POLSKY Center for Entrepreneurship and Innovation
THE UNIVERSITY OF CHICAGO

Preventing Protein Aggregation: "Molecular Tweezers"

SUMMARY

Alzheimer's is an incurable neurodegenerative disease afflicting millions of Americans. Current therapies target the symptoms rather than the cause of disease, which involves the deposition of the amyloid-beta (Aβ) and tau proteins into fibrous plaques or tangles in the brain. Researchers have developed "molecular tweezers," small molecules that inhibit the assembly of Aβ proteins. Similarly, there are no therapeutics that specifically target toxic protein aggregates following spinal cord and traumatic brain injury. CLR01 is a "molecular tweezer" that can be applied to the injury site of the spinal cord, and improve neuronal survival by inhibiting post-injury protein aggregation.

KEY RESULTS

Researchers have demonstrated that molecular tweezers can inhibit assembly of Aβ in both in vitro assays and vivo mouse models. Animal studies to further characterize efficacy and pharmacokinetics of the molecule and associated derivatives are underway, as well as experiments to reveal the structure and mechanism of interaction have been initiated. In addition, CLR01 has been tested in a lamprey model of spinal cord injury; significantly less synuclein aggregation was observed and neuronal survival was greatly increased.

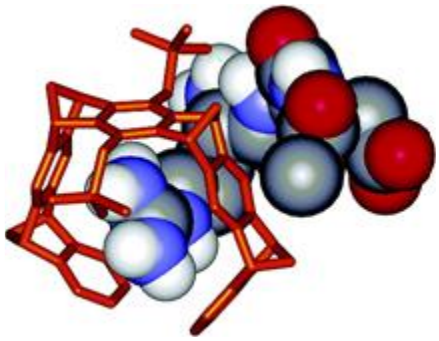
ADVANTAGES

- Targets cause of disease or tissue damage, not symptoms.
- Non-toxic at concentration up to 200 μM.

APPLICATIONS

- Treatment for Alzheimer's disease.
- Treatment for spinal cord injury.
- Treatment for traumatic brain injury.
- Potential for treatment of other amyloid-related diseases: Parkinson's disease, Creutzfeldt-Jakob disease, Gerstmann-Straussler-Scheinker disease.

Molecular tweezer with a high affinity for the amino acid lysine



Fokkens et al, 2005

TECHNICAL DESCRIPTION

Protein aggregation is associated with a number of diseases, such as Alzheimer's, and is believed to be responsible for tissue damage after traumatic injury to the spinal cord or brain. Aggregation of Aβ and tau proteins is neurotoxic, precipitates neuronal death and impairs cognitive signaling. Therapeutic research efforts for Alzheimer's focus on the drivers of disease by targeting inhibition of Aβ production, enhancement of Aβ clearance, or disruption of Aβ assembly. Recent findings allow for the development of therapies that target specific amino acids of Aβ fibers; this specificity holds promise for the treatment of Alzheimer's and other amyloid-related diseases such as Parkison's disease, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker disease. CLR01 is a "molecular tweezer" that can disaggregate amyloidogenic proteins, such as amyloid-β. CLR01 could be applied to the injury site of the spinal cord or brain, improving neuronal survival by inhibiting the post-injury aggregation of α-synuclein.

REFERENCE
MBL 0015

DEVELOPMENT STAGE
Pre-clinical / animal studies

THERAPEUTIC AREAS
Alzheimer's disease,
Spinal cord injury,
Traumatic brain injury

PUBLICATIONS
Fokkens et al, 2005
Klarner et al, 2006
Attar et al, 2012
Attar & Bitan, 2014
Fogerson et al, 2016

INTELLECTUAL PROPERTY
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US 14/536,176

INVENTOR(S)
Dr. Gal Bitan, PhD is an Associate Professor in Residence of Neurology at the David Geffen School of Medicine at UCLA, a member of the Brain Research Institute at UCLA, and an associate member of the Molecular Biology Institute at UCLA. Dr. Bitan's expertise lies in chemistry and biochemistry.

Dr. Jennifer Morgan, PhD is an Associate Scientist at the Marine Biological Laboratory and Associate Director of the Bell Center.; Dr. Morgan's expertise lies cellular and molecular neuroscience, using lampreys as a model system.

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