DNA repeat expansion disorders are genetic disorders with abnormal expansion of repeated DNA sequences. More specifically, trinucleotide repeat disorders, a subtype of repeat expansion, are a series of three nucleotides repeated multiple times in a gene. A common example of this disorder is Huntington’s Disease (HD) which affects approximately 1 in every 10,000 people worldwide according to the Huntington’s Disease Society of America. This dominantly inherited, incurable, neurodegenerative disorder is a result of a CAG repeat expansion within exon 1 of the HTT gene. Symptoms of this disorder include progressive loss of motor control, speech difficulty, and most prevalently, cognitive deterioration. Research has shown the longer the length of the CAG repeat, the earlier onset of disease. To attempt to combat this disease, we are studying how to slow or even halt expansion to prolong the time before onset of symptoms. Overall, our goal is to understand the underlying mechanism of repeat expansions to develop potential therapeutic strategies to prevent disease progression and extend patient’s lives.

To further investigate the genetic properties of tissues affected by HD, polymerase chain reaction (PCR) was performed on various tissues in HD model mice to identify the HTT CAG repeat expansion size within these tissues. Furthermore, a comparison can be made between HD-model mice of different ages (6, 9, and 12 months). The tissues analyzed include the cerebellum and cerebral cortex of the brain, kidney, liver, gastrocnemius, and heart. Following a PCR procedure, agarose gel electrophoresis was performed to analyze the repeat size in the tissues and identify the degree of CAG expansion in each tissue. Gel imaging reveals repeat expansion to be most prevalent in the kidney and cerebral cortex, more so in older mice. This is consistent with the most prevalent symptom of those affected by HD: progressive cognitive decline due to expansion and subsequent neuron deterioration. Within HD patients, the striatum, found within the cerebral cortex of our samples, is most affected. My results show that a therapy targeting CAG repeat expansions in the cerebral cortex would be beneficial to treatment and delay symptoms of HD. Results of my research can be applied to other disorders also caused by repeat expansions, such as Friedreich’s ataxia (FRDA).