AD Antibody: passive immunization treatment for Alzheimer's disease

Organization
University of Missouri-St. Louis

Industry:
Human Health: Alzheimer's Disease Therapeutics

Researchers:
Dr. Michael R. Nichols, Professor, Department of Chemistry & Biochemistry

Status of Intellectual Property:
Provisional Patent Application Filed 08/20/2019

Next Steps:
Animal studies, humanizing the mAbSL antibody

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Wanted

Experienced leader to commercialize a novel Alzheimer's disease antibody as a passive immunization treatment for AD.

Customer Problem

Alzheimer's disease is 100% fatal. There are no approved disease-modifying therapeutics currently available. Current drugs, such as Aricept and Namenda, treat only the symptoms of dementia. More than 5 million Americans are living with AD. It is the 6th leading cause of death in the United States, killing more than breast cancer and prostate cancer combined. In 2020, AD and other dementias will cost the nation $305 billion, which could rise as high as $1.1 trillion by 2050, according the Alzheimer's Association. They also note that 16 million Americans provide unpaid care for people with AD or other dementias – an estimated 18.6 billion hours valued at nearly $244 billion. And, it's not getting better. While between 2000 and 2018 the deaths from heart disease decreased 7.8%, the deaths from Alzheimer's disease increased 146%.

A disease-modifying therapeutic is desperately needed.

Potential Market Uses

The proposed therapeutic targets patients with mild cognitive impairment (MCI) due to AD and mild Alzheimer's – early stage AD. The monoclonal antibody solution would be delivered intravenously to patients on a monthly basis.

Market Size

In the United States, there are 10 million MCI/mild cases of AD. First-year sales at 10% of the market would result in $100 million in sales. With market and case growth, sales are estimated to reach $1 billion after five years.

Innovation

Protein aggregation is at the core of Alzheimer's disease. Accumulation of proteins capable of forming amyloid deposits is a pathological mechanism for AD. The Alzheimer brain is characterized by the presence of extracellular amyloid plaques (Fig 1), which contain numerous proteins, the principal of which is Aβ.

Our solution is passive immunization treatment of early-stage AD patients with **mAbSL antibody**, which selectively targets a protofibril form of Aβ. There is substantial *in vitro* data indicating that these soluble precursors to Aβ fibrils cause many of the early deleterious neurodegenerative effects and are an important therapeutic target for AD.

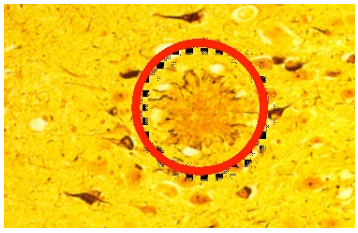

Fig 1. Aggregated amyloid-beta protein (Aβ) fibrils in a brain slice from AD patient. (Selkoe, *Trends Cell Biol*, 1998, 8, 447)

Stage of Development

We have obtained, cloned, sequenced, expressed, purified and characterized the Amyloid-β protein (Aβ) monoclonal antibody (mAbSL). We have also developed methods for expression and purification of mAbSL antibodies.

Our next research milestones include 1) strengthening the case that mAbSL is an effective regulator of AD progression via AD transgenic mice studies, and 2) humanizing the mAbSL antibody.

Competitive Advantages

There is no therapeutic on the market that treats the actual disease; they only modify the Alzheimer's disease symptoms. The mAbSL antibody has higher selectivity for the Aβ protein that anything currently in trials.

Intravenously administered Aβ-targeting antibodies are thought to work via the "peripheral sink hypothesis,"in which they draw Aβ from the brain into the periphery for subsequent disposal.

Thus far, amyloid antibodies have not been successful in human clinical trials, yet two antibodies currently in Phase 3 trials, adacunumab and BAN2401, are showing promise and both target aggregated Aβ.

One potential weakness for these antibodies is their lack of selectivity between protofibrils and fibrils. Our antibody demonstrates this selectivity and may have the potential for greater efficacy.

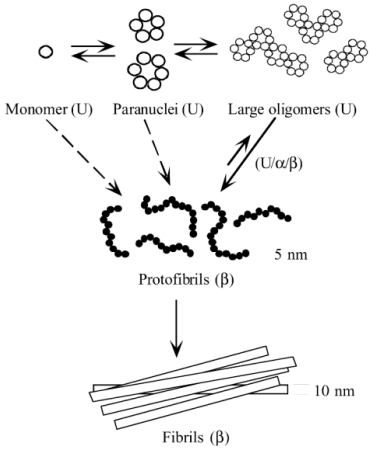

Fig 2. Aggregation pathway of Aβ (Bitan et al., *PNAS*, 2003, 100, 330).

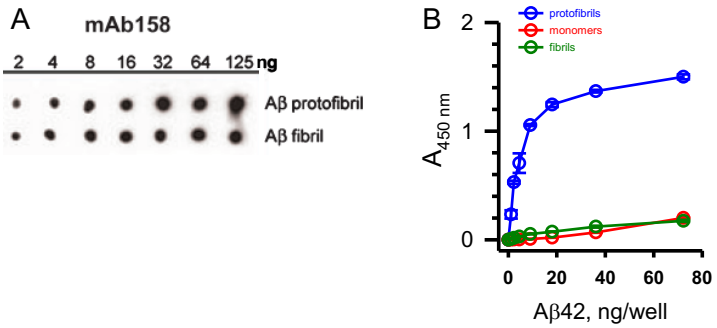

Fig 3. Selectivity differences between mAb158 and mAbSL. ***A.*** Dot blot assay showing recognition of Aβ protofibrils and fibrils by mAb158, the precursor antibody to BAN2401 (Englund et al., *J Neurochem*, 2007, 100, 330). ***B.*** Indirect ELISA showing selectivity of mAbSL for protofibrils.