# TECHNOLOGY BRIEF

Therapeutic

# A new treatment approach for DNA repeat expansion diseases

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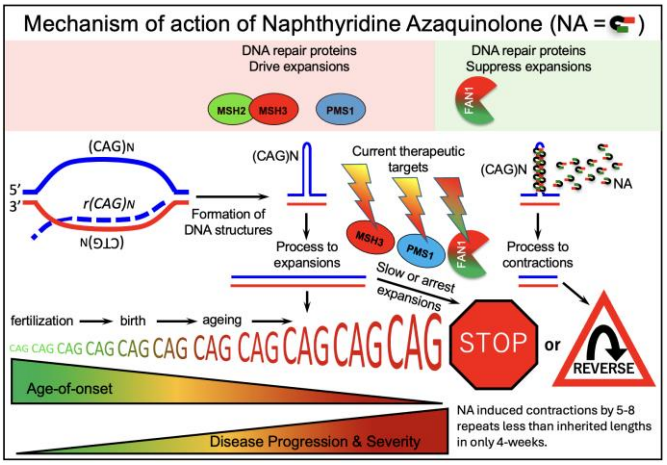
## Background

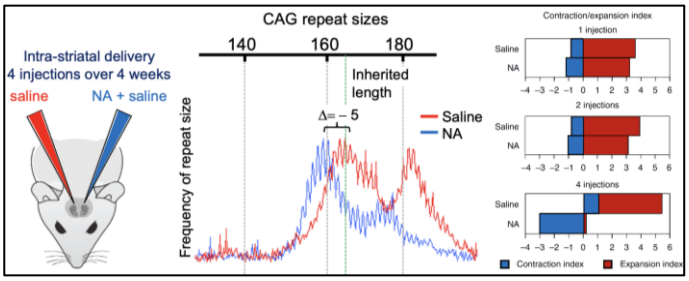
Genetic expansions of repeat sequences, like CAG tracts, in certain genes have been linked to at least 74 neurodegenerative, neurological, and neuromuscular diseases, including Huntington's disease (HD), various spinocerebellar ataxias (SCAs), myotonic dystrophy (DM1), amyotrophic lateral sclerosis (ALS), and frontotemporal dementia (FTD). The inherited repeat expansion continues to somatically expand in affected tissues as the individual ages, resulting in earlier age of disease onset, increased disease progression and severity. Decreasing the number of repeats could delay disease onset by years, and arresting or reversing somatic CAG/CTG expansions could be used to arrest or even reverse disease onset, progression, and severity.




DNA repair proteins drive or suppress repeat expansions by aberrant processing of slipped-DNAs, which drive or suppress disease onset, progression and severity. Targeting DNA repair proteins will slow or arrest expansions. Targeting mutation-specific slipped-DNAs with Naphthyridine-Azaquinolone (NA) can rapidly and specifically induce contractions to less than the inherited repeat length, rapidly leading to clinical benefit.

## Description of Invention

The Pearson Lab has developed a platform to discover chemical matter (small-molecules) specific to CAG and other repeat diseases. Indications include various CAG expansion diseases (HD, SCAs, and DM1, ALS, and FTD).




*NA induces repeat contractions in vivo over 4 weeks.*

## Commercial Applications & Advantages

Inducing contractions of expanded repeats can be a transformative therapy for individuals with a range of neurodegenerative conditions, for which there is currently no disease-modifying treatment. Unlike competing approaches, targeting disease-specific slipped-DNAs induces contractions with an efficacy that suits the rapid timeline of a clinical trial.

## Development Stage

Preclinical *in vitro* and *in vivo* data in disease-specific brain regions with phenotypic, pathological and biomarker improvement are promising. Next steps include medicinal chemistry, pharmacokinetic, animal efficacy, and toxicology studies.

## Publications

10.1038/s41588-019-05758
10.1016/j.nbd.2021.105604
10.1016/j.celrep.2021.110078

## Patent Status

Patent *Method of Treating diseases associated with Repeat Instability* issued in US 20210283114 on 13-06-2023, Japan JP 2019524160 A on 05-11-2023, EP 3496713 A1 on 13-03-2024, CA 3033590 A1 pending in Canada.

**IP&C is seeking investors to launch a start-up company.**