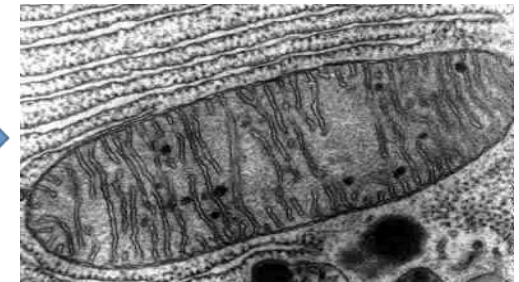




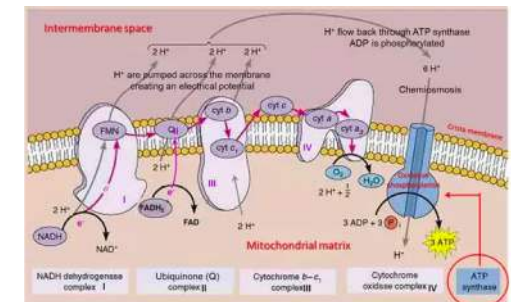
# Whole genome sequencing with comprehensive re-analysis in undiagnosed or unclear causes with mitochondrial dysfunction: How this can lead to improved diagnosis, treatment, and clinical outcomes.



```
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```



Richard G. Boles, M.D.  
 Chief Medical & Scientific Officer, NeuroNeeds LLP  
 Director, Neurabilities NeuroGenomics Program  
 MitoAction November Expert Series  
 November 5, 2021



# Mitochondrial Dysfunction

## Case Report: Payam

- Autistic spectrum disorder diagnosed at age 18 months
- Unexplained vomiting at age 15 months
- Hypotonia
- Mental health issues:
  - OCD
  - anxiety
  - irritability
  - aggression
- Functional disease issues:
  - constipation, severe and since birth
  - easy fatigue
  - sleep problems
  - night twitches



- Very rare variant identified in the creatine transporter
  - Required to transport creatine from blood to brain.
  - Creatine is important for brain as a source of stored energy.
- Trial of cyclocreatine
  - decreased anxiety
  - more expressive language output
  - many fewer behavioral manifestations, particularly less aggression and self-injury
  - much better able to handle change, frustration, and denied requests.
  - greater awareness of his environment
  - improvements in visual attention
- Transporter is located on the cell membrane, not in the mitochondria
  - Example of secondary mitochondrial dysfunction – not a mitochondrial disorder

# Mitochondrial Dysfunction

## Case Report: Payton

- Cyclic vomiting syndrome from ages 1-10
- Episodes then morphed into daily migraine
- Chronic pain throughout her body
- Multiple admissions for bowel clean-outs
- **Chronic fatigue syndrome = chief complaint**
- Excellent student

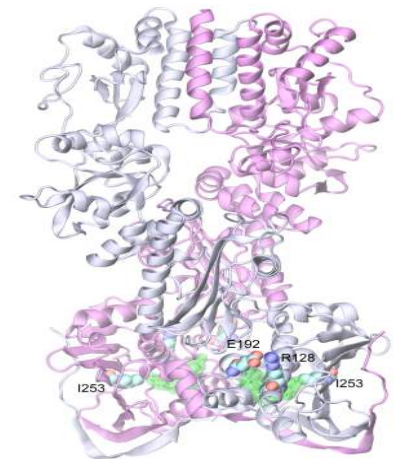


- Cyclic vomiting syndrome from ages 1-10
  - Episodes then morphed into daily migraine
  - Chronic pain throughout her body
  - Multiple admissions for bowel clean-outs
  - Chronic fatigue syndrome = chief complaint
  - Excellent student
- 
- DNA sequencing revealed the p.Ile253Val variant in the *TRAP1* gene.
  - This variant is present in about 1% of the general population.
    - Average is about 3,000 rare variants at prevalence less than 1% per person!





- This gene encodes for a chaperone that protects mitochondrial proteins from oxidative stress.
- This variant was also found in many other patients with “functional” symptoms such as chronic pain, fatigue and GI dysmotility.
- Granisetron (Kytril) was predicted by computer modeling to tightly bind in the mutant 253-valine ATP-binding pocket, but not the wild-type 253-isoleucine pocket.
- Essentially all disease manifestations resolved on Granisetron (Kytril) therapy.





- Clinician treating patients
  - Primary interests in neurodevelopmental (e.g., autism) and functional (e.g., cyclic vomiting) disease
  - Past: Geneticist/pediatrician 20 years at CHLA/USC
  - Present: Director, Neurabilities NeuroGenomics Program (<https://neurabilities.com/neurogenomics>)
- Chief Medical & Scientific Officer of NeuroNeeds LLC
  - Present: The company that produces SpectrumNeeds® and EnergyNeeds® (<https://neuroneeds.com>)
- Medical Director for DNA sequencing companies
  - Past: 5 years at Courtagen Life Sciences; 6 months at Lineagen
  - Present: Free agent, ordering from multiple companies
- Expert witness in legal cases
  - Present: Medical child abuse, child neglect and custody cases ([drboles@molecularmito.com](mailto:drboles@molecularmito.com))
  - Vaccine Court, malpractice cases
- Researcher with prior NIH and foundation funding
  - Past: USC faculty for 20 years
  - Present: Study DNA sequence variation that predispose towards neurodevelopmental and functional disorders

In personalized medicine, treatments are individualized. All treatments discussed herein relate to case reports, are off-label per the FDA, and may not translate to other patients.

Dr. Richard G. Boles is a founder and officer of NeuroNeeds®, which makes dietary supplement products for people with neurological disorders, including autism and cyclic vomiting.





“Any sufficiently advanced technology is indistinguishable from magic.”

Clarke's Third Law



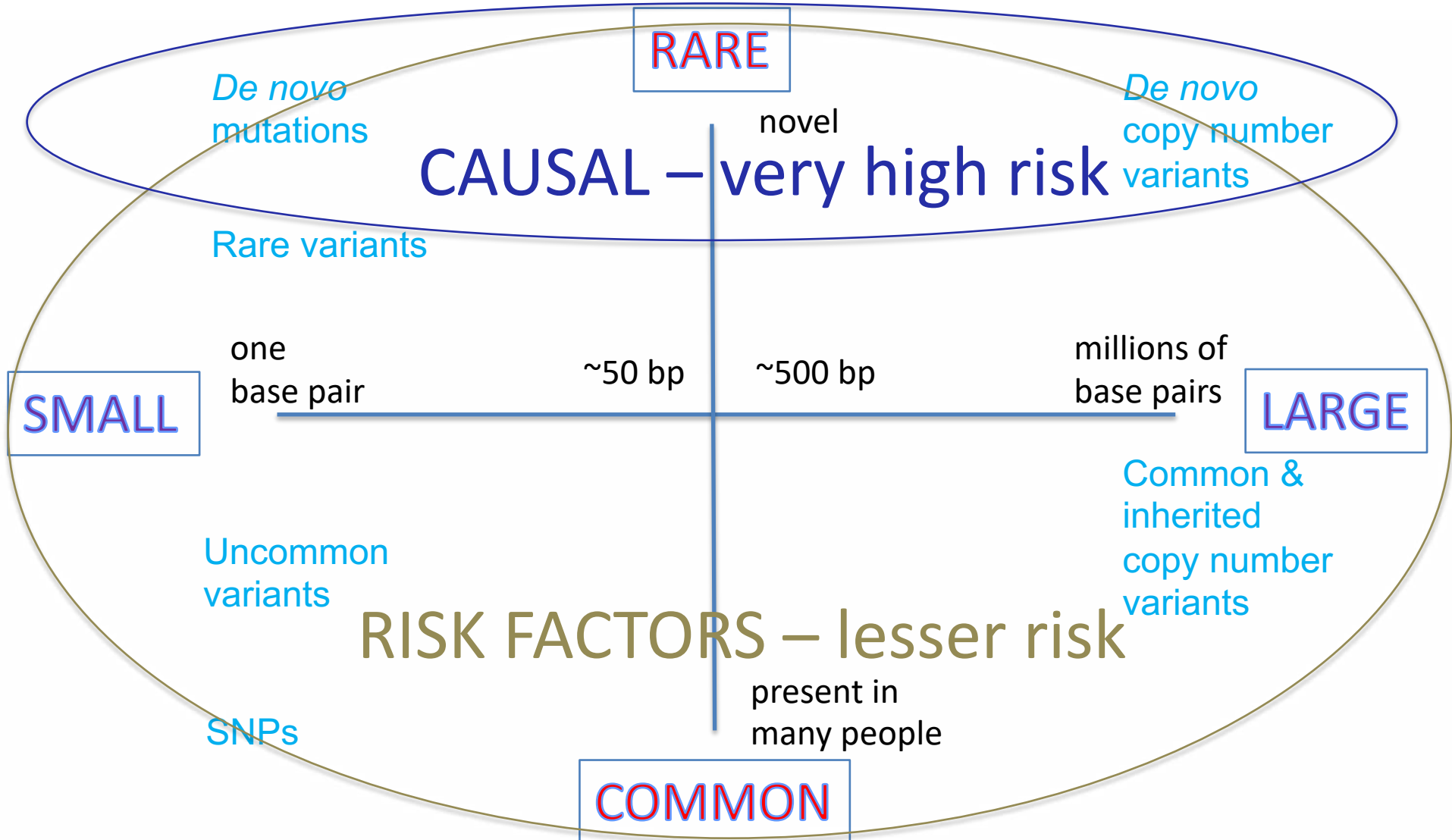
# DNA Sequencing: Illumina HiSeq 4000





NEURONEEDS.com

# Mitochondrial Dysfunction Causal Variants v. Risk Factors



# Mitochondrial Medicine

## The Spectrum of Mito

### Brain

- Developmental delays
- Dementia
- Neuro-psychiatric disturbances
- Migraines
- Autistic Features
- Mental retardation
- Seizures
- Atypical cerebral palsy
- Strokes

### Nerves

- Weakness (may be intermittent)
- Absent reflexes
- Fainting
- Neuropathic pain
- Dysautonomia - temperature instability

### Muscles

- Weakness
- Cramping

- Gastrointestinal problems
- Dysmotility
- Irritable bowel syndrome
- Hypotonia
- Muscle pain
- Gastroesophageal reflux
- Diarrhea or constipation
- Pseudo-obstruction

### Kidneys

- Renal tubular acidosis or wasting

### Heart

- Cardiac conduction defects (heart blocks)
- Cardiomyopathy

### Liver

- Hypoglycemia (low blood sugar)
- Liver failure

### Ears & Eyes

- Visual loss and blindness
- Ptosis
- Ophthalmoplegia
- Optic atrophy
- Hearing loss and deafness
- Acquired strabismus
- Retinitis pigmentosa

### Pancreas & other glands

- Diabetes and exocrine pancreatic failure (inability to make digestive enzymes)
- Parathyroid failure (low calcium)

### Systemic

- Failure to gain weight
- Fatigue
- Unexplained vomiting
- Short stature
- Respiratory problems

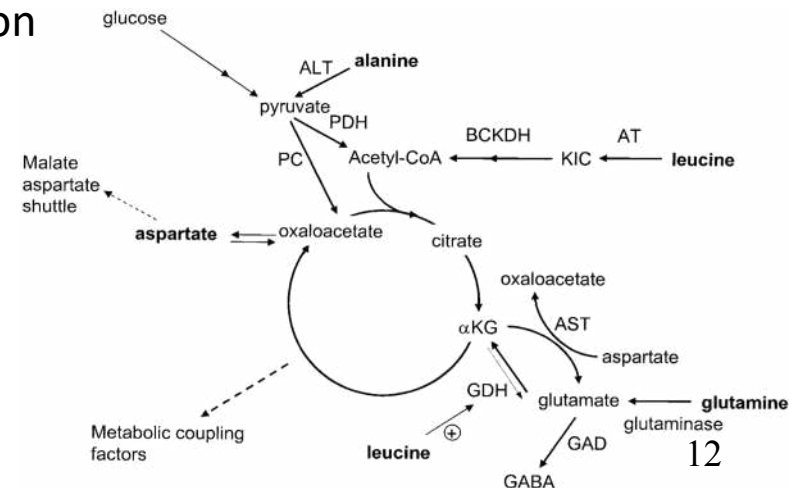
Neurodevelopmental disorders  
Functional neurological disorders



# Mitochondrial Dysfunction

## Case Report: Kelly

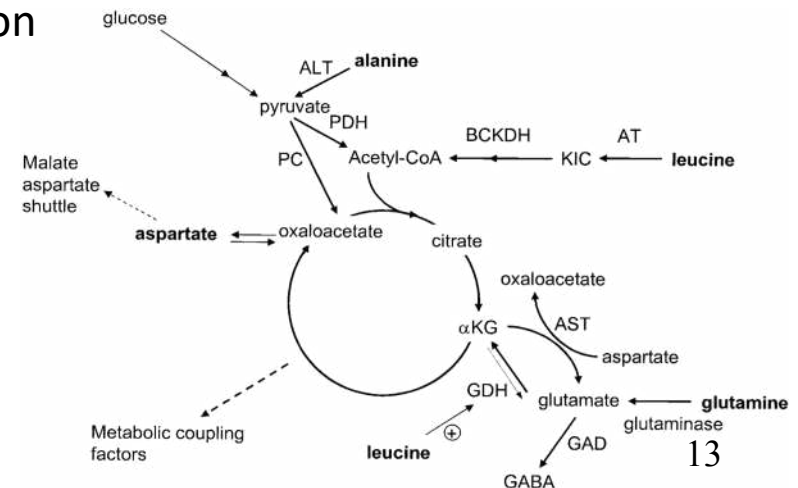
- Autistic spectrum disorder
- Severe migraine and fatigue
- Cyclic vomiting, IBS, POTS, depression, and anxiety
- Biochemical testing revealed signs of a mitochondrial disorder
- Physical manifestations improved on “mito-cocktail”:
  - CoQ10, L-carnitine, L-arginine, Mg, Vitamins B2, C and E
- Two mutations in glutaminase 2
  - the enzyme that converts glutamine to glutamate
- Improved on alpha-ketoglutarate supplementation





- 
- A black and white woodcut-style portrait of a young man with curly hair, wearing a ruff collar. The image is heavily stylized with puzzle pieces integrated into the face and clothing, and a jagged, serrated border.

This occurs INSIDE the mitochondrial, and Kelly thus has a “mitochondrial disorder”.



- 13-year-old female
- Presented with developmental regression in the first grade, recovered
  - Given autism diagnosis, but never typical
  - Auditory and visual processing delays dx at age 7y
- At age 12 years during a viral-like URI:
  - Lost all academic skills w/i one day
  - Regressed behavior, often “almost catatonic”
  - Seizure-like events: always preceded by headache, always with muscle weakness – more on left, often with ataxia, tachycardia, pallor, urinary incontinence, clammy, often nausea.
  - EEG never shown seizure activity
- Functional disease:
  - Status migrainosus
  - Chronic pain: spine>throat>neck
  - Chronic fatigue
  - POTS
- Frequent infections, dx CVID – treated with IVIG, high-dose steroids

## Diagnosis: Hemiplegic migraine/episodic ataxia due to calcium channelopathy

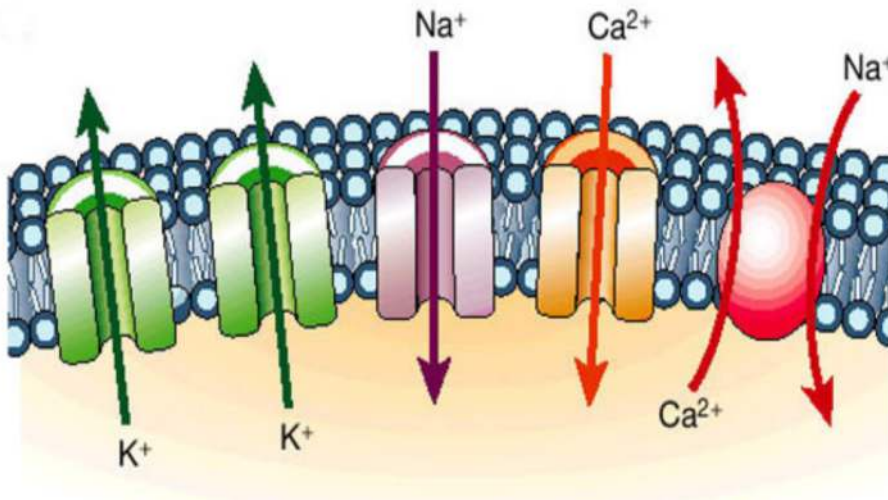
- Prolonged episodes of headache, confusion, ataxia, and other neurological signs and symptoms, including asymmetrical weakness, is consistent with and suggestive of hemiplegic migraine.
- Hemiplegic migraine is generally due to mutations in calcium channel genes and ion pumps. She has variants that may be disease related in three of these genes:
  - CACNA1A p.His2225dup
  - CACNA1S p.Pro1839Ser
  - ATP1A2 p.Arg564Gln

Each of these variants are rare and highly conserved and thus likely to affect protein function.

### Follow-Up:

- Interventions:
  - Mitochondrial cocktail
  - KCl and acetazolamide
- Dramatic return of cognitive functioning:
  - 2/2020: Academics tested at kindergarten in reading and 1<sup>st</sup> grade in math.
  - 2/2021: Same test – reading 8<sup>th</sup> grade and math 7<sup>th</sup> grade.
- Regressed behavior has resolved, and behavior age appropriate.
- Ataxia has resolved; POTS and anxiety improved.
- Chronic pain and fatigue remain and are presently being addressed.

- Ion Channels



- Ion:
  - Sodium
  - Potassium
  - Calcium
  - Chloride
- Membrane:
  - Plasma
  - Endoplasmic reticulum
  - Mitochondria
  - Endosome

Ion channelopathies are important causes of mitochondrial dysfunction, as well as comorbidities. Ion channels are particularly common causes of epilepsy, migraine, and cardiac conduction defects.



# Mitochondrial Dysfunction

## Case Report: Karl

- Presented with episodes of abdominal pain, nausea, vomiting and pallor.
  - Meets diagnostic criteria for both cyclic vomiting and abdominal migraine.
- Episodes became very frequent and coalesced to near-continuous.
- Status-post cholecystectomy and appendectomy
- On narcotics, fully disabled, and labeled as a drug addict
- Other issues: migraine headaches, fatigue, GERD, anxiety
- Seen in my clinic at age 23 and diagnosed with abdominal migraine
- Placed on amitriptyline, coenzyme Q10 and L-carnitine. Initial success with only rare episodes.
- Stopped treatment, and at age 26 was refractory to above therapy, including episodes every 4 to 7 days for several hours; again disabled. Had 10-15 ER visits in 5 months.

- Sequencing revealed 3 known mutations in the *RYR2* gene.
- The patient was placed on high-dose propranolol.
- Dramatic improvement with the resolution of episodes.
- Encodes a stress-induced calcium channel across the endoplasmic reticulum
- Dominant mutations are associated with adrenergic-triggered arrhythmia (often fatal) and right-sided cardiomyopathy
- Channel also present in neurons
- Highly-conserved variants are associated with the “functional triad”
  - Pain
  - Fatigue
  - GI dysmotility
- All are anxious people, with stress-triggered disease
- Disease responds favorably to beta blockade (propranolol)

# Mitochondrial Dysfunction

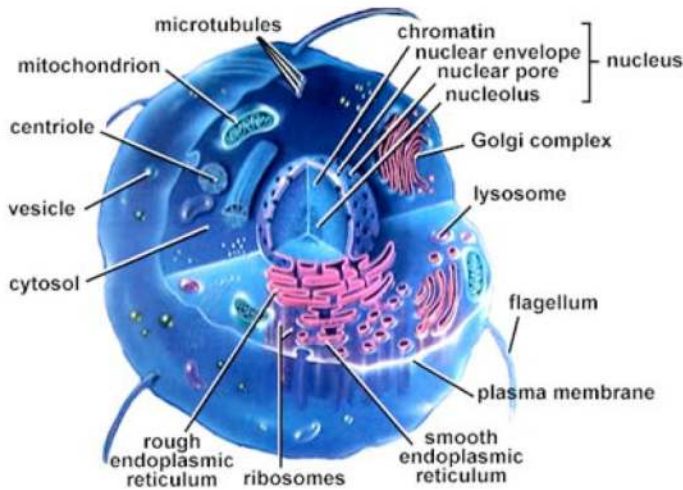
## Case Report: Margot

- Margot presented at age 10 years with a history of 1 to 3 daylong episodes of vomiting and dizziness since infancy.
- As time went on dizziness became the predominate symptom, and episodes sometimes lasted as long as 2 weeks.
  - By age 12, dizziness was chronic and unremitting, and she was unable to attend school.
- DNA sequencing revealed a disease-associated variant in the *RYR2* gene. Specific treatment was started aimed at this gene. Now, Margot is almost completely free of dizziness and back in school with a normal life.

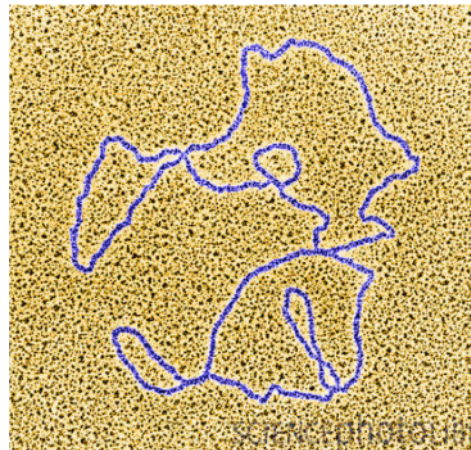


# Mitochondrial Genetics

## The Basics



### Mitochondrial DNA

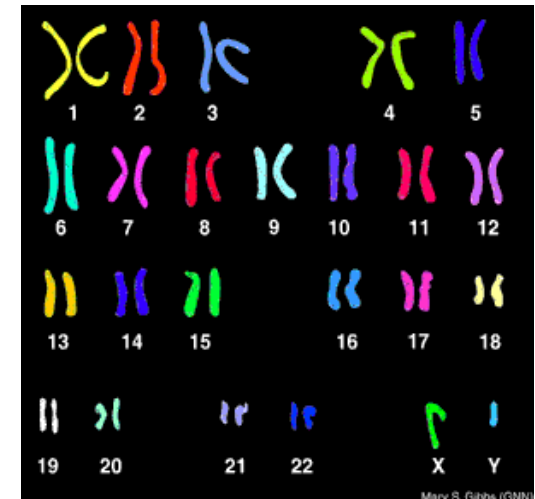


37 genes

16,000 base pairs

- Maternal inheritance

### Nuclear DNA



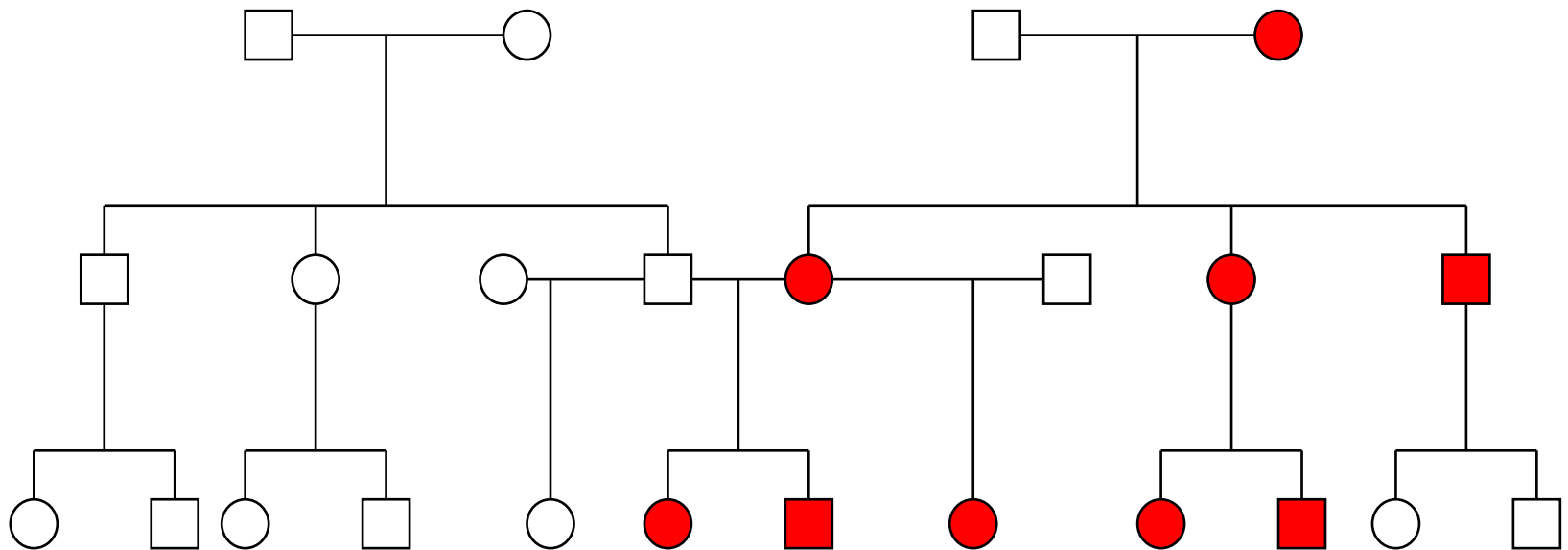
~22,000 genes

3,000,000,000 base pairs

1,013 genes encode mitochondrial proteins

- Autosomal recessive
- Autosomal dominant
- X-linked

## Maternal Inheritance

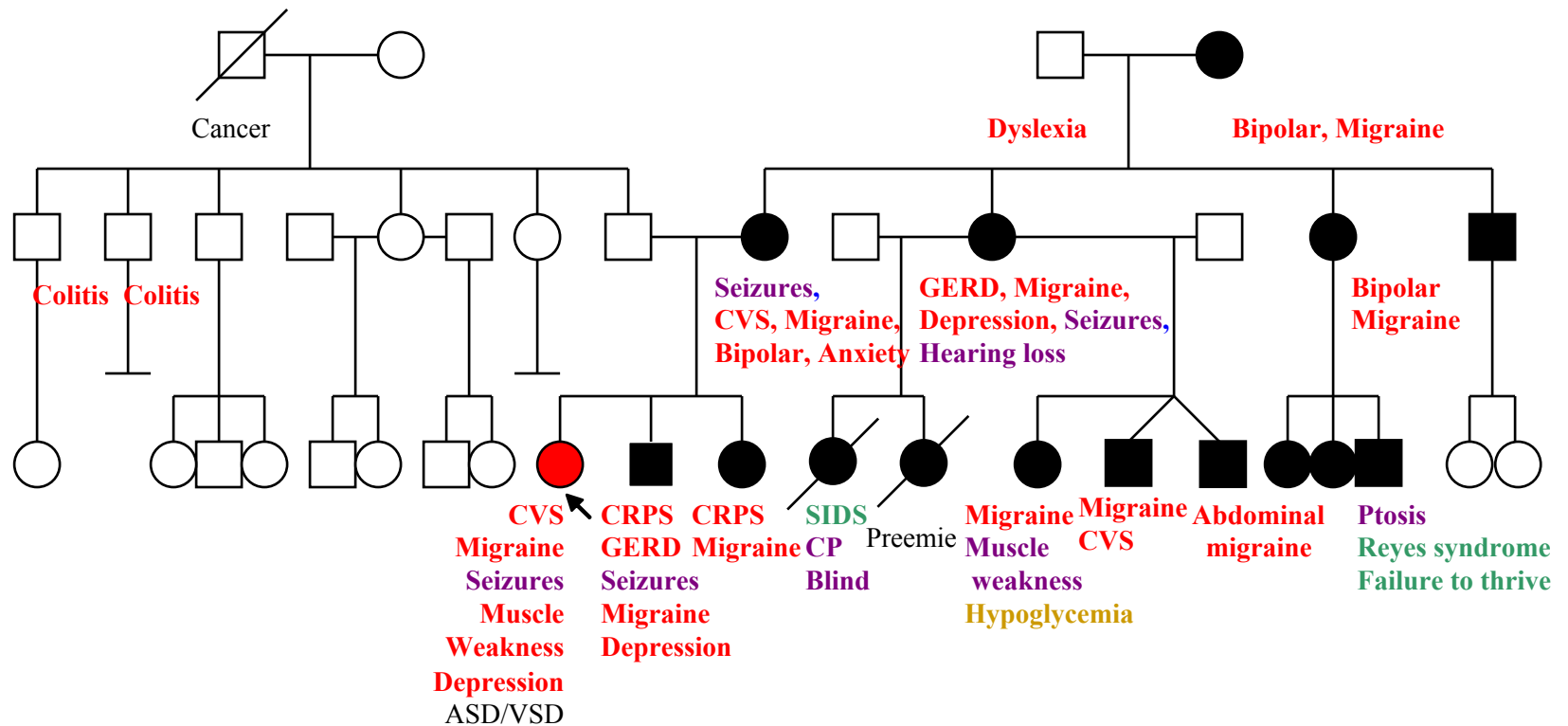


mtDNA is inherited exclusively from the mother.  
There is no recombination.

Thus, all relatives with red symbols have exactly the same mtDNA sequence, in the absence of a new mutation.



# Maternal Inheritance



# Mitochondrial Dysfunction

## Case Report: William

- William presented to my clinic at age 6 years.
- Chronic **pain**, including pain in the eyes, head and abdomen.
- Limb-girdle **myopathy**; chronic fatigue.
- **Constipation**, obstipation and encopresis.
- He is an excellent student.
- Body fluid biochemical testing and electron microscopy on a muscle biopsy specimen suggested mitochondrial disease.
- Pedigree: probable maternal inheritance, with multiple manifestations of functional disease in the mother, including chronic pain, fatigue, and bowel dysfunction.
- **mtDNA sequencing: revealed 14960G>A at 55%** in the mitochondrially-encoded *CYTB* gene encoding a subunit of complex III of the respiratory chain. His mother has 78% heteroplasmy for that nucleotide.
- On the "**mitochondrial cocktail**" he has shown much improvement in energy level, and the essential resolution of headache, muscle cramps and abdominal pain.

- Izzy presented to my clinic at age 6 years.
- Anxiety: Became severe at age 5 years. She could not get a teeth cleaning, attend birthday parties, or participate in gymnastic or scouting. Randomly cried over half the day (regarding various fears), especially with any changes in the routine. Severe separation anxiety and cries for hours when mother is not present, even if with other relatives.
- Pain: Developed chronic right ankle pain, occurring every day.
- mtSEEK (NextGen sequencing of the mtDNA) revealed 78% heteroplasmy for 14960G>A in the *CYTB* gene.
- Placed on "mitochondrial cocktail" and low-dose sertraline.
- Anxiety and pain resolved.

- Autistic spectrum disorder – high functioning
- Disease started at age 12 years with severe back and shoulder pain
- Vertigo
- Chronic fatigue – severe, with 3-6 “crashes” per month
- Family history of functional disease, especially migraine, in sister, mother, maternal grandmother, and maternal aunt

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- Genetic testing:
  - Large heteroplasmic mtDNA deletion
  - *CACNA1S* calcium channel variant
- Cyclic vomiting syndrome appeared at at 15 years

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- Conversion disorder diagnosis
- Genetic testing:
  - Large heteroplasmic mtDNA deletion
  - *CACNA1S* calcium channel variant
- Cyclic vomiting syndrome appeared at at 15 years
- Manifestations improved greatly on therapy, including “mito-cocktail” and medications (amitriptyline, acetazolamide, duloxetine)

- 16-year-old male with severe autism, intellectual disability, migraine, GI.
- Genetic testing revealed a *de novo* 84 kb deletion on chromosome 8p23.1 that includes the genes of two deubiquitinating enzymes: *USP17L2* and *USP17L7*.
  - mtDNA variants associated with migraine were also identified on WGS.
- Mother reports significant improvements on mitochondrial cocktail: better transitions, sleeping better, using some new words, trying new foods and activities.
  - She ran out and behavior worsened and improved again with restarting.

- Cyclic vomiting syndrome started at age 20 years.
  - 3-day episodes every 2 weeks.
- Other issues: Ulcerative colitis, and back pain
- Complex genetics:
  - RYR2 variant that is extremely rare, highly conserved, and predicted to alter protein function by computer models.
  - Deletion of 25 genes, 1.5 million base-pairs on chromosome 17, including the PMP22 gene. Mutation in this gene causes CMT.
  - 4-base-pair deletion in POLG mitochondrial gene, known pathogenic variant.
  - 4 variants of interest in NADH subunits on mtDNA.
- Genetics predicts channelopathy + mitochondrial dysfunction + CMT peripheral neuropathy.

- Primary mitochondrial dysfunction:
  - Defective cellular energy metabolism
  - Genetic anomaly is in the mitochondria
  - Can be called a “mitochondrial disorder”
  - Uncommon, not rare
  - TRAP1, glutaminase 2, CYTB, mtDNA deletion, POLG
- Secondary mitochondrial dysfunction:
  - Defective cellular energy metabolism
  - Genetic anomaly is NOT in the mitochondria
  - Has no good label at present.
  - Very common
  - Creatine transporter, RYR2, CACNA1A/S, ATP1A2, USP17L2/7



- Primary mitochondrial dysfunction:
  - Defective cellular energy metabolism
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Mitochondrial-targeted therapies are used in both.

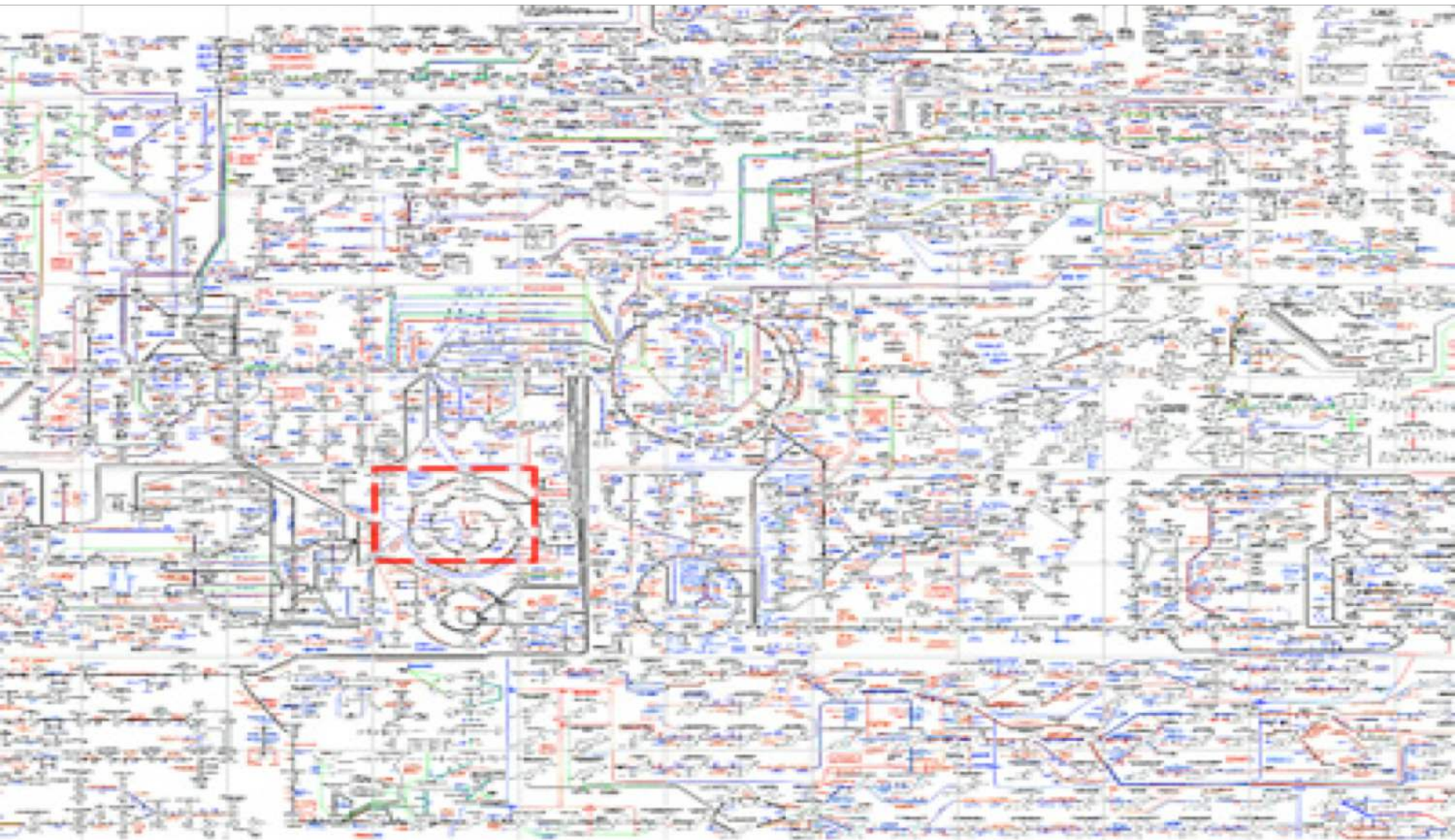
However, secondary dysfunctions may have additional options.

## General Principles of the Treatment of Mitochondrial Dysfunction

- Increase energy supply
  - Exercise
  - Cofactors (Co-Q, L-carnitine, creatine, riboflavin, etc.)
- Decrease energy demand
  - Avoid fasting
  - Avoid other high-demand situations: over-exertion, environmental temperature extremes, illness, etc.
- Protect mitochondrial from reactive oxygen species (ROS) produced
  - Anti-oxidants
- Treat symptoms
  - Neuropathic medications: amitriptyline, gabapentin
  - Channelopathy: propranolol, acetazolamide
  - Depression/anxiety: SSRIs, SNRIs
  - GI: many agents

# Key Metabolic Pathways

## Metabolism is Complicated!

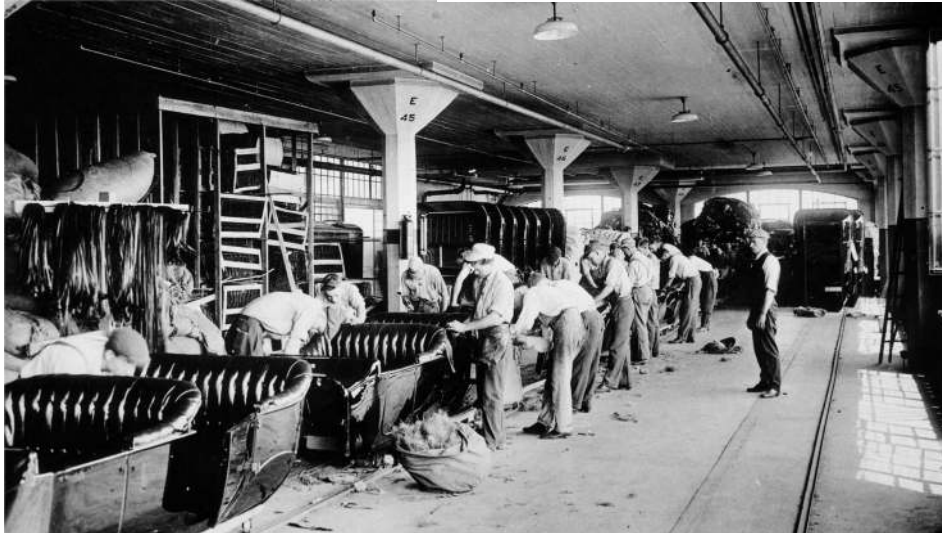
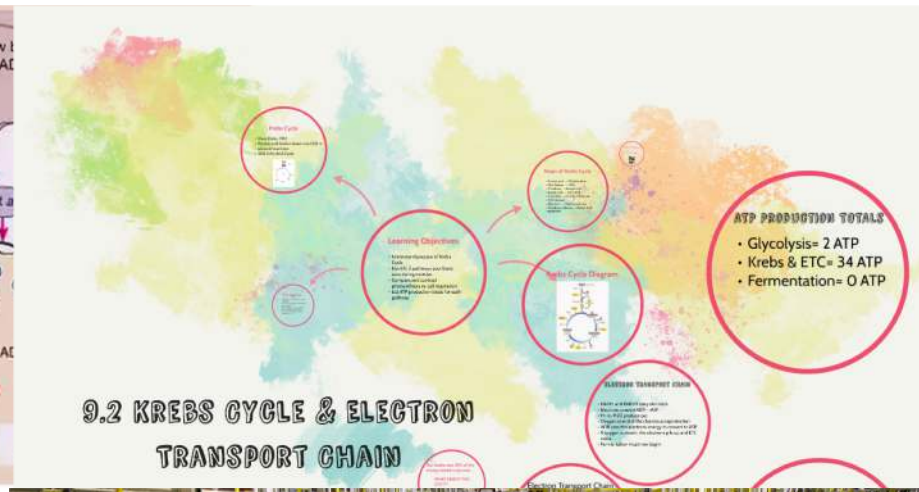
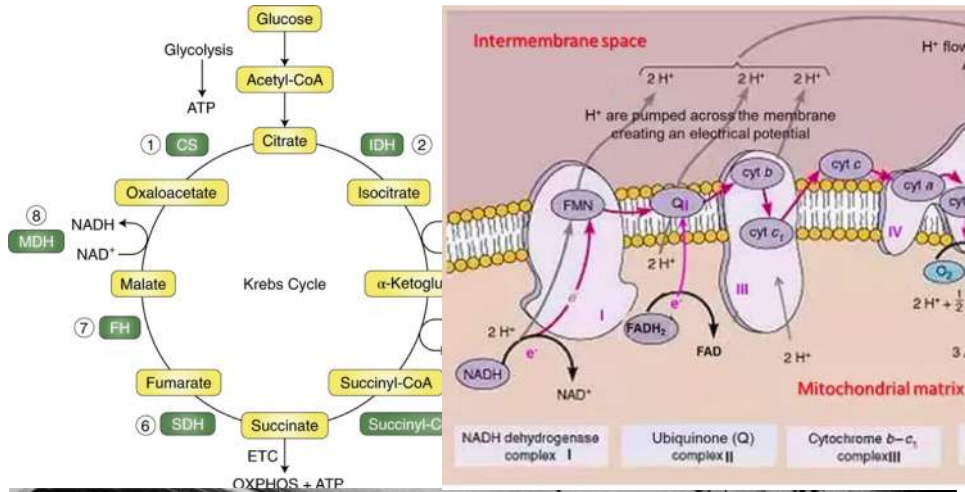


The following are common components of the **mito-cocktail**:

- Acetyl L-carnitine
- Alpha ketoglutarate
- Alpha lipoic acid
- Arginine
- Carnitine
- Coenzyme Q10
- Creatine
- Magnesium
- Selenium
- Zinc
- Vitamins
  - B1 (thiamine)
  - B2 (riboflavin)
  - B3 (niacinamide)
  - B5 (pantothenate)
  - B6 (pyridoxine, pyridoxal-5-phosphate)
  - B7 (biotin)
  - B12 (methylcobalamin)
  - C
  - D3
  - E



# Energy Is Produced on an Assembly Line





# The Science Behind Supplements

## The Adams 2011 Study

Effect of a vitamin/mineral supplement on children and adults with autism. Adams et al, 2011, PMID 22151477.

- Randomized, double-blind, placebo-controlled
- 141 children and adults with autism
- 3-months of placebo or a vitamin/mineral cocktail consisting of 31 ingredients
- **Improvements** in the PGI-R (Average Change,  $p = 0.008$ ), and on the subscores for **Hyperactivity** ( $p = 0.003$ ), **Tantruming** ( $p = 0.009$ ), **Overall** ( $p = 0.02$ ), and **Receptive Language** ( $p = 0.03$ ).
- Improvements in methylation, glutathione, oxidative stress, sulfation, ATP, NADH, and NADPH.

Simpson et al. *BMC Psychiatry* 2011, **11**:62  
<http://www.biomedcentral.com/1471-244X/11/62>



### RESEARCH ARTICLE

### Open Access

## Systematic review of safety and tolerability of a complex micronutrient formula used in mental health

J Steven A Simpson<sup>1</sup>, Susan G Crawford<sup>2</sup>, Estelle T Goldstein<sup>3</sup>, Catherine Field<sup>4</sup>, Ellen Burgess<sup>5</sup> and Bonnie J Kaplan<sup>6,7\*</sup>

### Abstract

**Background:** Theoretically, consumption of complex, multnutrient formulations of vitamins and minerals should be safe, as most preparations contain primarily the nutrients that have been in the human diet for millennia, and at safe levels as defined by the Dietary Reference Intakes. However, the safety profile of commercial formulae may differ from foods because of the amounts and combinations of nutrients they contain. As these complex formulae are being studied and used clinically with increasing frequency, there is a need for direct evaluation of safety and tolerability.

**Methods:** All known safety and tolerability data collected on one complex nutrient formula was compiled and evaluated.

**Results:** Data were assembled from all the known published and unpublished studies for the complex formula with the largest amount of published research in mental health. Biological safety data from 144 children and adults were available from six sources: there were no occurrences of clinically meaningful negative outcomes/effects or abnormal blood tests that could be attributed to toxicity. Adverse event (AE) information from 157 children and adults was available from six studies employing the current version of this formula, and only minor, transitory reports of headache and nausea emerged. Only one of the studies permitted a direct comparison between micronutrient treatment and medication: none of the 88 pediatric and adult participants had any clinically meaningful abnormal laboratory values, but tolerability data in the group treated with micronutrients revealed significantly fewer AEs and less weight gain.

**Conclusions:** This compilation of safety and tolerability data is reassuring with respect to the broad spectrum approach that employs complex nutrient formulae as a primary treatment.

SpectrumNeeds® is in a powder form.

- Contains 20 main ingredients of the mitochondrial cocktail
- Additional nutrients constitute a high-powered multivitamin
- High quality (USA CGMP)
- Easy use in children
- Great taste in 2 flavors



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860-434-7777  
NeuroNeeds.com • Manufactured in the USA

\*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

### Supplement Facts

Serving Size: 2 Heaping Scoops (4.4 g)  
Servings Per Container: 60

	Amount Per Serving	% Daily Value Children under 4 years of age	% Daily Value Children 4 or more years of age
Vitamin C (as ascorbic acid)	300 mg	2,000%	333%
Vitamin D (as cholecalciferol)	7.5 mcg (300 IU)	50%	38%
Vitamin E (as d-alpha-tocopheryl acetate and mixed tocopherols)	25 mg	417%	167%
Thiamin (as thiamin HCl)	12.5 mg	2,500%	1,042%
Riboflavin	12.5 mg	2,500%	962%
Niacin (as niacinamide)	12.5 mg	208%	78%
Vitamin B6 (50% as pyridoxine HCl and 50% as pyridoxal-5-phosphate)	10 mg	2,000%	588%
Folate (as 6S-5-Methyltetrahydrofolic acid glucosamine salt (Quatrefolic®) and calcium folinate)	1,667 mcg DFE	1,111%	417%
Vitamin B12 (as methylcobalamin)	250 mcg	27,778%	10,417%
Biotin	500 mcg	6,250%	1,667%
Pantothenic acid (as D-calcium pantothenate)	150 mg	7,500%	3,000%
Calcium	30 mg	4%	2%
Iodine (as potassium iodide)	50 mcg	56%	33%
Magnesium (as magnesium citrate and magnesium malate)	100 mg	125%	24%
Zinc (as zinc gluconate)	6 mg	200%	55%
Selenium (as selenomethionine)	25 mcg	125%	45%
Manganese (as manganese amino acid chelate)	0.5 mg	42%	22%
Chromium (as chromium picolinate)	25 mcg	227%	71%
Molybdenum (as sodium molybdate)	50 mcg	294%	111%
Potassium (as potassium citrate)	25 mg	<1%	<1%
Creatine monohydrate	625 mg	†	†
L-Arginine	500 mg	†	†
Carnitine Blend (acetyl L-carnitine HCl and L-carnitine)	250 mg	†	†
Alpha ketoglutaric acid	150 mg	†	†
Coenzyme Q10	125 mg	†	†
Choline bitartrate	75 mg	†	†
Inositol	50 mg	†	†
Alpha lipoic acid	50 mg	†	†
D-Beta, D-Gamma, D-Delta tocopherols	2.2 mg	†	†

† Percent Daily Values are based on a 2,000 calorie diet. †Daily value not established.

Other ingredients: Citric acid, natural flavors, organic glucosylated steviol glycosides, organic rebaudioside A, silica and monk fruit extract.

Take twice a day, amount of powder taken depends on weight. Discuss with your physician.

# EnergyNeeds®

## 40-Active Ingredients

Supplement Facts		
Serving Size: 5 Capsules Servings Per Container: 60		
	Amount Per Serving	% Daily Value
Calories	5	
Total Carbohydrate	<1 g	<1%**
Vitamin A (as retinyl palmitate and 89% beta-carotene)	3,900 mcg	433%
Vitamin C (as ascorbic acid)	500 mg	556%
Vitamin D (as cholecalciferol)	18.8 mcg (750 IU)	94%
Vitamin E (as d-alpha-tocopheryl succinate and mixed tocopherols)	70 mg	467%
Vitamin K (as phyloquinone)	50 mcg	42%
Thiamin (as thiamin HCl)	18.8 mg	1,567%
Riboflavin	20 mg	1,538%
Niacin (as niacinamide)	50 mg	313%
Vitamin B6 (as pyridoxine HCl and pyridoxal-5-phosphate)	1 mg	59%
Folate (as calcium L-5-methyltetrahydrofolate)	335 mcg DFE	84%
Vitamin B12 (as methylcobalamin)	25 mcg	1,042%
Biotin	750 mcg	2,500%
Pantothenic acid (as D-calcium pantothenate)	75 mg	1,500%
Choline (as choline bitartrate)	100 mg	18%
Iodine (as potassium iodide)	75 mcg	50%
Magnesium (as magnesium oxide and 33% magnesium citrate)	75 mg	18%
Zinc (as zinc gluconate)	7.5 mg	68%
Selenium (as selenomethionine)	50 mcg	91%
Manganese (as manganese sulfate)	0.75 mg	33%
Chromium (as chromium nicotinate glycinate chelate)	37.5 mcg	107%
Molybdenum (as molybdenum glycinate chelate)	75 mcg	167%
Potassium (as potassium citrate)	40 mg	<2%
Acetyl L-carnitine HCl	250 mg	†
L-Carnitine tartrate	250 mg	†
Creatine monohydrate	200 mg	†
Quercetin (as quercetin dihydrate)	150 mg	†
L-Arginine HCl	150 mg	†
Alpha-Ketoglutaric acid	125 mg	†
Coenzyme Q-10	100 mg	†
Glycine	100 mg	†
Alpha-lipoic acid	75 mg	†
Inositol	75 mg	†
Taurine	50 mg	†
Rutin	25 mg	†

\*\*Percent Daily Values are based on a 2,000 calorie diet. †Daily value not established.

Other ingredients: Hypromellose, rice flour, magnesium stearate, and silica.

\*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

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## EnergyNeeds® in a capsule form.

- Designed for adults and adolescents, but also for children who prefer capsules.
- One container is a one-month supply for an adult.
- Higher amounts of riboflavin, carnitine, and vitamin D.
- Immune booster, with vitamins A, B<sub>6,9,12</sub>, C, D, E, Se, Zn, beta-carotene, quercetin, rutin, coQ10.



Take twice a day; amount of capsules taken depends on weight. Discuss with your physician.



# Coenzyme Q10 Is Key!

## Ubiquinol v. Ubiquinone

- CoQ10 is such an essential component of the mitochondrial cocktail that [any mitochondrial-targeted approach is likely to fail unless sufficient CoQ10 is supplemented.](#)
- Present as ubiquinone in powdered products, but usually not enough.
- Ubiquinol is the most effective form of CoQ10.
- Most CoQ10 products on the market are poorly absorbed.
- No CoQ10 product is perfect or right for every person.
- Considerations in purchasing a CoQ10 product:
  - Ubiquinol v. ubiquinone
  - Liquid v. gel capsule, and capsule size
  - Oil base: soy v. limonene
  - Price
- Adjust dosing based on blood levels



# Is Our Destiny Written in Our DNA?

Almost all common conditions are polygenic/multifactorial.

Autism has the highest genetic component among all common conditions!

## *Ancient Greek Fates*



- Genetics determines risk, not outcome!
- Genes are regulated by the environment.
- *Metaphor – one hand in a card game:*
  - Genetic testing is the hand one is dealt.
  - Environmental factors are the hands of the other players.
  - Genetic testing is the careful reading of the cards in your hand.
  - The outcome depends on the cards we are dealt, the cards of our opponents, and HOW WE PLAY OUR HAND.



- Recommendations for Testing:
  - Whole exome sequencing (“**exome**”, “**WES**”)
  - CNV testing by chromosomal microarray (**CMA**) or sequencing equivalent
  - Mitochondrial DNA (**mtDNA**) sequencing
  - Pharmacogenetic (**PGx**) testing
- Whole genome sequencing (“WGS”):
  - Covers all of the above in premium laboratories
- Trio versus singleton

Phenotype: Neurodevelopmental: 72% (33/46)

Autism Spectrum Disorder, ADHD, Neuropsychiatric Disorders, Maladaptive Behaviors, Intellectual Disability

55% had a molecular diagnosis provided in total based off clinical correlation.

9% had a molecular diagnosis\* provided by lab based off clinical correlation.

52% had a molecular diagnosis\* provided by genomicist based off clinical correlation.

95% had a treatment recommended\*\*.

9% had a treatment recommended based on lab report data.

89% had treatment recommended per genomicist reading of data.

\* Pathogenic or Likely Pathogenic

\*\*Treatments include supplements, medications or dietary



## For More Information

### **NeurAbilities**

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Neurabilities healthcare (Instagram)

NeurAbilities Healthcare (LinkedIn)

### **NeuroNeeds®**

<https://www.neuroneeds.com>

*For more information on nutritional therapy for mitochondrial dysfunction.*

**Thank You,** Richard Boles, M.D.

