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ABSTRACT

ProSAAS is the descendant of several peptides in brains as well as other tissues. In previous studies, scientist have discovered that proSAAS could function as an amyloid anti-aggregant for Alzheimer's disease (AD). In a twelve-month old brain of a mice, proSAAS was exceedingly colocalized along with amyloid pathology in the cortex of an AD-affected human brain. Therefore, protein aggregation and misfolding is a typical cause of neurodegenerative diseases. On the other hand, chaperones place the proteins on the precise pathways for folding. Overall, proSAAS has an involvement in AD.

INTRODUCTION

Neurodegenerative diseases is the process of neurons deteriorating inside of the brain and spinal cord. When neurons begin to break down, they cannot be restored or replicated. An example of a neurodegenerative disease is Alzheimer's Disease (AD). Alzheimer's is the most common type of dementia, which is memory loss. Early signs of Alzheimer's Disease consist of having difficulties remembering current events or even conversations. Once the disease progresses, an individual will begin to have critical memory loss and become unable to perform daily tasks. A person with Alzheimer's has critical brain damage, which affects the size of the brain. An AD brain is much smaller than a healthy brain because it shrinks to as much as one-third of the usual size as the disease advances. A healthy brain has nourished folds that are tightly packed together. In contrast, an AD brain has slight, narrow folds and broad openings in the middle of each fold. Alzheimer's Disease could be derived from family history or genetics. A person could be at risk of developing AD if a first-degree relative possesses the disease. Although, the risks of Alzheimer's disease could be lowered by having a balanced diet. Consuming fresh produce and fruits manages the blood pressure and cholesterol. Exercising on a

daily basis allows the body to engage in a type of physical activity which benefits the body. All in all, Alzheimer's Disease is a type of neurodegenerative disease that breaks down neurons.

BACKGROUND

Protein aggregation occurs when misfolded proteins inhibit a conformation, which causes the polymerization to aggregate and arrange fibrils. Protein misfolding occurs as a protein does not fold into the native functional conformation. Protein misfolding and aggregation results in the formation of neurodegenerative diseases such as Huntington's disease (HD), Alzheimer's disease (AD), Parkinson's disease (PD), etc. The aggregates and misfolded proteins seem to be harmful which causes illness or death towards the cells. As a result, the higher the aggregation, the higher the harshness of the disease.

Chaperones are a group of proteins which acts as an essential role stabilization of unfolded proteins. Chaperones are important because they lead proteins to the correct pathways for folding. In fact, they help avoid non-specific aggregation through binding to proteins that are not native. Majority of chaperone proteins are called "heat shock" proteins since they are produced in huge amounts when cells are revealed to heat. Consequently, proteins are destabilized by heat. Also, heat causes misfolding to become more common. Therefore, cells need additional help with proteins when the heat increases. On the other hand, researchers are seeking whether proSAAS acts as a role in AD pathology. In AD patients, proSAAS immunoreactivity has already been discovered in neurofibrillary tangles and neuritic plaques in the brain tissues. This implies a potential involvement of proSAAS within AD pathology.

EXPERIMENRAL METHODS

Initially, an immunofluorescence of human brain tissues were marked for proSAAS and AD targets. A sample of hippocampal tissue was acquired from a seventy-three-year-old donor

who suffers from AD. The tissue was separated, formalin-fixed and cryoembedded at 16 μm. The portions were placed in a blocking solution for an hour. Also, the rabbit anti-proSAAS and monoclonal mouse antibody were placed in an overnight blocking solution at 4°C. Then, the portions were cleansed and nurtured by Cy3-conjugated anti-rabbit or Cy2-conjugated donkey anti-mouse within a blocking solution for two hours at a steady room temperature. For the animal models, the amyloid plaques of twelve-month old mice were inspected and sacrificed for their brains to be projected with Accustain. Next, an immunofluorescence of brain tissues in mice were conducted for proSAAS and AD targets. Ten μm brain portions were processed with Aqua DePar and Reveal antigen recovery solutions. The portions were placed in various incubations and blocking solutions to ensure the development. Eventually, the portions were cleansed substantially and observed under a microscope. Moreover, the recombinant was prepared, and the N-terminal diminished the His-tagged proSAAS. Then, a peptide was nurtured by a concentration of 1 mM for roughly an hour. The samples were then analyzed and compared to determine whether proSAAS is involved in Alzheimer's disease pathology.

A cytotoxicity assay was performed to determine whether cells have loss any functions in the membrane. The cells were cleansed and nurtured with a vehicle in order to calculate the cell's viability. The viability was evaluated by the WST-1 cell proliferation reagent, then absorbed for every thirty minutes. The cell viability was analyzed through marking the cells with calcein AM and images were taken by a microscope.

In this experiment, proSAAS was speculated to have an active part in Alzheimer's disease. An amplified incidence of co-localization occurred between proSAAS and $A\beta_{1-42}$ plaques in AD human brain tissues alongside AD mouse brains. This led to the data proposing that proSAAS has a duty in Alzheimer's disease pathogenesis.

DISCUSSION

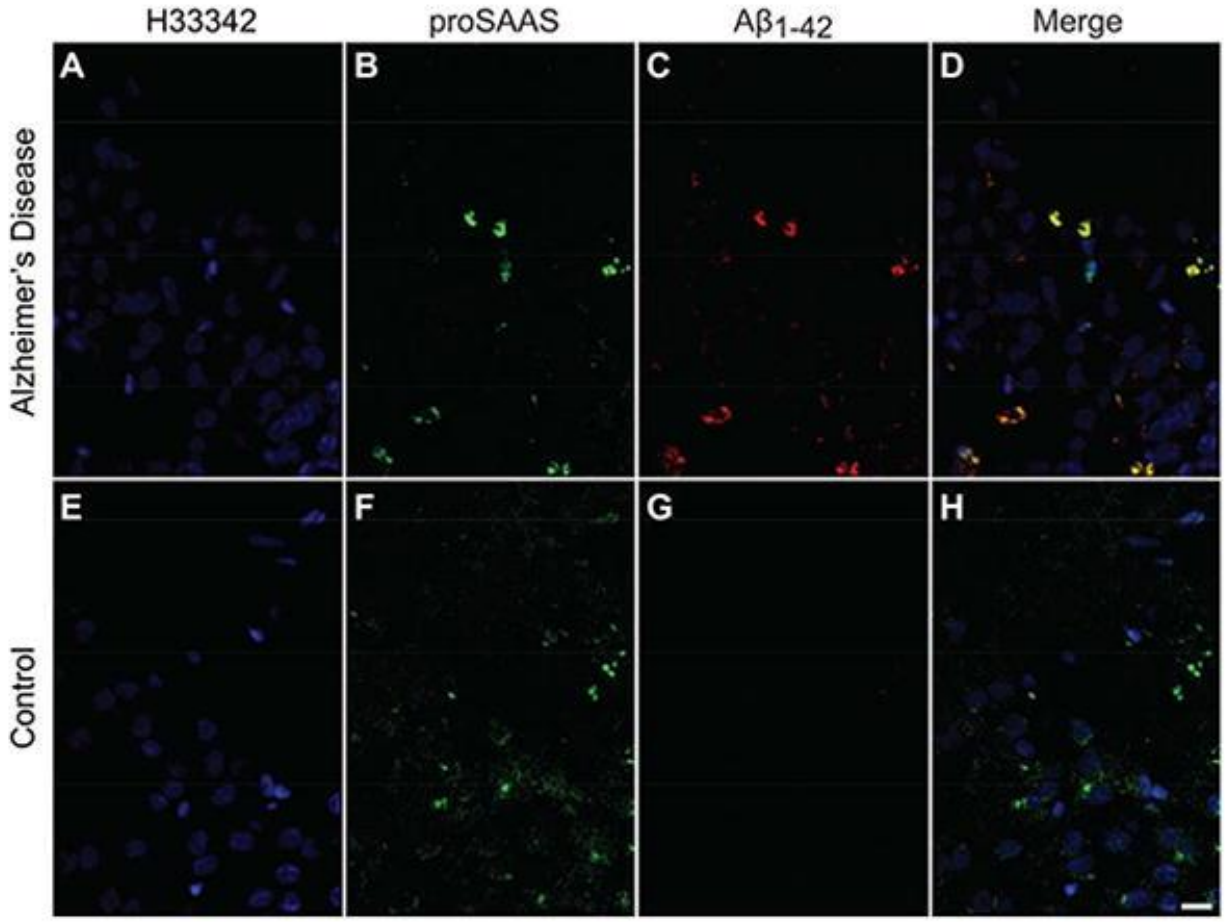

Figure 1 'proSAAS co-localizes with $A\beta_{1-42}$ inside a human AD brain.'

The figure above shows the co-localization of proSAAS in an AD brain. Portions A-D shows the coronal portions of the human hippocampus derived from a patient with AD. Next, portions E-H shows the healthy control. Image B, F, C, and G were stained for proSAAS and $A\beta_{1-42}$. The staining of $A\beta_{1-42}$ was viewed exclusively in the hippocampus of the patient with AD. The combined photos display the co-localization of proSAAS and $A\beta_{1-42}$.

In this experiment, the methodology conducted could be useful for future research about other diseases. The research materials used could lead to discovering the activity of proSAAS in

other neurogenerative diseases. Also, proSAAS could be discovered in cardiovascular diseases. Therefore, the methodology performed could achieve future discoveries in the medical field.

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