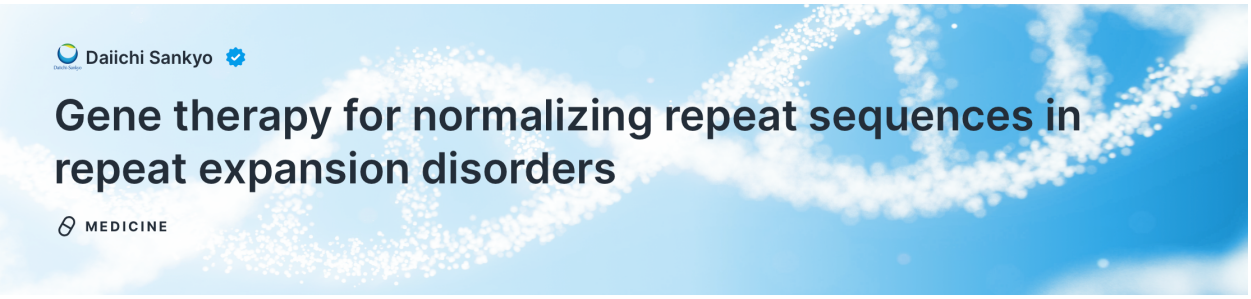

Background
Repeat expansion disorders are a group of hereditary diseases characterized by the abnormal repetition of specific DNA sequences within genes. These expansions lead to the loss or gain of function of gene products, resulting in a range of debilitating clinical manifestations. Notable examples of these disorders include Huntington's disease, spinocerebellar ataxia, and myotonic dystrophy type 1. Despite ongoing research into therapeutic agents for these conditions, the development of effective gene therapies remains elusive. Gene therapies targeting repeat expansion hold significant promise, as they could potentially provide sustained, long-term effects with a single administration. This approach could effectively halt the progression of these debilitating disorders and may even offer a pathway toward their cure. Given that most repeat expansion disorders exhibit autosomal dominant inheritance, strategies focused on selectively reducing the expression of the mutated gene or normalizing the repeat expansions are particularly desirable. Furthermore, emerging evidence suggests that several repeat expansion disorders share common underlying mechanisms. This presents an exciting opportunity for the development of a therapeutic strategy that could be applicable across multiple conditions, despite their rarity.

What we're looking for
We are seeking novel gene therapeutic technologies to selectively normalize or reduce the expression of abnormal repeat expansions. This includes approaches that utilize Adeno-Associated Virus (AAV)-derived nucleic acids, proteins (peptides), and regulatory factors to inhibit transcription or promote the degradation of repeat sequences. Additionally, we are interested in AAV-derived genome editing technologies that have unique features regarding editing efficiency, versatility, and safety for normalizing repeat sequences.

Solutions of interest include:

- AAV-mediated allele-specific gene silencing to selectively target mutated alleles while preserving normal gene function.
- CRISPR-based editing or other high-fidelity genome editing tool to ensure precise repeat sequence targeting and minimize off-target effects.
- Models that mimic human repeat expansion mutations for in-depth testing and preclinical evaluation, including patient-derived induced pluripotent stem cell (iPSC) models, organoid models, and transgenic animal models.

Our must-have requirements are:

- The technology should be easy to incorporate into AAV for gene therapy applications.
- The approach should be designed to specifically target and modify abnormal repeat expansions, minimizing the risk of off-target effects.

Our nice-to-have's are:

- The technology should ideally be unique and applicable to multiple trinucleotides repeat disorders.
- Animal or in vivo data available.
- Data showing low risk of immunogenicity and genetic variation.
- In vitro data should demonstrate the effect of shortening (repairing) elongation repeats in cultured cells.

What's out of scope:

- Small molecules
- Simple antisense oligonucleotides (ASOs) targeting disease-specific target genes

Acceptable technology readiness levels (TRL): Levels 1-5

1. Basic principles observed
2. Concept development
3. Experimental proof of concept
4. Validated in lab conditions
5. Validated in relevant environment
6. Demonstrated in relevant environment
7. Regulatory approval
8. Product in production
9. Product in market

What we can offer you
Eligible partnership models:
Sponsored research

Benefits:
Sponsored Research
Funding is proposal dependent, with up to $ 100K for 12-month project with potential follow-on funding for 1 year.

Who we are
At Daiichi Sankyo, we attach significant importance to working with academic institutions, startups and bioventure companies to discover new therapeutics in the place where hypotheses are brought and tested in order to expand possibilities for scientific innovation breakthrough. We build sustainable relationships with partner institutions and companies through open and fair alliance management and trust based on mutual respect as the

foundation for effective collaborations. Our goal is to jointly create new value for patients by maximizing each other's expertise and strengths.

Reviewers

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