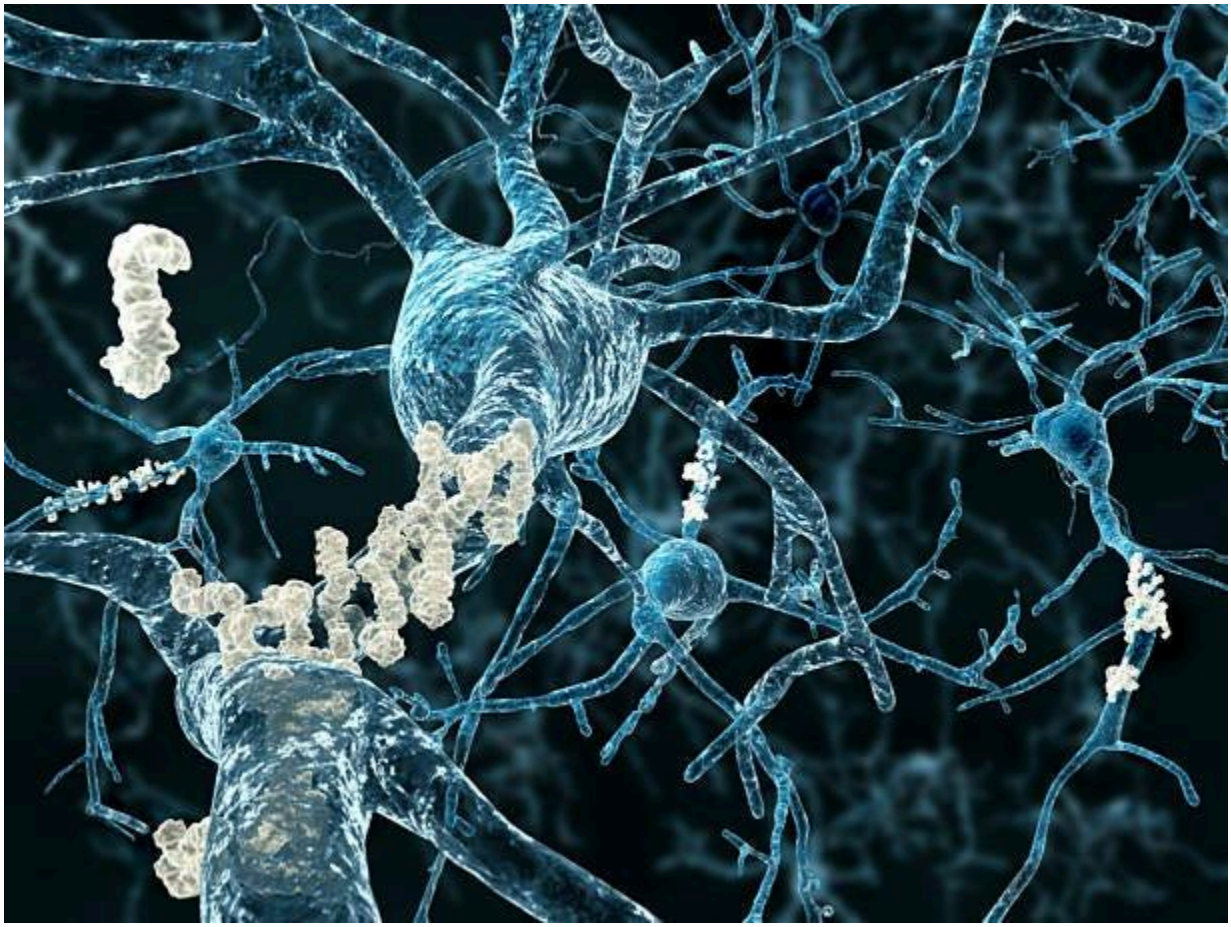
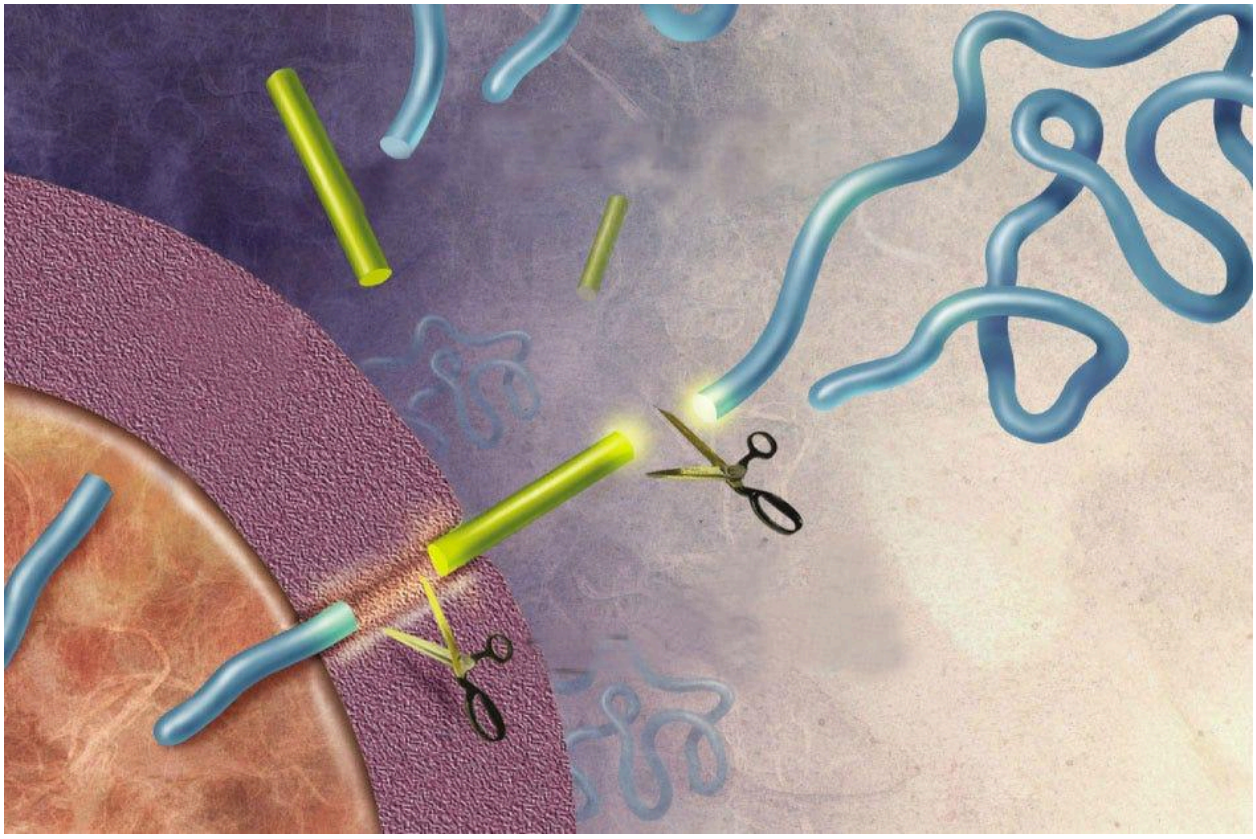
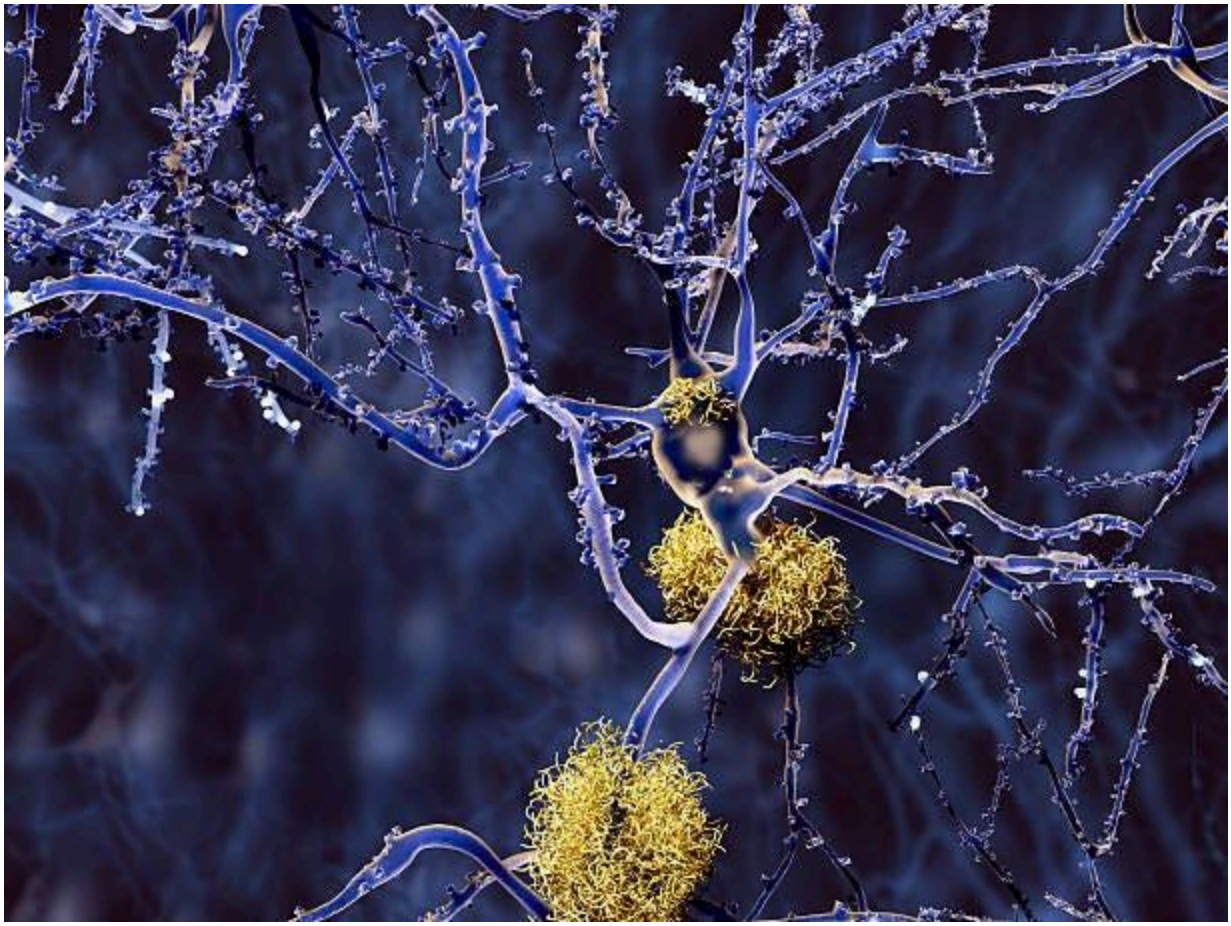
In Alzheimer's Disease (AD), essential brain cells that receive, process, and store information degenerate. Although scientists do not have a definitive answer on the underlying causes, there are many theories on what it could possibly be. One of these theories highlights a microscopic brain protein fragment called beta-amyloid. Scientists suggest that errors in the processes controlling production, accumulation or removal of beta-amyloid are the primary cause of AD. This is known as "The Amyloid Hypothesis," first proposed in 1991, by John Hardy and David Allsop.



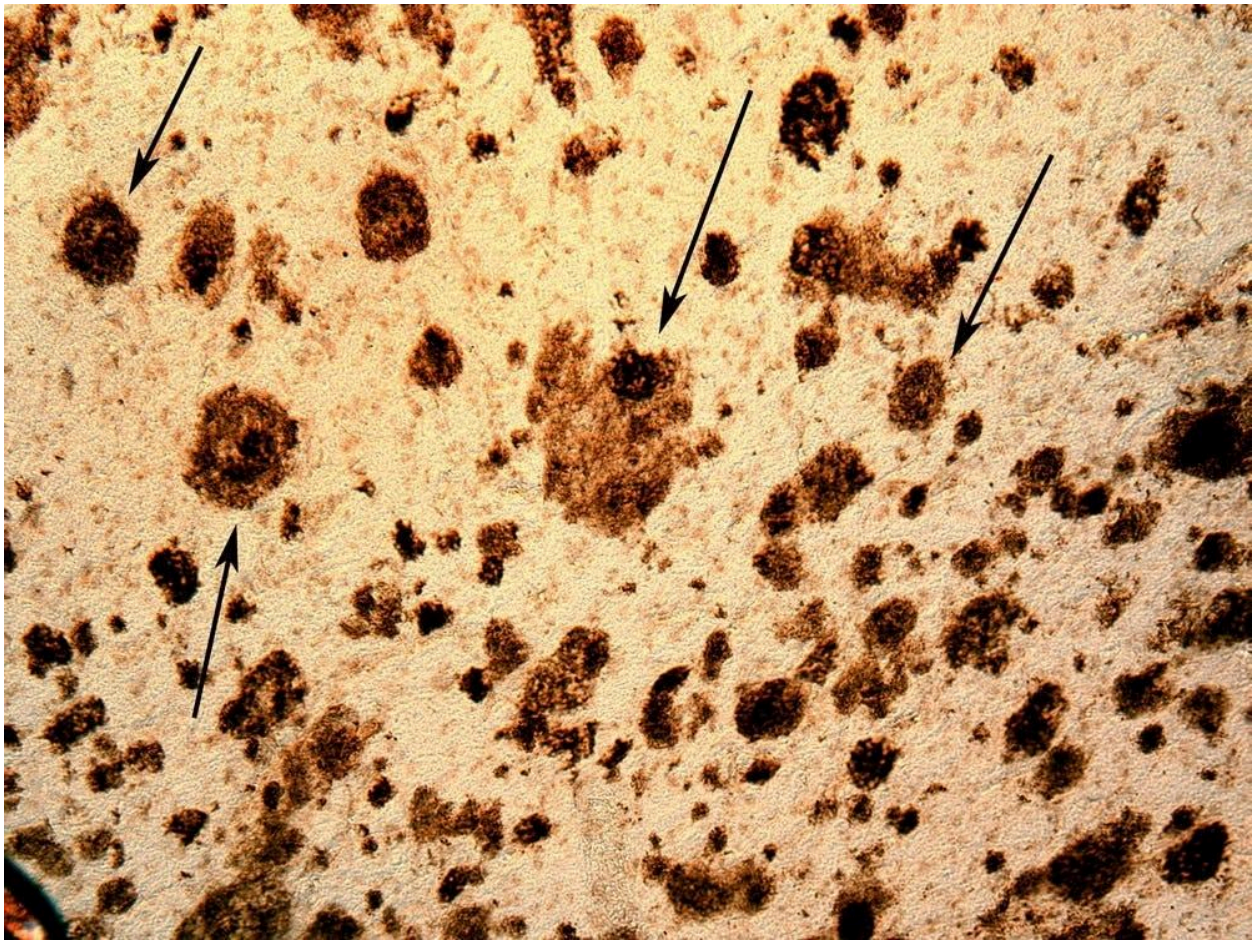
Beta-amyloid is a portion of a larger protein named "amyloid precursor protein (APP)," a substance that little is known about. However, scientists have been able to observe its function when it is active. During this time, proteins cut the APP into smaller pieces that stay inside and outside of cells, dependent on their function. Sometimes when APP is being cut, it results in beta-amyloid.



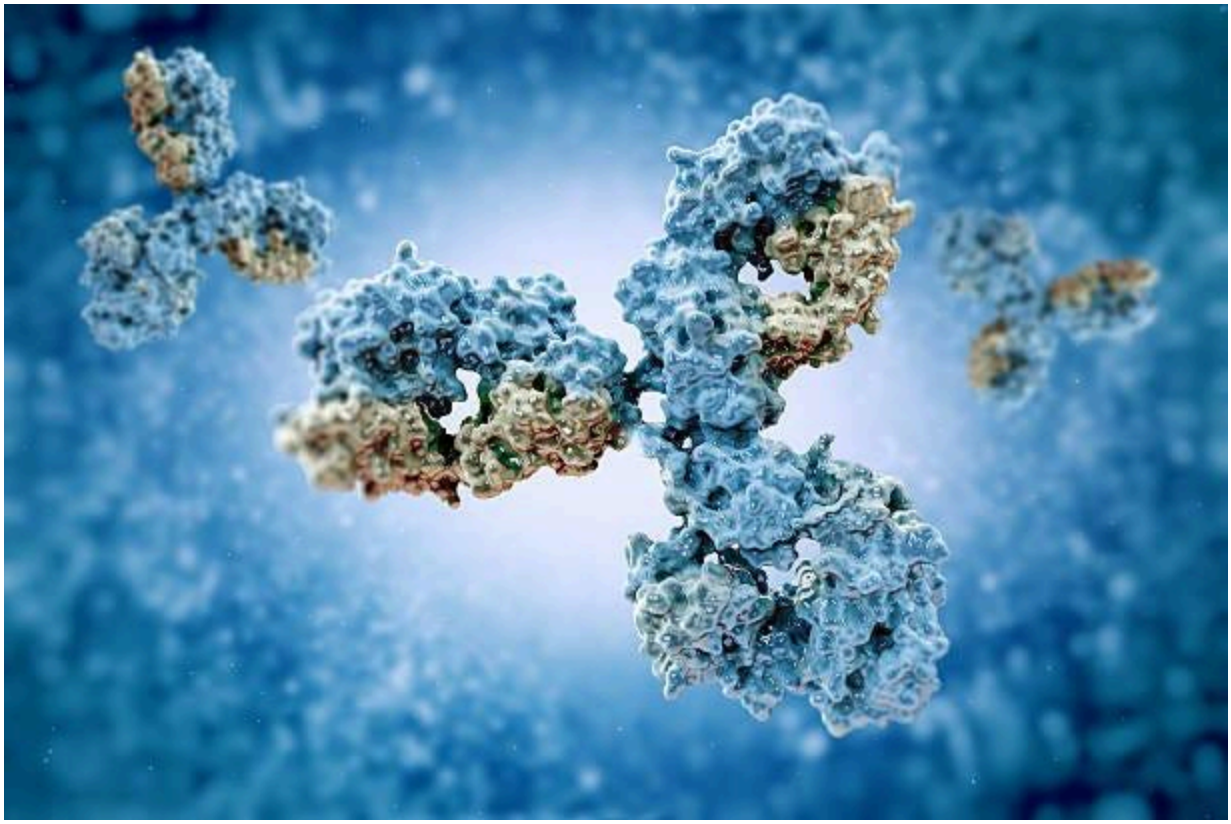
Amongst all of the other segments APP is cut into, beta-amyloid is proposed to be the AD causing factor due to its sticky properties. Scientists suggested that in the brain, beta-amyloid first forms small clumps called oligomers, then arrays of these clumps called fibrils, then layers of fibrils called beta-sheets. Lastly, beta-sheets and other substances combine to form plaques. Researchers speculated that these amyloid plaques were a key feature in many brains diagnosed with AD. The Amyloid Hypothesis states that when these plaques are formed they inhibit neurological communication and signaling. Furthermore, immune cells are activated, causing inflammation amongst the brain cells of a certain region, ultimately leading to their death.



When defending the hypothesis, scientists use three main arguments and pieces of evidence. Individuals with Down syndrome have three copies of Chromosome 21, which carries the APP gene. As a result, they have three genes instead of two, and almost always develop amyloid plaques by age 40. Scientists explain that due to having more APP genes, the probability of an individual with Down Syndrome (DS) to produce beta-amyloid, and subsequently amyloid plaques is increased. Moreover, data collected in multiple experiments reveals that 50% of individuals with DS, 60+ years of age, have been diagnosed with AD. Additionally, scientists have discovered that a few rare genetic mutations guarantee that an individual will be diagnosed at some point during their lifetime. They have observed that these mutations occur in any of three genes. All of these genes are associated with beta-amyloid production or regulation, causing scientists to conclude that it is due to the subsequent amyloid abnormalities that AD is caused. For the third argument, scientists further prove the effect of these mutations. The experiment contained mice that were genetically engineered to contain the aforementioned gene mutations. After the span of a few days, the mice began to develop amyloid plaques and had trouble remembering the ways through mazes, all while continuing to show AD symptoms.



After an increasing amount of evidence that supported the hypothesis, researchers began clinical testing on medication that would battle AD by targeting beta-amyloid or APP. Primarily, scientists attempted to administer lab-grown antibodies into AD patients, in the hopes that it would trigger an immune system response against the plaques. Going along the same route of removing the plaques, scientists injected natural agents with anti-amyloid characteristics into sample organisms. However, most present-day research involves the prevention of these plaques before they even form. There have been very little advancements in this field, but scientists are hoping that they can find a correlation between how amyloid plaques interact with nerve cells, and how they inhibit neurological activity.



The Amyloid Hypothesis continues to be a relevant component of AD research years after its initial discovery. However, controversy has seemed to engulf it in recent years. Many pharmaceutical companies that provide AD relief medication, using the hypothesis's principles, were exposed to have altered data to have their products passed by the Food and Drug Administration (FDA). Additionally, others seem to have found contradicting information to many staple experiments that support the hypothesis, leaving us with the question on the validity of data AND researchers have accepted it to be true for so long.