## Biomarker Testing

1. Was a biomarker analysis done?

Yes

No

If yes, please answer questions below:

1. Sample/method used to assess the biomarker:

Blood (serum/plasma)

Urine

CSF

Fibroblasts

Leukocytes

Neutrophils

Monocytes

Platelets (high OXPHOS)

Lymphocytes

Lymphoblasts (EBV)

Muscle biochemistry

Muscle histology

Myotubes

Liver histology

Liver biochemistry

Genetic

1. Which biomarker(s) were assessed from the specimen's blood (serum/plasma) sample?

Lactate

Pyruvate

Lactate/pyruvate ratio

Leukocyte coenzyme Q10

Amino acids (emphasis on alanine, alanine/ lysine ratio, alanine//phenylalanine + lysine ratio, citrulline)

Carnitine levels

Acylcarnitines

CPK

Creatine

Free glutathione (fGSH), oxidized disulfide (GSSG), fGSH/GSSG ratio

Plasma carbonyl content

Fibroblast growth factor 21 (FGF21)

Metabolic profiling

Hepatic enzymes (AST, ALT, GGT)

Ammonia

Thymidine

Deoxyuridine

Lactate accumulation level:

Increase in lactate

Normal lactate

Decrease in lactate

1. Pyruvate accumulation level:

Increase in pyruvate

Normal pyruvate

Decrease in pyruvate

1. Lactate/pyruvate ratio level:

Increase in L: P ratio

Normal L: P ratio

Decrease in L: P ratio

1. Which biomarker(s) were assessed from the specimen's urine sample?

Organic acids

3-methylglutaconic acid

Amino acids

lactate/creatinine

1. Which biomarker(s) were assessed from the specimen's cerebrospinal fluid (CSF) sample?

Lactate

Pyruvate

Lactate/pyruvate ratio

Amino acids (alanine, alanine/lysine ratio, alanine/phenylalanine + lysine ratio)

Cell count

Protein

Glucose (with simultaneous blood glucose)

1. Which biomarker(s) were assessed from the specimen's fibroblasts sample?

High resolution respirometry

OXPHOS enzymology

Lactate/pyruvate ratio

Pyruvate dehydrogenase enzymology

Pyruvate dehydrogenase subunit western blot

Pyruvate dehydrogenase immunohistochemistry

ATP synthesis

Fibroblast OXPHOS subunit immunohistochemistry

OXPHOS subunit western blot

Blue native gel electrophoresis (OXPHOS)

Clear native gel OXPHOS immunoblot

Clear native gel OXPHOS enzymology

Coenzyme Q10

1. Which biomarker(s) were assessed from the specimen's leukocytes sample?

Intracellular free glutathione (fGSH), oxidized disulfide (GSSG), fGSH/GSSG ratio

Intracellular coenzyme Q10

Pyruvate dehydrogenase enzymology

Thymidine phosphorylase enzymology

Coenzyme Q10 level

mtDNA deletion/duplication

mtDNA copy number

1. Which biomarker(s) were assessed from the specimen's neutrophils sample?

OXPHOS enzymology

High resolution respirometry

Coenzyme Q10

Intracellular glutathione

1. Which biomarker(s) were assessed from the specimen's monocytes sample?

Intracellular free glutathione (fGSH), oxidized disulfide (GSSG), fGSH/GSSG ratio

Pyruvate dehydrogenase enzymology

Thymidine phosphorylase enzymology

OXPHOS enzymology

High resolution respirometry

Coenzyme Q10

Intracellular glutathione

1. Which biomarker(s) were assessed from the specimen's platelets (high OXPHOS) sample?

OXPHOS enzymology

High resolution respirometry

Coenzyme Q10

Peripheral-type benzodiazepine receptor binding kinetics

1. Which biomarker(s) were assessed from the specimen's lymphocytes sample?

OXPHOS enzymology

High resolution respirometry

Coenzyme Q10

Intracellular glutathione

DNA strand breaks by comet assay (cultured cells)

Micronucleus assay followed by fluorescence in situ hybridization

Pyruvate dehydrogenase

1. Which biomarker(s) were assessed the specimen's lymphoblast sample?

ATP synthesis

High resolution respirometry

## PLACEHOLDER

1. Which biomarker(s) were assessed from the specimen's muscle biochemistry?

OXPHOS enzymology

High resolution respirometry

mtDNA copy number

mtDNA deletion/duplication

Pyruvate dehydrogenase enzymology

Pyruvate dehydrogenase subunit western blot

Coenzyme Q10

Glutathione content

OXPHOS subunit western blot

Blue native gel electrophoresis

Clear native gel immunoblot

Clear native gel enzymology

Human mitochondrial transcription factor A (hmtTFA or Tfam)

mtDNA absence sensitive factor (midas)

Biogenesis regulator peroxisome proliferator-activated recerptor-gamma-coactivator-1alpha (PGC-1alpha)

8-oxoguanine DNA glycolase-1 (OCG-1)

Manganese superoxide dismutase (MnSOD)

AIF

Bcl-2

Aconitase enzymology

1. Which biomarker(s) were assessed from the specimen's muscle histology?

Gomori trichrome

Succinate dehydrogenase (SDH)

Cytochrome C Oxidase (COX) (Complex IV)

Combined SDH + COX

Fibroblast growth factor 21 (FGF21)

OXPHOS subunit immunohistochemistry

Humanin immunohistochemistry

1. Which biomarker(s) were assessed from the specimen's myotubes?

Metabolic profiling

High resolution respirometry

1. Which biomarker(s) were assessed from the specimen's genetics?

Cellular energetics gene sequencing (NDS) (nDNA + mtDNA)

mtDNA sequencing

Exome sequencing (NGS) (nDNA)

mtDNA deletion/duplication (leukocytes)

mtDNA deletion/duplication (muscle)

mtDNA copy number (leukocytes)

mtDNA copy number (muscle)

Mitochondrial haplotype

Mitochondrial gene expression profiling

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