Huntington’s Disease: Pathophysiology and Clinical Prospects

Nina Stöberl and Nicholas D. Allen, School of Biosciences, Cardiff University, The Sir Martin Evans Building, Museum Avenue, Cardiff, UK, CF10 3AX

Huntington’s disease (HD) is a severe monogenic neurodegenerative disorder. It is caused by a dominantly inherited CAG trinucleotide repeat expansion in the huntingtin (HTT) gene, which encodes for an elongated glutamine stretch in the HTT protein. The progressive brain degeneration in HD is characterized by the prevalent loss of GABAergic medium spiny neurons (MSN) in the striatum. Clinical features include progressive motor dysfunctions and cognitive impairments.

Genetic and Clinical Manifestations

Juvenile Onset: >50 CAG

Somatic expansions

Huntington’s Disease Brain Pathology

The left hemispheres show a normal healthy brain, while the right hemispheres show HD-specific histopathological hallmarks. The most striking feature of HD is neuronal loss in the striatum along with enlarged lateral ventricles. In progressed stages of the disease, degeneration also occurs in the cortex.

Therapeutic Strategies

Currently, there are no curative treatments for HD that can halt or reverse the disease. Commonly used symptomatic treatments can improve the quality of life of affected patients by addressing the movement, cognitive, and psychiatric symptoms. Novel therapeutics with the intent of slowing disease progression are being developed. These approaches target pathways specific to HD biology. Among these approaches, mHTT lowering therapies hold great promise.

References

1. Massey & Jones (2018). Huntington’s Disease Brain Pathology
2. Tabrizi et al. (2020). Huntington’s Disease Brain Pathology
3. Cattaneo et al. (2020). Huntington’s Disease Brain Pathology
4. Saudou & Humbert (2016). Huntington’s Disease Brain Pathology
5. Jimenez-Sanchez et al. (2021). Huntington’s Disease Brain Pathology
6. HD iPSC Consortium (2012). Huntington’s Disease Brain Pathology
7. Takahashi & Yamanaka (2006). Huntington’s Disease Brain Pathology
8. Arrasate & Finkbeiner (2014). Huntington’s Disease Brain Pathology
9. Hong & Tae Do (2019). Huntington’s Disease Brain Pathology
10. Cold Spring Harb Perspect Med. 910. Huntington’s Disease Brain Pathology
11. Hong & Tae Do (2019). Huntington’s Disease Brain Pathology
12. Cell Stem Cell. 34. Huntington’s Disease Brain Pathology
13. Nat Rev Neurosci. 17. Huntington’s Disease Brain Pathology
14. Cell Death Diff. 23. Huntington’s Disease Brain Pathology
15. Dis Model Mech. 16. Huntington’s Disease Brain Pathology
16. Mol Neurodegeneration. 15. Huntington’s Disease Brain Pathology
18. Mol Neurodegeneration. 13. Huntington’s Disease Brain Pathology
20. Neuron. 11. Huntington’s Disease Brain Pathology
22. Cell Stem Cell. 9. Huntington’s Disease Brain Pathology
23. Science Transl Med. 8. Huntington’s Disease Brain Pathology
24. Nat Chem. 7. Huntington’s Disease Brain Pathology
25. Cell Stem Cell. 6. Huntington’s Disease Brain Pathology
26. Cell Stem Cell. 5. Huntington’s Disease Brain Pathology
27. Cell Stem Cell. 4. Huntington’s Disease Brain Pathology
28. Cell Stem Cell. 3. Huntington’s Disease Brain Pathology
29. Cell Stem Cell. 2. Huntington’s Disease Brain Pathology
30. Cell Stem Cell. 1. Huntington’s Disease Brain Pathology

NOTE: This poster conveys a general overview and should be considered neither comprehensive nor definitive.

Learn more | tocris.com

Bio-Technne® | R&D Systems™ | Novus Biologicals™ | Tocris Bioscience™ | ProteinSimple™ | ACD™

bio-techno.com

© 2022 Bio-techno