The Utilization of Bioluminescence for the Diagnosis of Alzheimer's Disease and Related Tauopathies

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In 2013, over 400,000 Americans died from Alzheimer’s disease. Early diagnosis may play a key role in increasing the success of potential preventive treatments, thus we sought to develop a new diagnostic tool for Alzheimer’s. Tau, a microtubule binding protein that contributes to Alzheimer’s disease pathology by aggregating and forming neurofibrillary tangles, is recognized as a potential biomarker for the disease, as levels of tau increase in Alzheimer’s patients. We hypothesized that, by fusing fragments of a luminescent protein to tau, we could take advantage of the process of Protein Fragment Complementation (a biological method to detect protein-protein interaction) to detect early steps in tau aggregation, which might prove to be a sensitive diagnostic tool to detect changes in tau levels and tau aggregation. In our cell-based Protein Fragment Complementation assay using tau, a luciferase molecule is divided into two halves, each half of which is attached to tau. Upon interaction of two (or more) tau molecules the two halves of luciferase are brought close together, leading to reconstitution of the luciferase enzyme which is detected by emission of a light signal. We further demonstrate that, upon addition of extracellular tau fibrils, which are present in Alzheimer’s patients, this light signal increases considerably. These data serve as proof-of-principle that call for further experimentation, including eventual plans to test our cell-based assay using cerebrospinal fluid and blood samples from Alzheimer’s versus control patients. Our results are an encouraging first step toward the development of a more efficacious diagnostic tool for Alzheimer’s disease, and possibly other diseases in which tau accumulates.

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