BBS (? secretase Blocking Site) Ab -A novel target for Alzheimer's and ALS immunotherapy (Ramot)

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THE TECHNOLOGY

BBS is a monoclonal antibody that binds specifically and blocks beta-secretase (BACE1) cleavage site on its substrate, APP. BBS inhibits Ab production, a hall-mark of AD and other neurodegenerative diseases such as ALS.

The mechanism of action of BBS is based on binding of the antibody at the cell surface before internalization to the early endosome where BACE cleaves the APP.

AD and ALS share several similar pathological aspects and mechanisms including aberrant protein aggregation, increased neurodegeneration, mitochondrial dysfunction, oxidative stress, transcriptional dysregulation, aberrant apoptosis, altered proteosomal function and several downstream targets that were reduced by BBS (GSK3, p53).

DATA-TO-DATE

AD: In triple transgenic mice model of AD (3x Tg-AD), BBS

- Decreases both intracellular Ab levels including toxic oligomers and reduction in total and phosphorylated tau levels.
- Increases the cognitive capabilities and reduces brain inflammation levels which accompany AD pathology

ALS: ALS SOD1G93A mice, BBS:

- Exerts beneficial effect in that overexpress mutant SOD1.
- Reduces APP, Aβ and SOD1 levels
- Reduces neuroinflammation
- Significantly prolongs life span

These results suggest that treatment of AD and ALS with BBS could be a promising neuroprotective strategy for treatment of these debilitating diseases

DEVELOPMENT STATUS

- CHO clone for the mice BBS antibody
- Analytical methods protocol (ELISA)
- cDNA of a humanized antibody
- humanized Ab hybridoma available

PATENT

Three patent families cover the antibodies and their use.

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