Applying the Surface Plasmon Resonance of Gold Nanoparticles to Denature Proteins Characteristic of Alzheimer's Disease

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Beta-secretase (BACE), an enzyme responsible for the endoproteolysis of amyloid precursor protein to produce the hallmark amyloid-beta plaques of Alzheimer's pathology, has been of considerable interest to the medical community as a target for drug development. Yet, numerous small-molecule therapeutic candidates developed for BACE have faltered in clinical trials due to a lack of specificity, adverse side effects, or an inability to cross the blood-brain barrier, demonstrating the need for innovative alternatives. In contrast with the small-molecule approach, this experiment investigated whether the surface plasmon resonance induced oscillation of 800 nm near-infrared resonant gold nanorods, and their consequent ability to generate localized heat, could serve as a mechanism to denature BACE. To determine whether gold nanorod-mediated photothermal therapy successfully denatured the enzyme, tryptophan fluorescence analysis was utilized to track its structural changes. The results suggest that by conjugating gold nanorods with BACE via polyethylene glycol and anti-BACE antibodies, the denaturation of BACE was induced upon irradiation with a 10W, near-infrared light. This novel tactic, which has never been translated from the cellular to the molecular level, indicates the potential of plasmonic nanogold in protein-specific therapeutics. These findings may serve as a platform for addressing the shortcomings of past drug development for Alzheimer’s disease, and for a diverse array of other therapeutic applications in protein-related illnesses.