Siemens Competition
Math : Science : Technology
Regional Finalist

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Project Title: *Structural Insight into the Ultrasensitivity of the Newly Developed Calcium Indicator GCaMP6* (Biophysics)

Ca2+ signaling is important for numerous physiological processes and Ca2+ imaging has become increasingly popular for studying the cellular and molecular mechanisms. The newly developed GCaMP6 shows superior brightness and ultrasensitivity to calcium concentration change. To understand the structural basis underlying the outperformance of GCaMP6, I crystallized Ca2+-bound GCaMP6 monomer and dimer and, by collaboration, determined their crystal structures at 2.7 and 2.49 Å, respectively. Comprehensive structural analyses provide mechanistic insights into how the superior properties of GCaMP6 are achieved from substitution mutations of the parent version GCaMP5G. Three substitution mutations and the resulting changes of local structure and interaction explain the ultrasensitivity and increased fluorescence intensity common to all three versions of GCaMP6. Each particular substitution in the individual GCaMP6 variants is also structurally consistent with their differential sensitivity, intensity, and speed, maximizing the potential of using GCaMP6 in solving diverse problems in calcium signaling. Based on the protein structure of GCaMP6 and the construction of previously developed multi-color calcium probes with lower sensitivity, I propose the rational design to generate ultra-sensitive calcium indicators of different colors. This study has the potentials of contributing to more precise monitoring of Ca2+ dynamics and revealing the functions of Ca2+ related signaling processes.