Computational Study of Amyloid Fibril Inhibition Mechanism by Hydrogen Sulfide

Aldarondo Torres, Wester (School: CROEM HS)
Santiago-Russe, Ana (School: CROEM HS)

Amyloid fibrils are small or slender fibers that can be found all around the human body and are formed by misfolded proteins. These fibers are resistant to degradation and can cause many diseases which are characterized by the protein which misfolded. These diseases include Alzheimer's disease, type 2 diabetes, Parkinson's disease, vascular dementia and others. In human insulin and hen egg white lysozyme, which were the proteins chosen for experimentation due to their availability, fibril formation can cause diseases or complications such as episodes of severe hypoglycemia, fatal insomnia, and the Creutzfeldt-Jakob disease. However, research has demonstrated that hydrogen sulfide inhibits amyloid fibril formation by causing significant rearrangements in the proteins' disulfide bonds. Little is known about how and where hydrogen sulfide docks within the insulin and lysozyme proteins and which disulfide bond causes the inhibition mechanism of amyloid fibrils, but understanding this would help thousands of lives. Hydrogen sulfide docked approximately 2.543 angstroms from insulin's Gly23 peptide and 3.023 angstroms from the Phe24 peptide. In the lysozyme protein, it docked around 14.004 angstroms from the Glu35 peptide and 14.011 angstroms from the Asp54 peptide. Insulin's closest disulfide bond to the H2S molecule connects the Cys19 and Cys20 peptides and was approximately 5.230 angstroms from the molecule. Lysozyme's closest disulfide bond was approximately 9.170 angstroms from the molecule and it connects the Cys76 and Cys94 peptides. This means that these bonds are most likely responsible for the inhibition mechanism of amyloid fibril formation and opens a new path for research.