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Therapeutic Medication Using the Oligomer Aβ₂₂Δ With the New Aβ₂₂Δ

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Beta-amyloid (also called Aβ) is a protein fragment that aggregates into amyloid plaque, a characteristic feature of Alzheimer pathology. Beta-amyloid also aggregates into smaller clusters called oligomers, which cannot be detected as easily as amyloid plaque. Both clusters and oligomers are toxic to nerve cells, but recent evidence suggests that oligomers may be the main cause of neurodegeneration. This idea, however, has not been proven.

Hiroshi Mori, Ph.D. and colleagues have identified a unique inherited form of Alzheimer's disease that may help to solve this dilemma. Persons affected by this form of Alzheimer's disease have a mutation in the gene that codes for amyloid precursor protein (APP), which is eventually cut into pieces yielding beta-amyloid. This genetic mutation leads to the formation of a mutated form of beta-amyloid known as Aβ₂₂Δ. Like normal beta-amyloid, Aβ₂₂Δ forms oligomers, but it is not able to form amyloid plaques.

Dr. Mori and colleagues have observed that persons with the Aβ₂₂Δ mutation exhibit many of the features of Alzheimer's disease, but they do not have amyloid plaques in their brain. The researchers now plan to perform detailed studies of mice that have been genetically altered to carry the Aβ₂₂Δ mutation. They will study how this mutation affects the cognitive function and behavior of the animals, as well as the biochemical and electrical properties of their nerve cells. The researchers will also test whether the mutated form of beta-amyloid, or antibodies to oligomers can reduce the detrimental effects of normal beta-amyloid. These studies will help to answer one of the key questions about the causes of neurodegeneration in Alzheimer's disease, and may suggest targets for potential treatments.