

# ENERGY DEFICIENCY IN ORGANIC ACIDEMIAS

Kimberly A. Chapman, M.D., Ph.D.  
Children's National Medical Center



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*Medical Center*



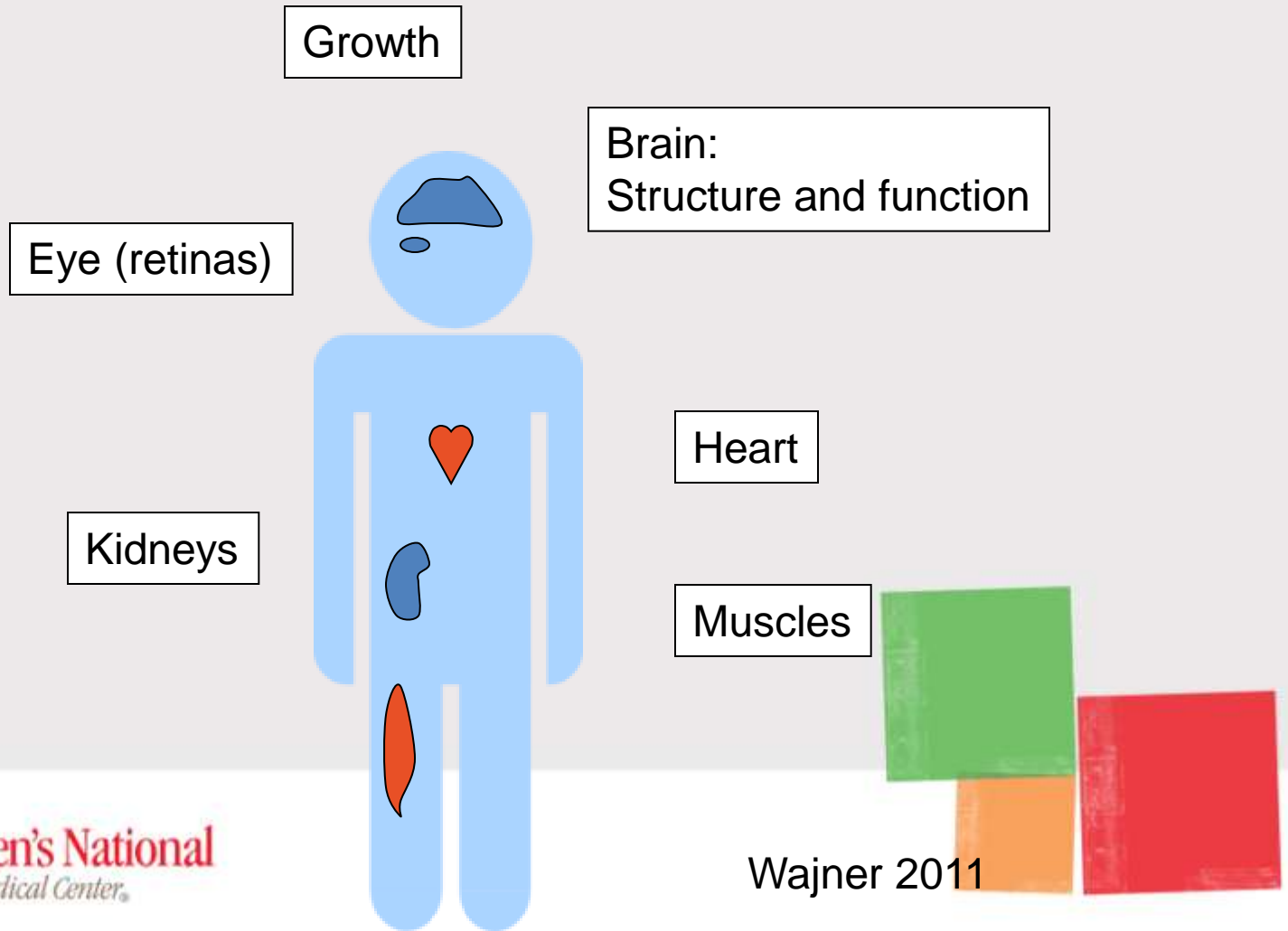
# What is energy?



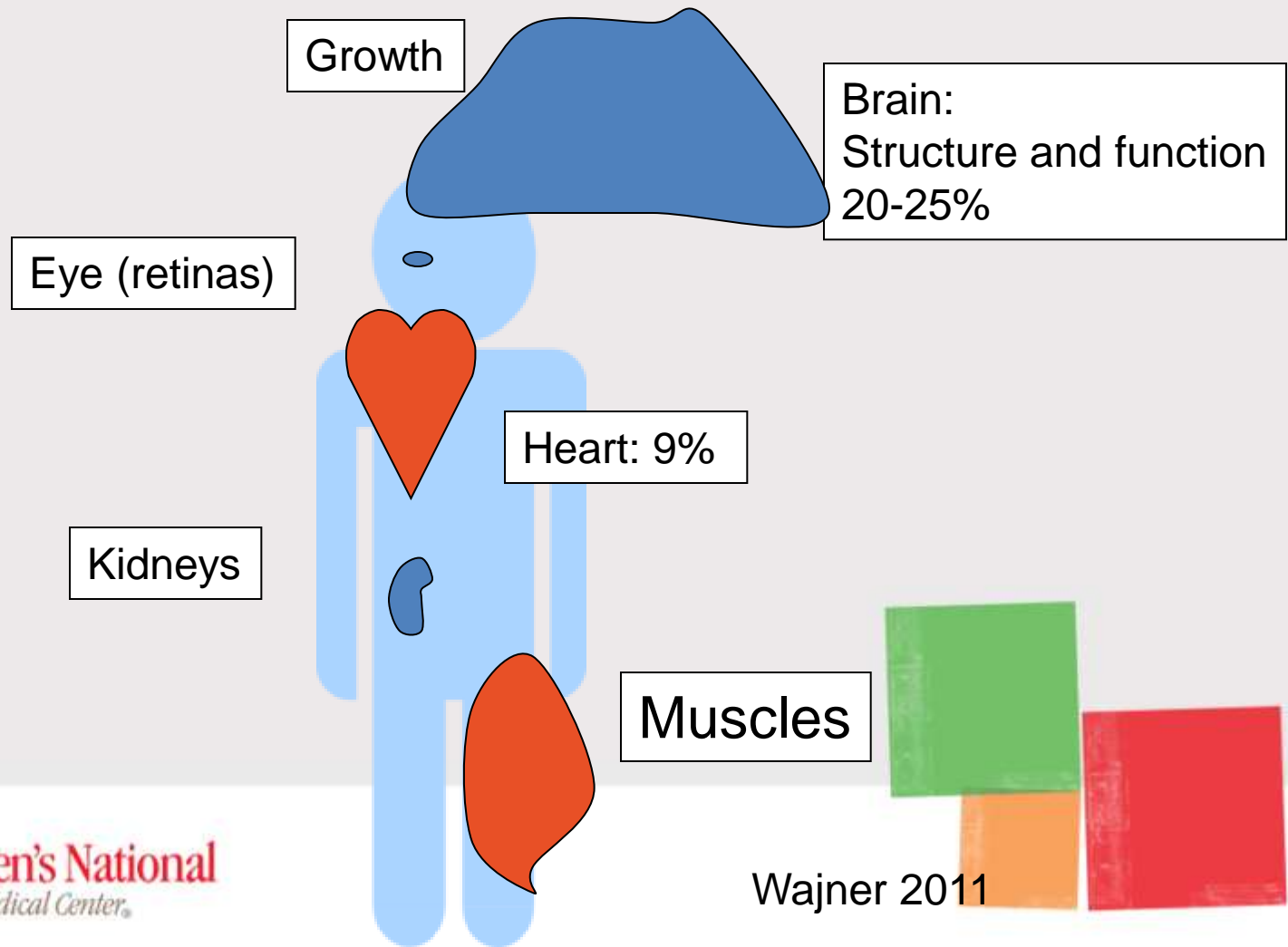
- Energy is the money that drives all biological processes
- Protein (amino acids), carbohydrates (CHOs), fatty acids



# Big Energy Users



# Energy phenotype

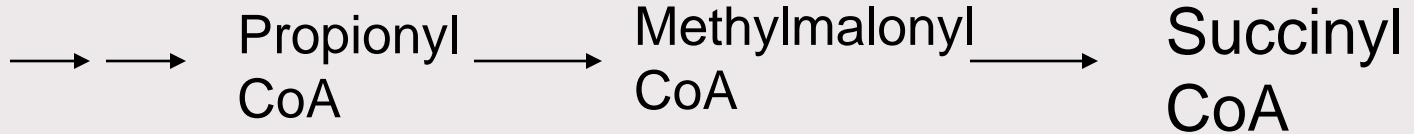


# Complex



# PA and MMA

V  
O  
M  
I  
T

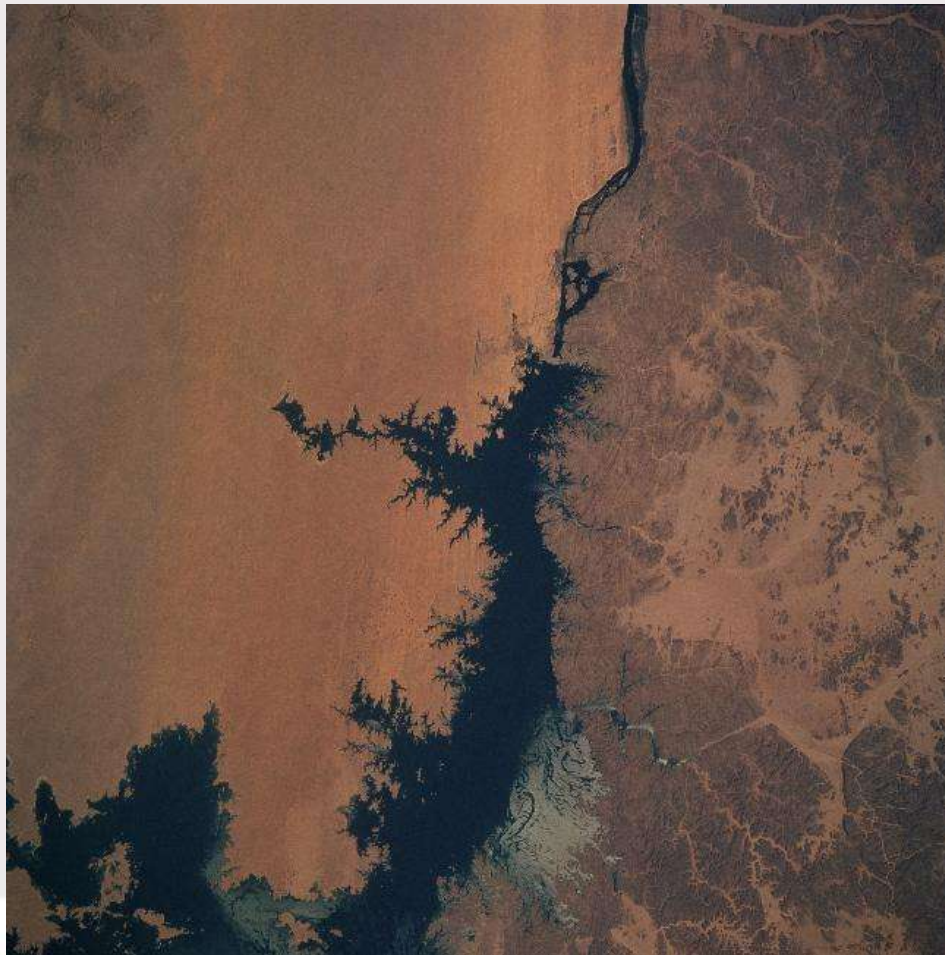


# PA and MMA

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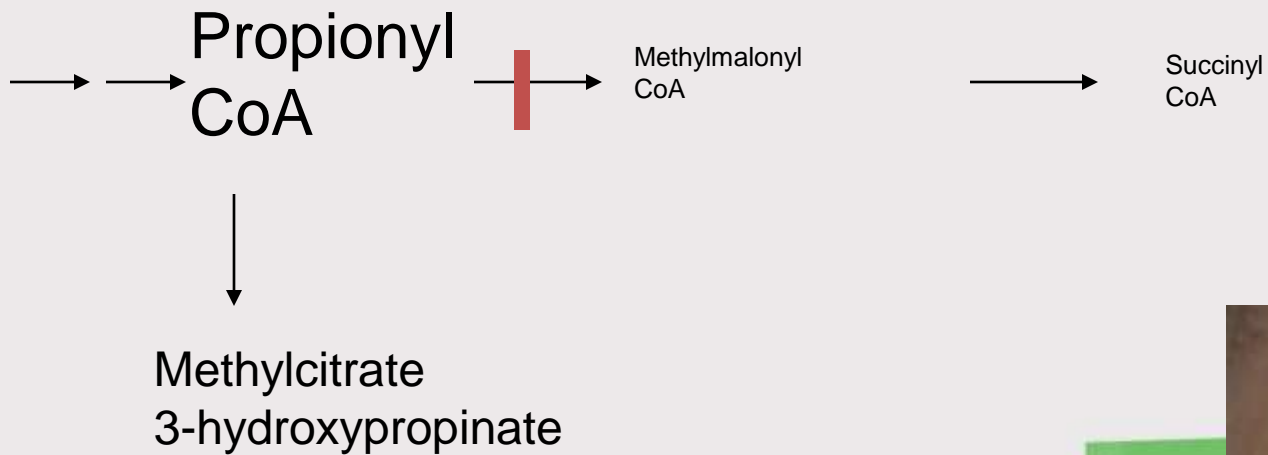
# What happens if block





# PA and MMA

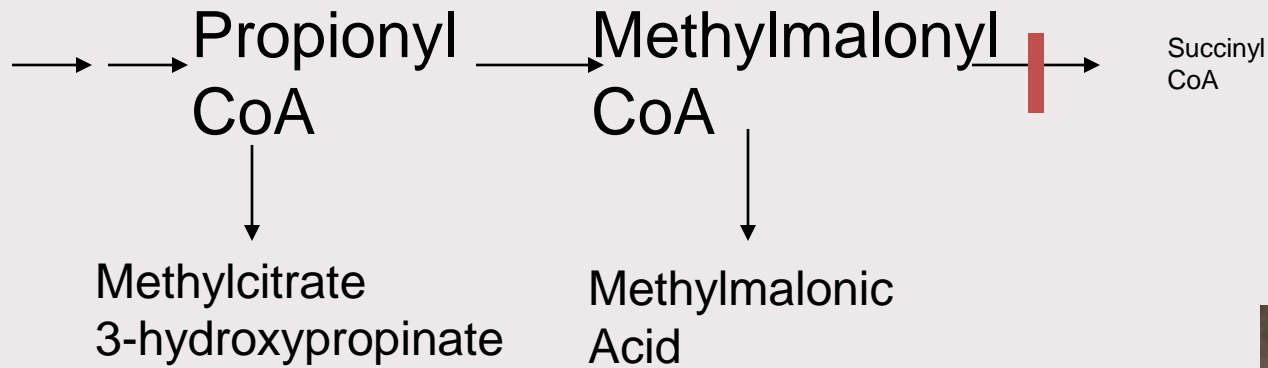
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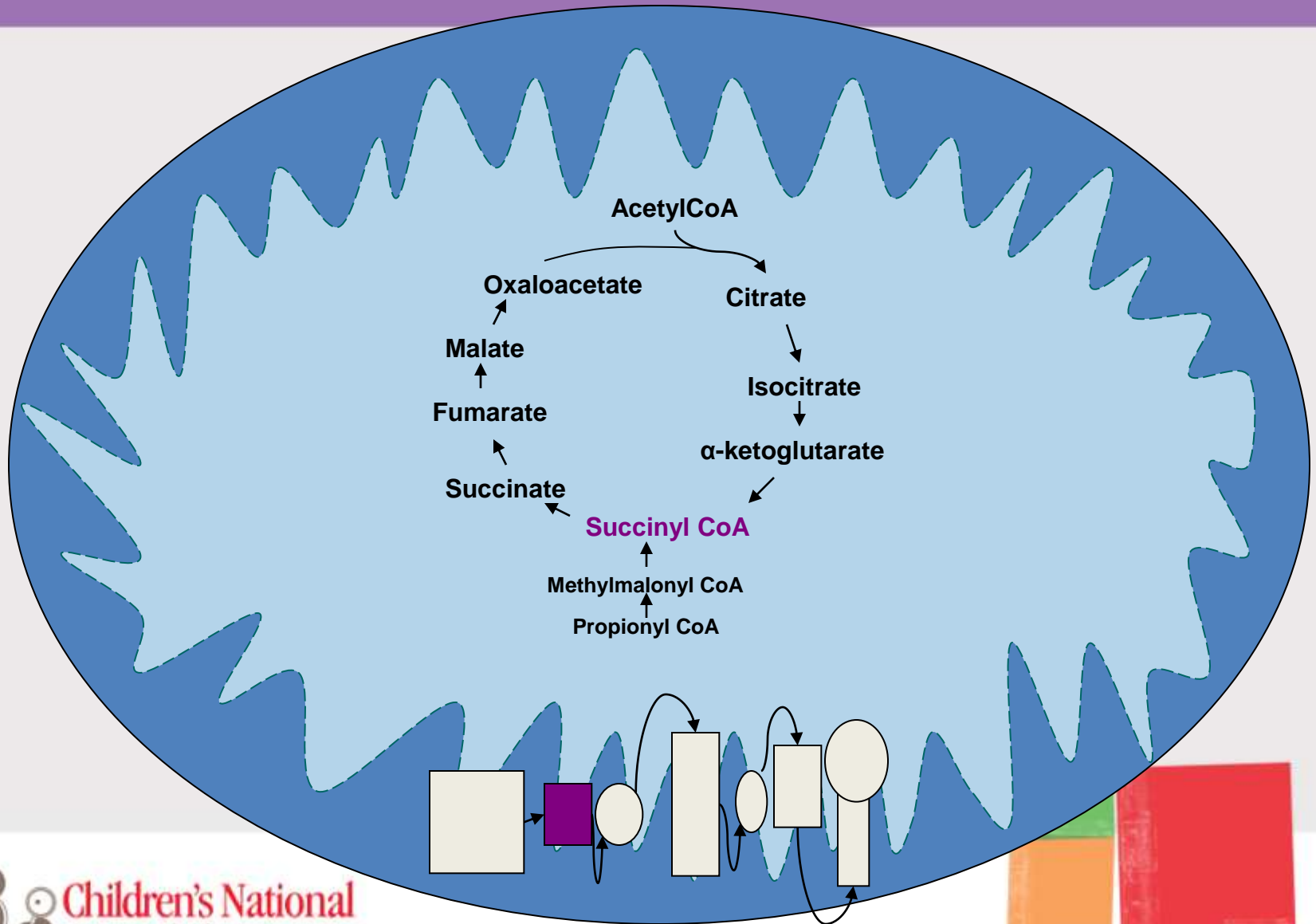
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# PA and MMA

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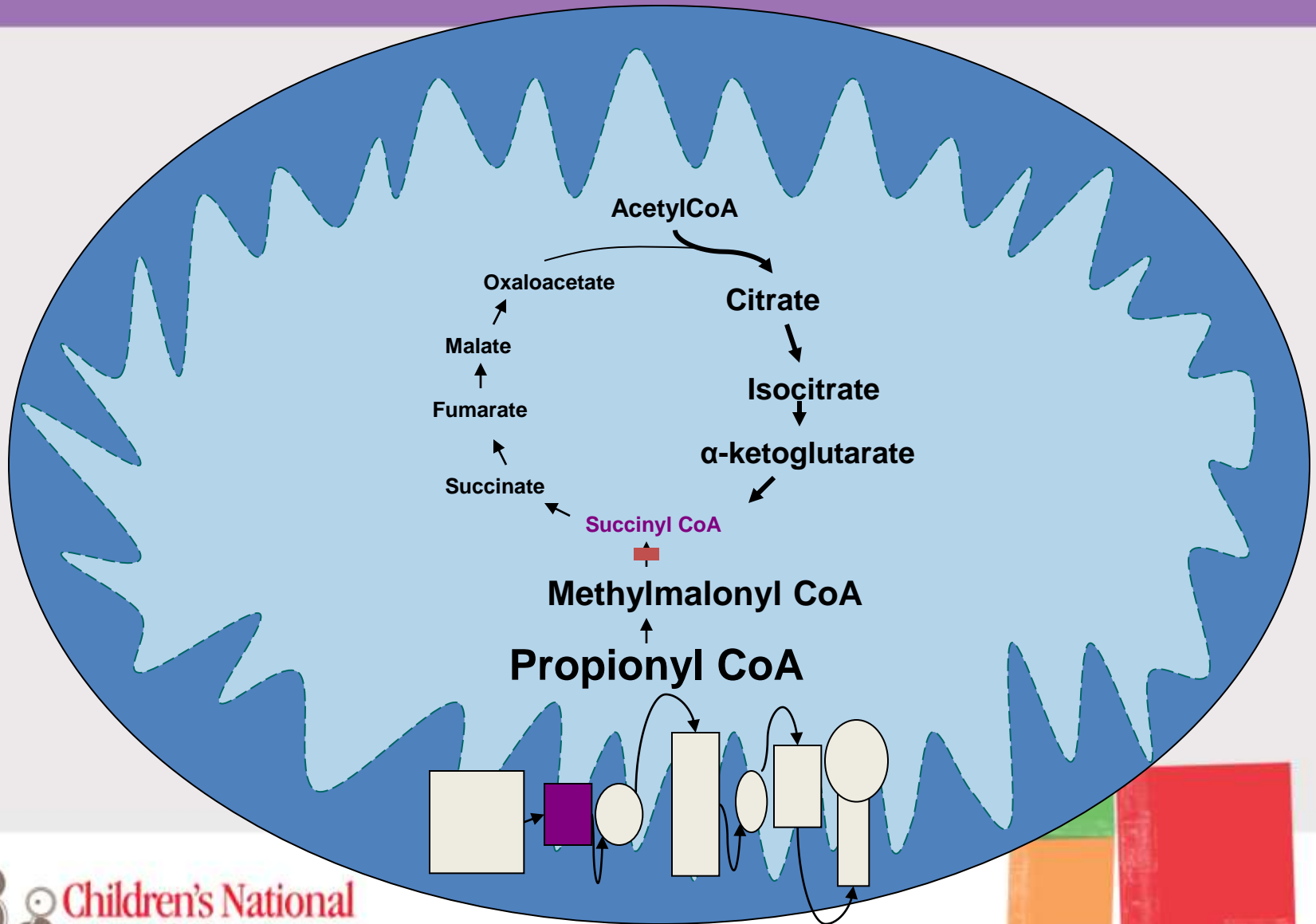


# Energy makes



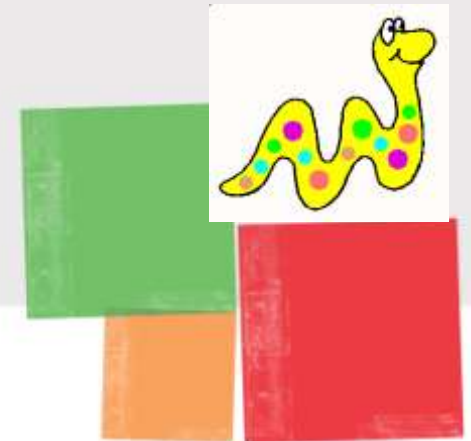
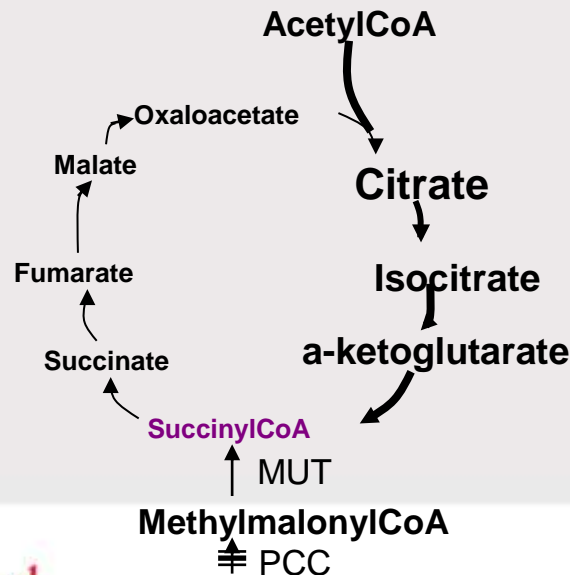


# PA/MMA effects

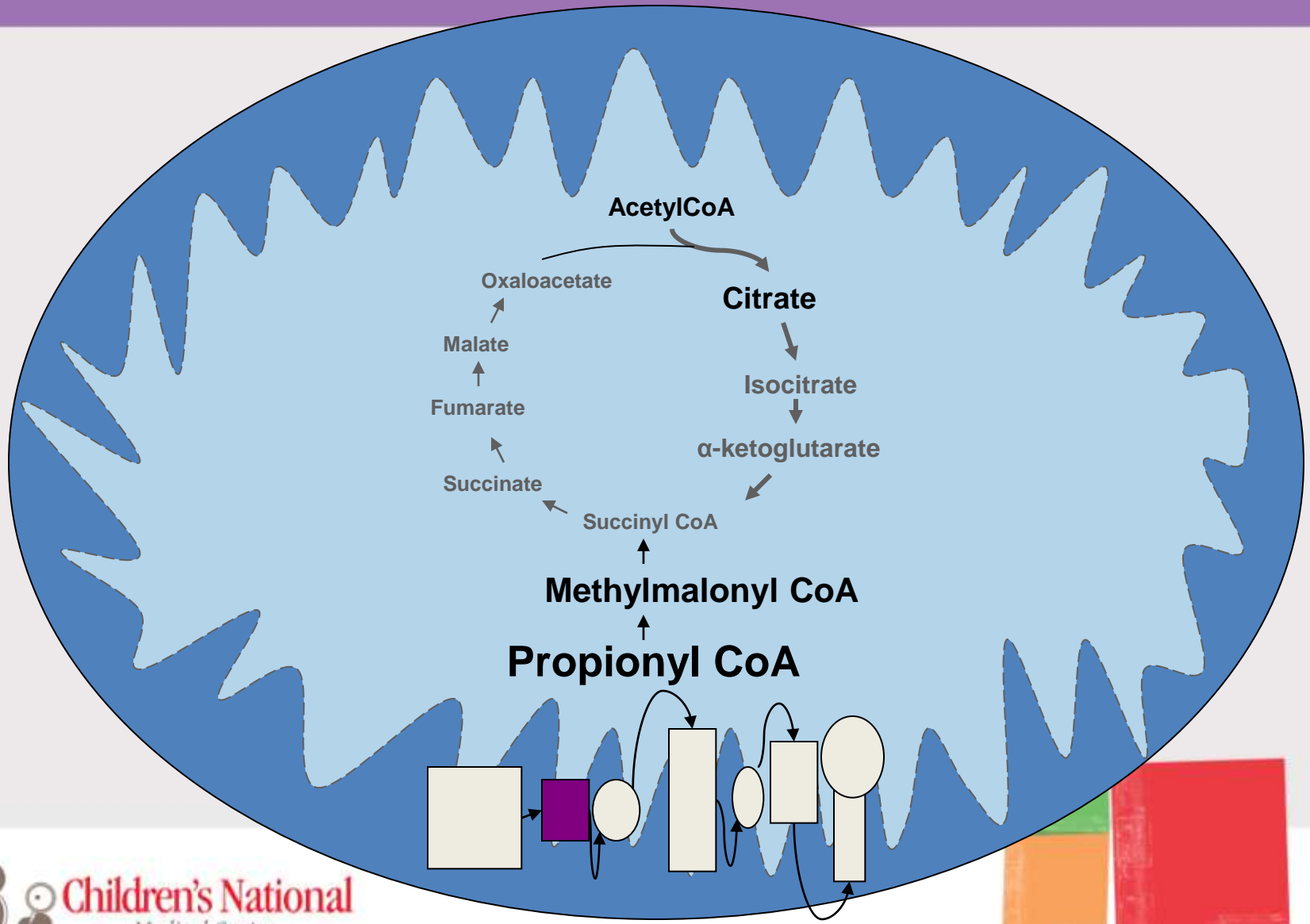


# How do you know this?

- *C. elegans* who missing *pcca* or *pccb* accumulate citrate and have deficient malate compared to controls (submitted)



# With time....we think



# Why not significant at birth?

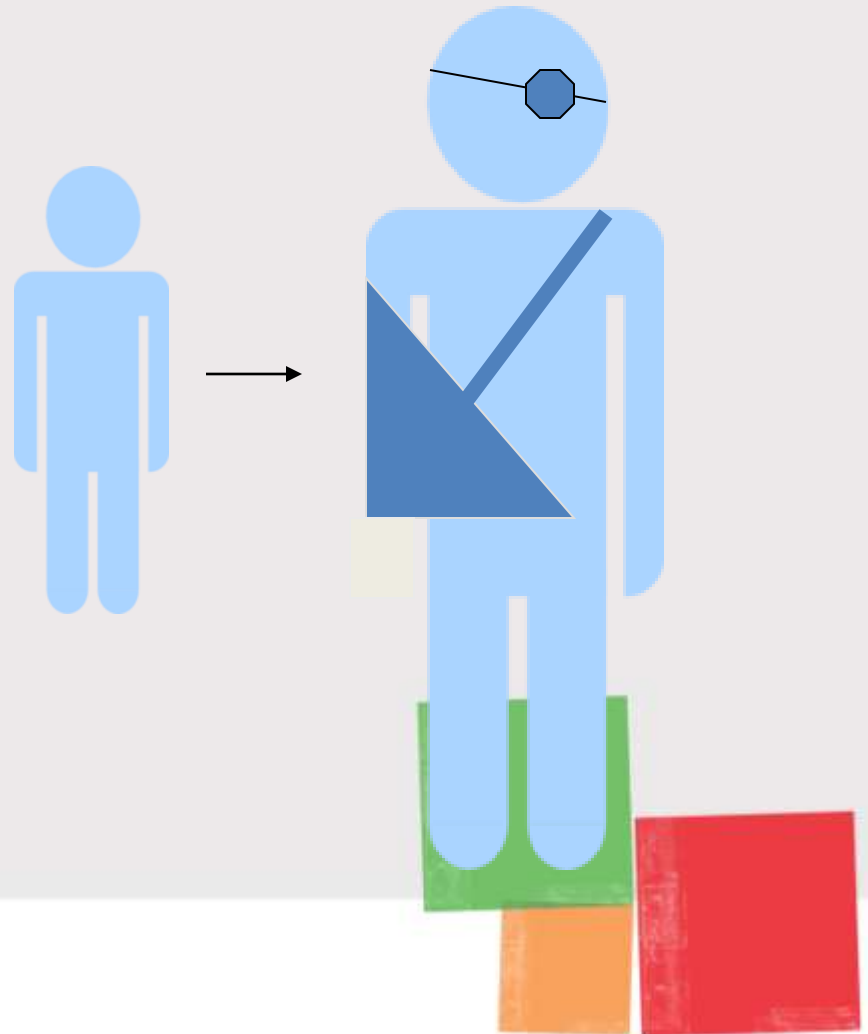
- Other systems to make energy (multiple generators)
- Cell may compensate with time (changing normal balances of other things to make up)
- More responsibilities as get older





# As age

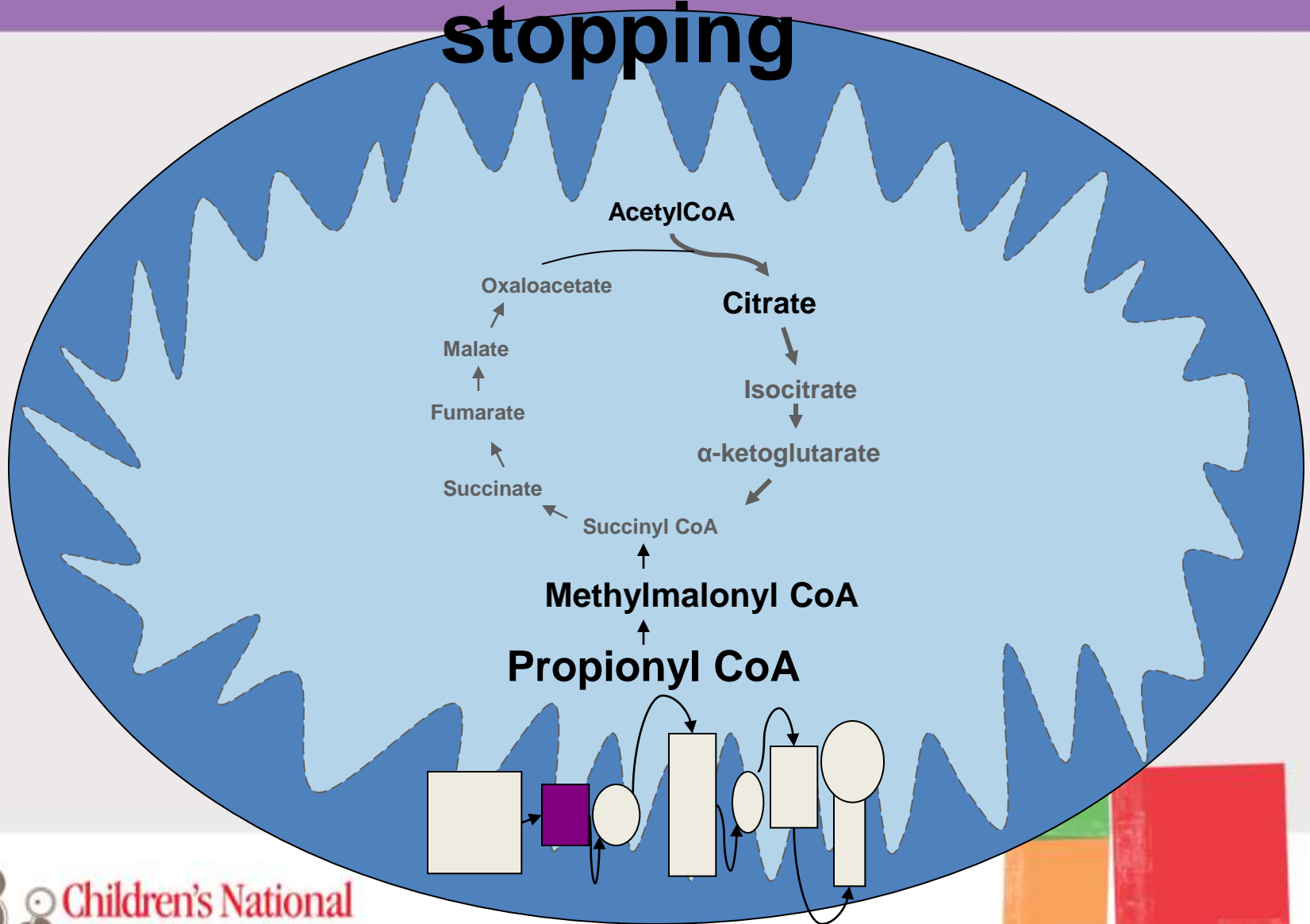
- More demand
  - Functional
  - New Construction
- Energy for repair



# But those generators and side reactions get old

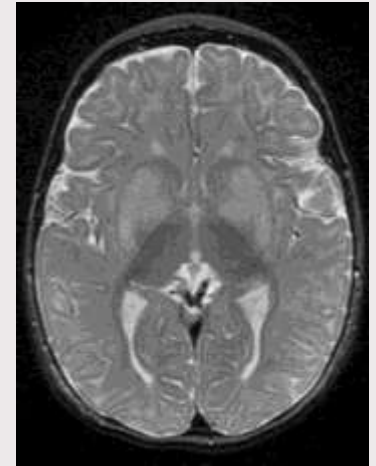


# Slowing to very slow and stopping

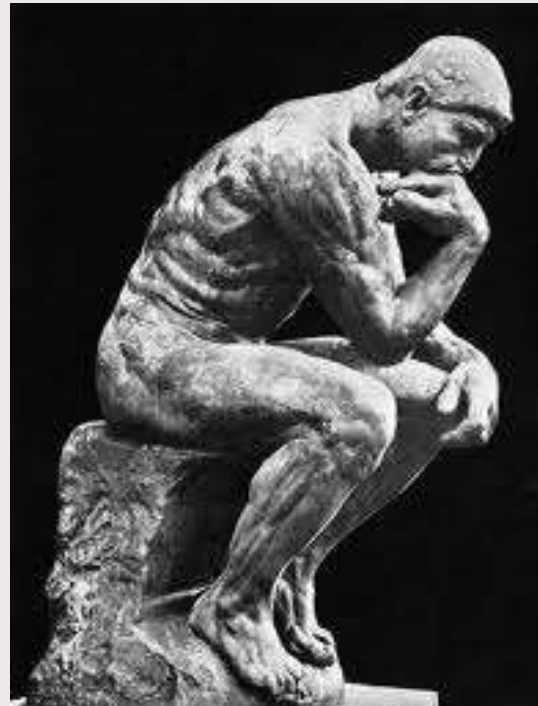


# Energy Presentations

- Metabolic “Strokes”
- Renal dysfunction
- Cardiomyopathy and Long QTc
- Optic Atrophy
- Myopathy
- Elevations of Lactate
- Increased free radical products in urine



# Now what?



# Tasks for doing...

- Measuring energy needs accurately
- Are there ways to work around the block (using alternative pathways)?



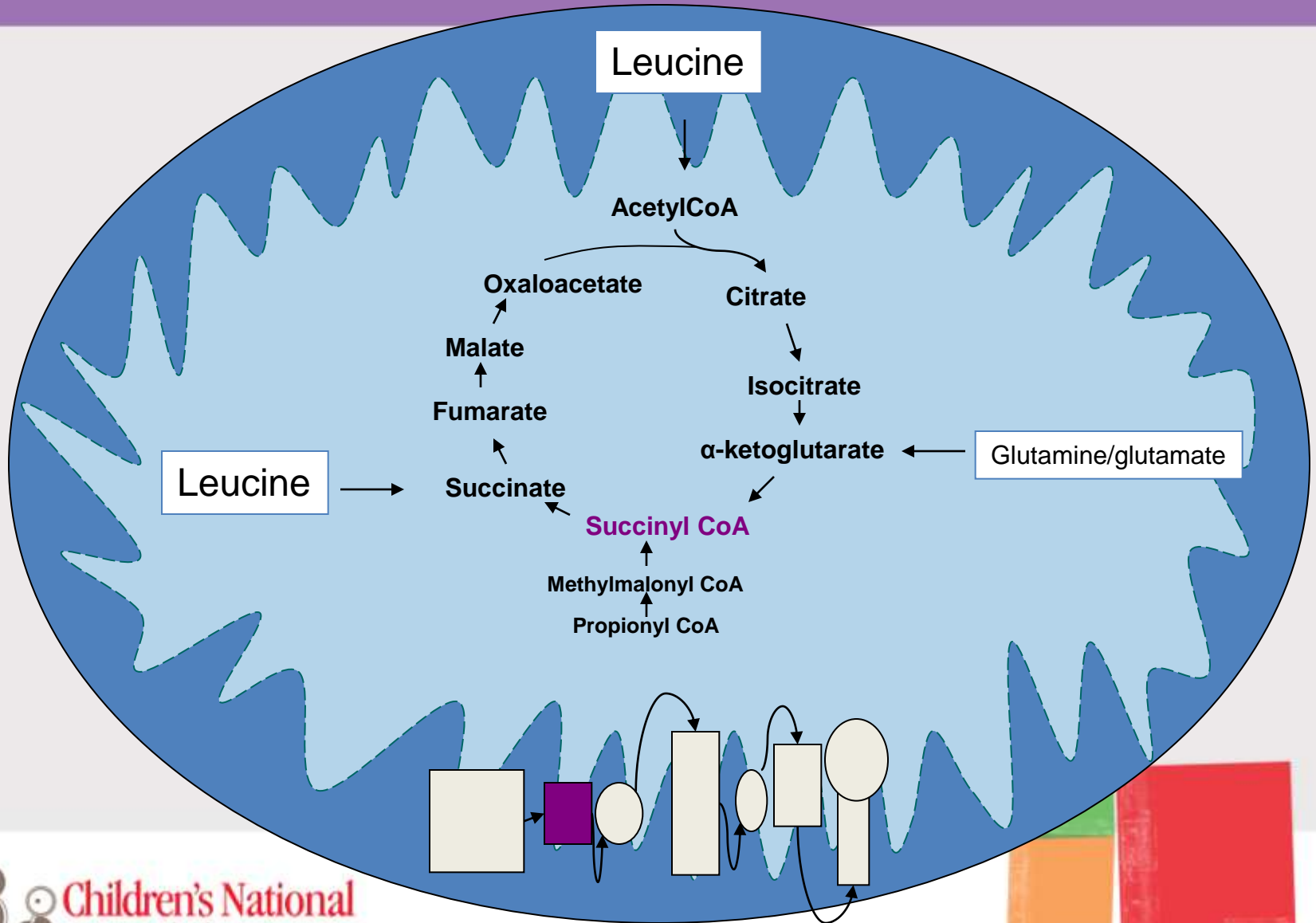
# Approaches to doing

- Measuring Energy Needs accurately
  - Resting Metabolic Rate (RMR)



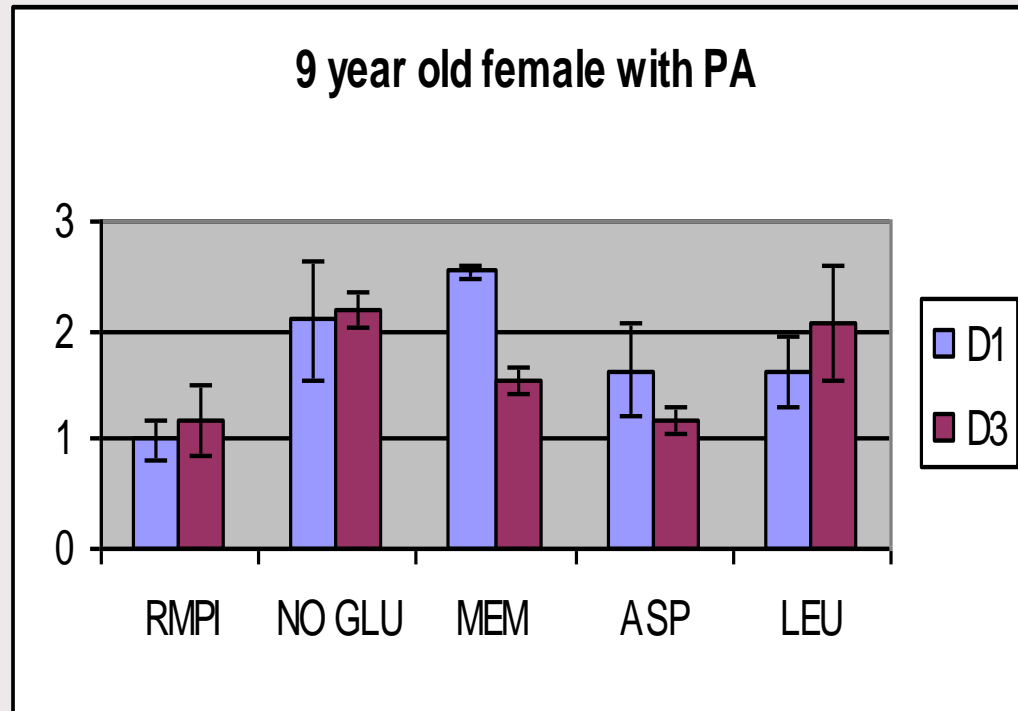
- Hauser et al. published in 2010 that individuals with MMA have about 20% less energy than predicted by math

# Alternative pathways

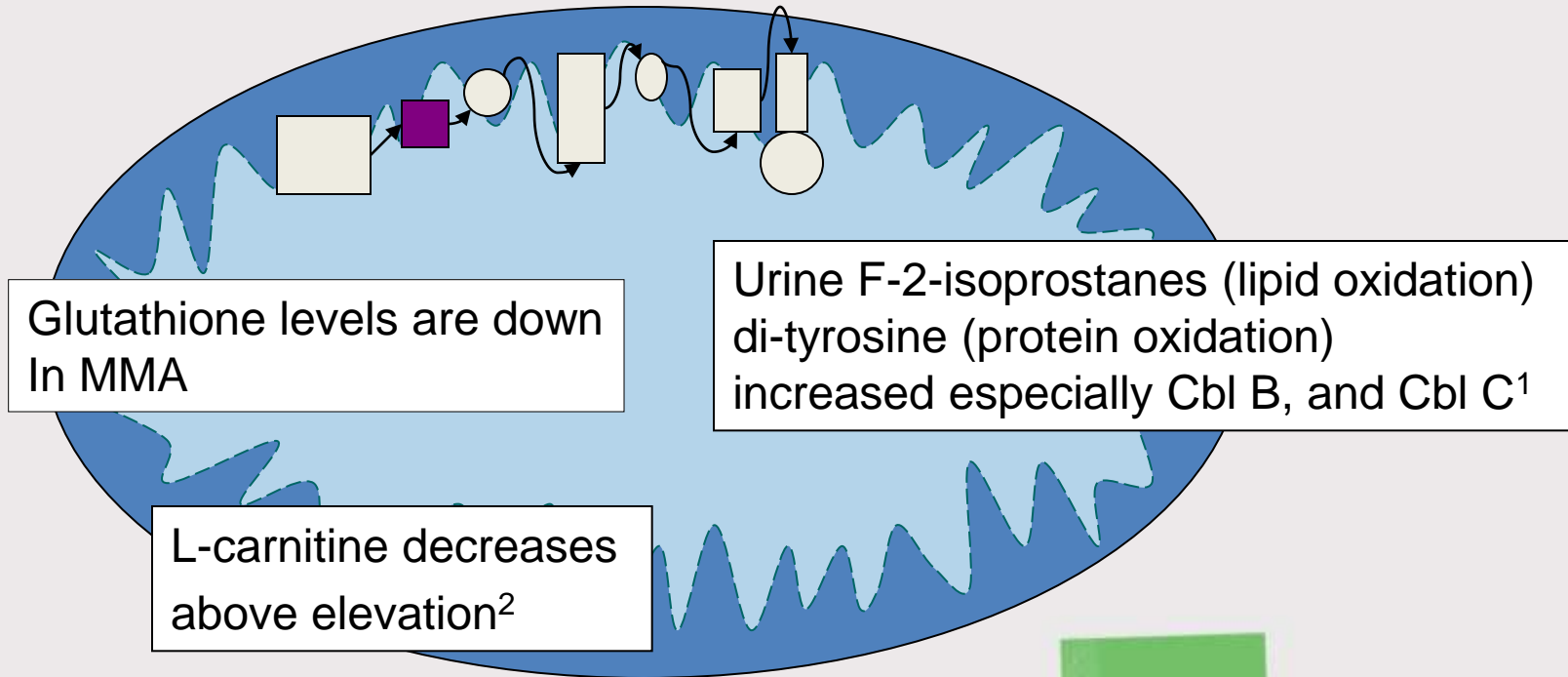




# Leucine does not kill PA cells



# Free Radical release



# Can we use antioxidants to better protect the mitochondria?

- Vitamin E and C
- CoEnzyme Q
- Thiamine (B vitamins)
- Gamma-glutamyl-cysteine
- N-acetylcysteine
- L-carnitine
- Others



# Should I do these thing now?

- No
- Clinical trials are really important
  - We don't know if any of these things will help
  - We need good markers if they are working (like RMR)
  - Trial designs are in preparation



# What can I do for my child?

- Maximize nutrition
- Wash hands (prevent infection)
- Flu shots and immunizations



# Questions and Discussion



# Acknowledgements

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