Discovery and Engineering of an Excitation Ratiometric Chloride Biosensor

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Over the last two decades, fluorescent protein-based biosensors have become important tools to monitor and measure cellular chloride in populations of cells with spatial and temporal resolution using microscopy. Due to the omnipresence of chloride transporters across diverse biological processes, researchers must be equipped with a suite of biosensors with a range of properties. These include excitation/emission profiles, chloride binding affinity, and operational pH, to name a few. However, progress to this end has been limited to single domain, intensiometric and multi-domain, ratiometric sensors. To expand the chloride biosensor toolkit, we are identifying and engineering new chloride-sensitive fluorescent proteins for cellular imaging applications. In this presentation, I will describe 1) how structure-guided bioinformatics has led to the discovery of naturally chloride sensitive cgreGFP from the hydrozoa Clytia gregaria and 2) how directed evolution has unlocked a single domain, excitation ratiometric sensor.