OFFICIAL ABSTRACT and CERTIFICATION

Stimulating Innate Immunity via TLR9 agonist CpG ODN in a Non-Human Primate Model

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Alzheimer's disease (AD) is the most common dementia characterized by hallmarks such as neurofibrillary tangles, amyloid plaques, and cerebral amyloid angiopathy (CAA). Additionally, inflammation and glial function have been recognized to play an important role in neurodegeneration. There is currently no effective treatment for AD. Previous research indicates immunomodulation has been successful in reducing AD pathology in mice. The current study aims to determine if squirrel monkeys are an appropriate model to use for AD research, innate immune stimulation via TLR9 agonist class C CpG ODN is safe to use in squirrel monkeys, and class C CpG ODN is an effective treatment for AD. To decide if the monkey model was acceptable for AD research, the current study compared young and old monkeys for the presence of astrocytes, T-cells, and glial cells via histological staining. Results indicated that old monkeys had a greater presence of T-cells and glial cells present, suggesting that aging had taken place in older monkeys, like that of humans. Through histological staining and semi-quantitative analysis, it was determined that CpG ODN did not cause any adverse effects in squirrel monkeys when compared to the monkeys receiving a saline control, suggesting its safety. Additionally, CpG ODN injections increased microglial activation, reduced T-cells in the squirrel monkey model, and increased cytokine presence in plasma associated with inflammatory, and anti-inflammatory response.

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