Question/Biological Problem

Huntington's disease is a inherited disease that causes degeneration of nerve cells in the brain and impacts a person's functional abilities resulting in movement, cognitive and psychiatric disorders [1]. This disease is caused by mutations in the short arm of chromosome 4 also known as the Huntington gene [2]. This mutation known as the HTT mutation involves the CAG trinucleotide repeat DNA segment; which is made up of cytosine, adenine, and guanine repeating several times. This segment normally repeats 10-35 times within the gene, however, in the HTT mutation it repeats 36 to more than 120 times [3]. Furthermore, recent studies have found that calcium signaling is abnormal in Huntington's disease and the HTT mutation can be attributed to this abnormality.

Biological Question: My aim is to investigate how HTT mutation affects calcium signaling.

Research Plan:

- To see how expression of mutant HTT disturbs calcium signaling, a genetic probe named Camgaroo, developed to measure calcium dynamics, would be transiently transfected into the mutant HTT gene.
- Camgaroo is based on the fluorescence properties of YFP and its interactions with calmodium (CaM). Camgaroo has a single excitation peak at 490 nm and after calcium saturation the emission intensity will increase eight-fold.
- If mutant HTT facilitates the activity of the N2RB subtype of NMDA receptors and inositol triphosphate receptors, calcium signaling will be disturbed and will be detected then compared to control cells.

References

[1] Mayo Foundation for Medical Education and Research. (2020, April 14). Huntington's disease. Mayo Clinic. Retrieved September 28, 2021, from https://www.mayoclinic.org/diseases-conditions/huntingtons-disease/symptoms-causes/syc-20356117.

[2] Huntington's disease. NORD (National Organization for Rare Disorders). (n.d.). Retrieved September 28, 2021, from https://rarediseases.org/rare-diseases/huntingtons-disease/.

[3] U.S. National Library of Medicine. (2020, August 18). Huntington disease: MedlinePlus Genetics. MedlinePlus. Retrieved September 28, 2021, from https://medlineplus.gov/genetics/condition/huntington-disease/#causes.