

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)

- 24 ▪ Cardiomyopathy
- 25 ▪ CPEO (Chronic progressive external ophthalmoplegia)
- 26 ▪ CPEO "plus" (Chronic progressive external ophthalmoplegia)
- 27 ▪ Diabetes and deafness (DAD)
- 28 ▪ Kearns-Sayre syndrome
- 29 ▪ LHON (Leber hereditary optic neuropathy)
- 30 ▪ Leigh syndrome
- 31 ▪ Maternal-inherited deafness
- 32 ▪ MELAS (Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like
33 episodes)
- 34 ▪ MNGIE (Mitochondrial neurogastrointestinal encephalopathy)
- 35 ▪ Multi-systemic syndrome
- 36 ▪ MERRF (Myoclonic epilepsy with ragged-red fibers)
- 37 ▪ Myopathy
- 38 ▪ NARP (Neuropathy, ataxia, and retinitis pigmentosa)
- 39 ▪ Pearson syndrome
- 40 ▪ Reversible infantile myopathy with cytochrome c oxidase deficiency
- 41 ▪ SANDO (Sensory ataxia neuropathy dysarthria ophthalmoplegia)
- 42 ▪ Aminoglycoside-induced deafness
- 43 ▪ Barth syndrome
- 44 ▪ Encephalomyopathy
- 45 ▪ Hepatocerebral syndrome
- 46 ▪ 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

- 92 • Q6: What year did you first notice the onset of the symptom(s) that motivated you to see
93 a doctor? [Drop down list of years from DOB year to present]
- 94 • Q7: What year did you first see a doctor to discuss the symptom(s)? [Drop down list of
95 years from DOB year to present]
- 96 • Q8: Was the doctor with whom you first discussed your symptoms your primary care
97 physician? [Yes/no]
- 98 ○ If yes Q8: NEXT QUESTION
- 99 ○ If no Q8: Q8A: Was the doctor with whom you first discussed your symptoms a
100 specialist? For example, a Neurologist and a Gastroenterologist are both types of
101 specialists. [yes/no]
- 102 ▪ If yes Q8A: Q8A1: What type of specialist was the doctor? [Drop down list]
- 103 • Neurologist
- 104 • Gastroenterologist
- 105 • Endocrinologist
- 106 • Clinical Geneticist
- 107 • Metabolic Disease Specialist
- 108 • Cardiologist
- 109 • Pulmonologist
- 110 • Ophthalmologist
- 111 • Ear, Nose, and Throat Specialist (Otolaryngologist)
- 112 • Other: Please enter [text box]
- 113 ▪ If no Q8A: NEXT QUESTION

- 114 • Q9: Was the doctor with whom you first discussed your symptoms the same doctor that
115 informed you that you have a mitochondrial disease? [yes/no]
- 116 ○ If yes Q9: NEXT QUESTION
- 117 ○ If no Q9: Q9A: Between the time when you first discussed your symptoms with a
118 doctor and the time that you were informed that you have a mitochondrial
119 disease approximately how many doctors did you see and discuss your
120 symptoms with? [drop down list 1-20]
- 121 • Q10: What was the specialty of the doctor that informed you that you have a
122 mitochondrial disease? [Drop down list]
- 123 ○ Neurologist
- 124 ○ Gastroenterologist
- 125 ○ Endocrinologist
- 126 ○ Clinical Geneticist
- 127 ○ Metabolic Disease Specialist
- 128 ○ Cardiologist
- 129 ○ Pulmonologist
- 130 ○ Ophthalmologist
- 131 ○ Ear, Nose, and Throat Specialist (Otolaryngologist)
- 132 ○ Other: Please enter [text box]
- 133 • Q11: Including the doctor with whom you first discussed your symptoms and the doctor
134 who diagnosed your mitochondrial disease, how many doctors did you consult? [double
135 digit numeric field]

- 136 • Q12: Between the time when you first discussed your symptoms with a doctor and the
137 time that you were informed that you have a mitochondrial disease did you receive any
138 other disease diagnosis/diagnoses that you were told was/were the cause of these
139 symptoms *but was not a mitochondrial disease?* [yes/no]
- 140 ○ If yes Q12: Q12A: What non-mitochondrial disease(s) diagnosis did you receive?
141 [text box]
- 142 ○ If yes Q12: Q12B: After receiving a non-mitochondrial disease diagnosis what
143 motivated you to seek out a different diagnosis? Please check all that apply.
144 [radio buttons]
- 145 ▪ The treatment did not help me.
 - 146 ▪ Consultation with other doctors motivated me to explore other diagnoses.
 - 147 ▪ Consultation with other individuals not in the medical profession motivated
148 me to explore other diagnoses.
 - 149 ▪ Information I learned at a medical conference motivated me to explore other
150 diagnoses.
 - 151 ▪ Information I learned on the internet motivated me to explore other
152 diagnoses.
 - 153 ▪ Information I learned on television motivated me to explore other diagnoses.
 - 154 ▪ Information I read in a magazine, journal, or other print media motivated me
155 to explore other diagnoses.
 - 156 ▪ I did not believe that the diagnosis I received was correct.
 - 157 ▪ Other: Please enter [text box]
- 158 ○ If no Q12: NEXT QUESTION

159 • Q13: Between the time when you first discussed your symptoms with a doctor and the
160 time that you were informed that you have a mitochondrial disease what tests did you
161 undergo that were specifically related to the symptoms you discussed? Do not enter test
162 that were performed for reasons unrelated to your mitochondrial disease symptoms.

163 Please check all that apply. [radio buttons]

164 ○ Blood testing

165 ▪ If yes to blood testing: Lactate

166 ▪ If yes to blood testing: Pyruvate

167 ▪ If yes to blood testing: Amino acids

168 ▪ If yes to blood testing: Genetic testing

169 ○ Nuclear DNA sequencing

170 ○ Mitochondrial DNA sequencing

171 ○ Whole exome sequencing

172 ○ Magnetic Resonance Imaging (MRI)

173 ○ Electroencephalogram (EEG)

174 ○ Electromyography (EMG), which also includes “Nerve conduction study”

175 ○ Urine organic acids

176 ○ Skin biopsy

177 ○ Muscle biopsy

178 ○ Other: Please enter [text box]

179 • Q14: As a result of receiving a diagnosis of a mitochondrial disease have you begun a
180 treatment or disease management plan? [yes/no]

- 181 • Q15: As a result of receiving a diagnosis of a mitochondrial disease did you join a
182 patient support group, patient advocacy group, Facebook group, online message board,
183 or any other sort of community for individuals with mitochondrial disease? [yes/no]
- 184 ○ If yes Q15: Q15A: Do you feel participation and or membership in such a
185 community has been beneficial to you? [yes/no]
 - 186 ○ If no Q15: NEXT QUESTION
- 187 • Q16: If you were to learn today that the mitochondrial disease diagnosis you received is
188 incorrect, and that you do not in fact have a mitochondrial disease, how would this affect
189 you? [drop down list]
- 190 ○ It would affect me very negatively.
 - 191 ○ It would affect me negatively.
 - 192 ○ It would not affect me at all.
 - 193 ○ It would affect me positively.
 - 194 ○ It would affect me very positively.
- 195