

## Guide to the UK MND Collections

### Background

The UK MND Collections include a DNA and Cell Bank and an Epidemiology Dataset. They were established to provide the international research community with a resource to identify and understand causative and disease modifying factors in motor neurone diseases. Initially conceived as a DNA bank from people with MND, spouse controls and family members, with EBV transformed lymphoblastoid cell lines as an everlasting supply of DNA, the Collections have now evolved. The lymphoblastoid cell lines are now available as a cell line to understand the aetiopathogenesis of MND (rather than solely as a supply of DNA). Combined, the genomic DNA and the cell lines form the DNA and Cell Bank part of the Collections. More information on the DNA and cell bank is available in Smith et al BMC Genetics (2015) 16:84. Two hundred people with MND who donated a blood sample for the DNA and Cell Bank also completed epidemiology questionnaires. Together with questionnaire data from age and gender matched (non-spouse) controls these data form the Epidemiology Dataset part of the UK MND Collections.

### DNA and Cell Bank Collections



The MND Association has established partnerships with UKBioCentre and the European Collection of Cell Cultures (ECACC). They house, maintain and store samples that form our DNA and cell bank within the UK MND Collections respectively. Samples are available from people with inherited and sporadic MND, spouse controls and family members of people with MND. Family member samples are available in very limited numbers, from family members of people with inherited MND, and from sporadic trios (either both parents or a parent and sibling of people with sporadic MND). Please contact the MND Association with enquiries about access to these family member samples. For more information on how the samples were collected, extracted and processed please see Smith et al BMC Genetics (2015) 16:84.

### Genomic DNA

UKBioCentre manages access to DNA samples in the DNA and cell bank part of the UK MND Collections. Where there are low yields of genomic DNA, users may be offered cell line DNA as an alternative.

### **Cell lines**

As one of the Public Health England collections, ECACC manage and store EBV-transformed lymphocytes derived from blood samples from participants. Two collections are housed here: a familial cell line range and a sporadic cell line range.

*Familial cell line range:* Samples within the familial cell line range were derived from people with inherited MND. 'Master and working cell banks' have been created for each participant's original cell line to ensure that the characteristics of the cells are as close to those of the original participant's blood sample as possible (thereby avoiding phenotypic drift). STR-profiling checks have matched the available cell lines to the Guthrie card from the blood sample received at ECACC and to the DNA samples stored at UKBioCentre. Quality control checking for mycoplasma and other organisms has also been performed. Please see the ECACC webpage for a searchable list of the samples available (searchable by their minimum dataset) or contact the MND Association.

*Sporadic cell line range:* This contains samples from people with sporadic MND, spouse controls and family members (see above for a description of the family member samples available). These form a larger part of the DNA and cell bank where individual samples are less in demand. The sporadic collection has a lower standard of quality control. Quality control checking (described above) has been done on a % of samples, STR profiling (to ensure participant identity) has not been performed and no master and working cell banks exist. (Where STR profile checking is required, this may be feasible, at the users' / applicants' expense).

A limited number of samples from family members of people with MND are also available. Specifically, cell lines are not available for family members of people with sporadic MND. (ie No trios are available as cell lines).

Cell pellets, growing cultures and DNA extraction services are available from ECACC on request.

### **Use of samples to date**

All sporadic patient DNA samples within the DNA and Cell Bank are in the process of being whole genome sequenced as part of the Project MinE initiative. Familial patient DNA samples are being whole genome sequenced in a separate project. More information on other analyses conducted on these samples is available from the MND Association.

## Epidemiology Dataset

### Introduction

The study resulting in the Epidemiology dataset was established alongside the DNA and Cell Bank collections to provide genetic, clinical and lifestyle information on a cohort of individuals, in order to identify potential environmental components contributing to disease in people with motor neurone disease.

### Objectives

The principal objective of the study was to investigate the association of risk factors with aspects of MND such as age of onset, survival or phenotype and interactions between risk factors. To investigate the association of risk factors with MND, using genotype-phenotype correlations, those participating in the epidemiology study were also invited to participate in the DNA and Cell Bank study. Participation in the DNA Bank study was not a requirement for entry into the epidemiology study.

### Recruitment

Two hundred patients and 200 controls were recruited into this epidemiology study.

People with MND were recruited from those attending MND clinics at King's College London, Sheffield and Birmingham (these were the co-ordinating centres of the DNA and Cell Bank study).

Age and sex matched controls were recruited for each patient. Wherever possible they were recruited from the same GP practice as a participating patient, or a GP practice in close vicinity. Controls were considered as eligible for the study if they were over 18 years of age, had no history of any neurological condition and were within 5 years of age of a participating patient.

All participants were asked to complete a self-report questionnaire and take part in an interview with a trained specialist nurse. The data are presented to researchers in one database, rather than separate self-report and interview databases. The data are pseudo-anonymised where each participant was assigned a study ID. Where appropriate these are linked to sample IDs for the DNA and cell bank.

In order to maximise power and the future utility of the data collected, many questions are the same as those used in a US study and lead investigators of this study are part of the ALS Consortium of Epidemiological Studies (ACES, Stanford University School of Medicine, CA, USA). Similarly, this study draws on a European collaboration, and members of this group are part of the European ALS Register (EURALS) initiative.

**DNA and cell bank overlap with epidemiology dataset**

DNA and cell lines are available for those whose data forms part of the epidemiology dataset. This includes a small number of age and gender matched non-spouse controls. Please contact the MND Association with enquiries about access to these samples.

**Appendix 1: Minimum Dataset**

### **Minimum dataset of the UK MND Collections**

All approved users of the samples from the MND Collections will receive a minimum dataset of anonymised information on participants. The minimum dataset includes the following information, as finalised and agreed by the MND Collections (DNA Bank) Management Committee at their meeting in September 2006.

- age
- gender
- affection status (control, familial ALS, sporadic ALS etc)
- diagnostic certainty (El Escorial status)
- age of onset

### **Appendix 2: Extended dataset for the DNA Bank and Cell lines of the UK MND Collections**

An extended dataset has been collected from as many participants as possible but is not a complete dataset.

Researchers wishing to access the additional phenotypic data must first liaise with principal investigators to explore collaborative opportunities. However, formal collaboration may not be required for access to the extended dataset.

When requesting fields from the extended dataset, please consider the most important information you require, the priorities of the information will affect the samples available to you (due to the incomplete data set mentioned above).

#### **Clinical history**

- Site of presentation
- Family history of: MND, Parkinson's Disease, Alzheimers Disease, Frontotemporal dementia, other neurological condition
- Inconsistent features: sensory, autonomic, sphincter, Parkinsonian, cognitive change

#### **Family tree pedigree**

- Parent, Grandparents, siblings, children and 'other'
- Affected/unaffected, age now, sex, alive (y/n), age at death, year of death, cause of death

#### **Investigations and results**

- Nerve conduction studies: central motor, motor, Sensory conduction respectively and conduction block
- EMG: right and left upper limbs, right and left lower limbs and tongue respectively • Blood: CK, antiganglioside Abs, Kennedy's mutation, SOD1 mutation\*
- MRI of brain, cervical, thoracic, lumbosacral spinal cord respectively

All individual investigations above are recorded according to one of the following categories: Unknown, normal, abnormal, abnormal relevant, abnormal irrelevant, not taken

### **Current medications**

- Current medications – drug and notes
- Disease modifying medications- drug, date started and notes

### **ALSFRS**

Divided into each of the 12 categories (including the with and without gastrostomy sub-categories) and a total score

### **Physical examination history**

- Upper motor neurone signs in bulbar, lower limb and upper limb
- Lower motor neurone signs in bulbar, lower limb and upper limb
- Weight in kilos (at time of giving sample)
- %FVC
- %VC

### **MRC scores:**

- Neck flexion and extension respectively
- Upper limb: shoulder abduction, elbow flexion, wrist flexion, wrist extension, thumb abduction, each for right and left side respectively
- Lower limb: hip flexion, knee flexion, knee extension, ankle dorsiflexion each for right and left side respectively

### **Notes fields:**

- Significant past medical history
- Family history

- Nerve conduction notes
- EMG studies
- Blood results
- MRI examinations
- Other significant abnormal investigations
- Physical examination history

## **Appendix 3: Epidemiology Dataset**

### **Personal details**

- Gender
- Age
- Marital status
- Ethnicity
- Country of birth
- Parental birthplace

### **MND History**

- Year of symptom onset
- Year diagnosed
- Familial/sporadic

### **Health/Hospital Admissions**

- Head injuries
- Skeletal fractures
- Neurological illnesses – loss/change of taste/smell
- Serious illnesses
- Surgical procedures – general anaesthetic required
- Medications
- Vaccinations
- Allergies
- Body build (weight/height)
- Reproductive history – no. of children
- Dominant hand
- Female only – menstrual cycle

### **Family history**

- Medical conditions
- Siblings/parents/children - Current age or age at death

### **Socio-Economic Background**

- Education
- Employment
- Parental Occupation
- Income

### **Lifestyle**

- Alcohol consumption e.g. age started, frequency of drinking

- Smoking – Cigars, cigarettes and pipe
- Air travel
- Physical Activity – team sports, frequency, age

**Electrical/Radio wave Exposure**

- Electric shocks/burns
- Work with radio waves
- Lived near pylons
- mobile/cordless phone usage

**Exposure (from employment and hobbies)**

- Chemical
- Pesticide
- Metal
- Solvent

**Employment History**

- Type, duration, hours per year, physical activity, exposure to (see above)

**Hobbies**

- Age started/finished, how many hours, exposure to (see above)

**Residence History**

- Area type, near agriculture, water from well

**Discrepancies/notes table for surveys**