Mitochondrial Disease Version 2.0 NINDS CDE Project
Ophthalmology Outcomes Subgroup Summary

Primary mitochondrial diseases comprise clinically, genetically, and biochemically diverse disorders that are caused by genetic defects that primarily affect intrinsic mitochondrial functions including: oxidative-phosphorylation[1], mitochondrial protein synthesis[2], mitochondrial mRNA synthesis/processing[3], mitochondrial fission and fusion[4], mitochondrial protein quality control and degradation[5], iron-sulfur protein assembly[6], mitochondrial sulfide oxidation[7], mitochondrial nucleoside/nucleotide metabolism[8], mitochondrial DNA maintenance[9], pyruvate dehydrogenase complex[10], primary defects of mitochondrial protein importation[11], and ATP/ADP transport[12] (specific examples are listed in the Appendix).

Some diseases that affect mitochondrial functions are excluded because they are classified as other types of disorders or cause secondary mitochondrial dysfunction such as: defects of mitochondrial fatty acid oxidation, Krebs cycle disorders, urea cycle disorders of intra-mitochondrial enzymes, mitochondrial phospholipid metabolism, congenital disorders of glycosylation, exogenous mitochondrial toxins, and drug-induced mitochondrial dysfunction.

The NINDS Mitochondrial Disease v2.0 Common Data Element (CDE) Ophthalmology Outcomes Subgroup addressed conditions outlined by the definition above with potential to involve the eye, its adnexa, and the visual system.

Summary of Recommendations

Subdomain	Guidance Document Name	Classification
Vision	Mitochondrial Disease Ophthalmology Test Guidance	N/A

Appendix: Specific examples of primary mitochondrial diseases.

[1]Oxidative-phosphorylation

Complex I: *NDUFS1*, *NDUFS2*, *NDUFS3*, *NDUFS4*, *NDUFS6*, *NDUFS7*, *NDUFS8*, *NDUFV1*, *NDUFV2*, *NDUFA1*, *NDUFA2*, *NDUFA9*, *NDUFA10*, *NDUFA11*, *NDUFA12*, *NDUFA13*, *NDUFAF2*, *NDUFAF6* and *NDUFB11*

Complex II: *SDHA*, *SDHB*, *SDHC*, *SDHD* and *SDHAF1*

Complex III: *UQCRB, BCS1L, UQCRQ*, *UQCRC2*, *CYC1*, *TTC19*, *LYRM7*, *UQCC2* and *UQCC3*

Complex IV: *COA5*, *SURF1*, *COX10*, *COX14*, *COX15*, *COX20*, *COX6B1*, *ETHE1, FASTKD2*, *SCO1*, *SCO2*, *LRPPRC*, *TACO1* and *PET100*

Complex V: *ATPAF2*, *TMEM70*, *ATP5E, ATP5A1*, *USMGE5*

Coenzyme Q_{10} deficiency: *PDSS1*, *PDSS2*, *COQ2*, *COQ4*, *COQ5, COQ6*, COQ7, *COQ8A*, *COQ8B* and *COQ9*

[2]Mitochondrial protein synthesis

Aminoacyl-tRNA synthetases: *AARS2*, *DARS2*, *EARS2*, *RARS2*, *YARS2*, *FARS2*, *HARS2*, *LARS2*, *VARS2*, *TARS2*, *IARS2*, *CARS2*, *PARS2*, *NARS2*, *KARS*, *GARS*, *SARS2* and *MARS2*

tRNA modification: *MTO1*, *GTP3BP*, *TRMU*, *PUS1*, *MTFMT*, *TRIT1*, *TRNT1* and *TRMT5*

Mitoribosomal proteins: *MRPS16*, *MRPS22*, *MRPL3*, *MRP12* and *MRPL44*

Elongation factors: *TUFM*, *TSFM,* and *GFM1*

Release factors: *C12orf65*

[3]Mitochondrial mRNA synthesis/processing

LRPPRC, *TACO1*, *ELAC2*, *PNPT1*, *HSD17B10*, *MTPAP* and *PTCD1*

[4]Mitochondrial fission and fusion

OPA1, MFN2, MSTO1 and *MICOS13*

[5]Mitochondrial protein quality control and degradation

FBXL4, *AFG3L2, LONP1* and *SPG7*

[6]Iron-sulfur protein assembly

ISCU, *BOLA3*, *NFU1* and *IBA57*

[7]Mitochondrial sulfide oxidation

GFER

[8]Mitochondrial nucleoside/nucleotide metabolism

TYMP, *DGUOK*, *TK2*, *MGME1*, *SUCLG1*, *SUCLA2*, *GUK1, RRM1* and *RRM2B*

[9]Mitochondrial DNA maintenance

C10orf2, *POLG*, *POLG2, DNA2, RNASEH1*, *TFAM, TOP3A, SSBP1, LIG3*

[10]Pyruvate dehydrogenase complex

PDHA1, PDHB, LIAS, PDP1, PDHX, DLAT

[11]Primary defects of mitochondrial protein importation

TIMM8A

[12]ATP/ADP transport

ANT1