Siemens Competition
Math : Science : Technology
Regional Finalist

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Project Title: *Identification of α-Synuclein Peptides A29-V40 and G51-Q62 as Neuronal Toxicants and Peptides N65-A76 and G67-A78 as Neuroprotective Agents* (Biology; Genetics; Toxicology)

Malformed α-synuclein (α-Syn) aggregates contribute to the pathogenesis of synucleinopathies, such as Parkinson's disease (PD), either by directly attacking neurons or by activating microglia (innate immune cells in the CNS) to release neurotoxic inflammatory mediators. Although the ways by which the various domains (or peptides) of full-length α-Syn (FL-α-Syn) contribute to α-Syn aggregation have been well characterized, little is known about whether the individual peptides are neurotoxic themselves and whether these peptides influence α-Syn aggregate-induced neuronal damage. By monitoring superoxide production from α-Syn peptide-stimulated microglia, we identified A29-V40 and G51-Q62, which correspond to loci in FL-α-Syn that contain alanine 30 and alanine 53, respectively, and are capable of activating microglial NADPH oxidase and causing neuronal damage. Meanwhile, we also found two neuroprotective peptides, N65-A76 and G67-A78, which are located in the non-amyloid-β component (NAC) region and are able to attenuate α-Syn aggregate-induced neurotoxicity. Exploring the molecular basis of this reaction revealed that both these NAC peptides suppressed the ability of α-Syn aggregates to adhere to the microglial surface and precipitate their receptor, CD11b. Collectively, our study not only provides novel mechanistic information regarding how α-Syn causes neuronal injury but also suggests that NAC peptides may be applied toward PD therapy.