

Amyloid- β Signal Transduction Antagonist, A Possible Way to Relief Alzheimer's Disease

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Abstract. As a well-known common neurodegenerative disease in aging, Alzheimer's disease will cause the loss of the ability to talk, cognition and memorize. Amyloid beta is considered to be a major cause of Alzheimer's disease. It will form many different types and accumulate in human brain and cause Alzheimer's disease. However, a recent report about the plagiarism of the fundamental paper of this theory makes many people think that our research direction on Alzheimer's disease is wrong. The author agrees that the plagiarism of the paper is terrible and should be punished, but the author does not think that this will waste everything we have done about amyloid beta. Amyloid beta is still a major reason that causes Alzheimer's disease and find a way to stop the accumulation of amyloid beta in brain is a feasible way to cure Alzheimer's disease. Research on the role of amyloid beta in Alzheimer's disease, whether it is a major cause is the major purpose of the essay. What's more a new method that aim to reduce amyloid beta in brain to cure and relief Alzheimer's disease will be introduced in this article. This method aims to stop the signal transduction of amyloid beta to neuron cells, thus, stop amyloid beta from damaging our brain and cause Alzheimer's disease. The reason this article is written is to confirm the importance of amyloid beta for Alzheimer's disease. In addition, introduce a new cure method. Since this method is new, conclude the advantages and disadvantages of this method could inspire other researchers, and improve the performance of the drugs developed based on this method to reach the final goal, which is cure the Alzheimer's disease.

Keyword: Alzheimer's disease, Therapy, CT1812, Amyloid beta, academic integrity, Amyloid beta oligomer.

1. Introduction

Alzheimer's disease is one of the most common types of dementia. About 6.5 million people are suffered under the effects of Alzheimer's disease in the United States and the number of people infected increases every year. The number of patients is expected to be doubled in several years. The etiology of Alzheimer's disease is complex, with many irreversible changes of human body. One of the theories about the causes of Alzheimer's disease based on the paper that published on Nature on 2006 'A specific amyloid- β protein assembly in the brain impairs memory' [1]. In this paper, researchers inject a specific type of amyloid beta in to mice. After the injection, mice show several symptoms of Alzheimer's disease. Therefore, the researchers conclude that amyloid beta is one of the causes of Alzheimer's disease. Before this paper, the relationship between amyloid beta and Alzheimer's disease has been questioned for years, researchers cannot prove that amyloid beta is the cause of Alzheimer's disease. After this paper, amyloid

beta is proved and acknowledged to be the cause of Alzheimer's disease, and amyloid- β become the major research topic in academia. Researchers try to find a way to reduce the amount of amyloid beta in brain in order to cure Alzheimer's disease, how amyloid beta accumulate in brain and how amyloid beta cause the death of neuron cells. In order to find a cure for Alzheimer's disease, there are many problems like these need to be solved. Over the past few years, billions of dollars was invested in this field, hundreds of neuroscientists spent their time to research. However, a recent report in Science points out that about 70 of the images in that reigning paper are fabricated [2]. This means the basic about this theory is wrong, amyloid beta might not relate to Alzheimer's disease at all. After this report, many people believe that all the money and time people spent on the theory about amyloid beta seems become a waste.

However, that does not mean that all the researches that the academia have done about the relationship between amyloid beta and Alzheimer's disease is meaningless. First of all, there are many kinds of amyloid beta protein present in human brain. In Lesné's paper, only amyloid beta 56 is injected into mice and said to cause the Alzheimer's disease. Amyloid beta 56 is only one branch of many kinds' amyloid beta. A lot of the other amyloid beta, for example, amyloid beta 42 has been proven by many other researchers that it can affect human brain. Therefore, amyloid beta 56 is only a small part of all researches related to amyloid beta. The academic plagiarism on amyloid beta 56 does not mean the whole amyloid beta theory get denied. Therefore, the author still think amyloid is highly related to Alzheimer's disease and more researches about amyloid beta can eventually find a way to cure Alzheimer's disease. So, a new thought about design drug that aim to reduce the amount of amyloid beta in brain will be introduced.

2. Amyloid- β signal transduction antagonist

As the most causes of dementia, Alzheimer's disease cause people to lost memory and cognitive ability. Many patients can remember their family members and will be shocked when they saw their relatives in their home. Some of the severe patients will miss themselves when they step out their house while nobody noticed. It is always a great hurt to people when their family members can remember them or lost one of them without expectations. Therefore, cure Alzheimer's disease is always one of the most concerned aspects. Many researchers dream that they can solve the problem of Alzheimer's disease one day in their life. NIH, national institutes of health spent billions on Alzheimer's disease every year. Although many new discoveries have been published every year, scientists have not found a drug that can be called cure to the accumulation of amyloid beta in human brain and Alzheimer's disease. Because the effective methods and drugs that can cure Alzheimer's disease are still not existed, and the huge amount of people it affected, causes Alzheimer's disease is one of the major difficulties that need to be overcome in the medical profession.

3. The relevant studies on the effects of gene mutations on Alzheimer's disease

Recent studies have shown that some gene mutations is responsible for the genetic risk of Alzheimer's disease, for example, apolipoprotein E, amyloid precursor protein, presenilin 1, and presenilin 2. The mutation of these genes causes the dysregulation of amyloid precursor protein [3]. Amyloid precursor protein is one kind of transmembrane proteins that play an important role in the nervous system. It can regulate several important cellular functions, for example, synaptogenesis and synaptic plasticity. β -secretase and γ -secretase can cleave Amyloid precursor protein to produce amyloid beta. The dysregulation of amyloid precursor protein will disturb the regulation of amyloid beta in out brain, and finally, cause the accumulation of amyloid- β inside the brain and between neurons. This symptom of accumulation of amyloid beta is a key initiating event of Alzheimer's disease, and will ultimately cause neuronal dysfunction and death. It will also leads to the clinical and pathological features of Alzheimer's disease.

4. Amyloid beta is not always a bad thing

However, amyloid- β is not always a bad thing that causes Alzheimer's disease, amyloid- β is also present in a normal human's brain. Amyloid- β can improve neurons' survival rate when there is decent amount, but when amyloid- β start to aggregate, it will have opposite effects on the brain, it will cause neuron degeneration which is one of the key symptoms of Alzheimer's disease. Amyloid- β 42 is one kind of amyloid- β and is one of the most toxic amyloid- β . The reason that it is so toxic is that it will deposit early inside the brain and amyloid- β deposition is an essential early event in the pathogenesis of all forms of AD [4]. This also prove that amyloid beta is related to Alzheimer's disease.

When amyloid beta start to aggregate in human brain, they can become many different forms base on the number of amyloid beta the aggregation contained. Amyloid- β oligomers are one of them and are the most toxic form. The toxicity of the Amyloid- β aggregated form is related to its size of them. The smaller the aggregated amyloid- β is the more toxic it is. Amyloid- β oligomers are a very small group of aggregated amyloid- β . It contains only several amyloid beta and, that is the reason that they are so toxic. A large group of amyloid- β -like amyloid plaque also aggregated between nerve cells. However, there is no clear evidence to show that amyloid plaque can cause memory dysfunction, while amyloid- β oligomers are related to some symptoms of Alzheimer's disease[5]. What's more Amyloid- β 42 tends to form a small group of aggregated amyloid- β , which is also one reason that amyloid- β 42 is more toxic than other amyloid- β .

Since Amyloid- β oligomers are so toxic and are thought to be the major cause of Alzheimer's disease, many scientists have tried to cure Alzheimer's disease by developing drugs that target amyloid- β oligomers. Many drugs aim to clear out or reduce the number of amyloid- β oligomers. However, despite the billion dollars invested, these drugs keep failing. My opinion here is that we are still not very clear about the mechanism of Alzheimer's disease. Although amyloid- β oligomers have been proven to have a relationship with the cause of Alzheimer's disease, I think we might have some mistakes in the method we choose to use to develop new drugs. Also, I think the accumulation of amyloid- β oligomers has many different causes, and the use of several drugs together might be helpful. Although the etiology of Alzheimer's disease is still unclear, and drugs keep failing, I do not think we should stop researching on amyloid beta and Alzheimer's disease. We should keep trying new method and mechanism to develop new drugs that aim to control amyloid beta oligomers. The solution to Alzheimer's disease might be very close to us, we just need to keep trying.

Many drugs designed before aim to destroy amyloid beta or clear out amyloid beta by some other methods. However, none of these drugs have strong effects on cure or relief Alzheimer's disease during the clinical trials. Since these drugs that aim to clear out or reduce the number of amyloid- β oligomers are not so effective, I think developing drugs that target amyloid- β oligomers from a different perspective is a possible solution. Recent research on amyloid- β signal transduction antagonists seems to be a reliable solution. There are many neuronal receptors at synapses in our brain that can bind with amyloid- β oligomers. Most of them are surface proteins on neuron cells. Developing a drug that aims to bind with these receptors can inhibit amyloid- β oligomers from binding with these receptors, and cause an effect of relieving Alzheimer's disease.

Elayta(CT1812) is one of the represents of amyloid- β signal transduction antagonists. It can bind with the sigma-2 receptor and prevents and displaces the binding of amyloid- β oligomers to neurons. It can occupy up to 80 percent of sigma2 receptors and help restore behavioral deficits in APP transgenic mice [6]. What's more, more research on CT1812 has shown that this drug is well tolerated by all ages of people, and the side effects are not very severe, including headache and GI tract symptoms. Also, the human body can normally decrease the number of CT1812 within, Plasma concentrations of the drug keep decreasing as time pass. So, my conclusion is that CT1812 is an effective way to relieve Alzheimer's disease with small side effects and good effects[7].

However, despite all the advantages CT1812 has, there are also many defects of this drug. Since CT1812 is a relatively new aspect of Alzheimer's disease, the long-term side effects are still unknown, it seems that the short-term side effects are not severe, but there might be strong side effects if it is taken for a long period. Also, it is pretty useful for stage 1 Alzheimer's disease, its effect on late-stage

Alzheimer's disease is unknown. However, the early stage of Alzheimer's disease is hard to identify because amyloid- β is also present in normal people's brains. What's more, it cannot reduce the number of amyloid- β oligomers inside the brain so it cannot cure Alzheimer's disease from its origin. One last thing that needs to be considered is that amyloid- β oligomers can bind to many receptors, and inhibiting some receptors can have bad outcomes, so decide that which receptors the drug should bind to is also important. All these defects are shared by this kind of drug. In conclusion, the author think we can find a cure to Alzheimer's disease by researching amyloid beta and also, the author think the amyloid- β signal transduction antagonist has an optimistic developing future and can be one solution to Alzheimer's disease, but more research is definitely needed.

5. Conclusion

As one of the incurable disease, Alzheimer's disease has been researched for years. Although there are people doubt the effects of amyloid beta. The accumulation of amyloid beta can still be concluded as the cause of Alzheimer's disease. Since the drug developed aimed at amyloid beta before are not so effective, some new cure methods are necessary. The method introduced in this article, which is the amyloid- β signal transduction antagonist, has an optimistic developing future and can be one solution to Alzheimer's disease, but more research is definitely needed.

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