Development of ASOs for multiple system atrophy

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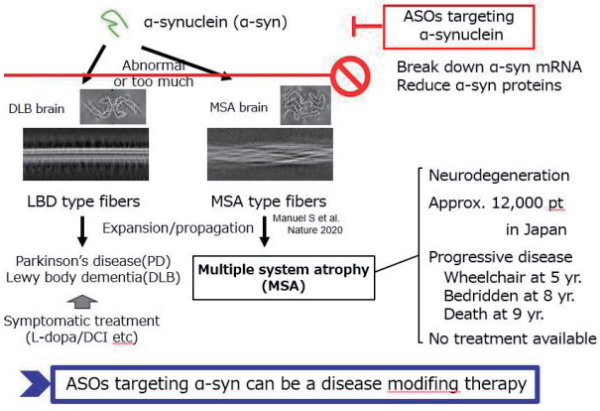
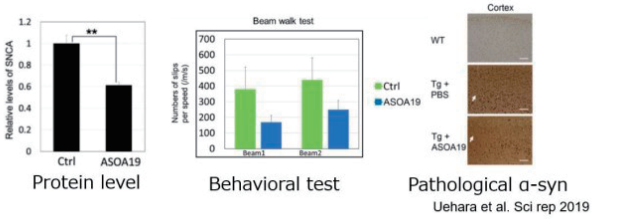
Project Outline

Multiple system atrophy (MSA) is the neurodegenerative disorder affecting about 12,000 people in Japan. Multiple symptoms including motor and autonomic symptoms progress, and patients eventually become bedridden. Currently, no effective treatment is available, thus vigorous researches have been conducted to elucidate the mechanism and develop treatment of MSA all over the world. Cumulative evidences indicate that pathological alpha-synuclein aggregates accumulate in oligodendrocytes and spread through brain, leading to neuronal death in MSA. That's why therapies targeting alpha-synuclein are considered as one of the promising strategies, and among them is the antisense-oligonucleotide(ASO).

We have developed ASOs targeting the coding sequences of alpha-synuclein. We've already had patents and found sequences that effectively suppress human alpha-synuclein *in vitro* and *in vivo*. The prototype ASO ameliorated the Parkinson's disease phenotype in transgenic mice model and suppressed alpha-synuclein expression in primates. Recently, we have developed next-generation ASOs that may be safer and more potent than the original version. We now test these ASO(s) to reveal whether they can suppress human alpha-synuclein in transgenic mice and ameliorate the disease progression and phenotype of mutant alpha-synuclein preformed fibrils-injected mice model with MSA-like parkinsonian pathology. Once we prove the concept that these modified ASO(s) are effective against aipha-synucleinopathy, we will transfer this seed to the stage of clinical evaluation.

Finally, our seeds could be applied to Lewy body diseases including Parkinson's disease and Lewy body dementia which suffer more than 6 million people worldwide.





Prototype ASO suppress α-syn and ameliorate related pathology

Targeted disease：Multiple system atrophy (approx. 12,000 persons in Japan)
Patent information：Application submitted
Characteristics of the technology ：Antisense oligonucleotide containing modified nucleic acids with optimized sequences
We are seeking for：Collaboration, license-out, and/or support for transfer to investigator-initiated clinical trial(s)