PRESENTING OUR

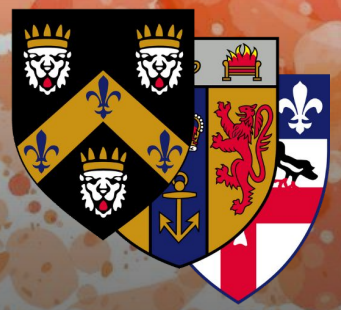
GKTEACH

STAGE 1 SERIES

MSA Education

~~FMS – CELL BIOLOGY AND SIGNALLING~~	~~MONDAY 13TH NOV 6PM~~
~~FMS – MOLECULAR AND CELL GENETICS~~	~~THURSDAY 16TH NOV 6PM~~
FMS – NUTRITION AND METABOLISM	TUESDAY 21ST NOV 6PM
ANATOMY OF RESPIRATORY AND CARDIOVASCULAR SYSTEMS	WEDNESDAY 29TH NOV 13:30PM
PHYSIOLOGY OF RESPIRATORY AND CARDIOVASCULAR SYSTEMS	WEDNESDAY 29TH NOV 4PM
FPP – PHARMACOLOGY	MONDAY 4TH DEC 6PM
RESPIRATORY PHYSIOLOGY	MONDAY 11TH DEC 6PM
RESPIRATORY ANATOMY	THURSDAY 14TH DEC 6PM

MAKE SURE TO COME ALONG!



MSA
Education

FMS NAM crash course

Slides and illustrations used with many thanks from Dr Despo Papachristodoulou and Dr Lauren Albee

Speaker: Jack Eaves

Anaerobic metabolism/glycolysis

- Red = ATP used up
- Green = ATP made
- * = non reversible reaction!

- *Glucose into glucose-6-phosphate via hexokinase/glucokinase and ATP phosphorylation
- Glucose-6-phosphate into fructose-6-phosphate via phosphohexose isomerase
- *Fructose-6-phosphate into fructose-1,6-bisphosphate via phosphofructokinase and ATP phosphorylation
- Fructose-1,6-bisphosphate into glyceraldehyde-3-phosphate and dihydroxyacetone phosphate via aldolase
- Dihydroxyacetone phosphate into glyceraldehyde-3-phosphate via triose phosphate isomerase
- Glyceraldehyde-3-phosphate into 1,3 bisphosphoglycerate via glyceraldehyde-3-phosphate dehydrogenase, NAD+ and Pi to form NADH and H^+
- 1,3 bisphosphoglycerate into 3-phosphoglycerate via 3-phosphoglycerate kinase via ADP
- 3-phosphoglycerate into 2-phosphoglycerate via phosphoglycerate mutase
- 2-phosphoglycerate into phosphoenol pyruvate via pyruvate kinase
- *Phosphoenolpyruvate into pyruvate via pyruvate kinase and ADP

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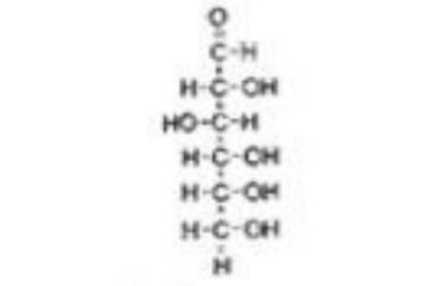
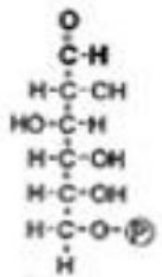


D-Glucose

Hexokinase or Glucokinase

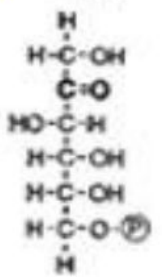
ATP

ADP

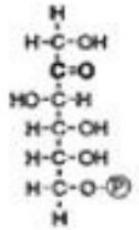


Glucose 6-phosphate

Phosphohexose isomerase



Fructose 6-phosphate

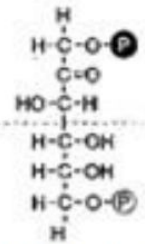


Fructose 6-phosphate

ATP

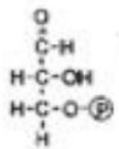
Phosphofructo-kinase

ADP

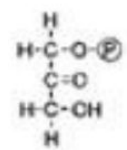


Fructose 1,6-bisphosphate

Aldolase

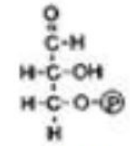


Triose phosphate isomerase



Glyceraldehyde-3-phosphate

Dihydroxyacetone phosphate



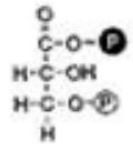
Glyceraldehyde-3-phosphate

Glyceraldehyde-3-phosphate dehydrogenase

P_i

NAD^+

$NADH + H^+$

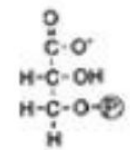


1,3-Bisphosphoglycerate

3-Phosphoglycerate kinase

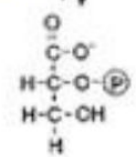
ADP

ATP

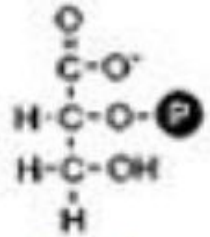


3-Phosphoglycerate

Phospho-glycerate mutase



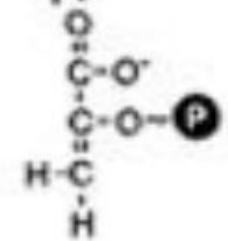
2-Phosphoglycerate



2-Phosphoglycerate

Enolase

H_2O



Phosphoenolpyruvate

Pyruvate kinase

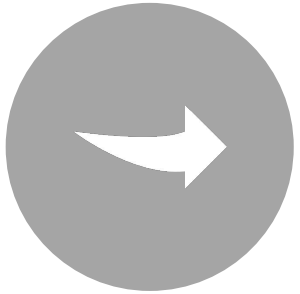
ADP

ATP

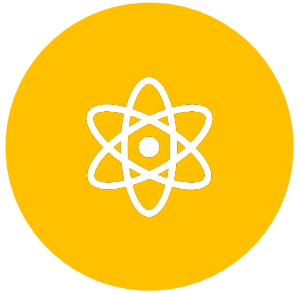
Pyruvate

Notes:

Glucokinase is only found in the Liver! - What do you think the Km is? Why do you think the Km is like this compared to hexokinase?



Any place where ATP is made is SUBSTRATE LEVEL PHOSPHORYLATION



If there is only two places where ATP is made – then how is this reaction sustainable? How are we actually producing ATP

Overall 2 ATP is used and 4 ATP are made as the net products of glycolysis, as well as 2 NADH produced

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Aerobic metabolism/Krebb's

CO2 lost
GTP made
NADH made
FAD made
*irreversible

- Pyruvate converted into acetyl coA with pyvurate dehydrogenase

Pyruvate+CoASH+NAD -> Acetyl CoA+CO2+NADH+H^+

- *Acetyl CoA and oxaloacetate into Citrate via citrate synthase
- Citrate into isocitrate via aconitase
- *Isocitrate into alpha ketoglutarate via isocitrate dehydrogenase and **loss of first CO2**
- *Alpha ketoglutarate into succinyl Co-A via alpha ketoglutarate dehydrogenase (uses CoASH and NAD^+ to make NADH, H+ and CO2) - **second loss of CO2**
- Succinyl Co-A into succinate via succinyl-CoA synthetase (via GDP and Pi to make GTP and Co-Ash)
- Succinate into fumarate via succinate dehydrogenase (via FAD into FADH2)
- Fumarate into malate via fumarase and addition of water
- Malate into oxaloacetate via malate dehydrogenase (via NAD into NADH and H+)

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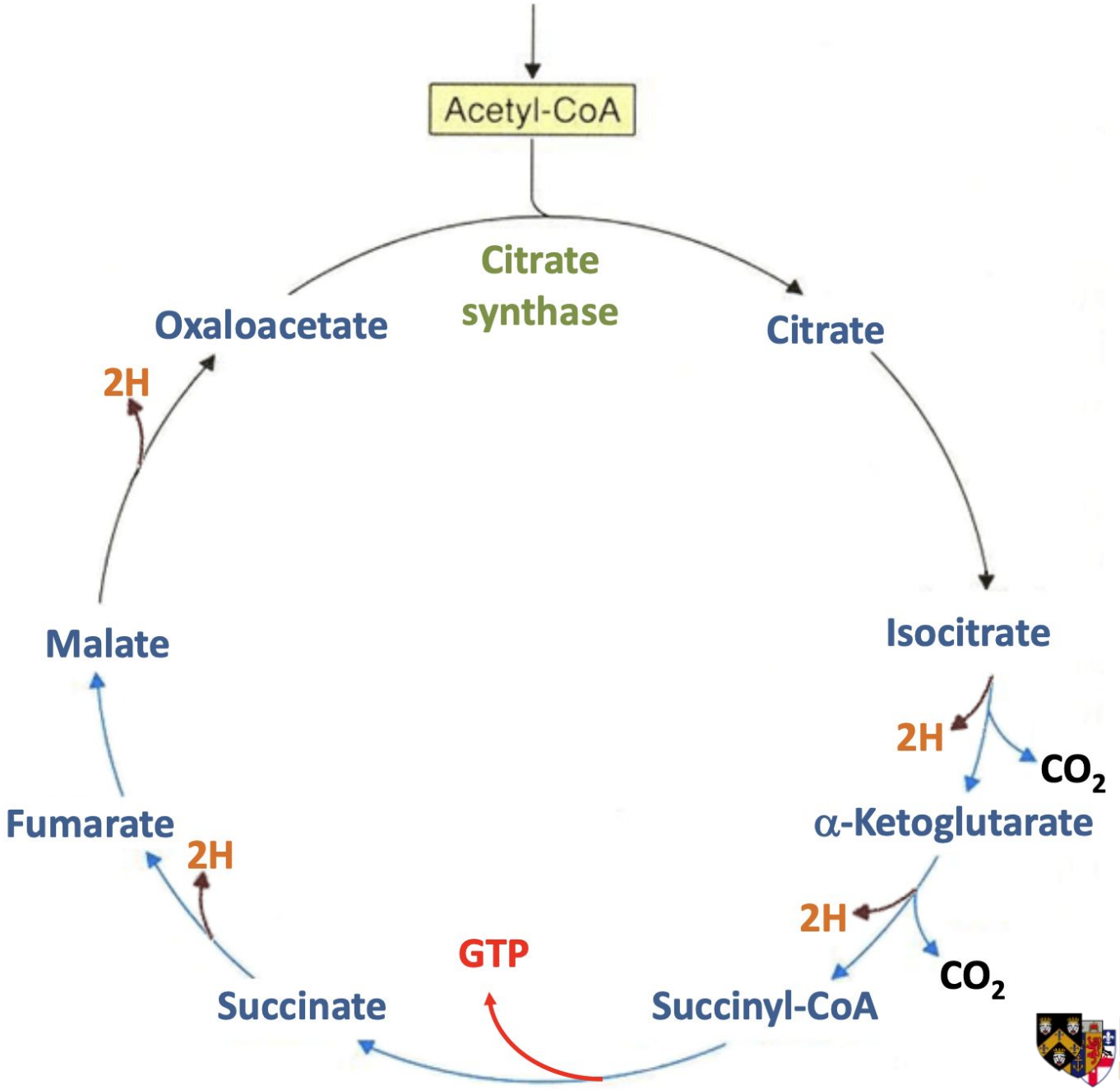
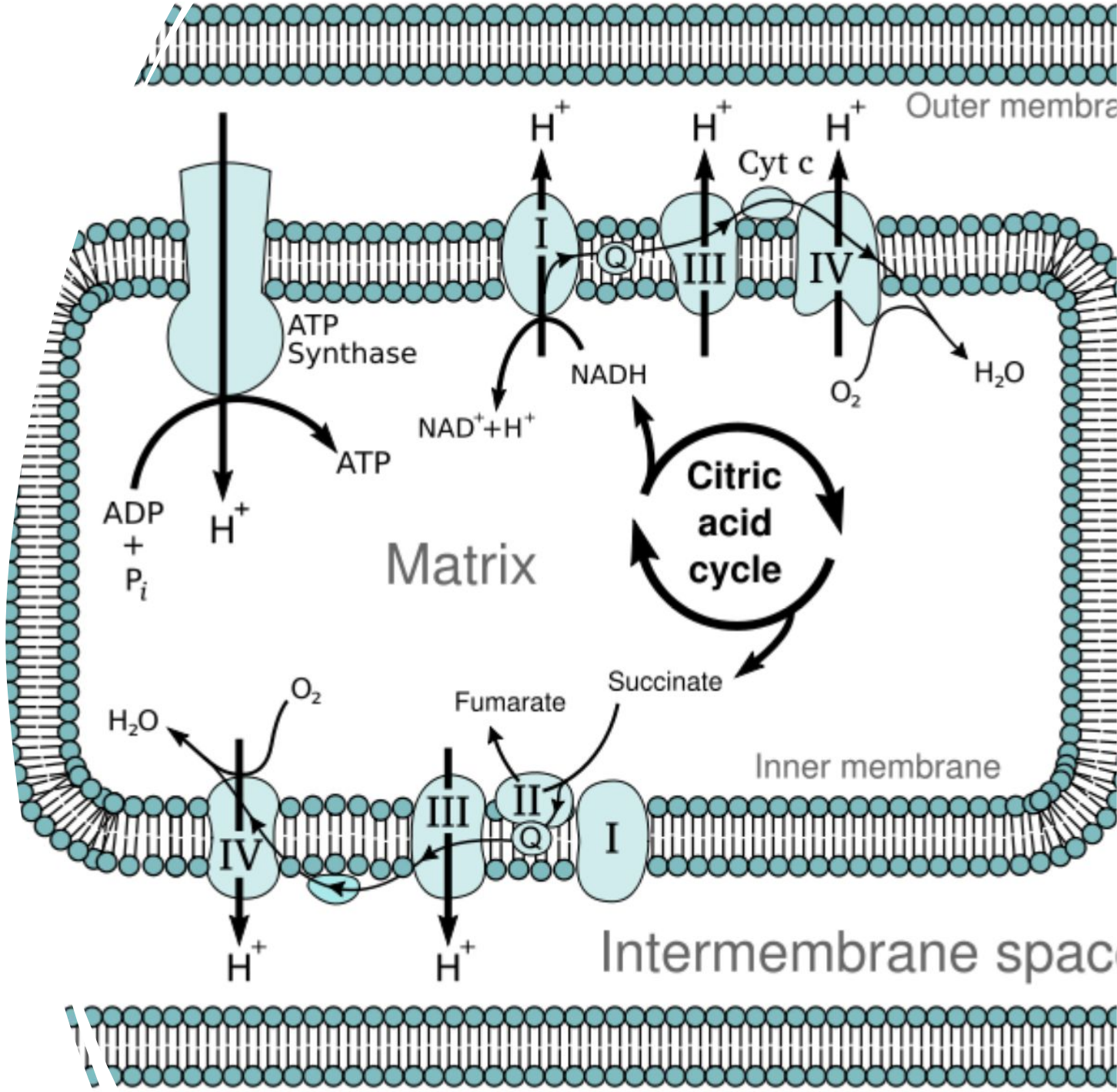
TCA cycle


Acetyl-CoA
Citrate synthase
Citrate
Isocitrate
2H
CO_2
α-Ketoglutarate
2H
CO_2
Succinyl-CoA
GTP
Succinate
2H
Fumarate
Malate
2H
Oxaloacetate

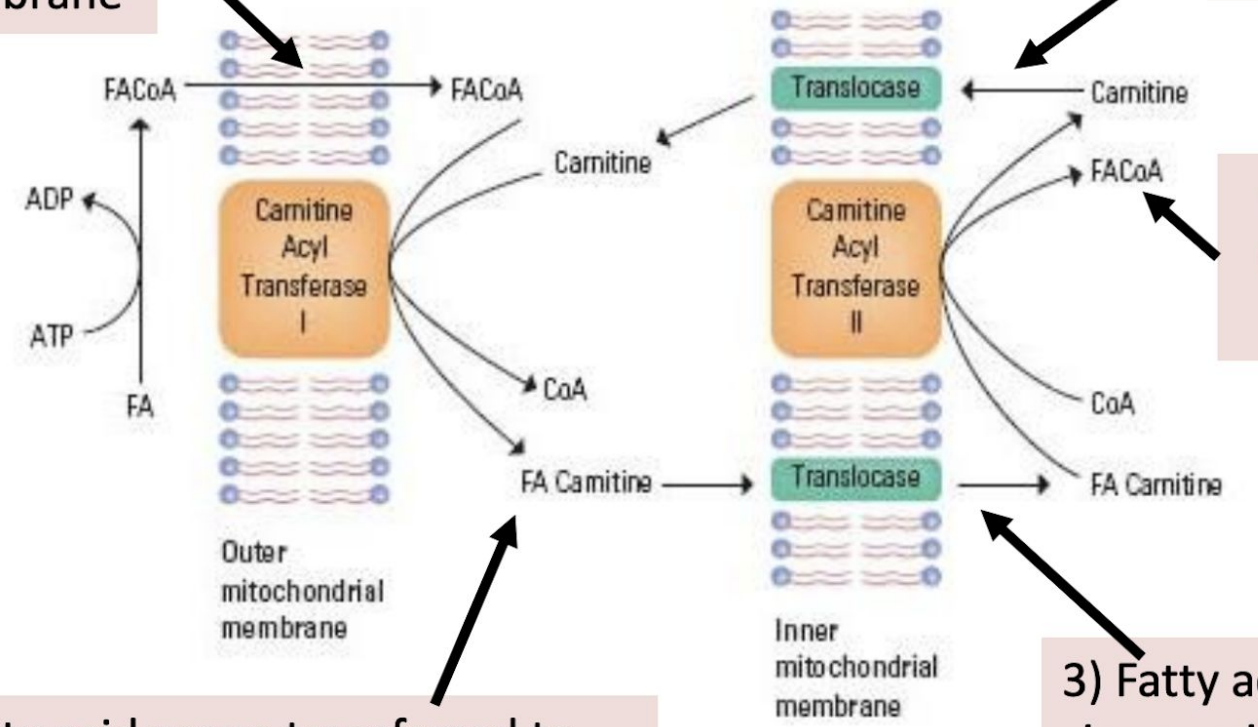
Notes

- It is a cycle
- Net products are 3 x NADH, 1 x FADH, 1x GTP
- NADH, FADH and GTP are all used to make ATP
  - Each NADH makes 2.5x ATP
  - Each FADH makes 1.5x ATP
  - Each GTP makes 1x ATP
- Overall – 10 ATP are made per cycle



Transport of fatty acyl-CoA into mitochondria: carnitine shuttle

1) Fatty acyl-CoA freely diffuses across the outer mitochondrial membrane



5) Carnitine transported back into the intermembrane space.

4) Carnitine is switched back for CoA by carnitine acyltransferase II, recreating fatty acyl-CoA.

2) Fatty acid group transferred to carnitine by carnitine acyltransferase I, creating fatty acyl-carnitine.

3) Fatty acyl-carnitine crosses the inner mitochondrial membrane via a translocase.

The process is energetically neutral.

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Glycogen synthesis and breakdown notes

- To make glycogen, a primer is needed
- The primer is made from adding UDP to glucose
- Glycogen is made from adding glucose molecules in a 1,4 bond via glycogen synthase
- Branching enzymes are used to make 1,6 bonds every 8-10 glucose molecules
- Glucose-6-phosphatase (the enzyme used to allow glucose to leave the cell) is only present in the liver – why?

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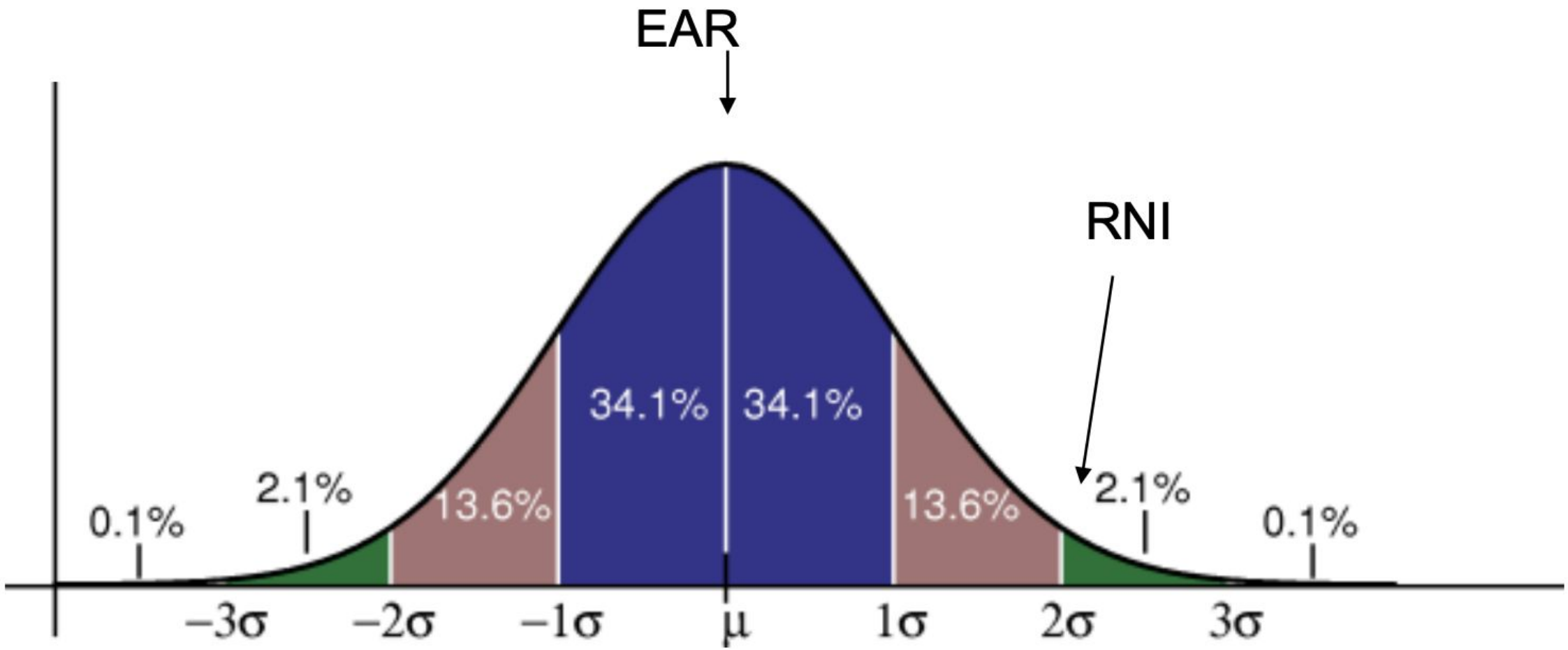
Nutrition and health questions

- What are macronutrients
- What are micronutrients
- How do we figure out the amount of macro and micronutrients we need?
- Do we use the same system for micronutrients as we do for calories? Why or why not?

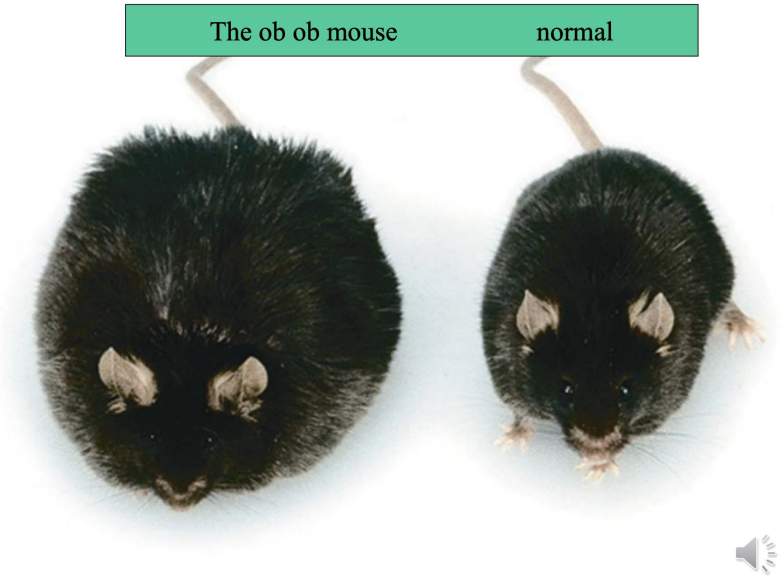
Nutrition and health answers

- Things we need in large amounts - protein, carbohydrates, lipids
- Things we need in small amounts – vitamins, minerals, amino acids, fatty acids
- Estimated average requirements and reference nutrient intake – scientists look at which levels make people sick from deficiency, and in what proportions. If people have the EAR, around 50% of people won't be deficient, if people use the reference nutrient intake, they take two σ above this, so 95% of the population won't be deficient
- If we all ate 2 σ above what we all needed, then we would all be fat


EAR
RNI
34.1%
34.1%
13.6%
13.6%
2.1%
2.1%
0.1%
0.1%
−3σ
−2σ
−1σ
μ
1σ
2σ
3σ

Hunger hormones

- Ghrelin is used to stimulate hunger (ghrelin sounds like a stomach growling)
- Neuropeptide Y is a hunger signal
- POMP and PYY suppress hunger
- Leptin indicates fat stores
- Insulin indicates carbohydrate stores



Note about cultural competency

- The "south asian diet" (doctor's words not mine) tends to be high in calories, saturated fats, sugars and salt
  - This leads to south asian communities facing higher prevelence of high blood pressure, heart disease, stroke, heart attacks, etc
- South asian women often wear modest clothing – why is this important in terms of nutrition?

Note about cultural competency

This means that south asian women not only have darker skin that leads to lower levels of vitamin D production, but they also don't receive much sunlight because of their clothing – leading to very low vitamin D levels that requires supplementation

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Thank you for attending the session -

Please fill in the feedback form:
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msa@kcl.ac.uk

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