Docket #: S19-058

Modulating Bone Morphogenic Protein (BMP) Signaling in the Treatment of Alzheimer's Disease

Technology Reference
Stanford ref. no S19-058
CZ Biohub ref. no. CZB-179S

Researchers at Stanford University have described a novel therapeutic target for Alzheimer's disease.

Alzheimer's disease (AD) presents a large public health burden, effecting an estimated 5.5 million people in the United States and occurring in 10% of individuals over the age of 65. Despite recent advances in therapies targeting plaques (monoclonal antibody therapies), there is currently no treatment currently available that can stop, prevent, or reverse the pathogenesis of AD. Additionally, AD pathology often begins decades before the onset of measurable clinical symptoms or neurologic deficits. In another vein, evidence in the literature suggests that adult neurogenesis is impaired in AD, specifically in the subventricular zone (SVZ) and the hippocampus, which may contribute to the neuropathogenesis of this disease. Neural stem/precursor cells (NPC) in this region have been reported to be abrogated in animal models of dementia, but it remains an open question whether this finding is a side effect or a causative factor in AD disease processes.

Stage of Research
The inventors have defined a novel therapeutic target for the treatment of AD through targeting important molecular pathways in adult NPCs. Through their research, the inventors have discovered that cell-intrinsic NPC deficits are at least partially regulated by Cdkn2a, which has been implicated in tumor formation. To avoid off-target effects, the inventors modulated bone morphogenic protein receptors (BMPRs) which are highly expressed in adult NPCs. By inhibiting BMPR

signaling, the inventors determined that BMPR inhibition rescues plaque formation via mutant amyloid precursor protein (APP). Prevention of the formation of mutant APP in turn prevents self-mediated renewal defects in human neurospheres. Taken together, this invention puts forth methods and compositions for treating AD patients with BMPR inhibitors. This invention provides a novel therapeutic pathway for AD, which has the potential to resolve an urgent unmet medical need in the AD field.

Stage of Development
Research -

in vivo

Applications

- Targeted, scientifically backed potential treatment avenue for AD using an inhibitor of BMPRs

Advantages

- Current understanding of BMPR signaling provides evidence of limited off-target effects of inhibition of these receptors
- This therapeutic target was discovered using human-derived neurospheres, lending to its applicability for use in humans

Publications

- Felicia Reinitz et al. "Inhibiting USP16 rescues stem cell aging and memory in an Alzheimer's model." eLife 11:e66037 (2022)

Patents

- Published Application: 20220186230
- Published Application: 20240102022

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