INTRODUCTION

Motor Neurone Disease (MND) is a fatal, rapidly progressing neurodegenerative disease that affects the brain and spinal cord. It kills a third of a person within six months and up to 90% within three years of diagnosis. So far, people are diagnosed only when it is too late to do much for them. The UK MND Collections [1] is the brainchild of UK MND Network [2] which is an internationally recognised and unique resource set up in 2003 to assist researchers in finding the cause behind MND [3].

>3000 people living with MND/Spinal cord injury (SCI) provided blood samples (DNA was extracted using Nuclear (ACAC) protocols) along with clinical/phenotypic data, between 2003 and 2012.

- Lymphoblastoid cell lines (e.g. Epstein-Barr virus transformation) were also produced from the white blood cells of the majority of these samples.

An epidemiology survey was conducted on 200 participants and 200 separately matched controls. Data examples include: Male/female, employment and environmental exposures.

Sample collection concluded and the resource became fully accessible in 2012 with >50 papers published to date and data/samples shared with over 20 countries across the world.

OBJECTIVES:

To map the full DNA profiles of at least 15,000 people with ALS and 7,500 control subjects, and to perform comparative analyses on the resulting data.

- To identify the last remaining major type of variation, namely rare or moderate frequency variants contributing to apparently sporadic ALS risk.

METHODS:

- WGS, GMA and methylated chip array.

RESULTS TO DATE:

- MND Collections has contributed over 1,600 samples (sporadic MND and controls), the largest contribution by any country outside the Netherlands. All of these have undergone WGS and the methylation chip array is almost complete.

- Analysis of resulting data is ongoing (>10,000 samples have undergone WGS, with 6 working groups now set up, demonstrating very good collaboration internationally, to focus on different analyses including epigenetics and phenotype-genotype associations.

- So far 6 at 8 new genes have been discovered to be associated with MND.

- Many peer-reviewed papers already published, this increases every year.

FURTHER COLLABORATION:

- MND Collections was the second cohort outside of the Netherlands to join the project initiative which helped give the project credibility to go global.

- Prof A/Chabali (the lead PI for the UK) shared his successful grant application, as a template, with many other countries to assist their funding applications.

- One of the working groups is focused on ethically optimising data sharing to accelerate drug discovery with commercial partners.

- Other countries are now sharing their WGS data (alone or separately) to enrich the data collected in Project MinE.

- New collaborations with Answer ALS, Target ALS and the New York Genome Center.

- Multiple government agreed to cover the huge cost for Project MinE to have dedicated space on a supercomputer.

- Data sharing is currently underway to enhance the ENRICHD (European Network for the Cure of ALS) survival prediction model.

- New citizen science project underway (in testing phase) to allow mobile phones to analyse small sections of genetic data to contribute to data analysis computing power.

- Most of our samples have a matching cell line available (the only ProjectMinE funded project who can offer this).

Discoveries in the data can be modelled very closely/confidently in the laboratory.

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