Seoul National University

Technology Overview

1. Background of Technology

1.1. Amyloid hypothesis in Alzheimer's disease

- Clinical association of amyloid42 oligomers with Alzheimer's disease

: Detection of amyloid42 oligomers in the brain of AD patients

: Apparent evidence for the role of amyloid42 oligomer in AD Pathology

: High ratio of Amyloid 42/40 for pathology

1.2. Amyloid42 receptors: not successful yet

- RAGE (Nature 1996)

: Role in amyloid transport in BBB (2008, 2009, ICAD)

: However, a role in the memory impairment of AD is not clear

- ABAD (Science 2005)

: Role in mitochondria for amyloid toxicity

: However, a role of ABAD in the memory impairment of AD is not clear

-**Prion (Nature 2009) etc.**

: Role in LPT

: However, a role in the memory impairment of AD is not clear yet.

1.3. Limited available targets in the amyloid pathology for drug development in AD

- Beta, gamma secretases are good targets but development of inhibitors have problems.

: Gamma-secretase: too many substrates

: Beta secretase: Difficulty to design inhibitor in brain

-Aggregation blockers, amyloid antibody etc.

: Long history, being tried by many groups.

1,4. Looking for New therapeutic targets

-Additional new targets are needed.

2. Description on Technology Applied

2.1. Amyloid 42-binding receptor (AIMP) discovered

-Interaction was confirmed in *in vitro* and cell level

-Amyloid42-selective interaction (Amyloid40 not bound))

-Monomer and oligomeric forms of amyloid42 bind to AIMP receptor

-Binding region was identified by *in silico* modeling and by mutagenesis

2.2. Role of the amyloid receptor in amyloid pathogenesis

-Increased expression of AIMP in the brains of AD and APP moce

-Essential role of AIMP receptor in neurotoxicity and Tau phosphorylation in cultured neuronal cells

-Inhibition of amyloid42-induced memory impairment in AIMP receptor KO mice (icv injection)

-No reduction in amyloid42-induced LTP in the brain of AIMP receptor KO mice.

-AIMP KO/PDAPP double transgenic mice rescue memory impairment of PDAPP mice.

-There is another ligand for the receptor and thus, selective inhibition is required to avoid unwanted effects.

2.3. Small compound inhibitor (inhibitor X) against amyloid receptor:

-AIMP inhibitor compound Isolated from in silico modeling

: Using in silico-modeling of the receptor and amyoid42, one million compounds were screened.

- In vitro, in vivo effects: Inhibition of receptor-mediated memory impairments

: AIMP inhibitor inhibits the interaction of amyloid42 with AIMP

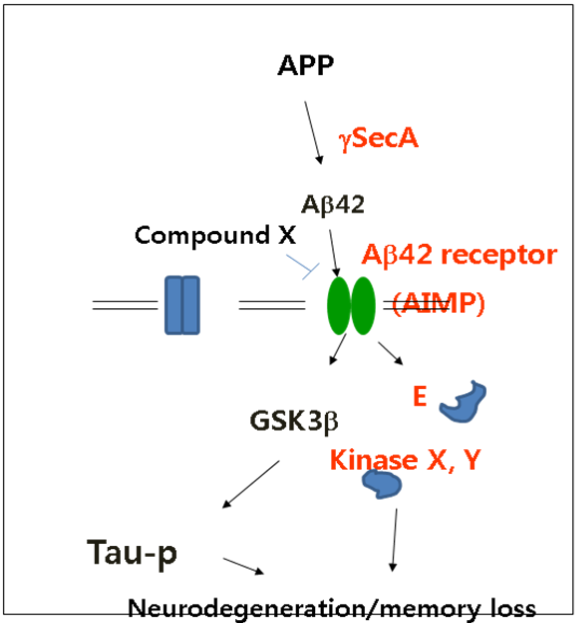
: AIMP inhibitor inhibits amyloid42-induced neuronal toxicity in vitro

: AIMP inhibitor inhibits amyloid42-induced memory impairment (memory test after amyloid42 i.c.v. injection).

: AIMP plays a role in neuronal transport of amyloid42

: Being tested for BBB transport.

Taken together, these in vitro and in vivo analysis of AIMP and its inhibitor provide a proof of concept that AIMP may serve as a receptor of amyloid42 (Fig. 1)



Role of AIMP

-selectively binds to Ab42
-role in Ab42 in neurotoxicity
-role in tau modification
-role in memory loss
-compound inhibitors available

(Fig. 1) **Schematic diagram for the role of AIMP receptor in amyloid pathology.**

3. Differential Point, Superiority or Characteristics of Technology Applied

3.1. New receptor of amyloid42 for amyloid pathogenesis

: AIMP receptor plays a key role in amyloid42-mediatedneurotoxicity and memory loss, while RAGE and ABABD have different roles.

: Role of AIMP in neuronal transport of amyloid42.

3.2. AIMP receptor Knockout mice are viable but show autoimmunity when it is getting old.

: Selective inhibition of the binding of amyloid42 to AIMP receptor

3.3. Competitive new target for AD therapeutics

: From analysis of double transgenic mice (AIMP receptor KO/PDAPP tg), we found that AIMP receptor may serve as a target for AD therapeutics.

3.4. Compound inhibitor interefering the binding of amyloid42 to AIMP receptor

: We have compounds that inhibit the binding of amyloid42 to AIMP and needs to further characterization for selective inhibition. However, the target may reserve as a novel target.

3.5. Receptor downstream mediator is being characterized for neuronal selectivity.

: We are also looking for neuronal specific amyloid42 signaling mediators as a target.

Specific Patent and Publication Information

No.	Name of Patent	Application No.	Date of application /approval	Country	Status (Applied/approval)	Cost for patent (KRW)
1	Compositions and method for the diagnosis, prevention and treatment of Alzheimer's disease	PCT/KR2008/006570	2008.11.7	PCT	applied	

※ *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.*