Lay Summary

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Genome and transcriptome analysis in DRPLA, other rare repeat expansion disorders and undiagnosed inherited ataxia tissue

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Repeat expansion disorders are inherited disorders where the disease gene has extra base pairs inserted (usually based CAGs), such as in Huntington's disease where the normal numbers of CAG repeats in the gene is under 36 but in patients it is usually above 40 and can be as high as 100 repeats. Other repeat disorders include ataxias (often called spinocerebellar ataxias or SCAs) and the rare disorders of Dentatorubral-pallidoluysian atrophy (DRPLA), Friedreich's ataxia.

Patients have progressive neurological problems characterised by ataxia, cognitive decline, often epilepsy and neuropathy. The cause of these disorders is poorly understood and the mechanism of repeat expansion is unknown and there are no known effective treatments. We would like to understand the mechanism and interesting pathways in patients with these disorders. For this we wish to obtain human tissue from as many patients and body regions as possible (brain, muscle and other tissue as well as blood and CSF where possible), numbers will be small as these are rare disorders. We will then investigate the repeat as compared to inherited ataxia without repeat expansions and compared with controls, in both DNA (genome) and RNA (transcriptome) and carry out sequencing on brain and other tissues, in comparison with control tissue.