R receptor as an upstream of cdk5 for Tau hyper-phosphorylation/aggregation**

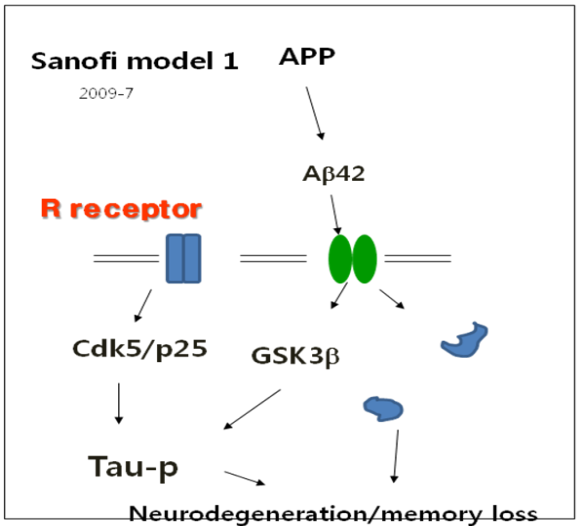
: R receptor seems to work at an upstream of cdk5 in cell level.

- in vivo characterization for neurotoxicity, providing proof of concept

: In fly rough eye model, R receptor increases Tau-induced neuronal degeneration, while dominant negative mutant rescues the toxic effects induced by Tau.

(* In R receptor knockout mice, R receptor seems to be viable but looks better smart).

- **Proposed role of R receptor in Tauopathy** (Fig. 2)



* **R receptor**

- Tau phosphorylation
- Tau aggregation
- Neurotoxicity
- Cdk5 upstream
- Rough eye degeberation
- KO mice are viable
- Memory (?)

(Fig. 2) **Schematic diagram for the role of R receptor in tauopathy.**

3. Differential Point, Superiority or Characteristics of Technology Applied

3.1. New receptor as an upstream of cdk5 for Tau Pathologic phosphorylation/aggregation

: R receptor is upstream of cdk5 for Tau phosphorylation/aggregation.

3.2. R receptor Knockout mice are viable but show increased memory, providing a good therapeutic targets

: In contrast to cdk5 or GSK3b, knockout mice are viable.

3.3. Competitive new target for AD therapeutics

: Though double transgenic mice (tau/R receptor-/-) remains to be further addressed, R receptor may serve as a good target for AD therapeutics.

3.4. Successful cell-based assay to further isolate Tauopathy modifiers

: By using cDNA collection, continuous screen can be performed to further isolate new pathway modifiers for Tauopathy. In addition, there are more signal mediators which were isolated from our screening.

Specific Patent and Publication Information

No.	Name of Patent	Application No.	Date of application /approval	Country	Status (Applied/approval)	Cost for patent (KRW)
1	R receptor as upstream of cdk5 for AD therapeutics	in preparation	2011	PCT		

※ *Please provide accurate information for Application No and Date of application/approval. It will be used for patent search.*

※ *In case of Cost for patent, please consider administrative cost for patent application only.*

※ *In case of PCT or overseas patent (application) except domestic patent, Please attach a certificate of application/approval (or patent abstract) as a separate file.*