Appendix e-1: The Survey Instrument

The purpose of this survey is to gain an understanding of the process by which individuals such as yourself or your child or your loved one receive a mitochondrial disease diagnosis. This survey is written to address a research subject. If, however, you will be answering this survey for your child or for someone for whom you are the caregiver the words ‘you’ and ‘your’ should be read as ‘your child’ or ‘the research subject’. Please answer the questions to the best of your ability.

- Q1: Are you completing this survey for yourself or for someone else? [myself/someone else]
    - If myself Q1: Next Question
    - If someone else Q1: Q1A: What is your relationship to the person you are completing this survey for? [drop down list]
        - I am their parent.
        - I am their caregiver.
        - Other
            - If other: Please enter [text box]
- Q2: In which country were you living when you (or the patient) was evaluated for a mitochondrial disease? [Drop down list]
- Q3: Have you been informed by a health professional that you have mitochondrial disease? [Yes/no]
    - If yes Q3: Q3A: What specific mitochondrial disease where you told that you have? [Drop down list]
        - Alpers-Huttenlocher syndrome (aka Alpers syndrome)

- Cardiomyopathy
- CPEO (Chronic progressive external ophthalmoplegia)
- CPEO "plus" (Chronic progressive external ophthalmoplegia)
- Diabetes and deafness (DAD)
- Kearns-Sayre syndrome
- LHON (Leber hereditary optic neuropathy)
- Leigh syndrome
- Maternal-inherited deafness
- MELAS (Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes)
- MNGIE (Mitochondrial neurogastrointestinal encephalopathy)
- Multi-systemic syndrome
- MERRF (Myoclonic epilepsy with ragged-red fibers)
- Myopathy
- NARP (Neuropathy, ataxia, and retinitis pigmentosa)
- Pearson syndrome
- Reversible infantile myopathy with cytochrome c oxidase deficiency
- SANDO (Sensory ataxia neuropathy dysarthria ophthalmoplegia)
- Aminoglycoside-induced deafness
- Barth syndrome
- Encephalomyopathy
- Hepatocerebral syndrome
- Leukoencephalopathy

47 - Encephalopathy
48 - Other
49 - If other: please enter [text box]
50 - If no Q3: NEXT QUESTION
51 - Q4: Have you been informed by a health professional that you have a “biochemical
52 deficiency”? An example of a biochemical deficiency would be “complex 1 deficiency” or
53 “thymidine phosphorylase deficiency”. A biochemical deficiency may also be referred to
54 as your “biochemical diagnosis”. [Yes/no]
55 - If yes Q4: Q4A: What specific biochemical deficiency where you told that you
56 have? [drop down list]
57 - Complex I deficiency
58 - Complex II deficiency
59 - Complex III deficiency
60 - Complex IV deficiency
61 - Complex V deficiency
62 - Multiple complex deficiency
63 - Coenzyme Q10 deficiency
64 - Thymidine phosphorylase deficiency
65 - Loose coupling of oxidation and phosphorylation
66 - Fatty oxidation
67 - Oxidative phosphorylation deficiency
68 - Pyruvate dehydrogenase complex (PDC) deficiency
69 - Other

- If other: please enter [text box]
  - If no Q4: NEXT QUESTION
  - If no Q3 and Q4: END SURVEY
- Q5: What symptom(s) first motivated you to see a doctor? Please check all that apply. [radio buttons]
  - Weakness
  - Fatigue
  - Difficulty walking
  - Impaired coordination
  - Droopy eyelids
  - Hearing loss
  - Loss of vision
  - Seizures
  - Developmental delay
  - Numbness, weakness, or both in your hands and/or feet
  - Diabetes
  - Gastrointestinal discomfort
  - Liver disease
  - Kidney disease
  - Heart disease
  - Other
    - If other: please enter [text box]

- Q6: What year did you first notice the onset of the symptom(s) that motivated you to see a doctor? [Drop down list of years from DOB year to present]
- Q7: What year did you first see a doctor to discuss the symptom(s)? [Drop down list of years from DOB year to present]
- Q8: Was the doctor with whom you first discussed your symptoms your primary care physician? [Yes/no]
    - If yes Q8: NEXT QUESTION
    - If no Q8: Q8A: Was the doctor with whom you first discussed your symptoms a specialist? For example, a Neurologist and a Gastroenterologist are both types of specialists. [yes/no]
        - If yes Q8A: Q8A1: What type of specialist was the doctor? [Drop down list]
            - Neurologist
            - Gastroenterologist
            - Endocrinologist
            - Clinical Geneticist
            - Metabolic Disease Specialist
            - Cardiologist
            - Pulmonologist
            - Ophthalmologist
            - Ear, Nose, and Throat Specialist (Otolaryngologist)
            - Other: Please enter [text box]
        - If no Q8A: NEXT QUESTION

- Q9: Was the doctor with whom you first discussed your symptoms the same doctor that informed you that you have a mitochondrial disease? [yes/no]
    - If yes Q9: NEXT QUESTION
    - If no Q9: Q9A: Between the time when you first discussed your symptoms with a doctor and the time that you were informed that you have a mitochondrial disease approximately how many doctors did you see and discuss your symptoms with? [drop down list 1-20]
- Q10: What was the specialty of the doctor that informed you that you have a mitochondrial disease? [Drop down list]
    - Neurologist
    - Gastroenterologist
    - Endocrinologist
    - Clinical Geneticist
    - Metabolic Disease Specialist
    - Cardiologist
    - Pulmonologist
    - Ophthalmologist
    - Ear, Nose, and Throat Specialist (Otolaryngologist)
    - Other: Please enter [text box]
- Q11: Including the doctor with whom you first discussed your symptoms and the doctor who diagnosed your mitochondrial disease, how many doctors did you consult? [double digit numeric field]

- Q12: Between the time when you first discussed your symptoms with a doctor and the time that you were informed that you have a mitochondrial disease did you receive any other disease diagnosis/diagnoses that you were told was/were the cause of these symptoms *but was not a mitochondrial disease*? [yes/no]
    - If yes Q12: Q12A: What non-mitochondrial disease(s) diagnosis did you receive? [text box]
    - If yes Q12: Q12B: After receiving a non-mitochondrial disease diagnosis what motivated you to seek out a different diagnosis? Please check all that apply. [radio buttons]
        - The treatment did not help me.
        - Consultation with other doctors motived me to explore other diagnoses.
        - Consultation with other individuals not in the medical profession motived me to explore other diagnoses.
        - Information I learned at a medical conference motived me to explore other diagnoses.
        - Information I learned on the internet motived me to explore other diagnoses.
        - Information I learned on television motived me to explore other diagnoses.
        - Information I read in a magazine, journal, or other print media motived me to explore other diagnoses.
        - I did not believe that the diagnosis I received was correct.
        - Other: Please enter [text box]
    - If no Q12: NEXT QUESTION

- Q13: Between the time when you first discussed your symptoms with a doctor and the time that you were informed that you have a mitochondrial disease what tests did you undergo that were specifically related to the symptoms you discussed? Do not enter test that were performed for reasons unrelated to your mitochondrial disease symptoms. Please check all that apply. [radio buttons]
    - Blood testing
        - If yes to blood testing: Lactate
        - If yes to blood testing: Pyruvate
        - If yes to blood testing: Amino acids
        - If yes to blood testing: Genetic testing
    - Nuclear DNA sequencing
    - Mitochondrial DNA sequencing
    - Whole exome sequencing
    - Magnetic Resonance Imaging (MRI)
    - Electroencephalogram (EEG)
    - Electromyography (EMG), which also includes “Nerve conduction study”
    - Urine organic acids
    - Skin biopsy
    - Muscle biopsy
    - Other: Please enter [text box]
- Q14: As a result of receiving a diagnosis of a mitochondrial disease have you begun a treatment or disease management plan? [yes/no]

- Q15: As a result of receiving a diagnosis of a mitochondrial disease did you join a patient support group, patient advocacy group, Facebook group, online message board, or any other sort of community for individuals with mitochondrial disease? [yes/no]
    - If yes Q15: Q15A: Do you feel participation and or membership in such a community has been beneficial to you? [yes/no]
    - If no Q15: NEXT QUESTION
- Q16: If you were to learn today that the mitochondrial disease diagnosis you received is incorrect, and that you do not in fact have a mitochondrial disease, how would this affect you? [drop down list]
    - It would affect me very negatively.
    - It would affect me negatively.
    - It would not affect me at all.
    - It would affect me positively.
    - It would affect me very positively.