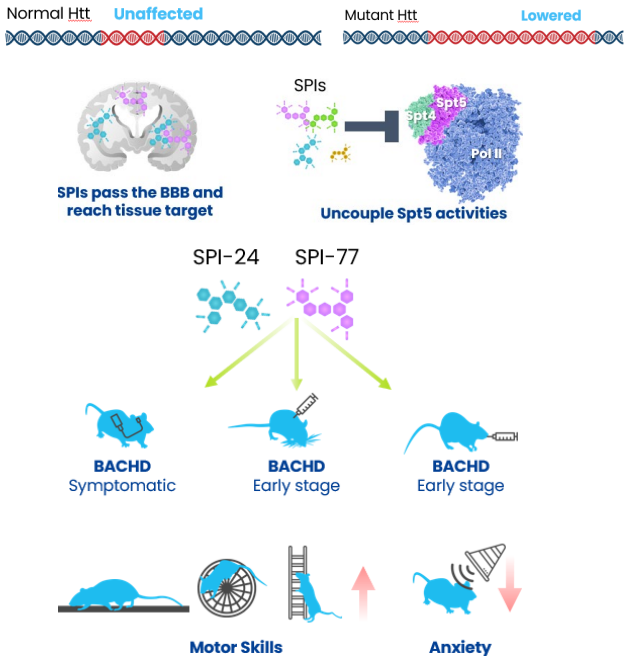
Small Molecules for Treatment of Huntington's Disease and Related Disorders

Therapeutics

Reference Number: **1947** \ Principal Investigator: **Prof. Rivka Dikstein** \ Patent Status: **2021-0379060-A1**

A new class of small molecules offers a targeted strategy for treating Huntington's disease (HD) and related trinucleotide repeat expansion disorders (TREDs). These compounds bind one of the interaction surfaces between transcription factor Spt5 and RNA Polymerase II—specifically required for expressing expanded, pathogenic repeats—thereby selectively silencing the mutant allele while preserving normal gene expression. This precision mechanism may reduce toxicity and improve therapeutic outcomes.



APPLICATIONS

- Treatment of Huntington's Disease (HD)
- Potential treatment of other TREDs, including: Spinocerebellar Ataxias 1, 2, 3 and 7, , Myotonic Dystrophy Type 1 etc.

DEVELOPMENT STAGE

- Hit compounds have been identified and validated in vitro, demonstrating selective activity
- In vivo studies in HD mouse models indicate a favorable safety profile, reduced anxiety, and improved motor skills
- Further compound optimization is ongoing, including testing in ALS models

DIFFERENTIATION

Allele-selective inhibition: targets mutant but not normal gene expression

Novel mechanism of action: binds the surface between transcription factor Spt5 and RNA Polymerase II

Demonstrated in vitro and in vivo efficacy

No apparent toxicity

REFERENCES

- Bahat et al, Mol. Cell. 2019
- Bahat et al, EMBO Mol Med, 2024