Development of protein molecular probes for detection of alpha synuclein oligomeric assemblies

Principal Investigators

KIM, JIN RYOUN

Institution

NEW YORK UNIVERSITY

Contact information of lead PI
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USA

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Development of protein molecular probes for detection of alpha synuclein oligomeric assemblies

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1

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Research Abstract
? DESCRIPTION (provided by applicant): The overall research objective is to develop a novel molecular probe for rapid, quantitative, sensitive and specific detection of toxic oligomeric forms of alpha synuclein (?S), implicated in Parkinson's disease. Rapid, quantitative, sensitive and specific detection of ?S oligomers is preferred for (1) accurate probing of structurally unstable

?S oligomers, (2) implementation of high-throughput assays for pharmaceutical applications and (3) correct profiling of ?S oligomeric states. The currently available compounds or methods either do not sensitively distinguish ?S forms in distinct aggregation states or are inappropriate for rapid, quantitative detection due to the requirement of additional sample preparation and incubation steps. Due to the uncertainty associated with the molecular structures of toxic ?S oligomers, it is extremely difficult to come up with a simple design principle leading to the creation of highly specific and sensitive probes. Instead, an exhaustive variation of the physico-chemical nature of a probe prototype, and rapid and reliable evaluation of such variation are strongly required to develop novel probes with desired properties. In the submitted project, the PI proposes to construct a new molecular platform where one can synthesize and test a large array of probe variants displaying a wide range of physico-chemical natures associated with binding to ?S oligomers and subsequent generation of optical signals. In specific aims, a pool of related probe structures will be created and rapidly tested to identify probes that generate specific optical signals upon binding to oligomeric forms of ?S. Our long term goal is to develop a pool of probes capable of detecting distinct forms of ?S. Such a panel of probes will allow for rapid and reliable testing of therapeutic agents, developing early diagnostics, and a better understanding of ?S oligomerization processes.

Further information available at:

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United States of America

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