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FRET Biosensors: Engineering Fluorescent Proteins as Biological Tools for Studying Parkinson's Disease

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ABSTRACT

Parkinson's Disease (PD) is a common neurodegenerative disease with over 200,000 new cases each year. In general, the cause of the disease is unknown, but oxidative stress inside of neurons has been associated with the disease's pathology for some time. Currently, techniques to study the onset of PD inside of neurons are limited. This makes treatments and causes difficult to discover. One solution to this has been fluorescent protein biosensors. In short, these proteins can be engineered to glow when a certain state is achieved inside a cell. The present research discusses the engineering of a genetically-encoded fluorescent protein (FP) sensor able to detect reactive oxygen species (peroxide, hydroxyl, superoxide, etc.) inside of neurons, giving one the ability to enhance their understanding of the role these species play in the onset of the disease. This sensor relies on Förster Resonance Energy Transfer (FRET) between a green fluorescent protein and a red fluorescent protein to facilitate red-shifting of the sensor's emission spectrum. Linked via a short polypeptide chain, the energy transfer efficiency of these combined FPs can vary greatly. Various linker lengths and FP combinations were experimentally tested to draw conclusions about their performance. The current trajectory of the research currently implies that those combinations with the shortest linker lengths will yield the highest-performing sensors. This sensor is another vital piece in the library of tools which can be used to help us begin answering the many questions we have about PD and its pathology.

KEYWORDS

FRET, Biosensors, Neurobiology, Parkinson's, Protein-Engineering