Siemens Competition
Math : Science : Technology
Regional Finalist

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Mentor: Dr. Alexander V. Birk
Project Title: *A Novel Peptide Alters the Alzheimer's β-amyloid Equilibrium to Protect Against Aβ Oligomer Neurotoxicity* (Biology)

A defining feature of Alzheimer's Disease (AD) is the presence of large deposits of amyloid β-peptide (Aβ) in the brain. This accumulation of Aβ is widely regarded as one of the most prominent pathogenic mechanisms of AD. The amyloid cascade hypothesis describes the self-assembly of Aβ into a large range of species with differing sizes, conformations, and toxicities. In the past decade, extensive studies have implicated soluble intermediates of the Aβ cascade called oligomers as the primary causative agent behind the disorder. These small oligomers, rather than large, insoluble amyloid fibrils, cause the neuronal cell death and loss of function characteristic of the AD brain. Here, a unique approach to AD treatment is presented where pharmacological modulation of the Aβ equilibrium promotes Aβ fibrillogenesis to reduce the concentration of neurotoxic Aβ oligomers. Detailed biochemical studies revealed that [ald]SS31, an aladan analog of the blood-brain barrier permeable, mitoprotective drug Bendavia (SS31), was able to alter the Aβ equilibrium to favor the assembly of nontoxic amyloid fibrils. By accelerating fibril formation, [ald]SS31 decreases the prevalence of harmful amyloid intermediates and protects N2A cells from the inherent reactivity and neurotoxicity of Aβ oligomers, demonstrating its potential as an AD therapeutic.