Evidence of Toll-like Receptor Nine-Mediated Amelioration of Amyloid Pathology in a TgSwDI Mouse Model of Alzheimer's Disease

Herber, Charlotte

Alzheimer’s disease (AD) is the most common and costly neurodegenerative disease, increasing in prevalence and expense annually. This study investigated a method of passive immunization to prevent and remove the amyloid plaques that cause AD without adverse side effects. By stimulating a nontoxic immune response via toll-like receptor nine (TLR9) using type B cytosine-guanine DNA oligodeoxynucleotides (CpG ODNs), we hoped to eliminate the neurotoxicity and cerebral microhemorrhage observed in previous vaccination studies. Previously investigated in Tg2576 and 3xTg mouse models of AD, these compounds were histologically and biochemically assessed for efficacy and toxicity in two age cohorts of TgSwDI mice. This murine model expresses extensive vascular amyloid resembling the prevalent complication of AD called congophilic amyloid angiopathy (CAA), known to increase hemorrhage risk. Behavioral tests and histological analysis of stained brain sections in two age groups indicated that CpG ODNs significantly improved cognitive function and reduced vascular amyloid burden by an average of 30% without associated neuroinflammation or hemorrhage, in both age cohorts. The stimulated innate immune pathways were currently subject to mechanistic studies. This suggests that TLR9 stimulation could constitute a safer method to successfully prevent and ameliorate amyloid-beta AD pathology in humans.

Awards Won:

Third Award of $1,000