Amyloid-Beta Protein Concentration Dependence of Reversible Aggregation Using Gold Colloid Particles

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Abstract

Although Alzheimer's and COVID-19 are different diseases, the commonality between them is during the process of them developing in a person by fibrillogenesis. The product of fibrillogenesis results in the development of these diseases. We study the first stage of fibrillogenesis where the amyloid-beta peptide monomers are assembled into an oligomer. We want to isolate this oligomer using gold colloids because this step can be reversed. Utilizing gold colloids allows us to freeze fibrillogenesis in the first step by folding and unfolding the protein repeatedly through a series of pH changes from 4 or below to 10 or higher. At an acidic state (pH~4), the protein is unfolded and aggregates while during a basic state (pH~10), the protein is folded and dispersed. A UV-vis spectrophotometer is used to view the results of the change in acidic to basic conditions. For our research we try to keep the amyloid-beta protein in a quasi-reversible state, so we are able to continue to switch between a pH of 4 and 10 to better observe the protein structures of Alzheimer's and COVID-19.

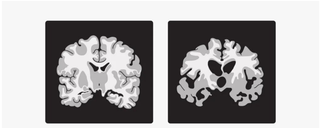

Figure 1. A sketch of what happens to the brain after Alzheimer's disease develops, provided by MedicalNewsToday, Diego Sabogal

Background

Alzheimer's is a neurodegenerative disease that impacts a person's ability to form new connections, recall new information, and causes a massive decrease in retrograde memory. When the disorder expresses itself, it slowly drains one's short-term memory weakening the path from short-term to long-term memory. Alzheimer's disease is not typically part of aging, however given its long development over time, it is more present in older people. Given the rise of seniors in many developed countries, there will be a larger number of elderly people who have a higher risk of developing Alzheimer's.

COVID-19 is an infectious respiratory disease that in short term can impact a person's ability to breath, causes fatigue, muscle aches, the loss of certain senses, and etc. Which has shown to be long lasting in some people infected by COVID-19. We still lack longitudinal research. But COVID-19 vaccines have been produced and given researchers more of an understanding about how virus proteins work, because of the work developed from the vaccines.

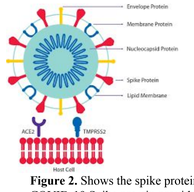

Figure 2. Shows the spike protein of COVID-19 Spike protein provided by Millpore Sigma

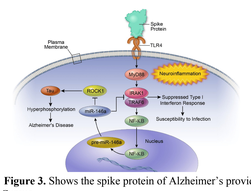

Figure 3. Shows the spike protein of Alzheimer's provided by Cureus

Methods

Amyloid-beta (Aβ1-40) proteins were coated with gold colloid particles so we could use an UV-vis spectrometer to allow us to examine the protein absorbance between 400nm and 1200nm wavelengths when alternating between acidic conditions and basic conditions. The protein absorbance essentially allowed us to examine the protein's color shifting from red to blue when going from a basic condition to an acidic condition. This was done while keeping the temperature of the solution at 25° C. For the experiment, hydrochloric acid and sodium hydroxide were used, respectively, to change the pH of the protein in solution.

pH 4

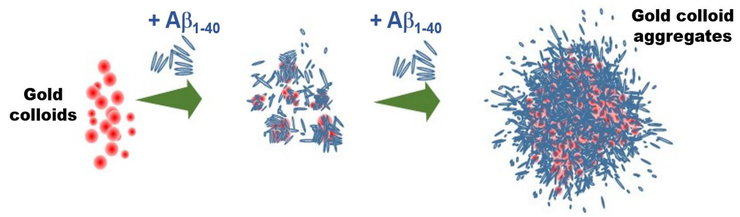

Figure 4. Sketch showing the aggregation of gold colloid when subjected to an acidic condition (pH~4)

pH 10

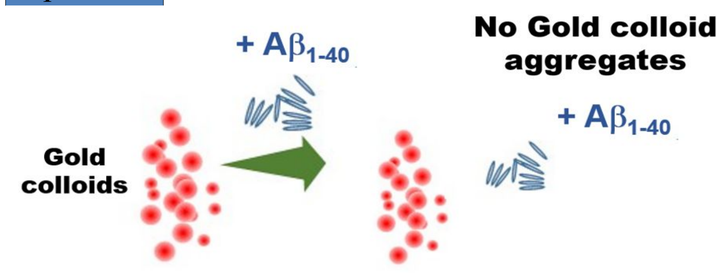

Figure 5. Sketch showing that gold colloid does not aggregate when subjected to an acidic condition (pH~10)

Acknowledgements

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References

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Results

Our group was able to determine that there is a concentration dependence. It was known that amyloid-beta proteins coated with certain-sized gold colloid particles demonstrated a form of reversibility in the protein structure. This was indicated by the folding and unfolding when placed in basic conditions after being exposed to acidic conditions - indicating the ability to return to its original state. However, our experiment showed that this reversibility does not depend only on the size of the gold colloid particles but also on the concentration of the amyloid beta proteins; increasing the concentration of the protein in solution increases the degree of reversibility the protein can sustain itself to. So far, we have analyzed the trend between concentration and reversibility of 30nm and 60nm gold colloid particles.

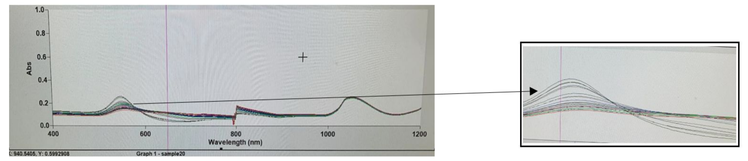

Figure 6. An image of the UV spectrum which shows the reversibility of the protein.

Future Directions

To further our studies, it would be imperative to study other nanoparticle sizes and amounts of protein in other diseases to observe the reaction of pH shifting. Applying this to other diseases like Parkinson's and Lou Gehrig's Disease, in which the process of protein aggregation can also be quasi-reversible through pH changes will help us better understand and create treatments for them. Another step would be to use the Raman Imaging System to further analyze the data. The Raman Imaging System is a specialized microscope that would allow us the examination of the protein's structure and size.

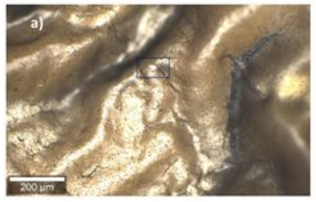

Figure 6. (b) The white-light image of a section of the tissue with x10 magnification

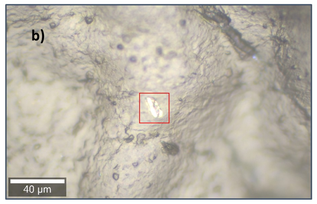

Figure 6. (b) The white-light image of a section of the tissue marked by a box in (a) with x50 magnification.