Protein-Energy Interactions: Horizontal Aspects

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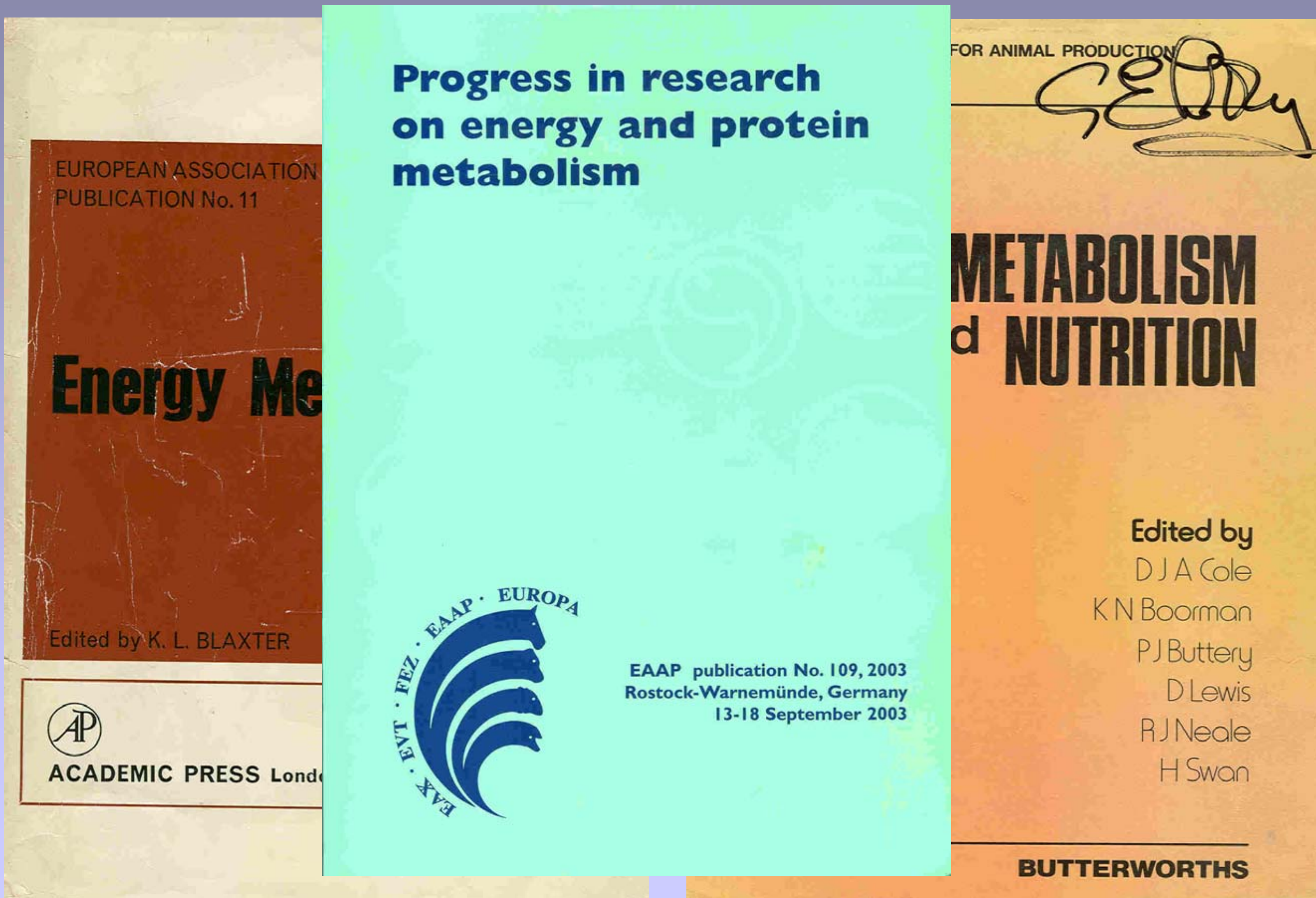
ROWETT
research institute
Improving food quality & preventing disease

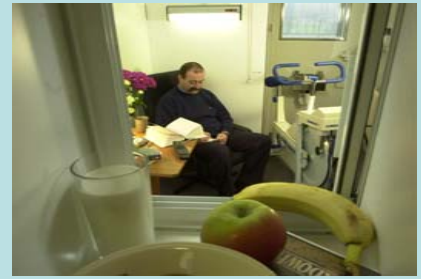
Long tradition



General P:E Interactions

Appetite

Efficiency

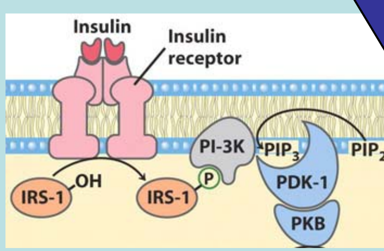


Bioenergetics

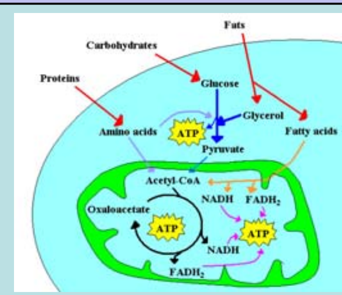
Epi-genetics

P E

Metabolic fuels



Hormonal sensitivity



Metabolite interconversion

Protein-Energy Interactions: Why are we interested?

Need to:

- **Understand**
- **Predict**
- **Manipulate**

Consequences

Agricultural efficiency

- Targeted outputs
- Better use natural resources
- Reduce environmental pollution

Health benefits

- Animal
- Consumer – added quality
- Target ‘Western’ diseases

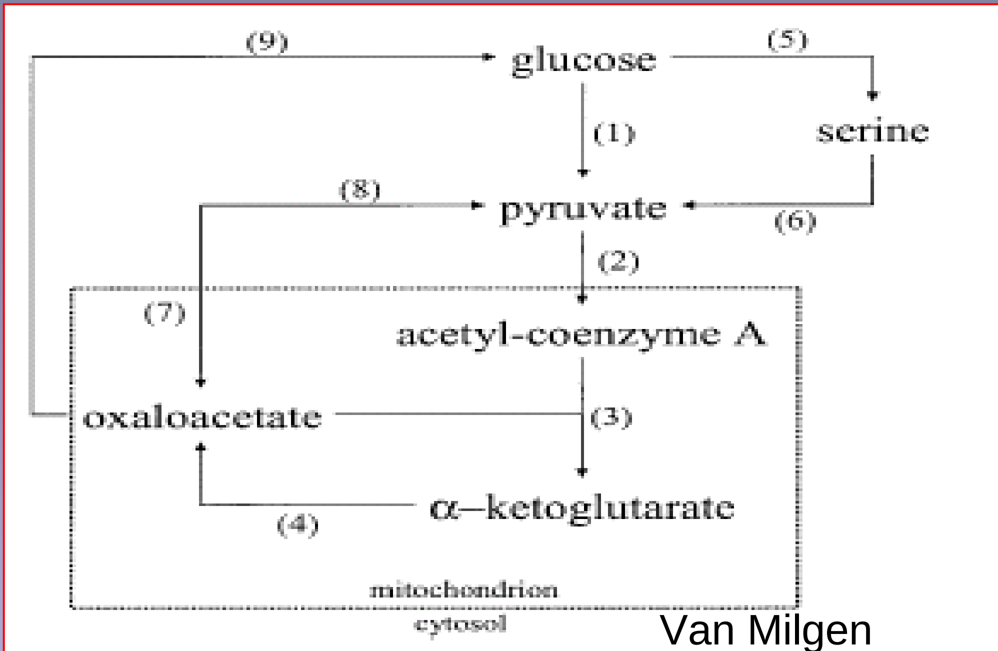
Prediction schemes

Current

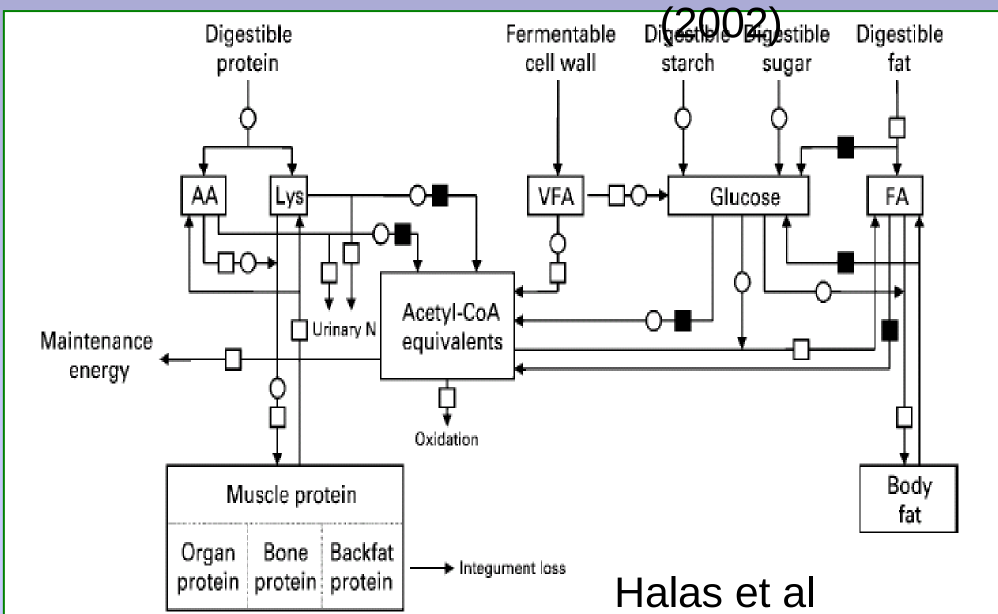
- Empirical
- ‘Crude’ assumptions
- Inflexible

Future

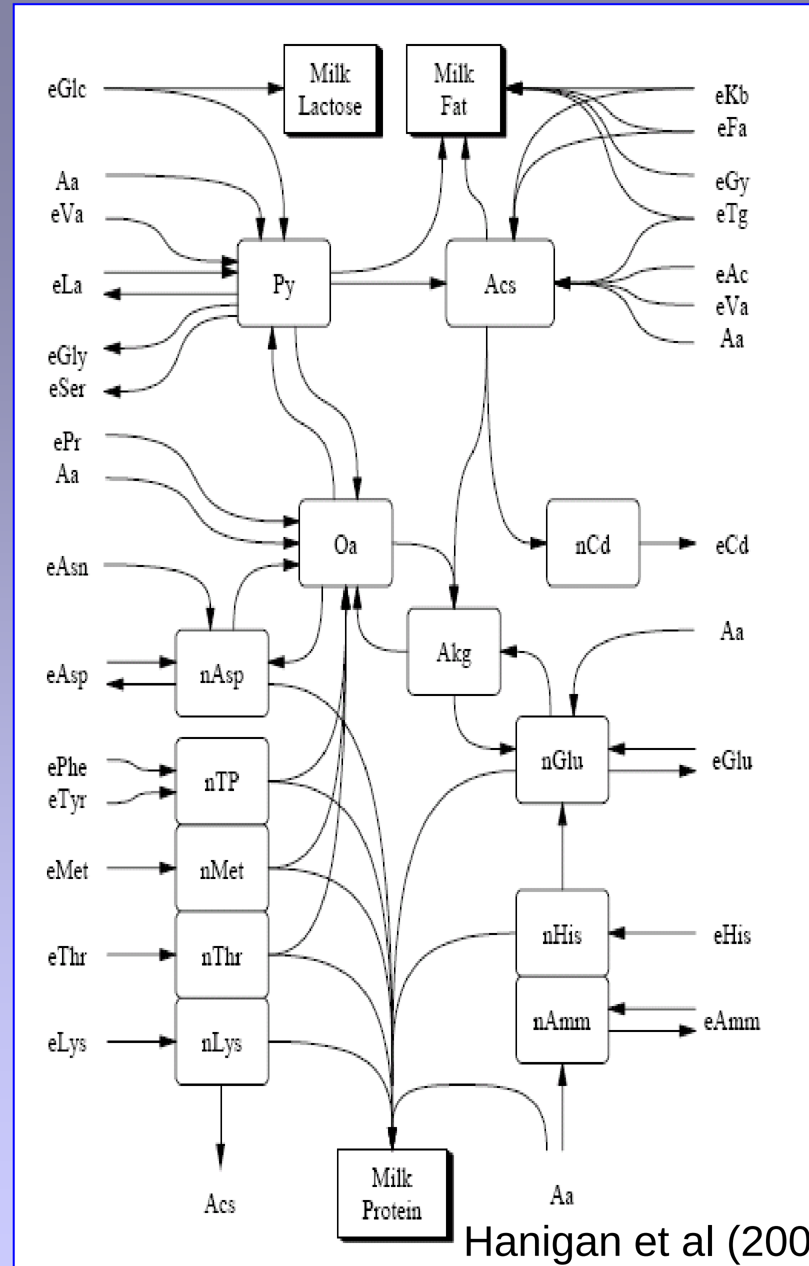
- Mechanistic
- Flexible
- More subtle knowledge



Van Milgen (2002)



Halas et al (2004)

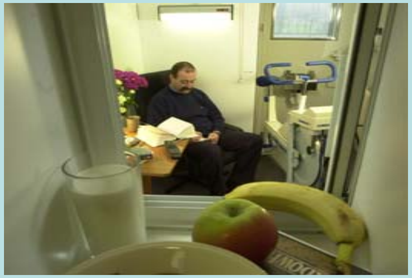


Hanigan et al (2002)

General P:E Interactions

Appetite

Efficiency

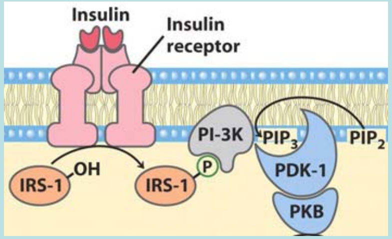


Bioenergetics

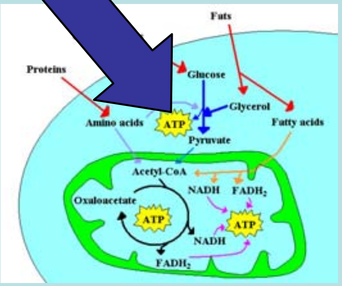
Epi-genetics

P E

Metabolic fuels

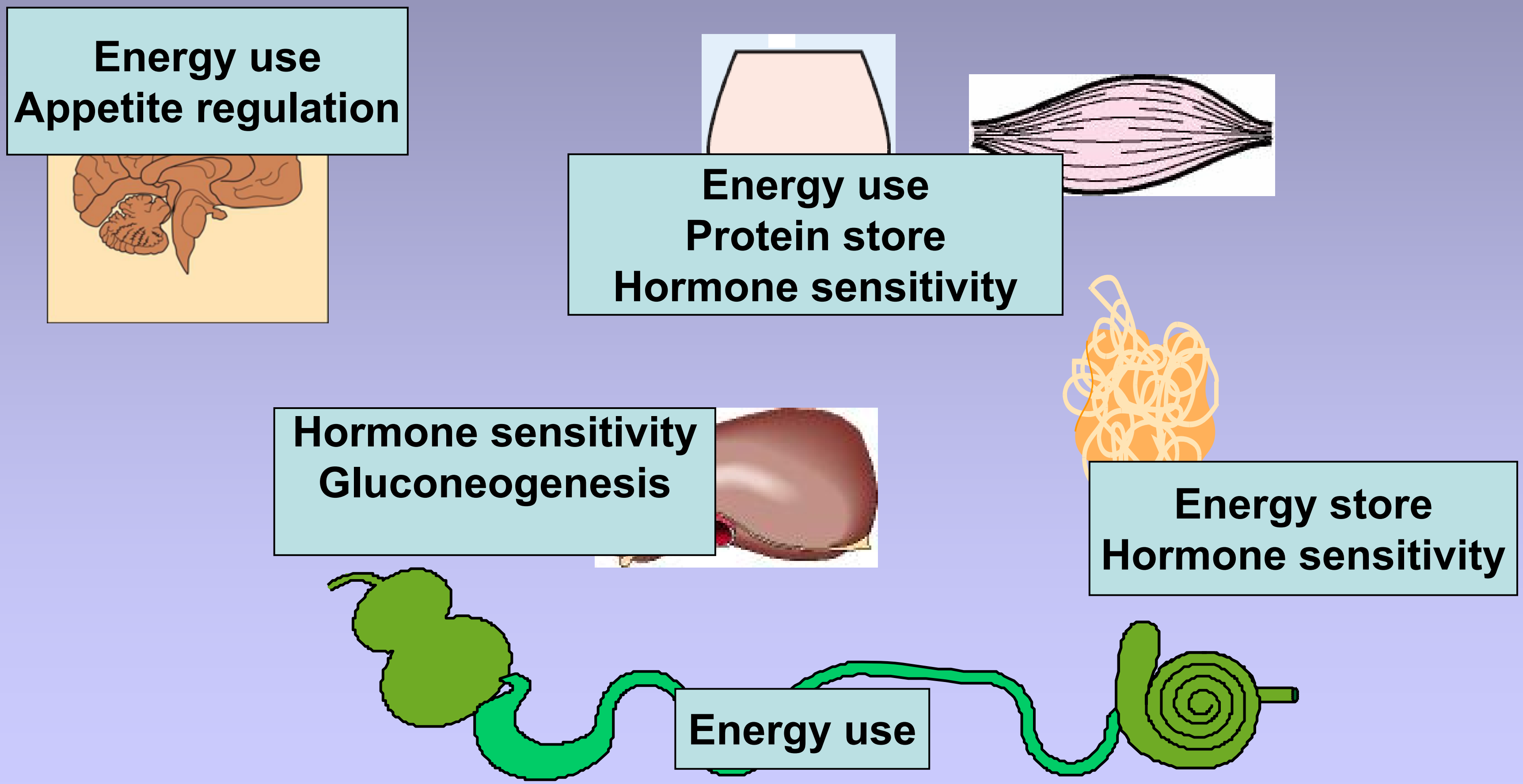


Hormonal sensitivity



Metabolite interconversion

Glucose – Amino Acids

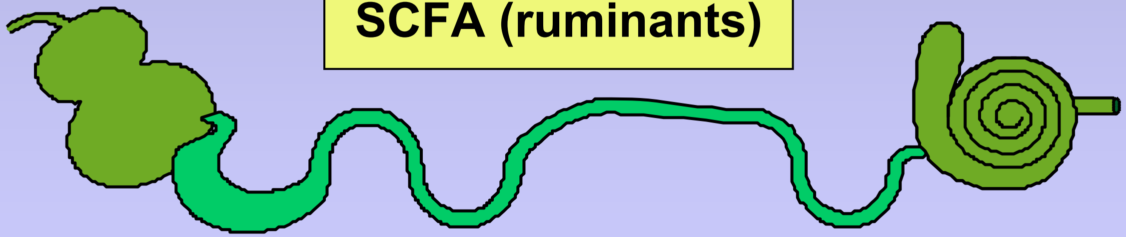


Glucose & AA – gut

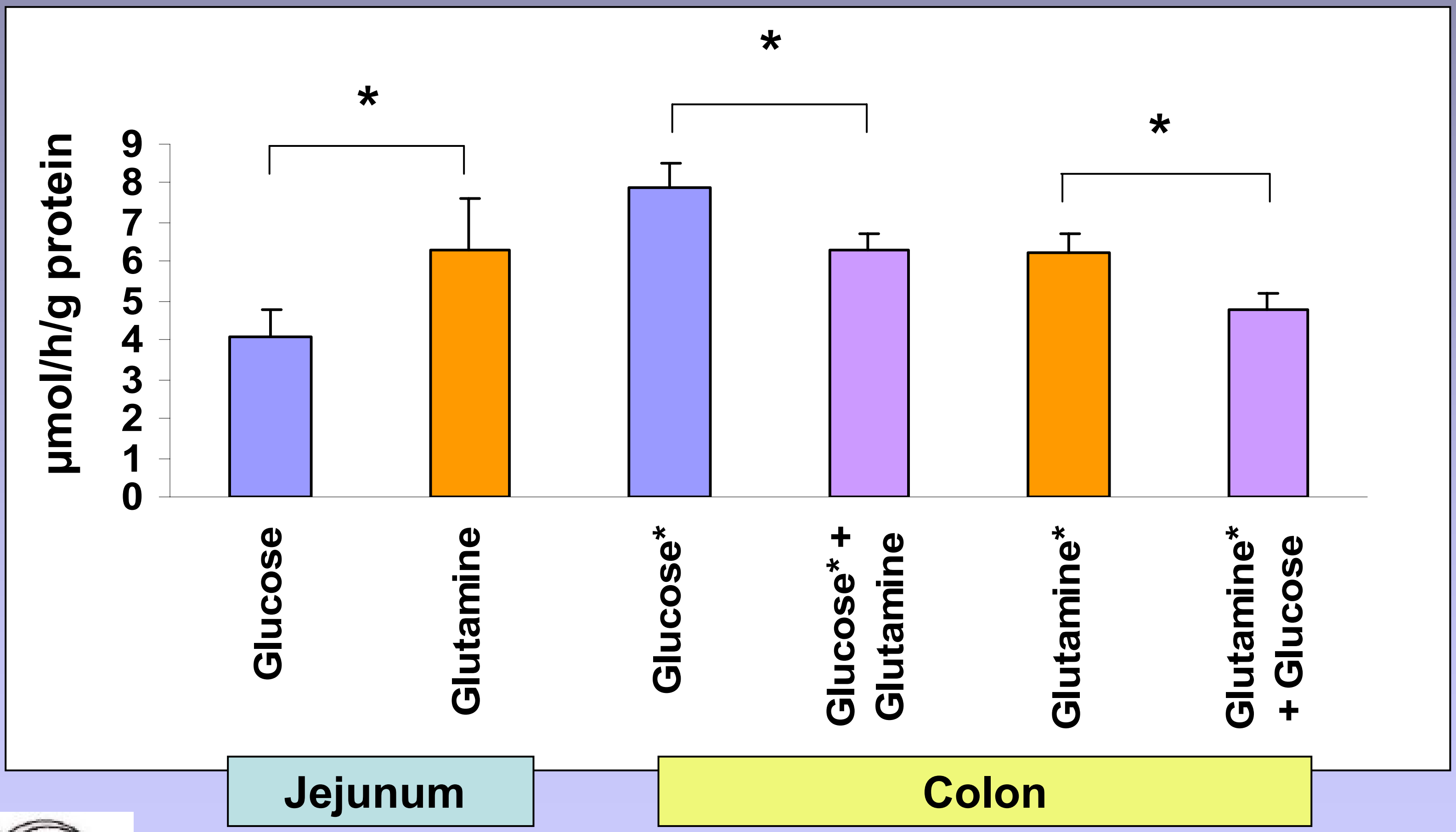
20-25% of WB energy expenditure

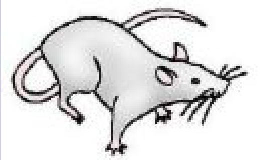
Major fuels
Glucose
Amino Acids
SCFA (ruminants)

Glutamate
Glutamine
BCAA (Leu)
Methionine
Threonine
Lysine?



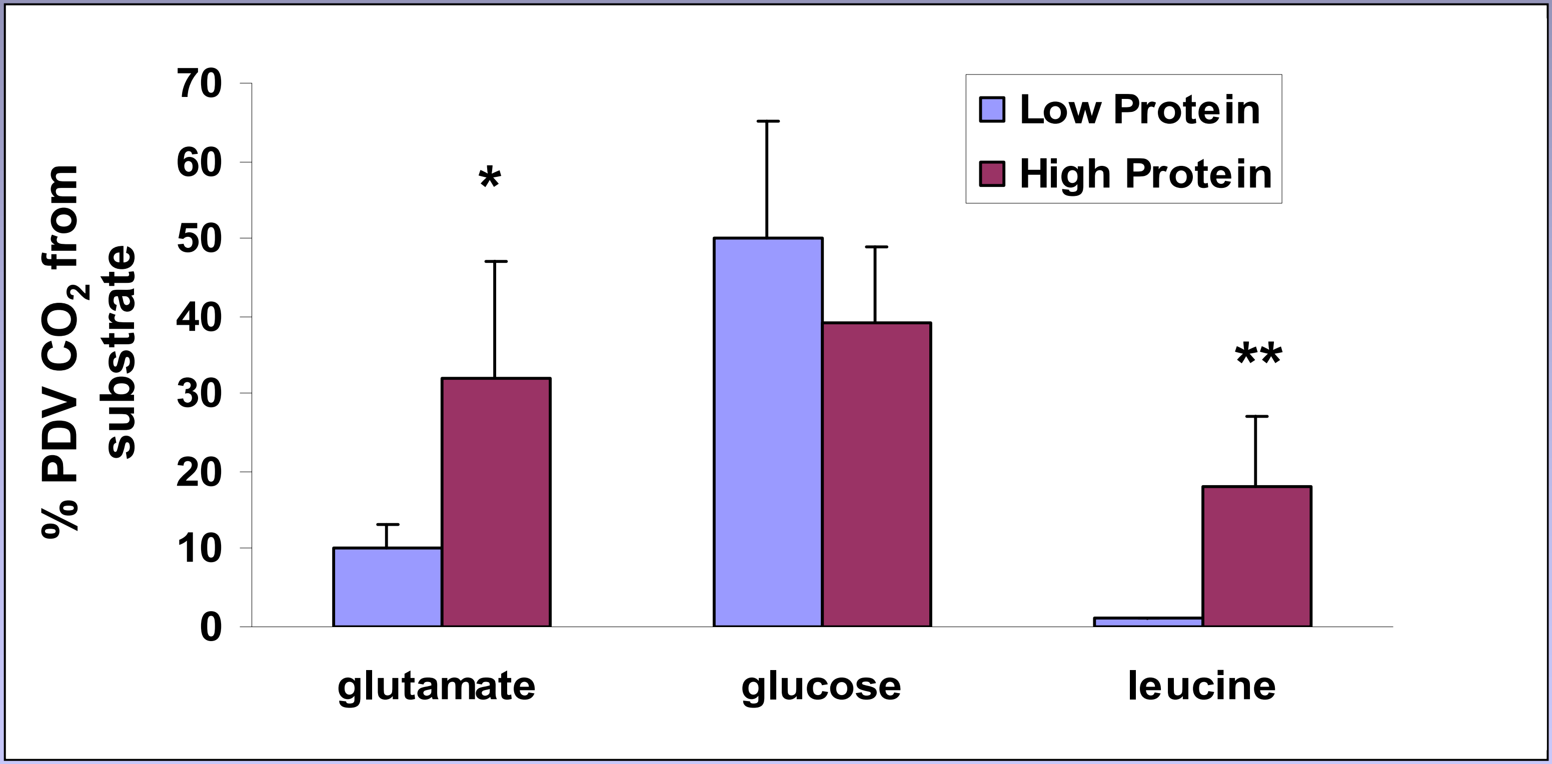
Substrate use by rat gut *in vitro*

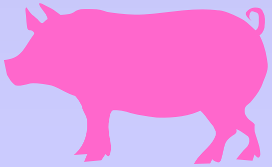




Fleming et al (1991)

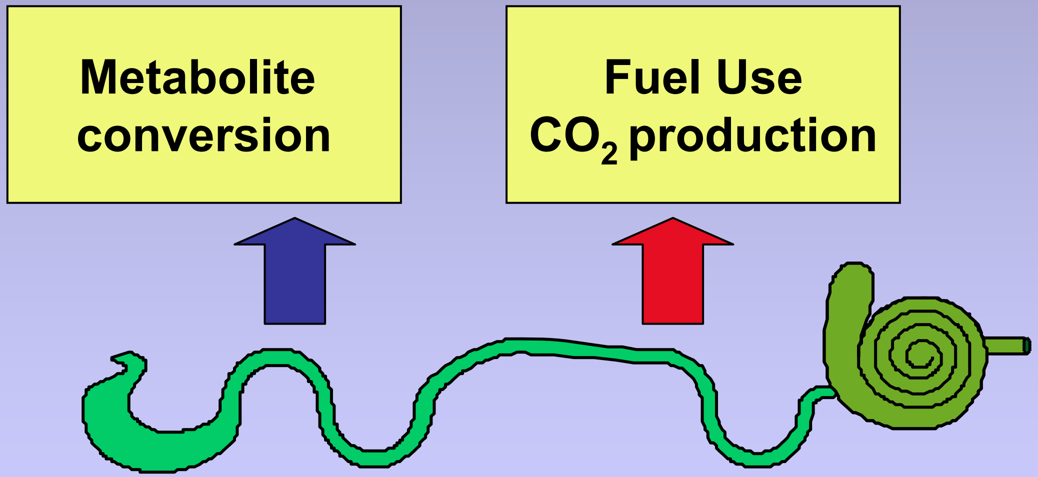
Substrate use by pig gut



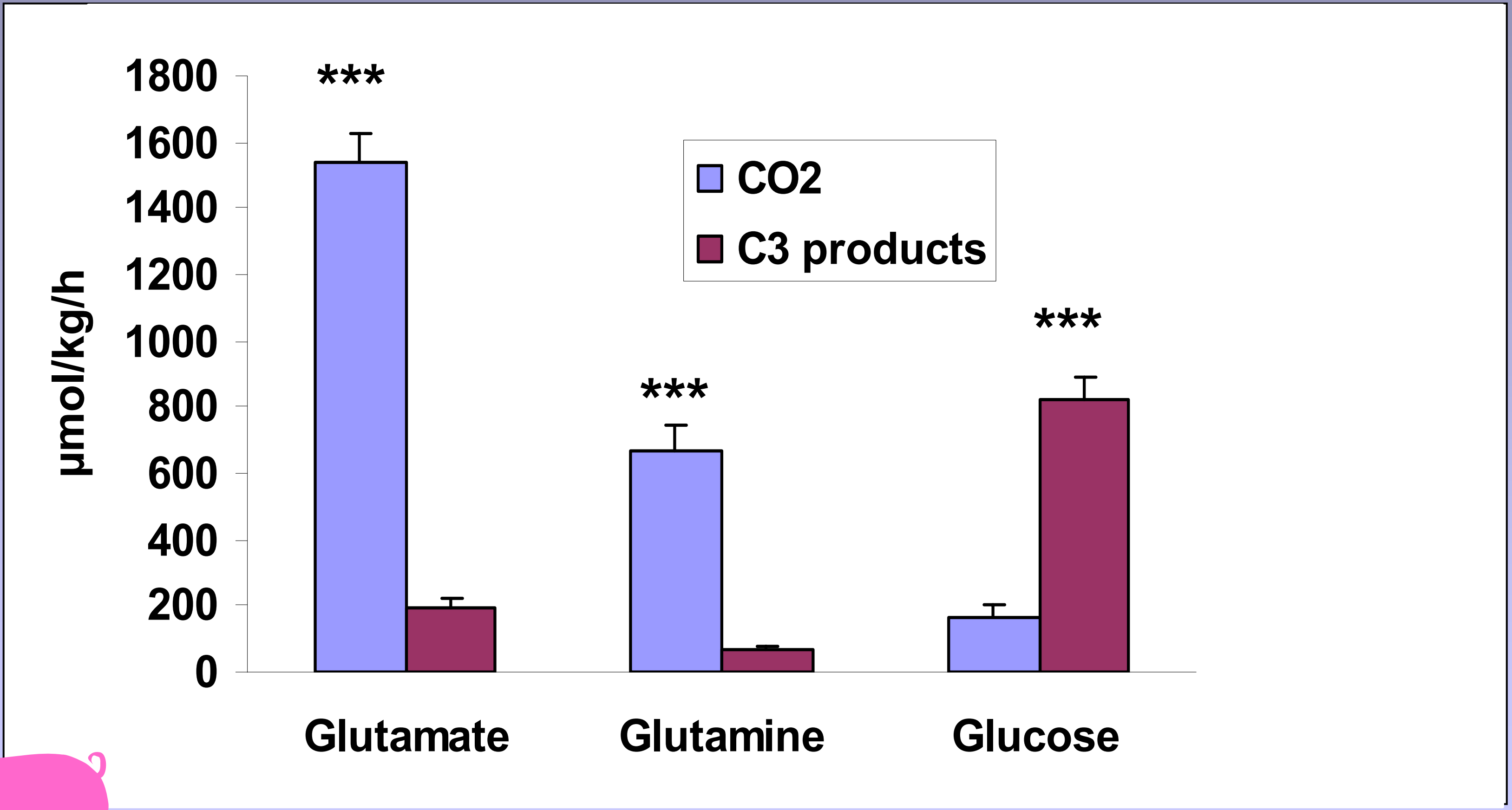


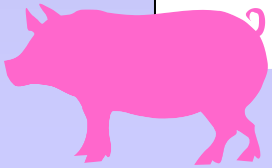
Van der Schoor et al (2001)

Metabolic fates



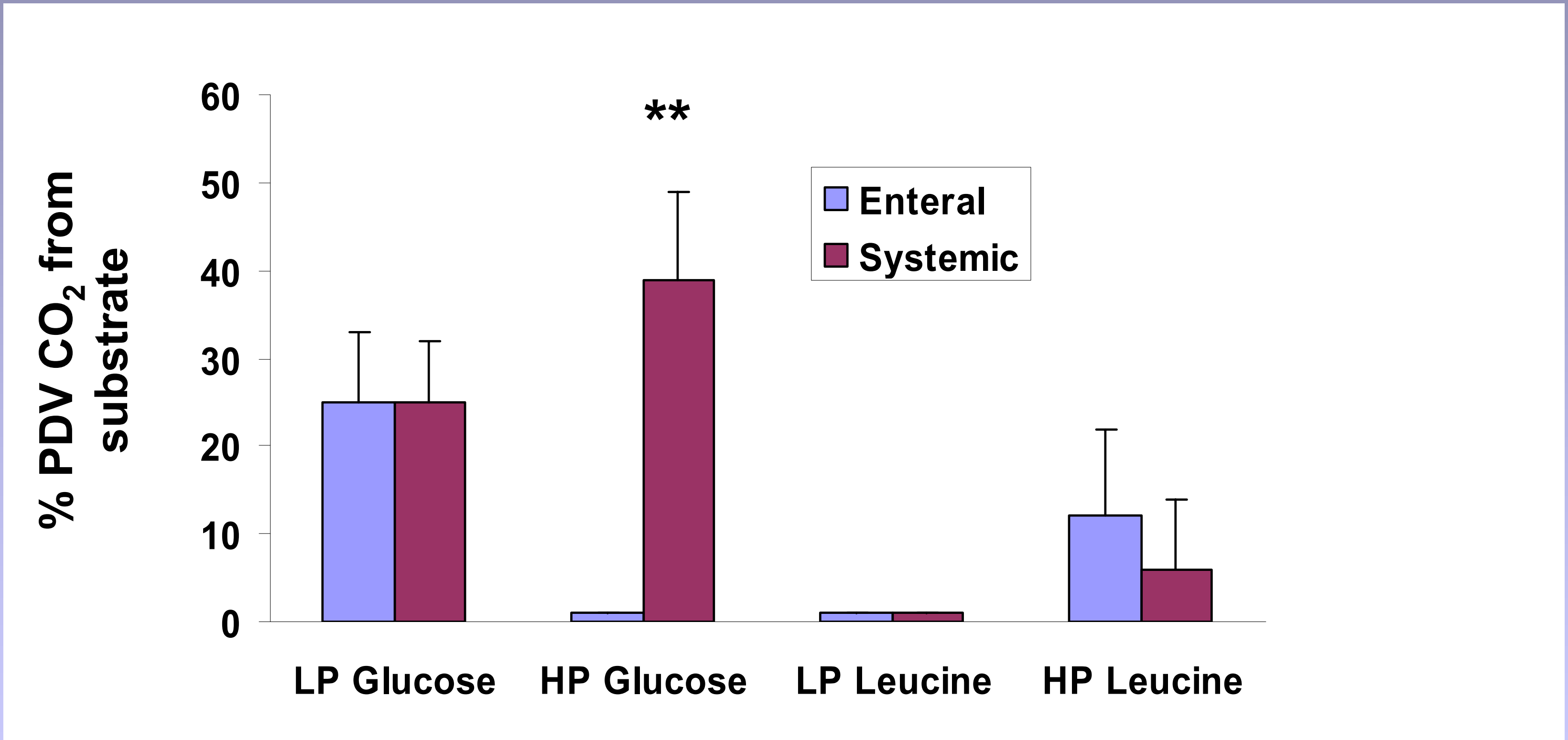
Substrate fate across pig gut

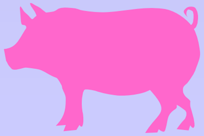




Reeds et al (2001)

Site of substrate oxidation by pig gut

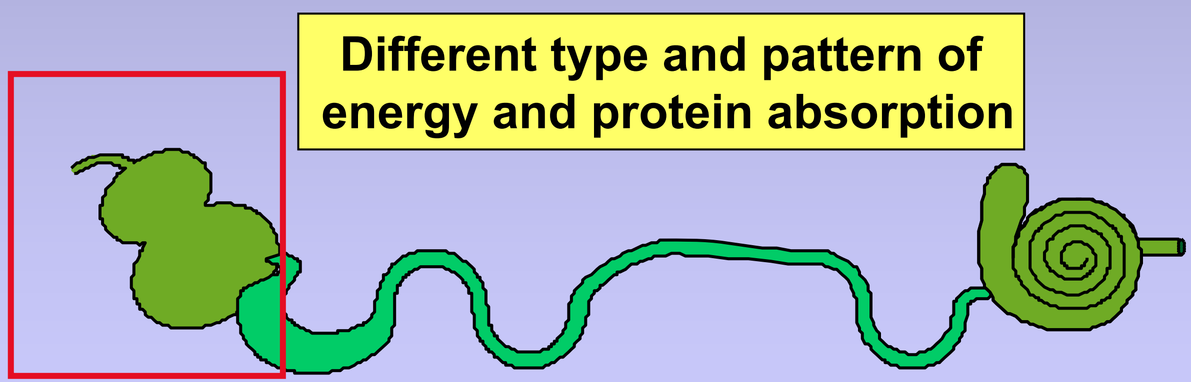


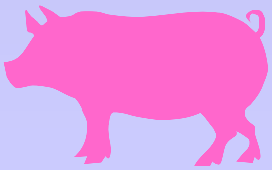


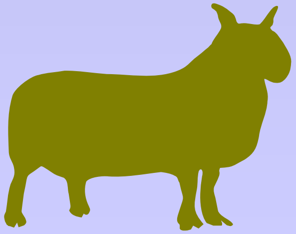
Van der Schroor et al 2001

Species differences

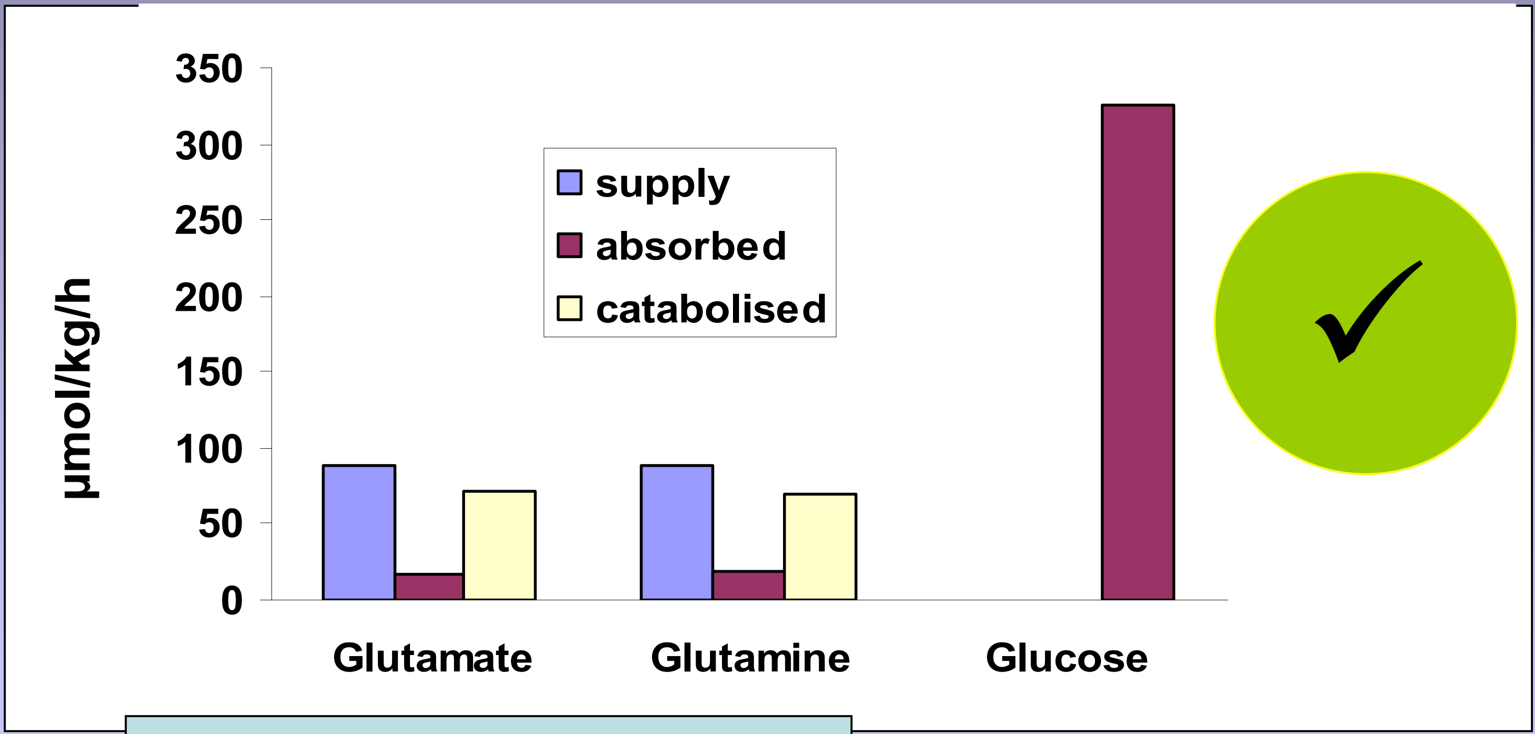
Does the ruminant behave as a non-ruminant?

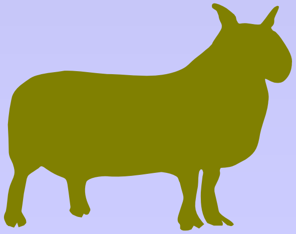






Glucose utilisation across sheep gut – effect of AA

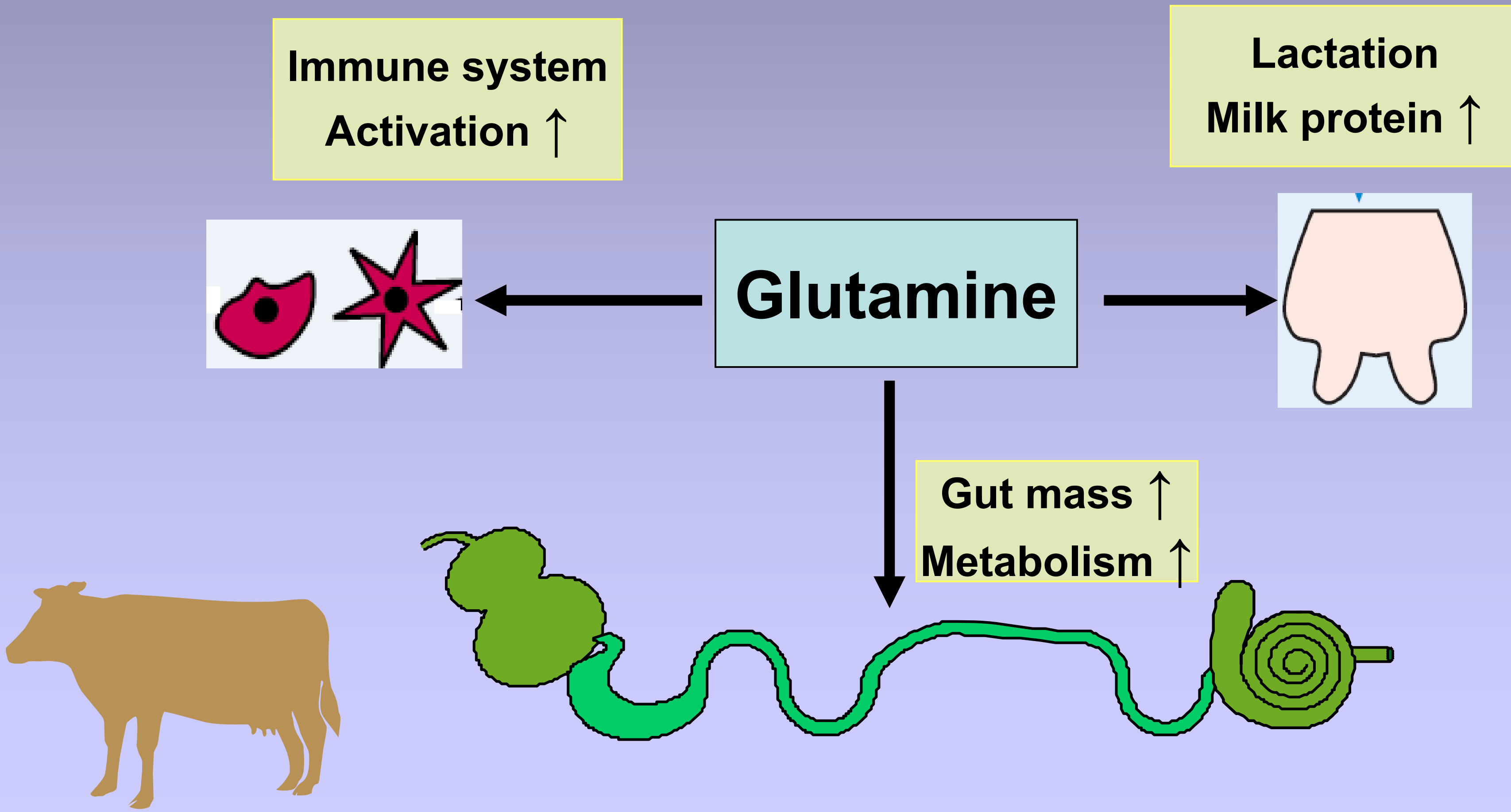




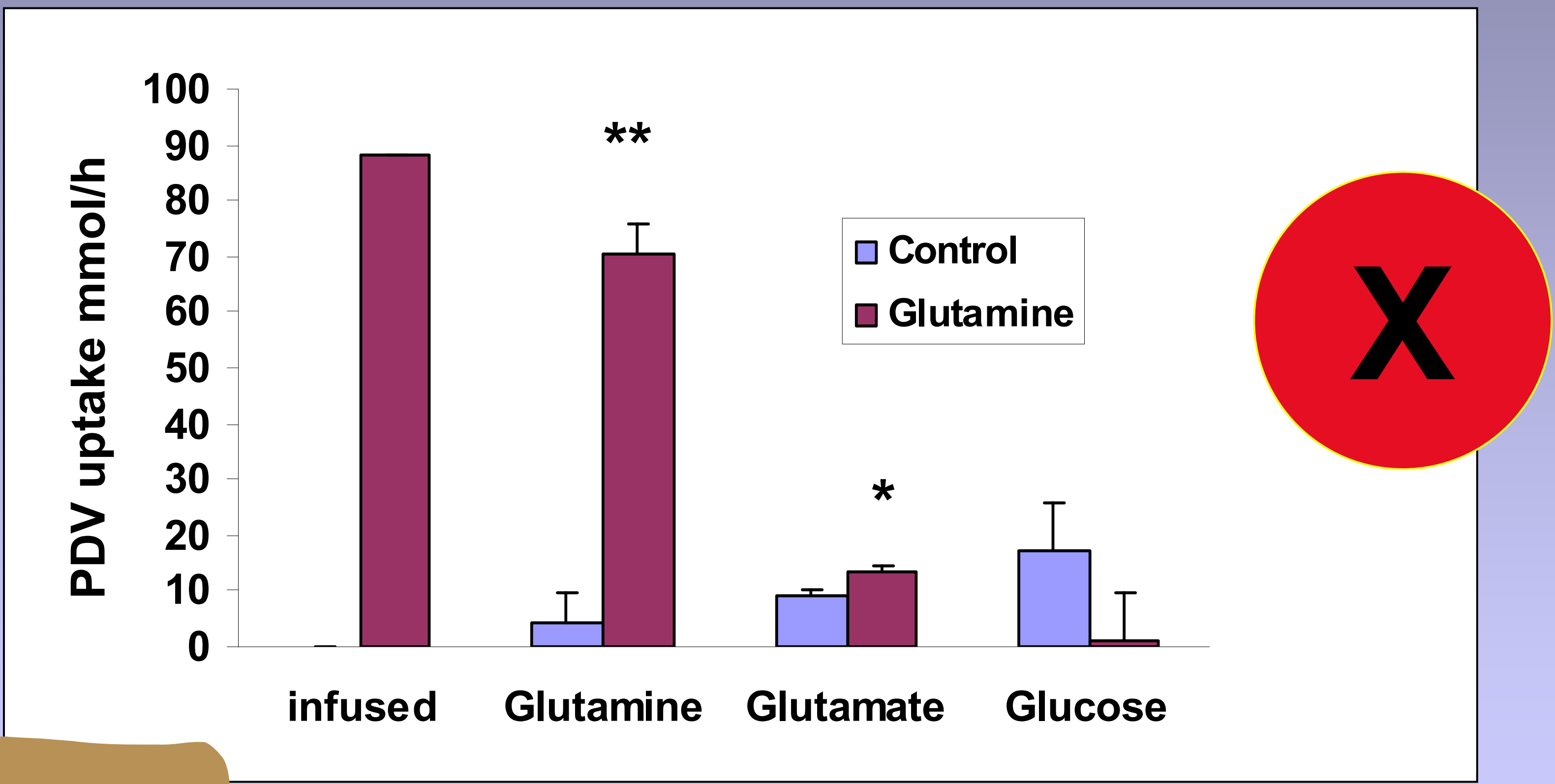
Infused (duodenum)
100 g/d casein
From 60 to 105% requirements

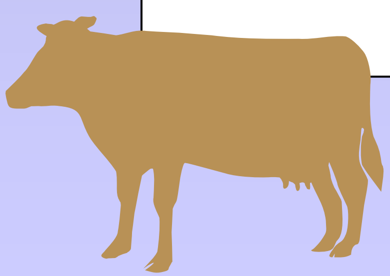
El-Kadi et al (2006)

Glutamine needs – dairy cow early lactation



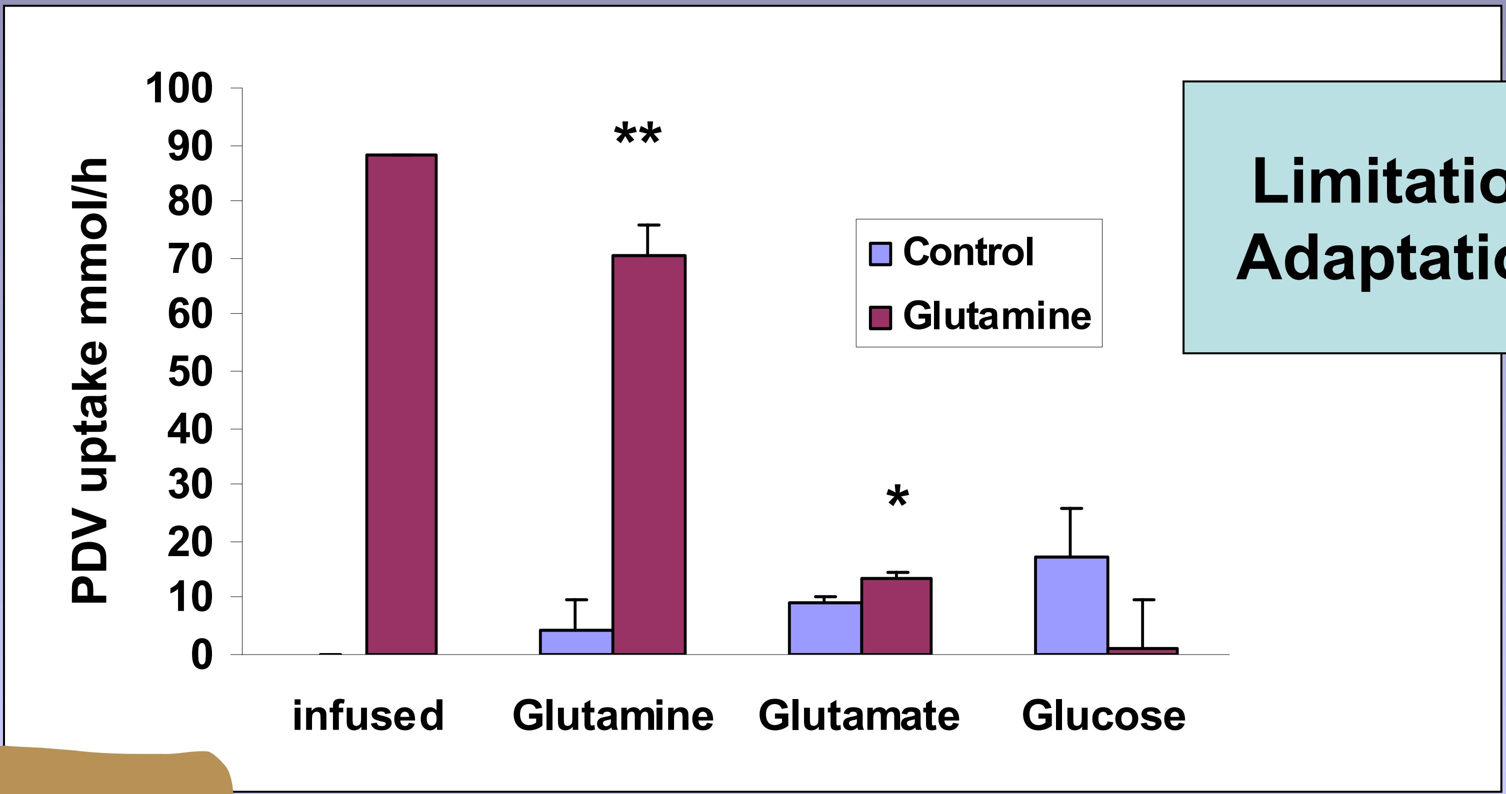
Gut responses to glutamine in peri-parturient dairy cows



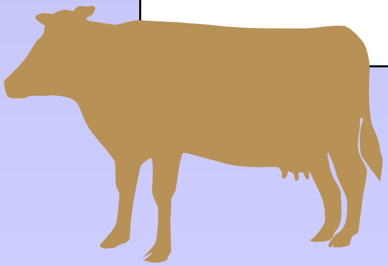


Doepel et al. (2007)

Gut responses to glutamine in peri-parturient dairy cows



Limitations?
Adaptations?



Doepel et al. (2007)

Energy substitutions

- Can occur across gut of pigs and ruminants
- Not obligatory
- Adaptation to metabolic needs?

P:E – mammary gland

FFA (preformed)

Acetate
3-OHButyrate

EAA ↑

Glucose ↑

mino
cids

NEAA ↓

Regulation:

Amino acid supply?

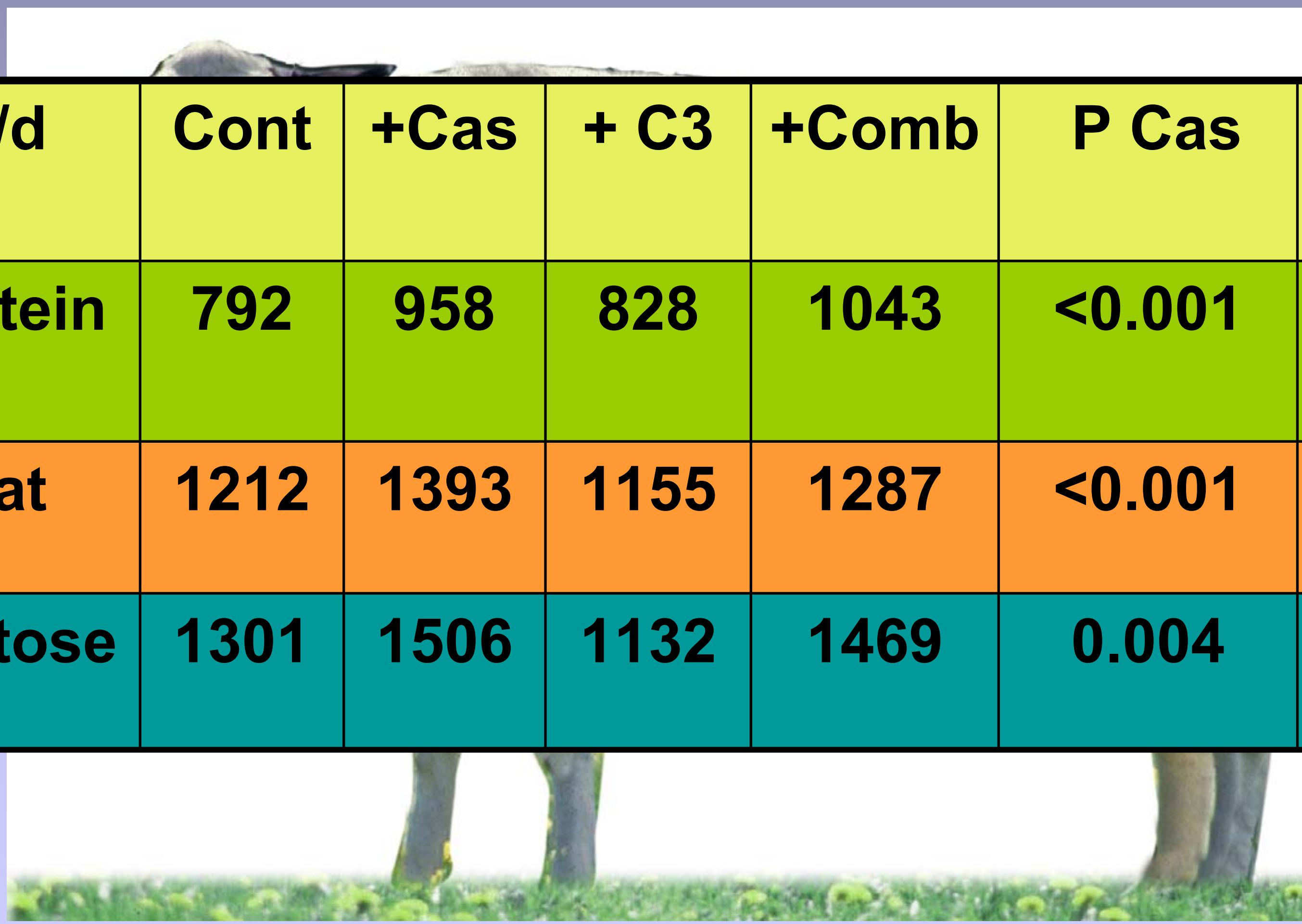
Energy provision?

Used for:
Lactose
Energy
C skeletons

Protein
Lactose
Fat

EAA-N used to make EAA-N
Needs C

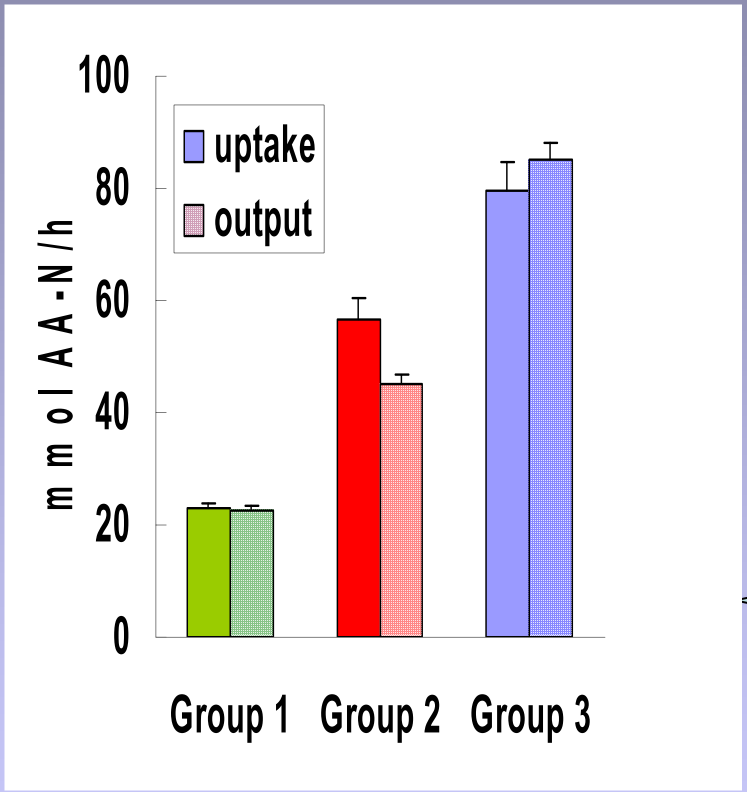
Impact protein & energy on MG

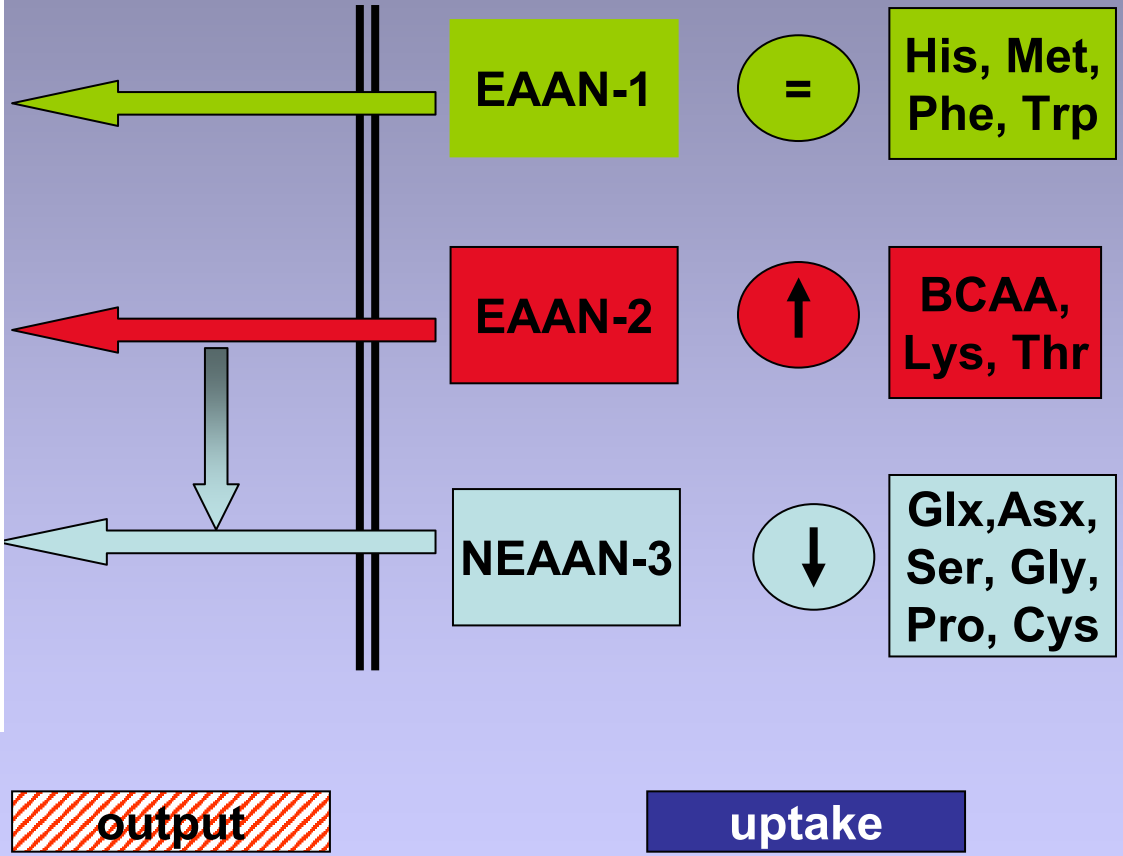


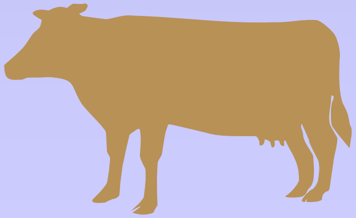
g/d	Cont	+Cas	+ C3	+Comb	P Cas	P C3
Protein	792	958	828	1043	<0.001	0.02
Fat	1212	1393	1155	1287	<0.001	0.02
Lactose	1301	1506	1132	1469	0.004	NS

Raggio et al (2006)

AA-N uptake across cow mammary gland

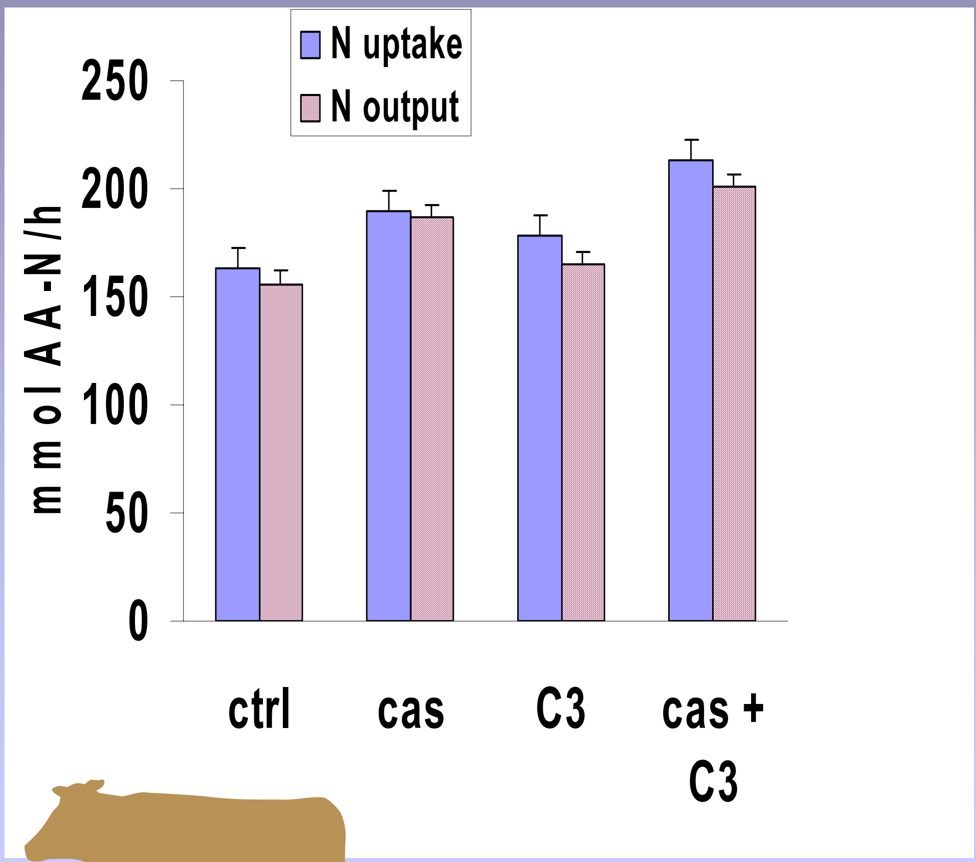


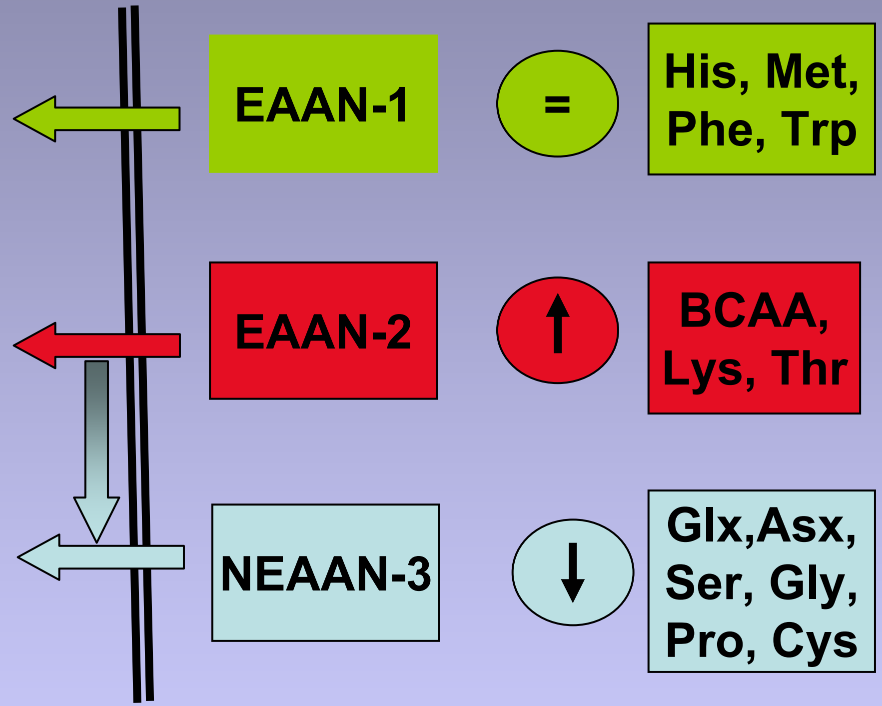


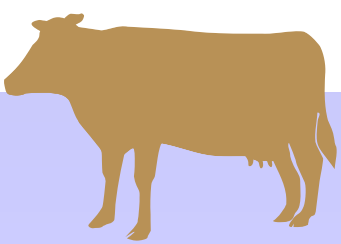


From Raggio et al (2006)

AA-N uptake across cow mammary gland

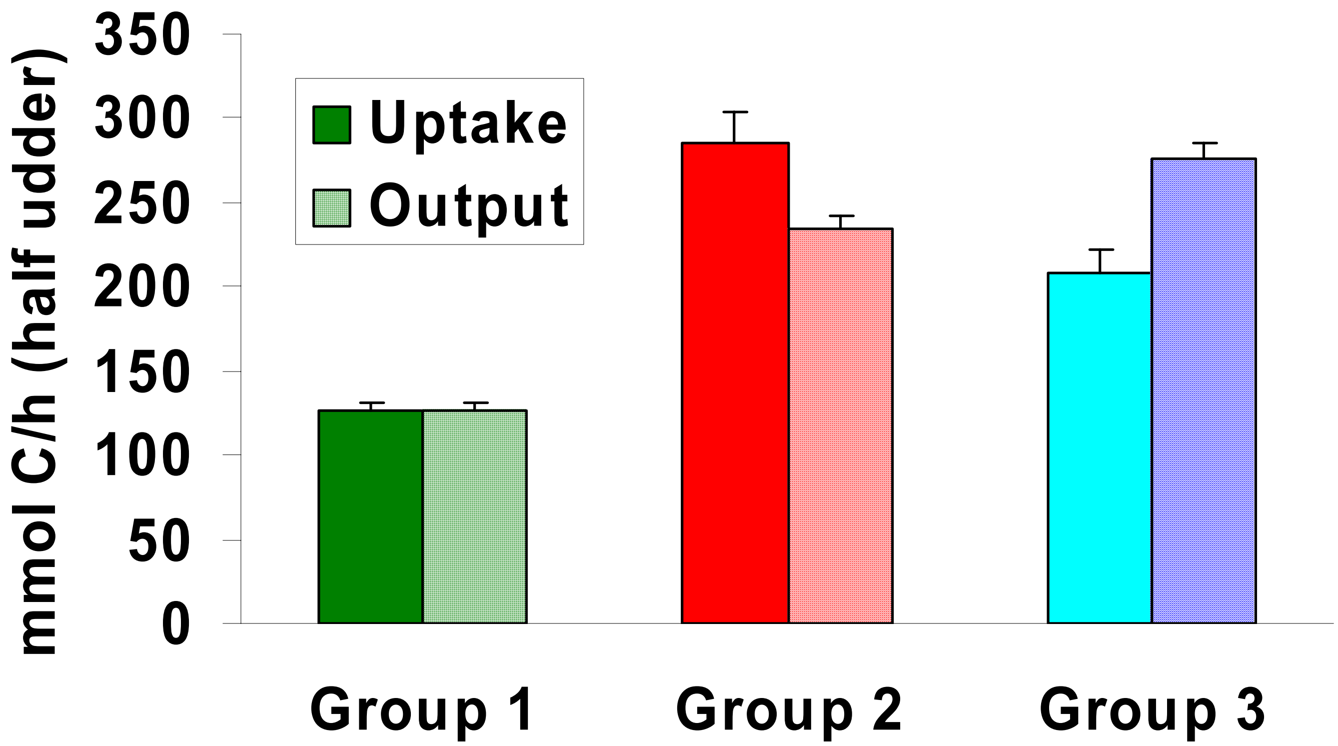


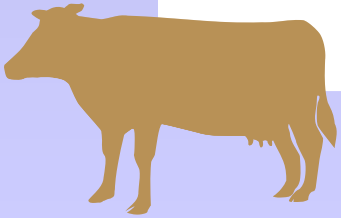




From Raggio et al (2006)

AA C balances across half udder

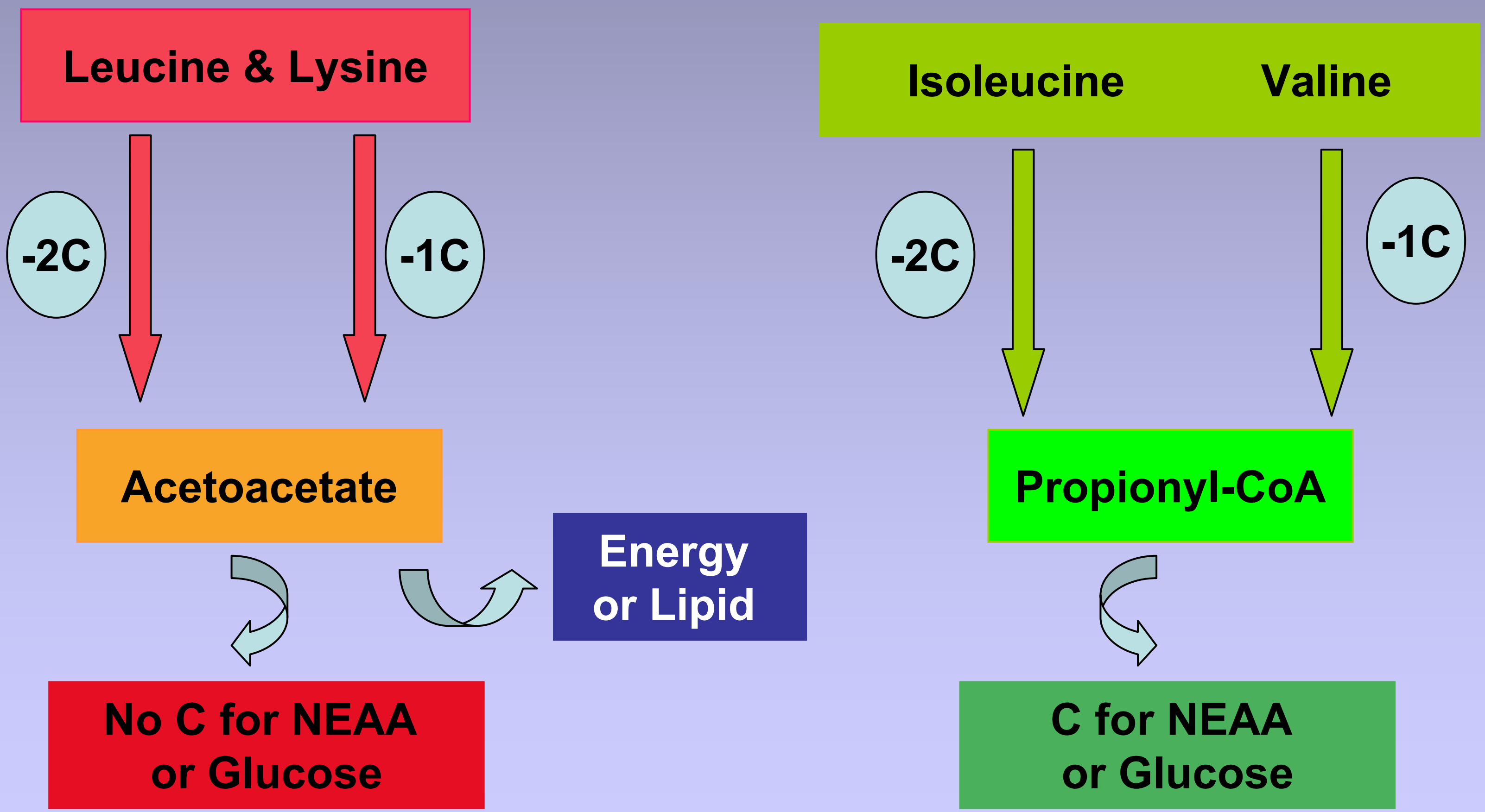




Total uptake = 621
Total output = 638

Lemosquet et al. (unpub)

EAA-2 to NEAA-C or E sources



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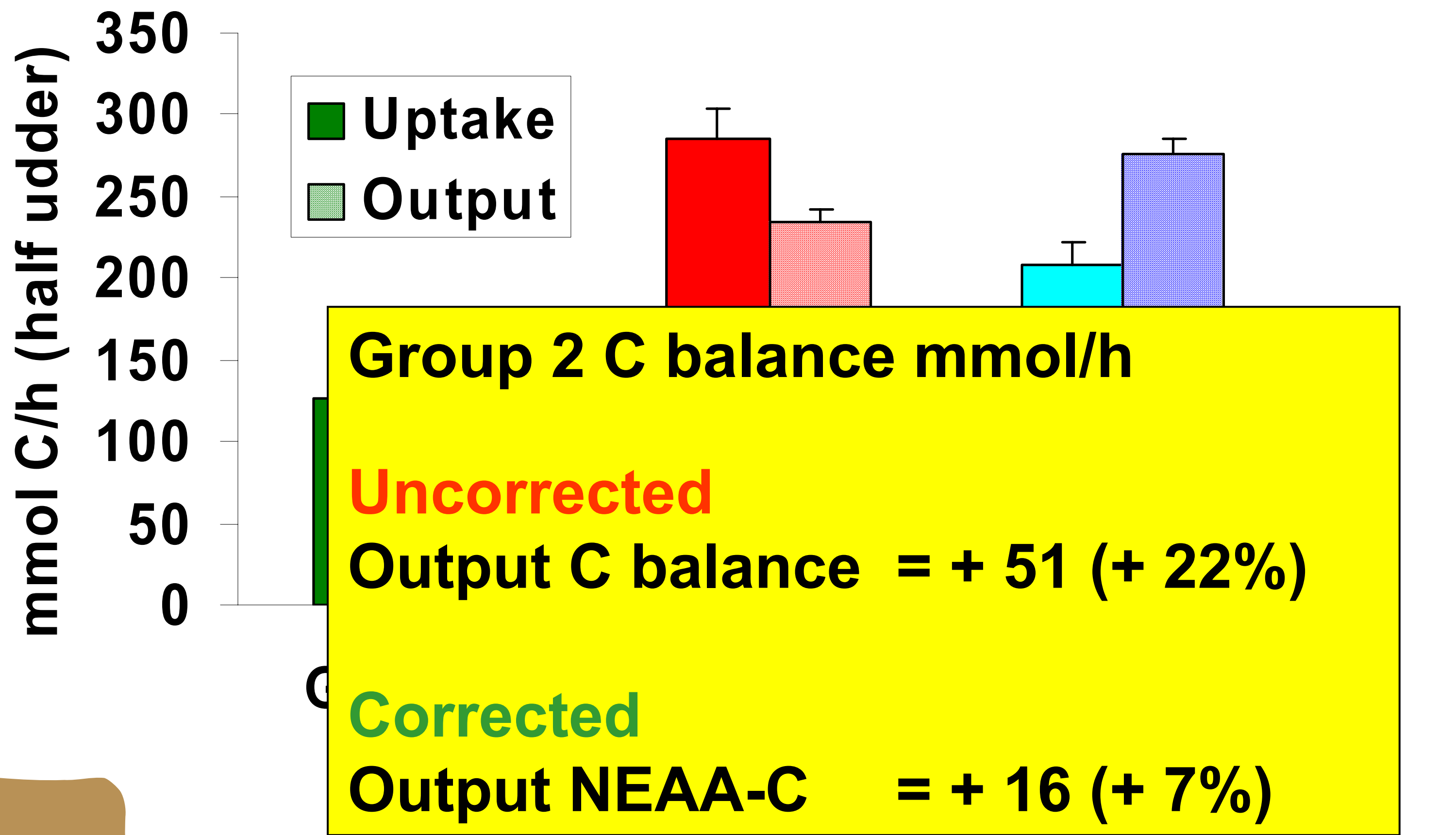


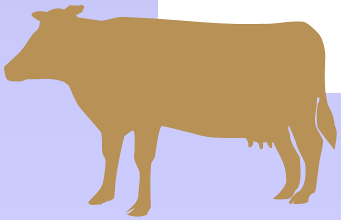
Group 2 C balance mmol/h

Uncorrected

Output C balance = + 51 (+ 22%)

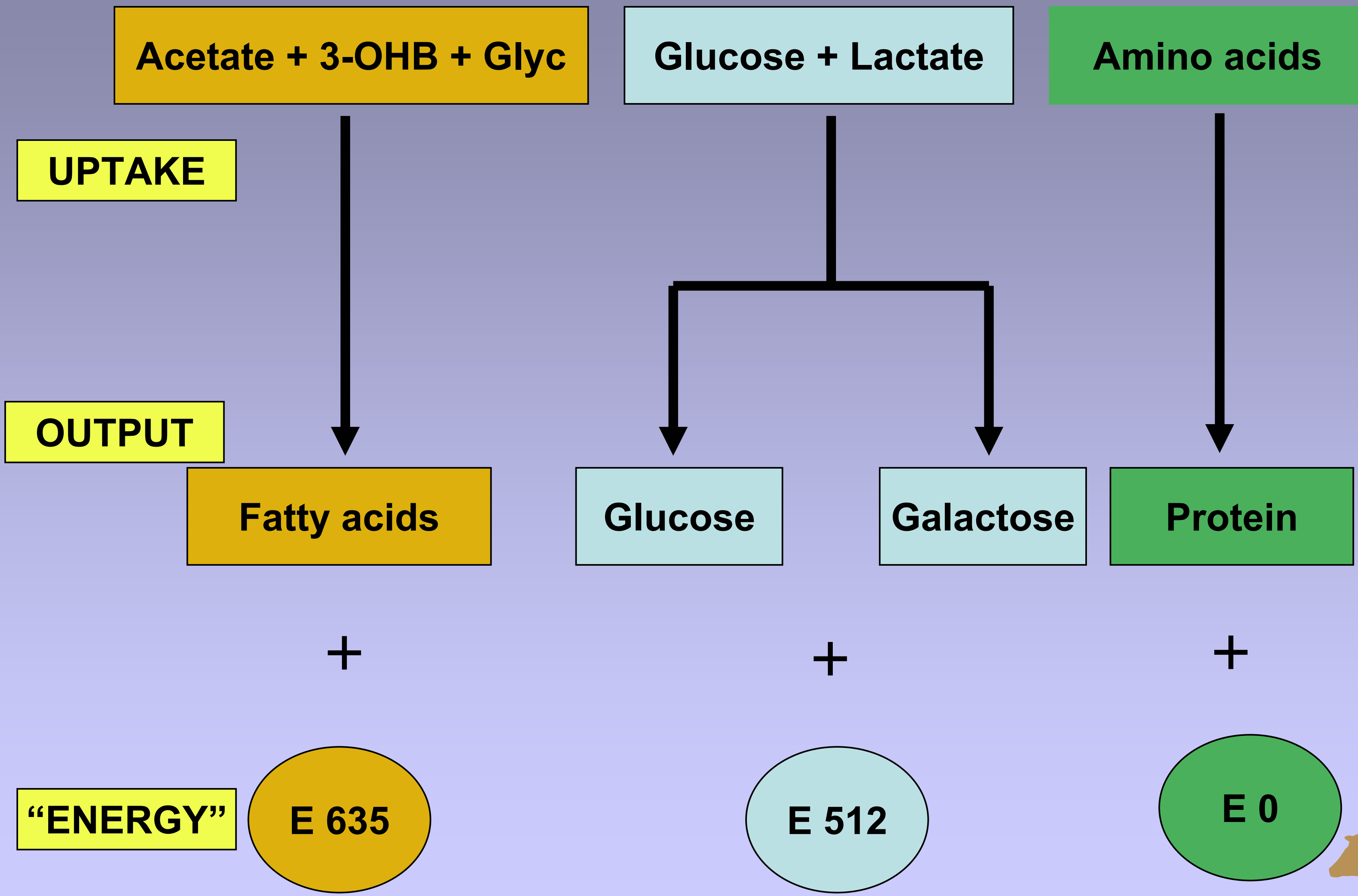
Corrected

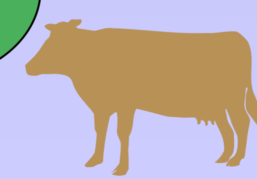
Output NEAA-C = + 16 (+ 7%)



Lemosquet et al. (unpub)

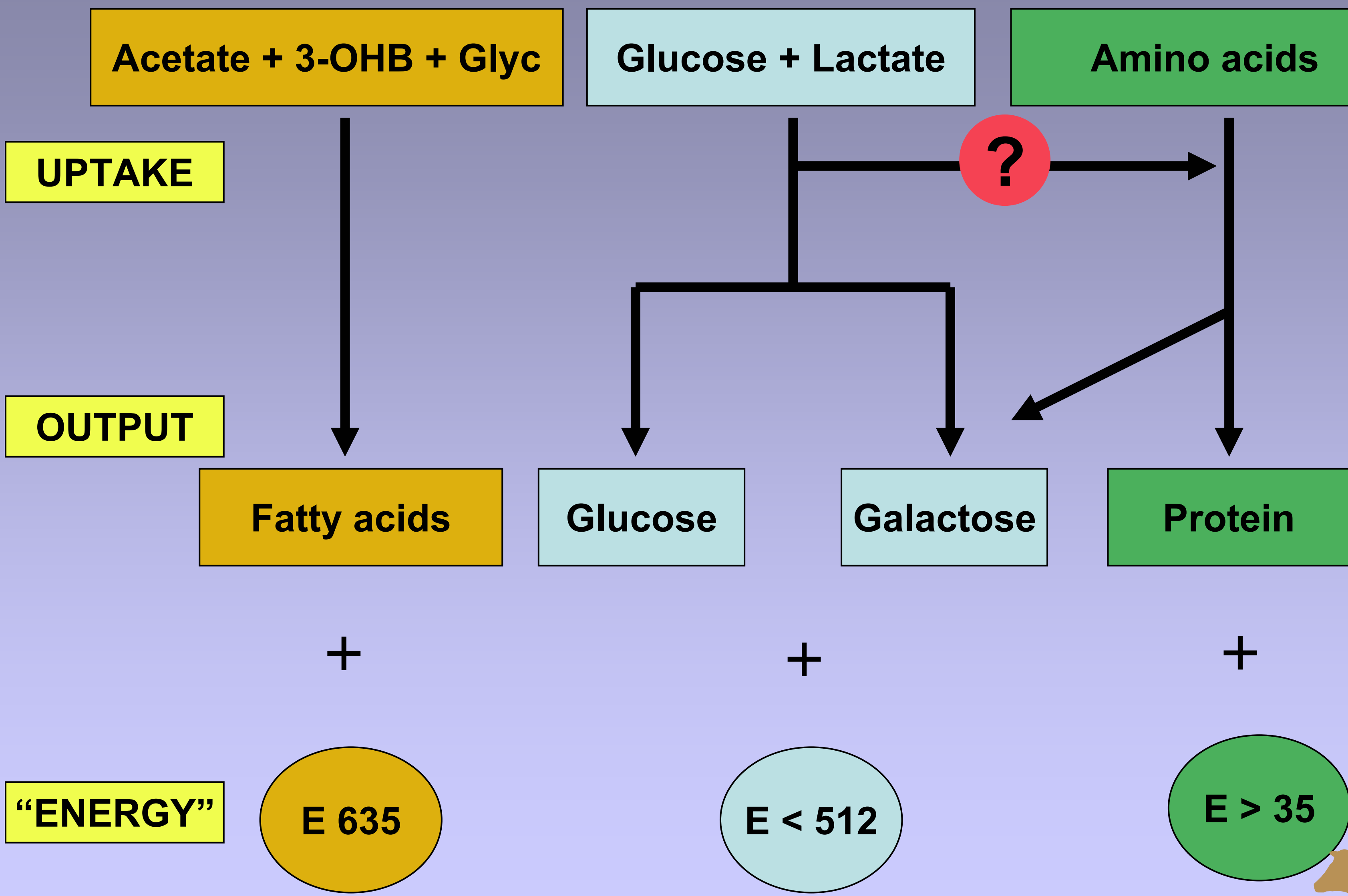
Apparent C transfers

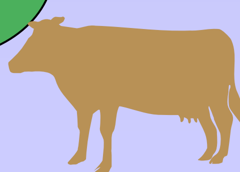




Lemosquet et al. (unpub)

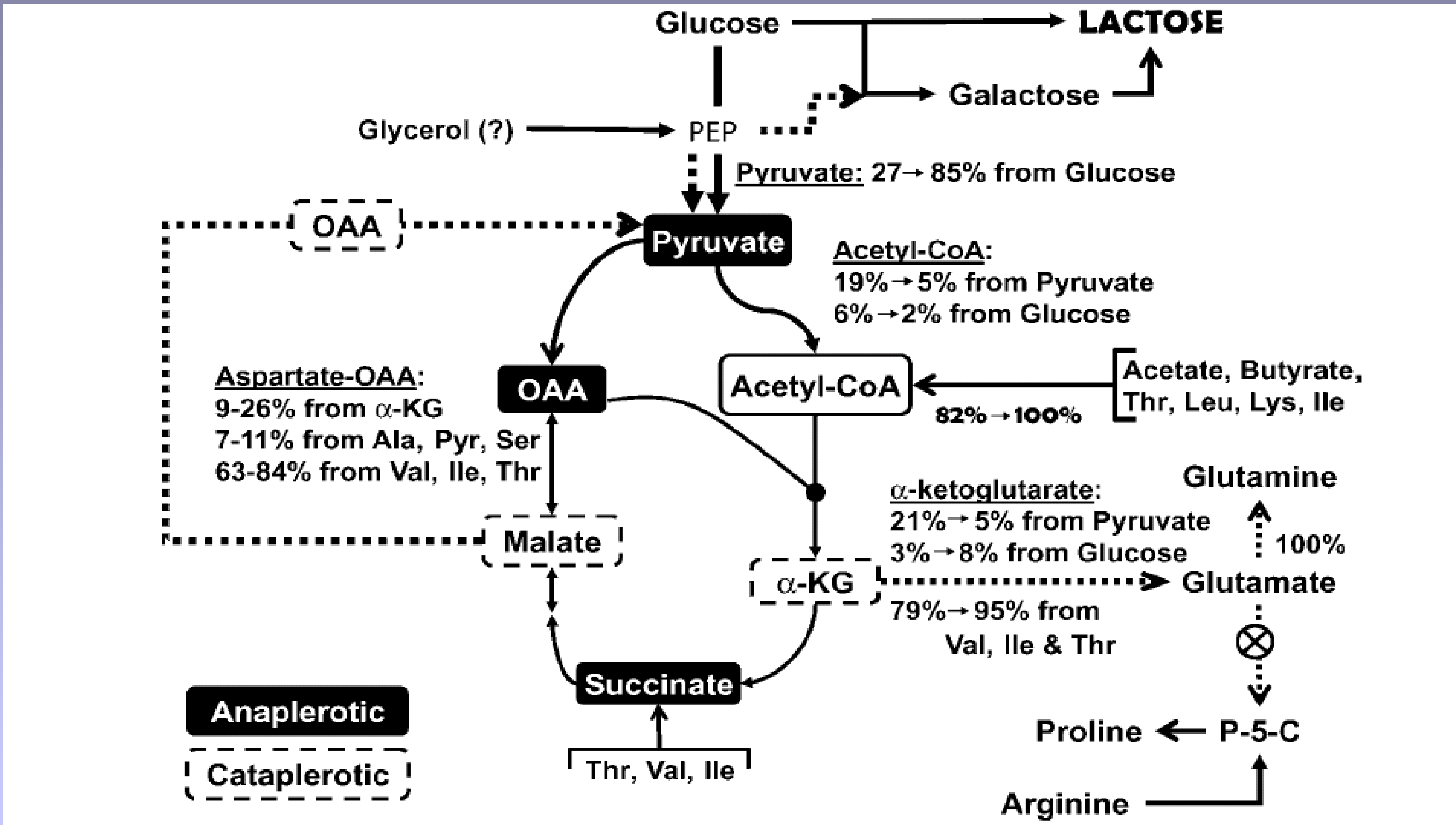
True? C transfers





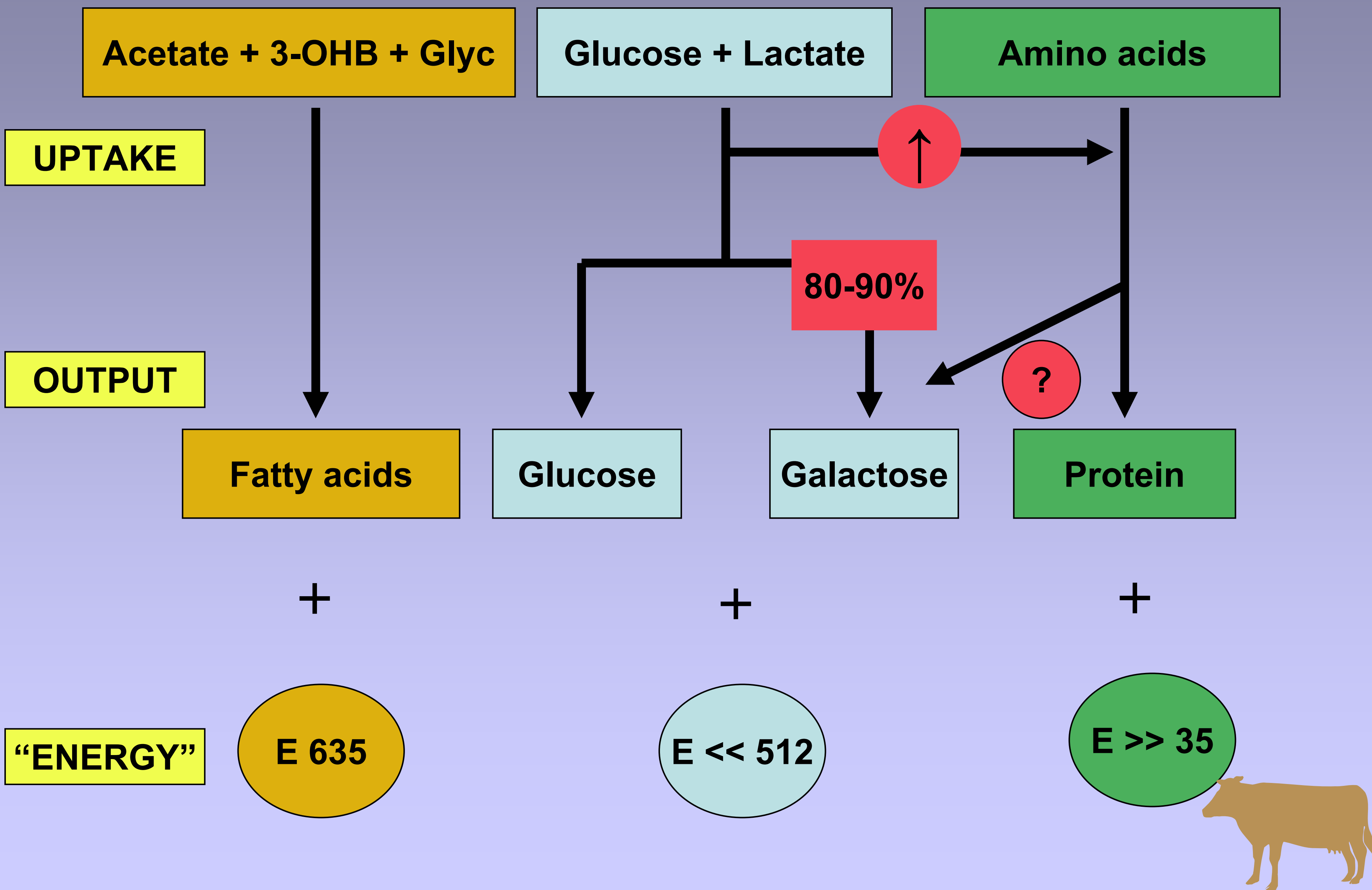
Lemosquet et al. (unpub)

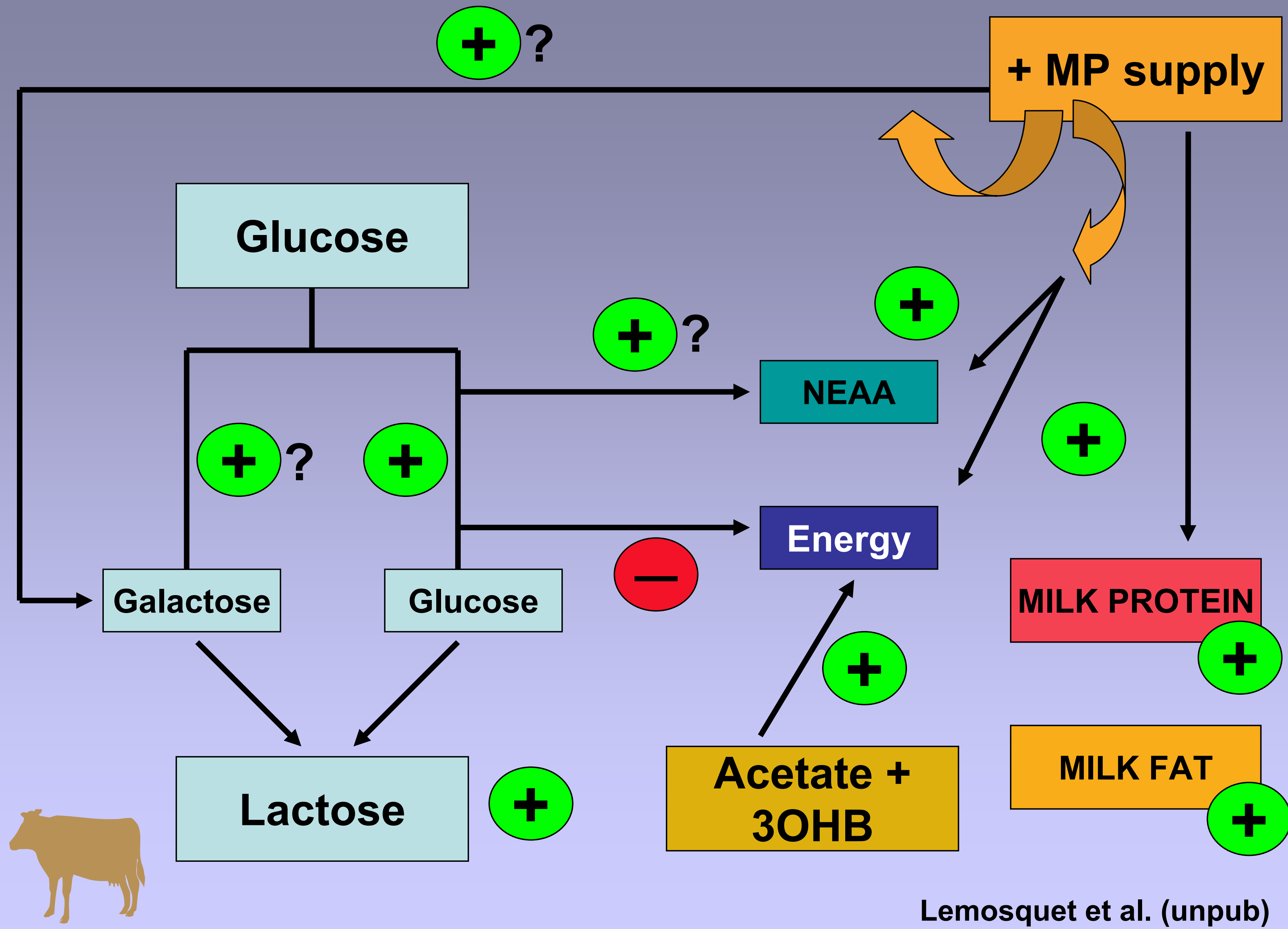
Inter-conversions in MG explants



Bequette et al. (2006)

True? C transfers




?
+ MP supply
Glucose
?
NEAA
?
Energy
Galactose
Glucose
MILK PROTEIN
Lactose
Acetate +
3OHB
MILK FAT
Lemosquet et al. (unpub)

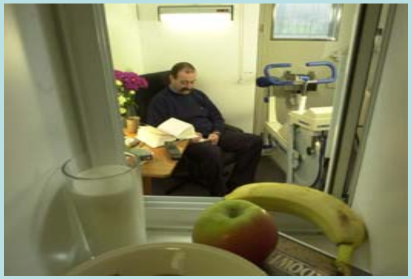
Implications

- Flexibility
- Limitations?
- Dynamic feed models
- Improved efficiency/resource use
- Selection parameters?

P:E - Efficiency & Health

Appetite

Epi-genetics

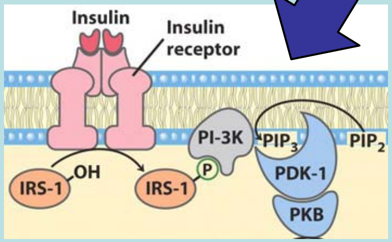


Bioenergetics

Metabolic fuels

P E

Efficiency



Hormonal sensitivity

Metabolic health

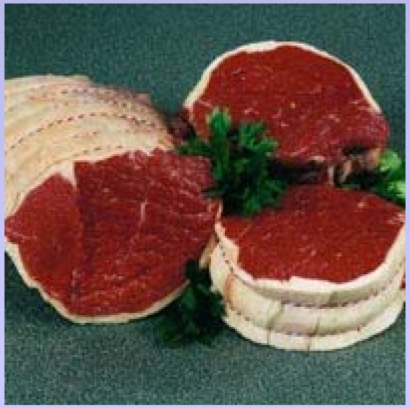
Is insulin sensitivity important?

Protein S & D

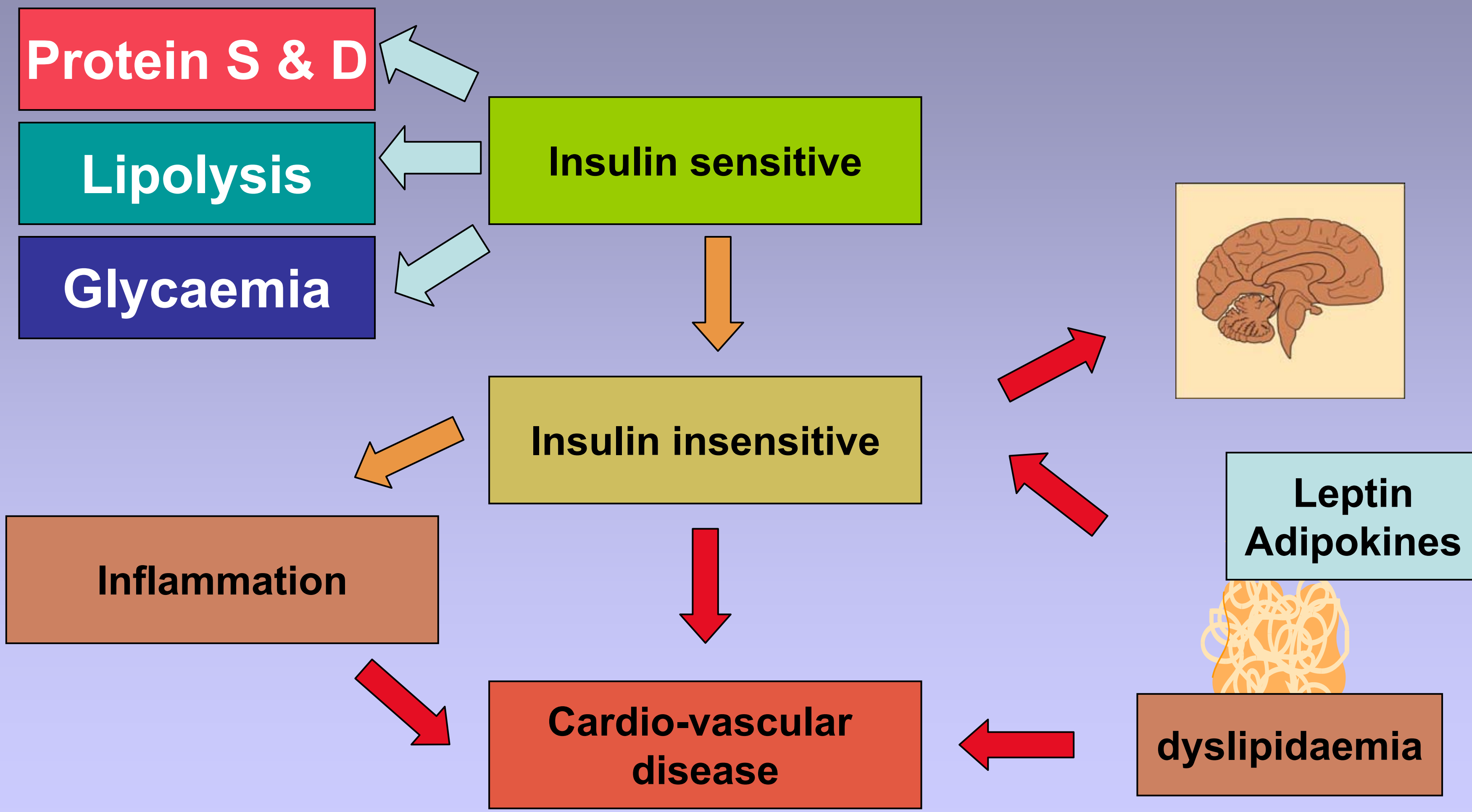
Lipolysis

Glycaemia

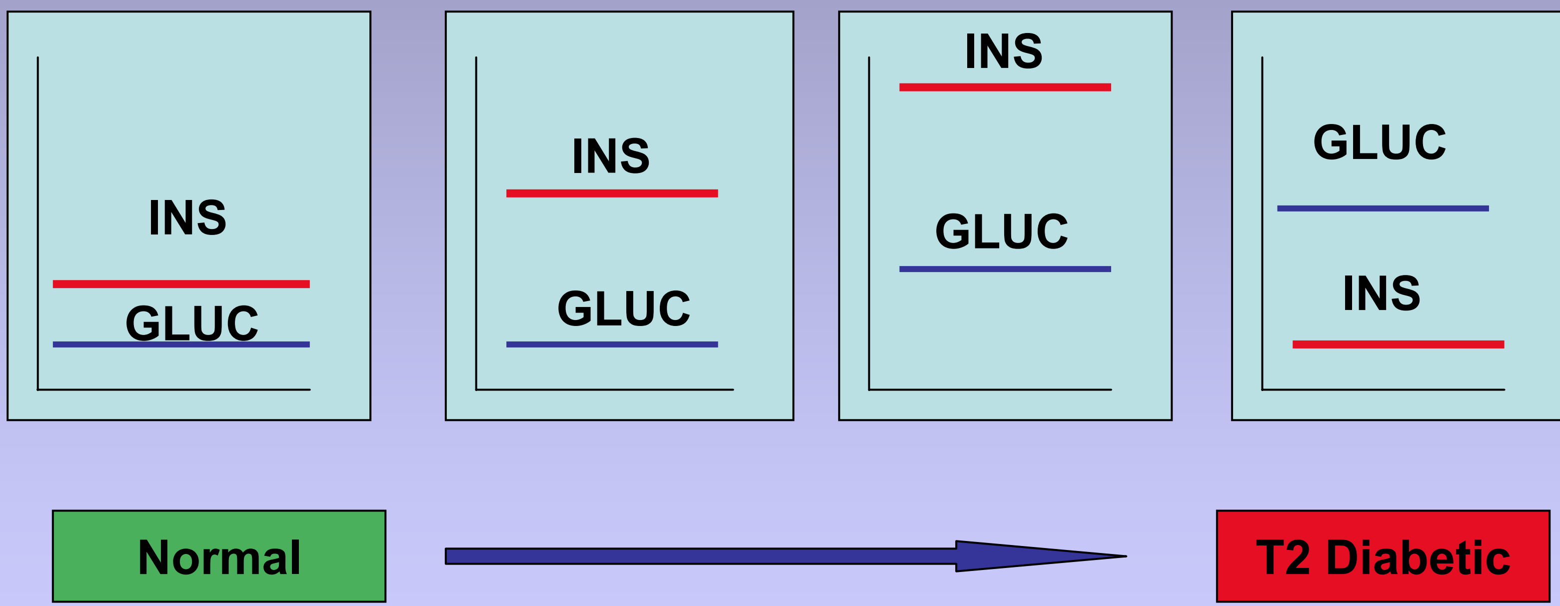
Insulin sensitive



Is insulin sensitivity important?

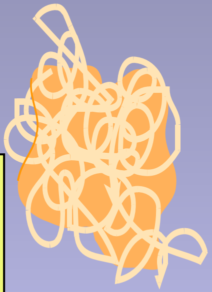


Insulin Resistance

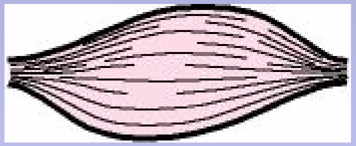


Insulin Sensitivity

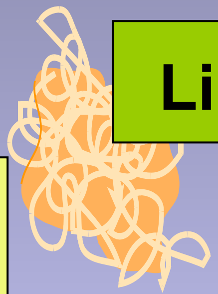
Gluconeogenesis
Glycogenolysis



Glucose
Uptake



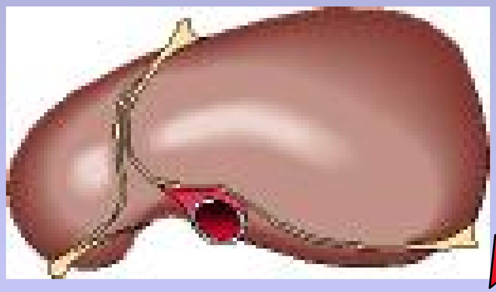
Insulin Sensitivity

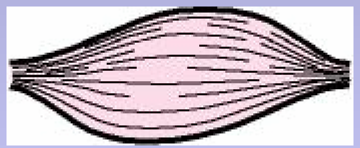


Lipolysis ↓

Glucose Uptake ↑

Gluconeogenesis ↓
Glycogenolysis ↓





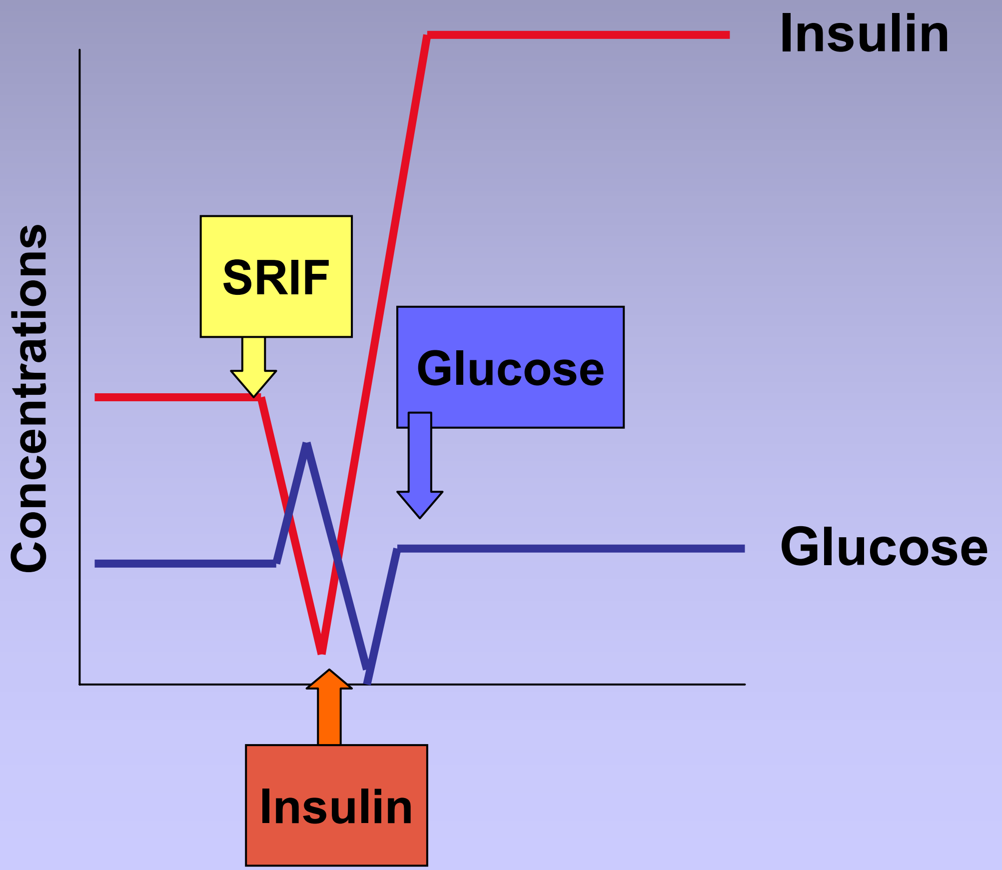
Protein synthesis ↑
Proteolysis ↓

Insulin

Less release

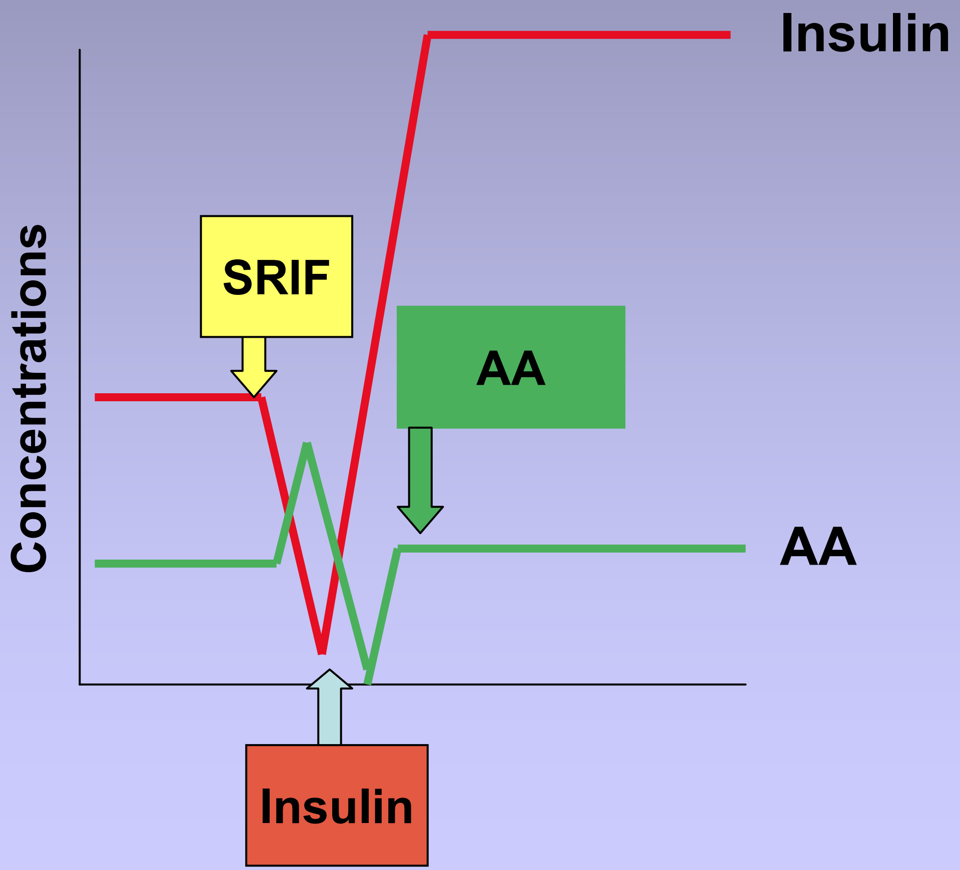
More disposal

Insulin Clamp - sensitivity



More glucose needed to restore euglycaemia the higher the insulin sensitivity

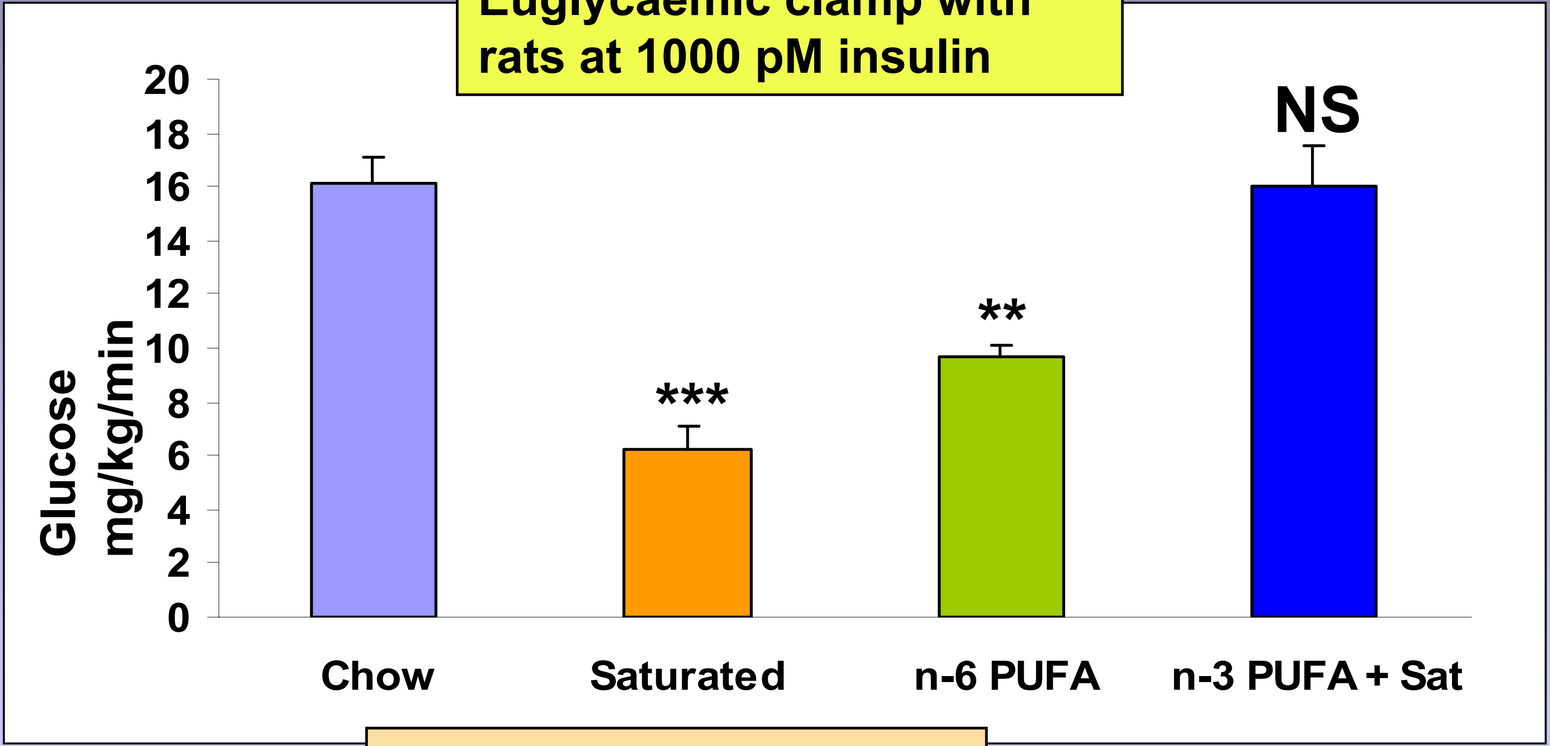
Insulin Clamp - sensitivity



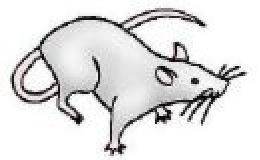
Similar with AA – decreased with insulin infusion, rate of replacement reflects insulin sensitivity

PUFAs and insulin resistance

Euglycaemic clamp with rats at 1000 pM insulin

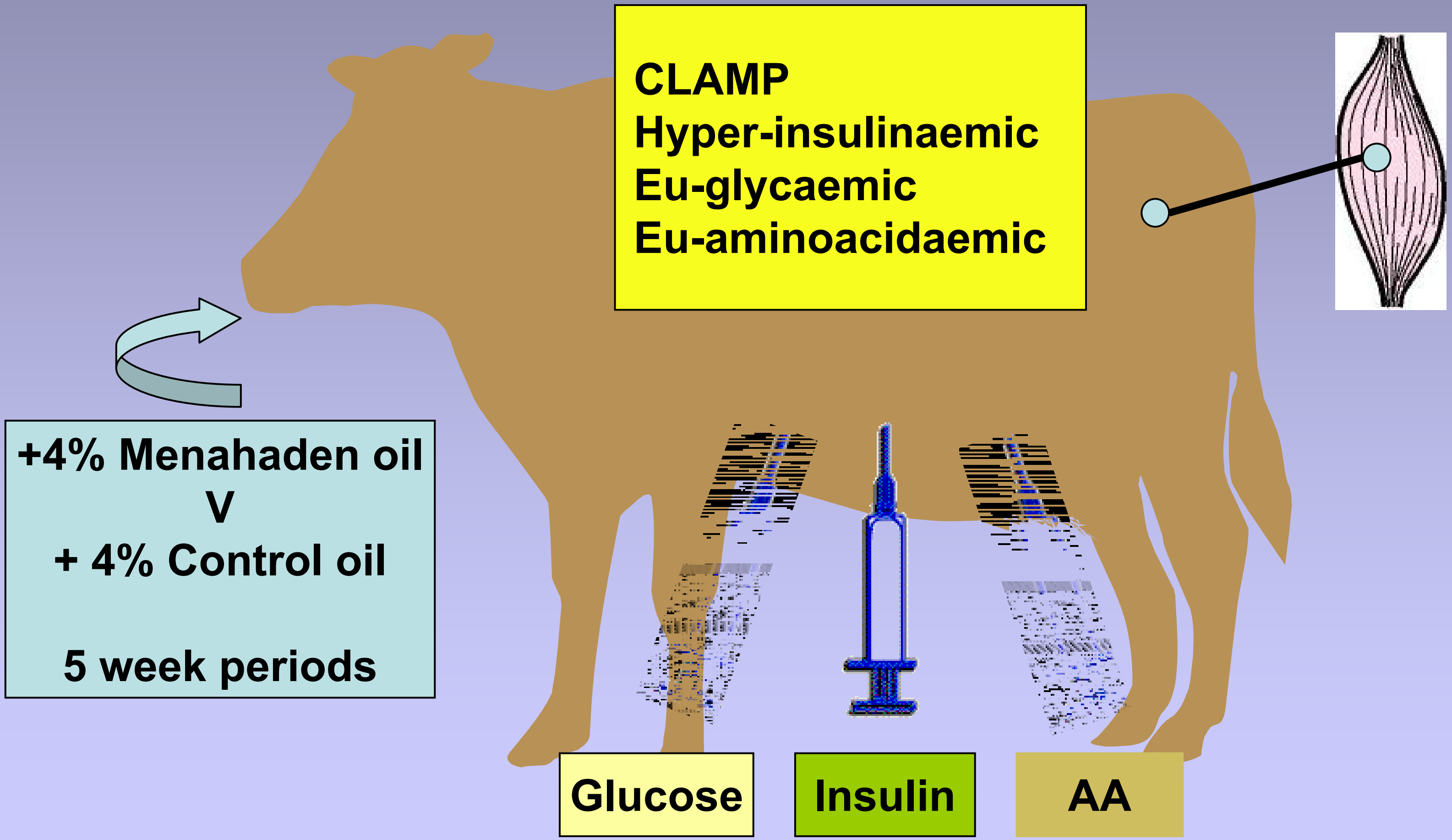


Responses in both liver and peripheral tissues



Storlien et al (1991)

n-3 PUFAs and IS in steers

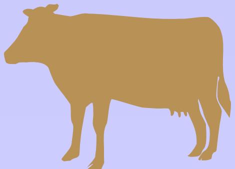


Gingras et al (2007)

n-3, n-6 PUFA content

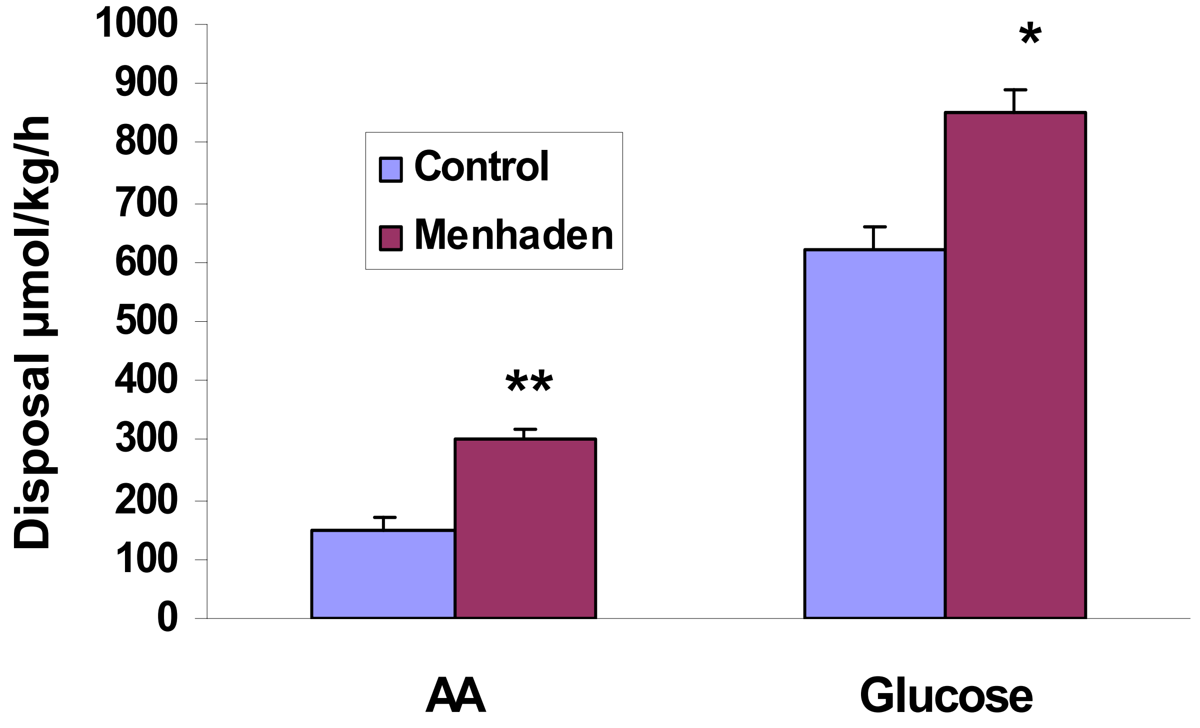
Diet	n-3	n-6	ratio
Control	0.6	35.8	0.02
Menhaden	38.2**	4.4**	8.8**

Muscle (PC)	n-3	n-6	ratio
Control	11.5	44.5	0.3
Menhaden	23.8**	32.2**	0.8**



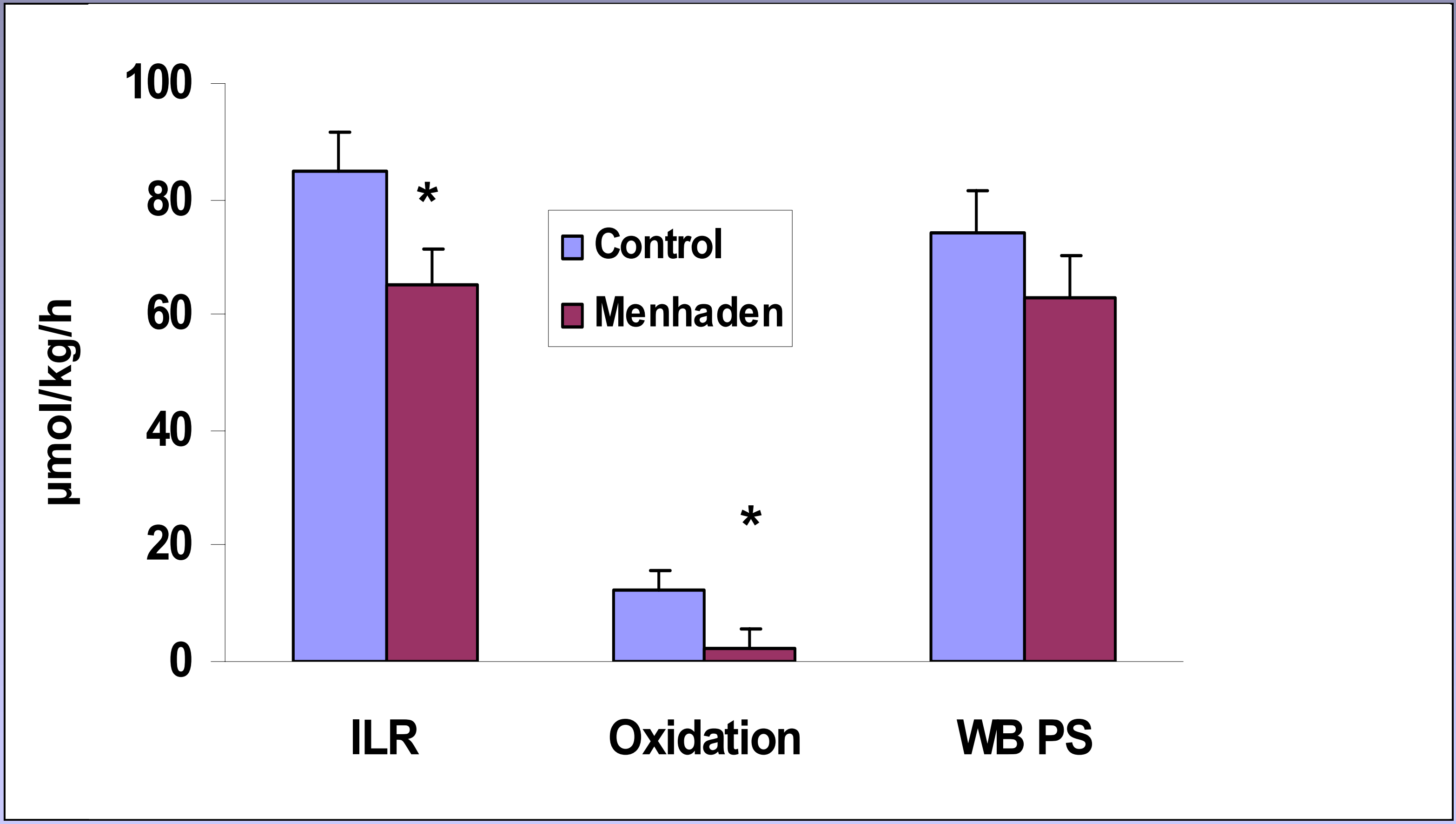
Gingras et al (2007)

Clamp - glucose and AA disposal



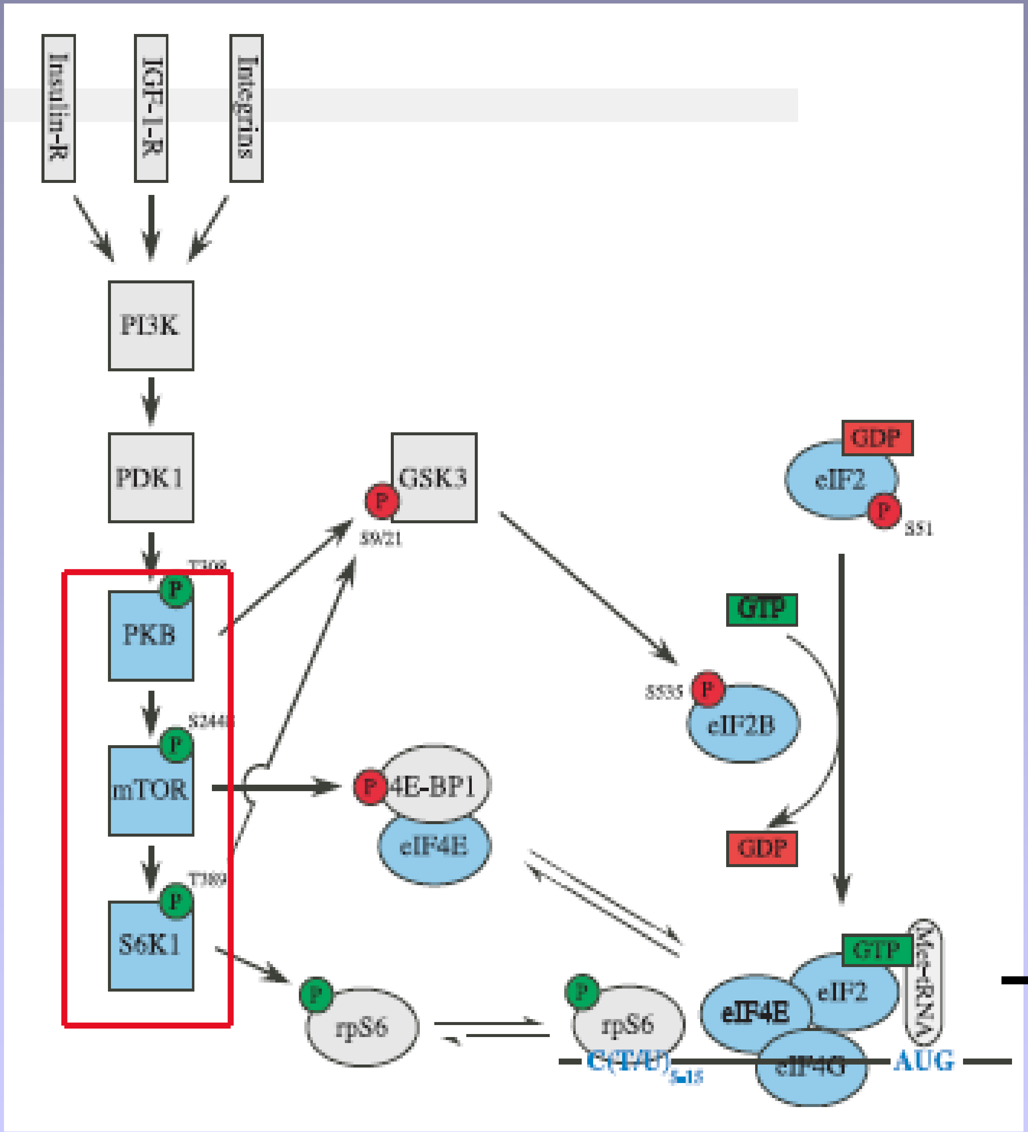
Gingras et al (2007)

n-3 PUFA and WB protein turnover



Gingras et al 2007

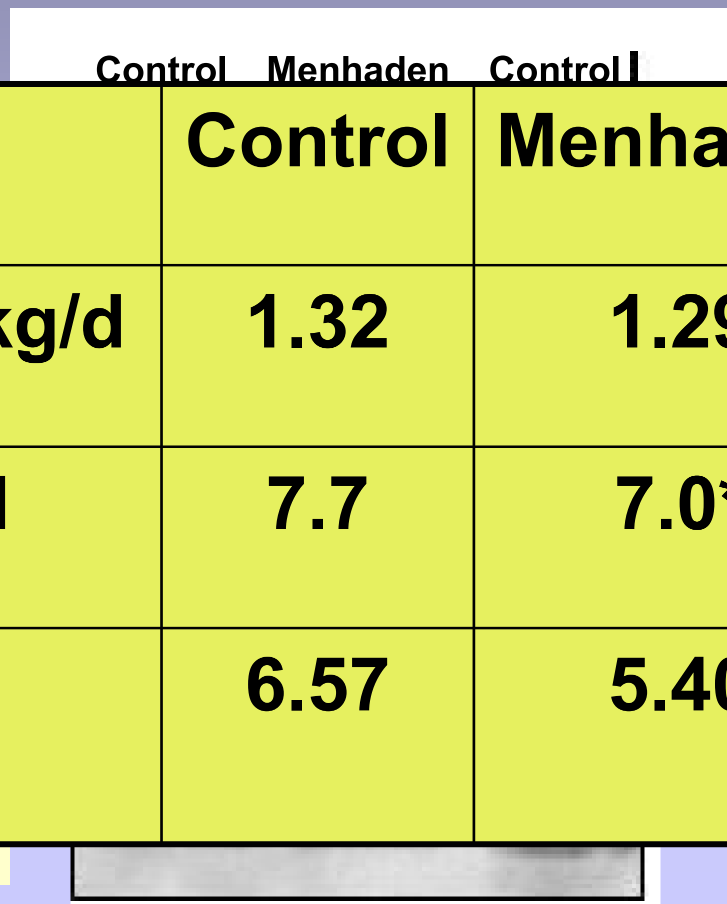
mTOR/S6K signalling pathway and protein synthesis



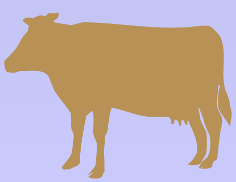
Protein Synthesis

Kimball et al (2004)

Muscle western blots



	Control	Menhaden
BW gain kg/d	1.32	1.29
FI kg/d	7.7	7.0*
FCR	6.57	5.40

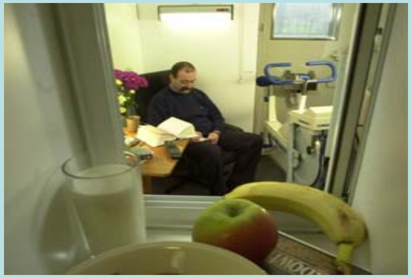


Gingras et al (2007)

P:E Human health

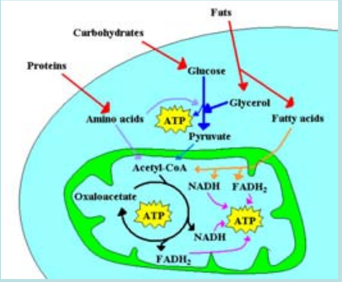
Appetite

Epi-genetics



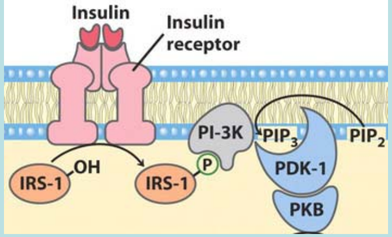
Bioenergetics

P **E**



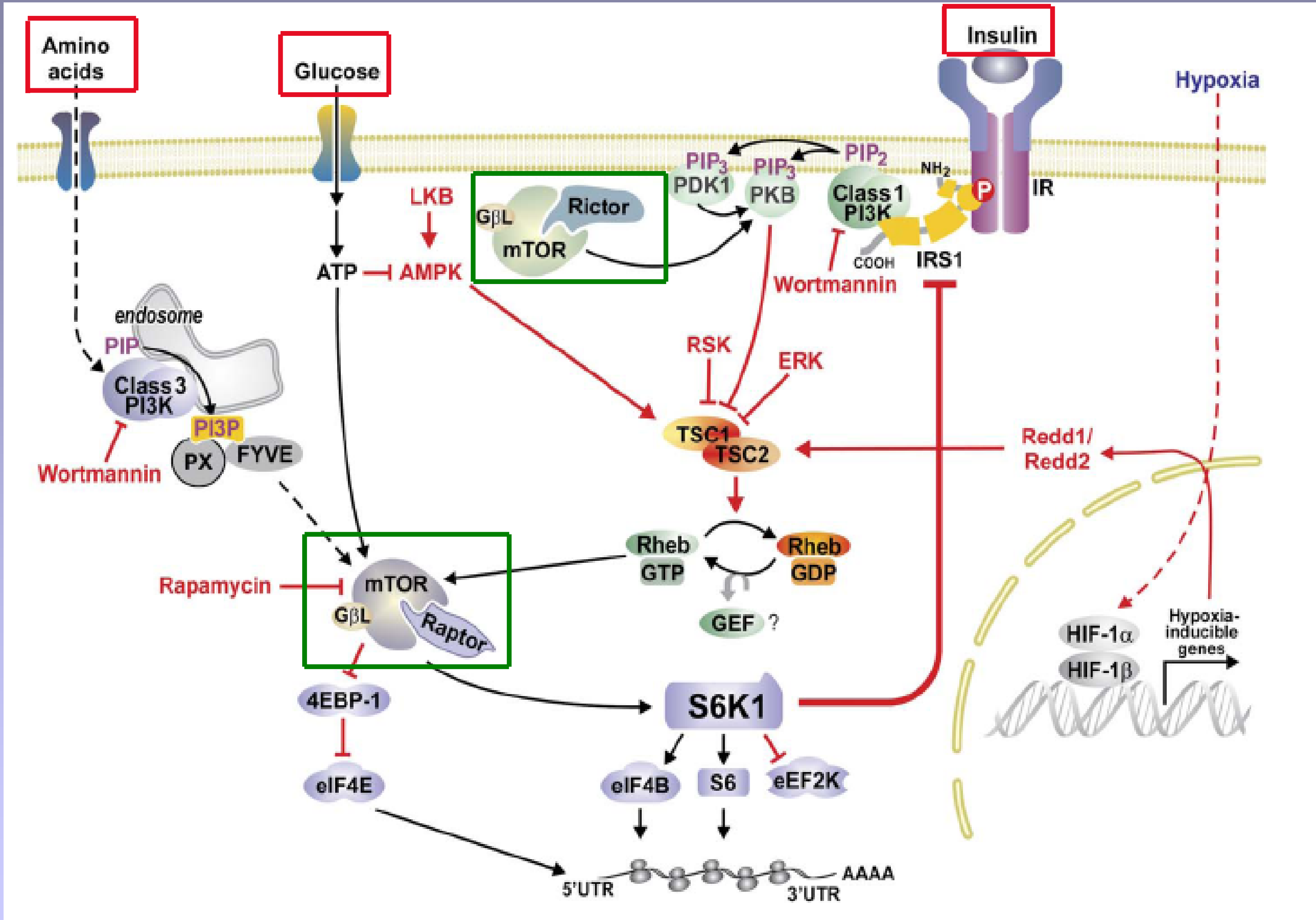
Metabolite interconversion

Metabolic health



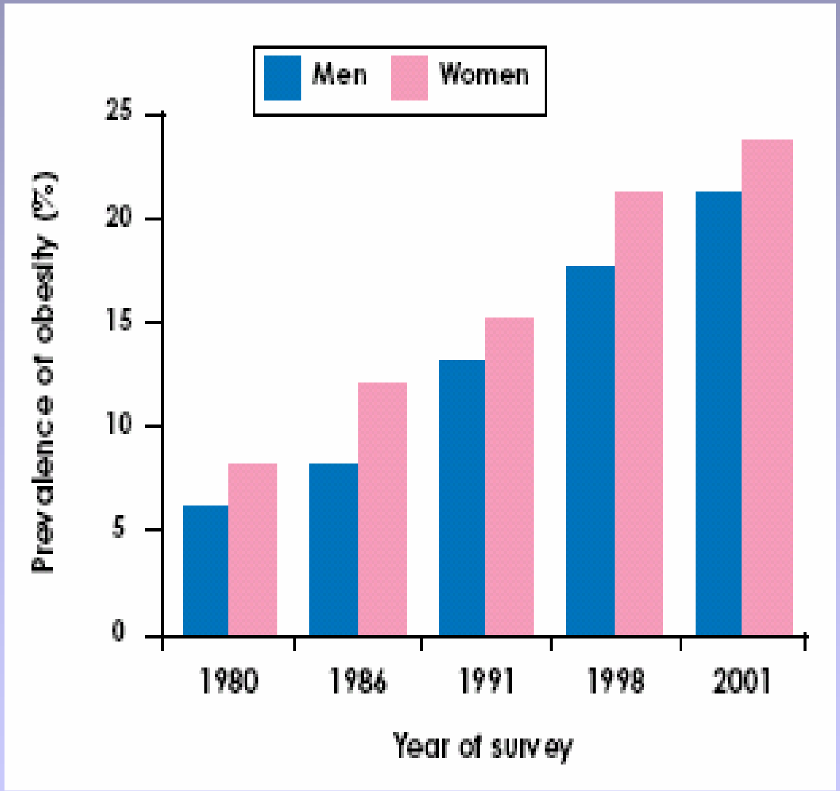
Hormonal sensitivity

mTOR/S6K signalling pathway in response to nutrients



Um et al (2006)

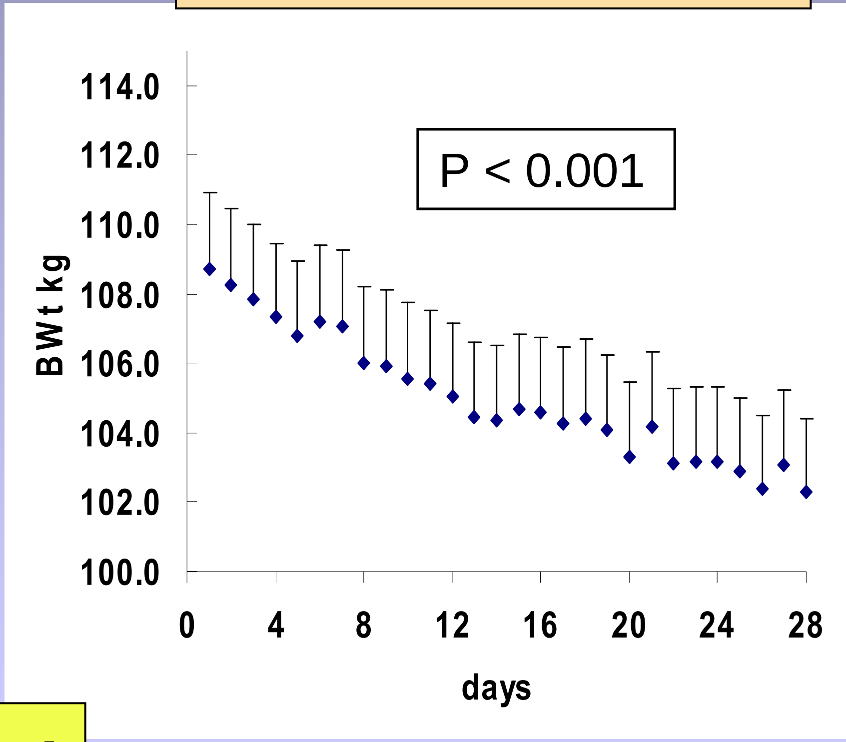
Positive E balance!!



Jebb & Steer (2001)

Positive E balance!!

High Protein diet ad lib



Another P:E interaction!

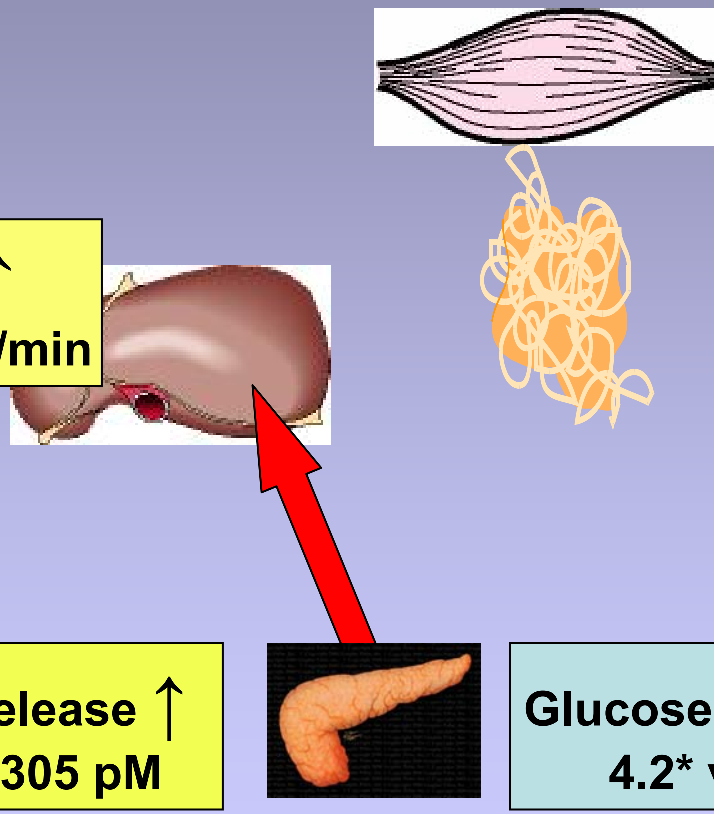
Johnstone et al (2007)

High Protein diet & Glycaemia

Glucose oxidation ↓
5.6* v 7.4 mg/kg/min

Glucose release ↑
12.2** v 10.9 μmol/kg/min

Protein oxidation ↑
1.12* v 0.82 mg/kg/min



Insulin release ↑
516** v 305 pM

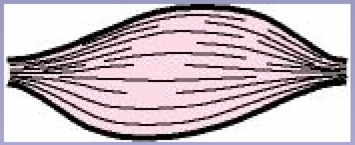
Glucose threshold ↓
4.2* v 4.9 mM

Glucagon ↑
38* v 28 pM

Linn et al (2000)

Amino Acids – possible actions on hyperglycaemia

Gluconeogenesis ↑?
Glycogenolysis ↑?



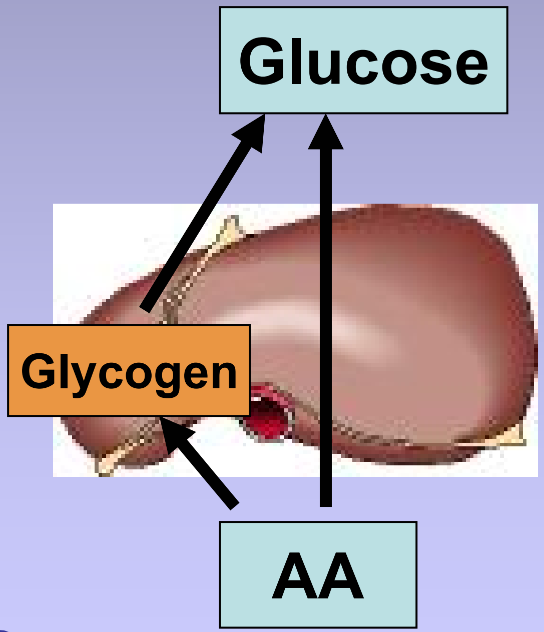
Glucose transport ↓?
Glucose substitution ↓?

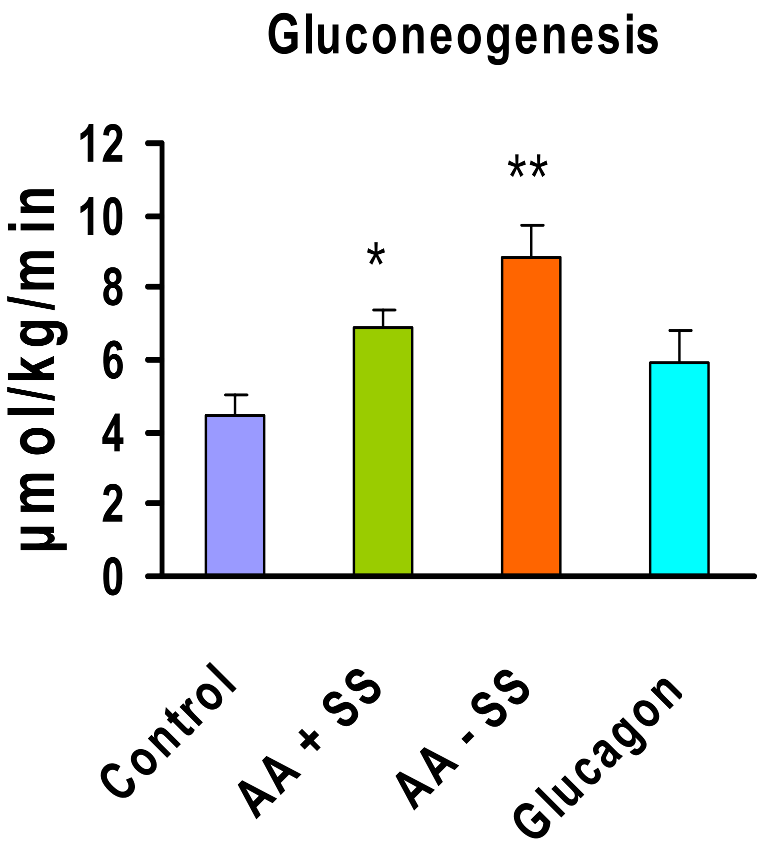
More release

Amino Acids

Less disposal

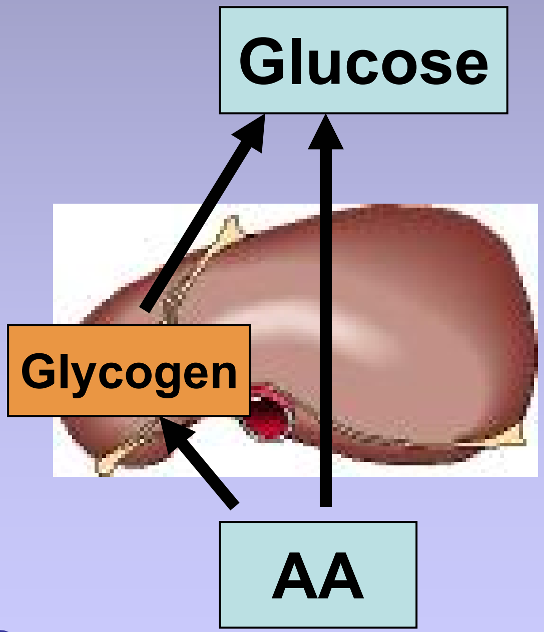
High Protein diet & Glycaemia

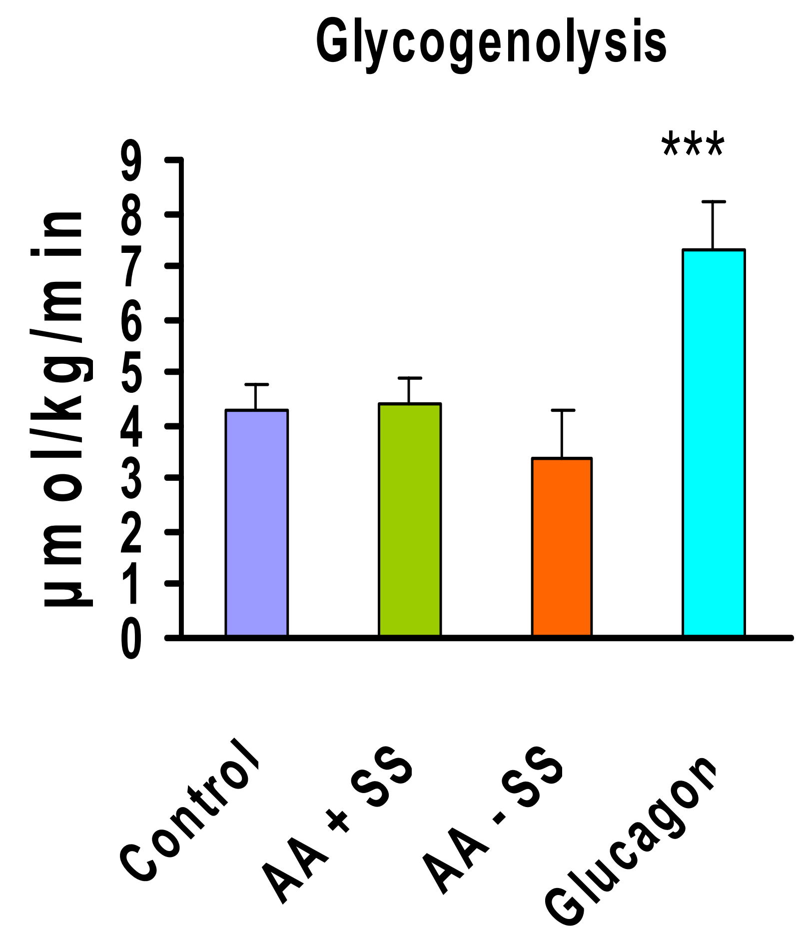




Krebs et al (2003)

High Protein diet & Glycaemia

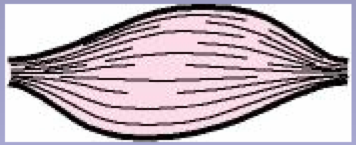




Krebs et al (2003)

Amino Acids – possible actions on hyperglycaemia

Gluconeogenesis ↑
Glycogenolysis =

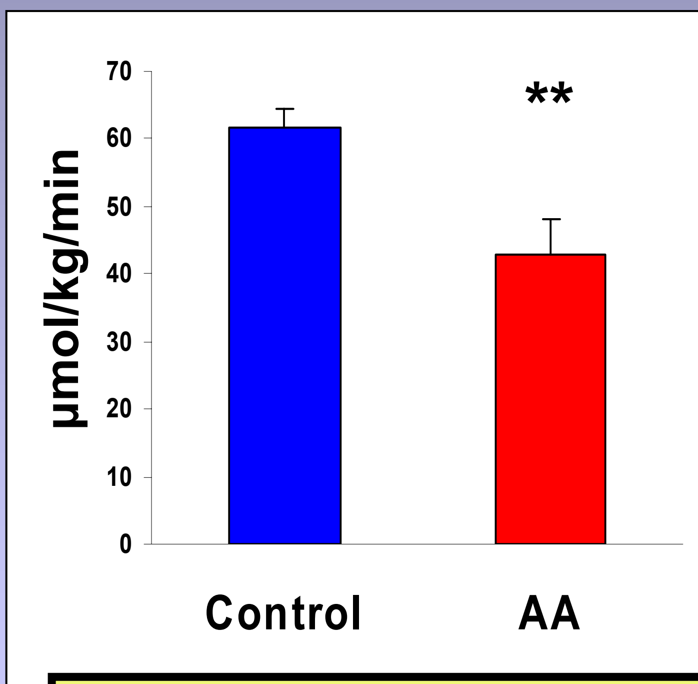


Glucose transport ↓?
Energy substitute ↓?

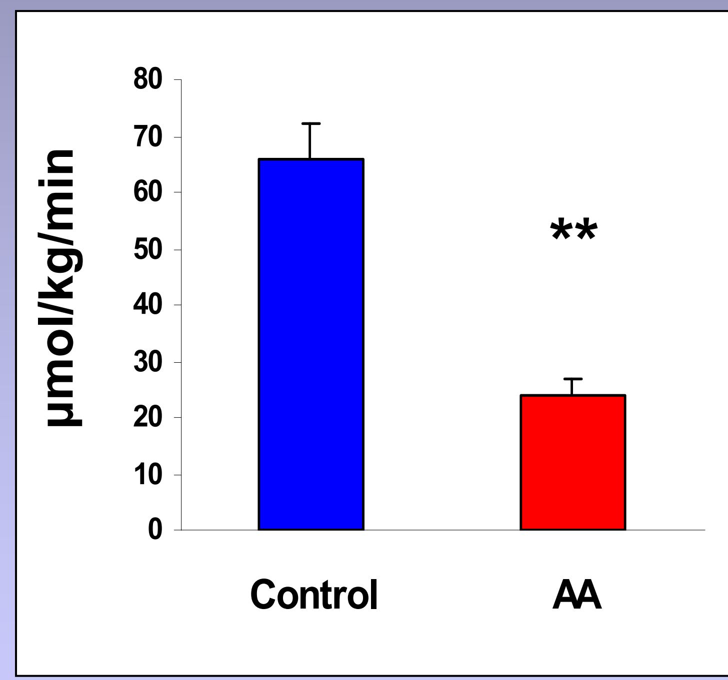
Amino Acids

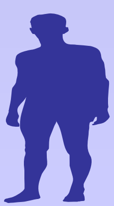
Amino Acids – Insulin Sensitivity

Glucose transport

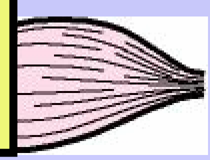


Glycogen synthesis



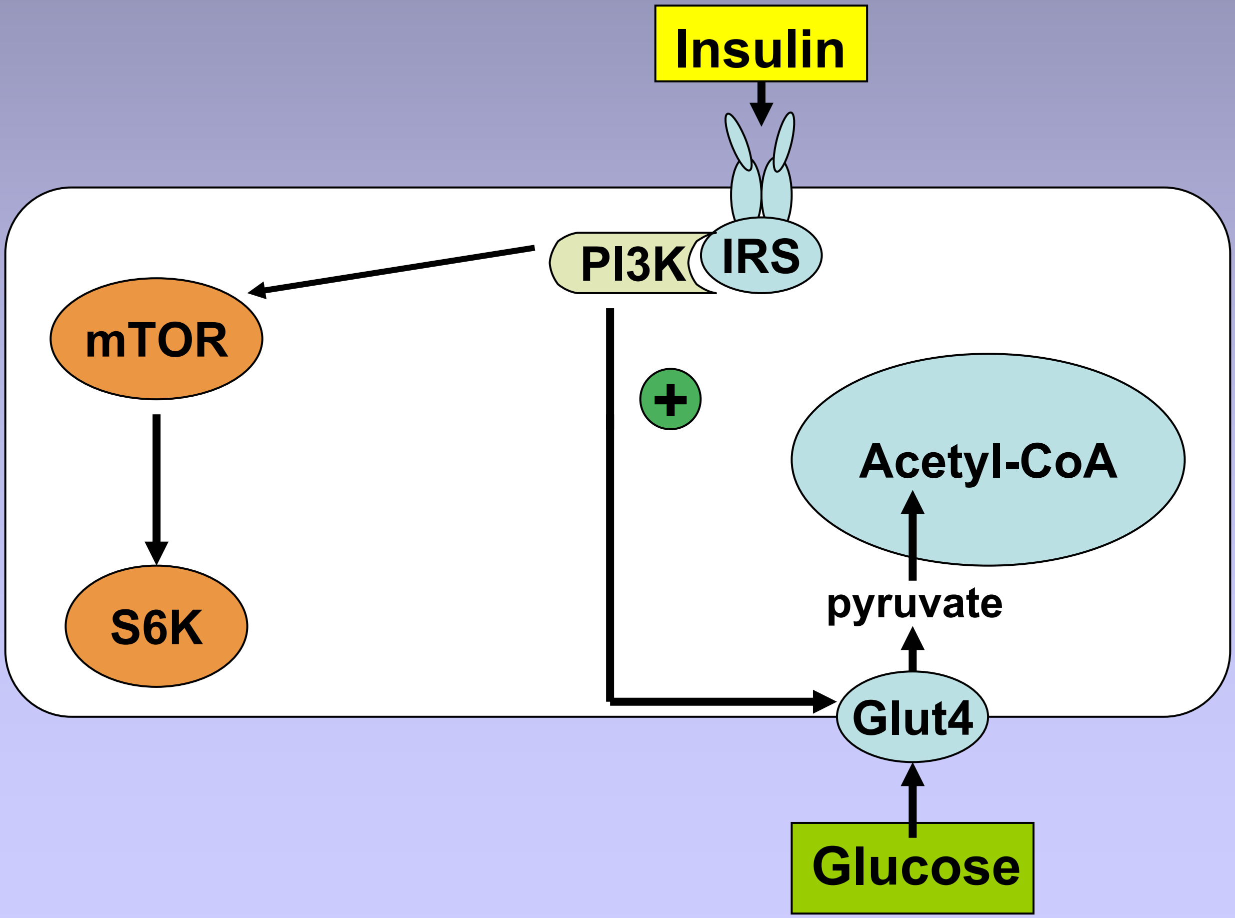


Glucose transport ↓
Energy substitute ↓

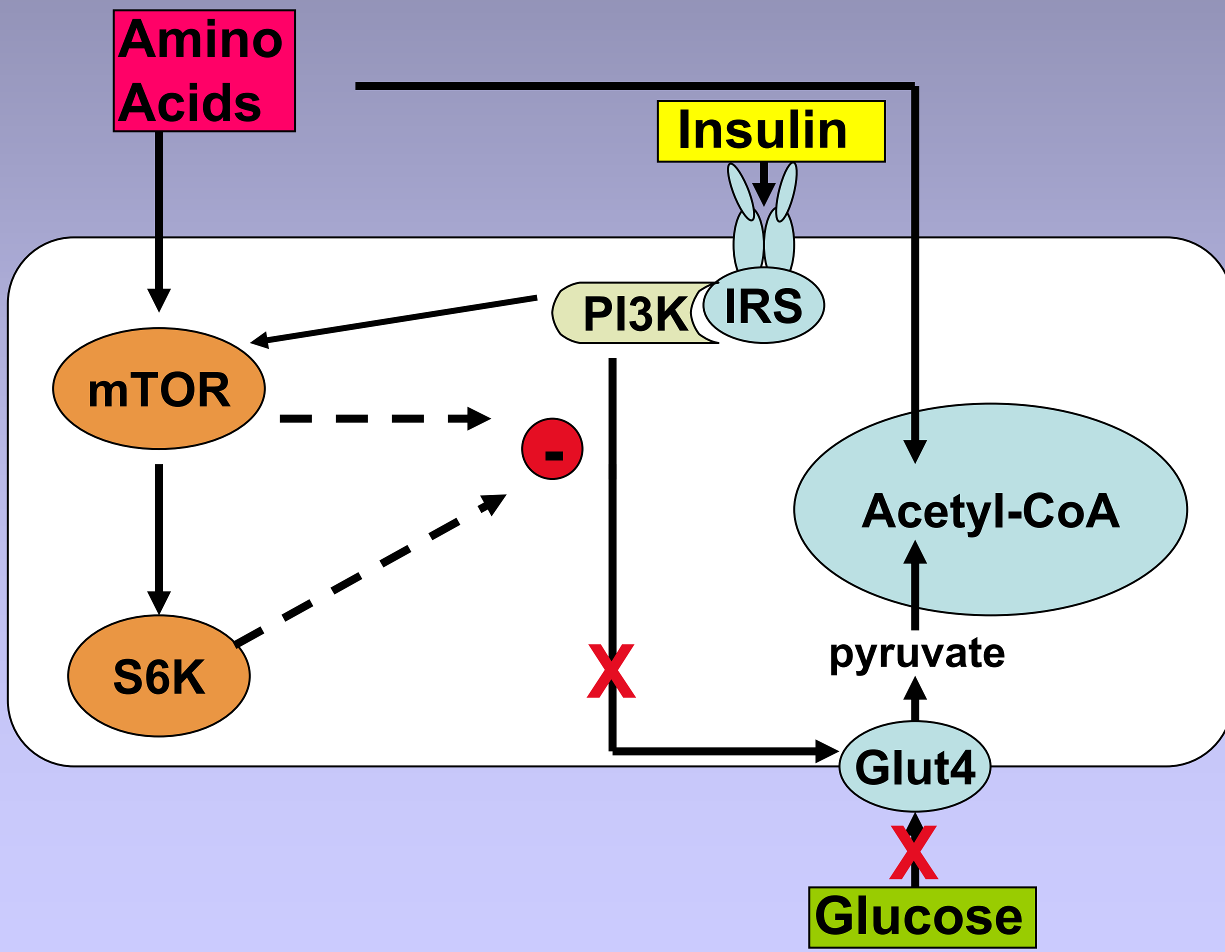


Krebs et al (2003 & 2005)

Amino acid signal pathways



Amino acid signal pathways



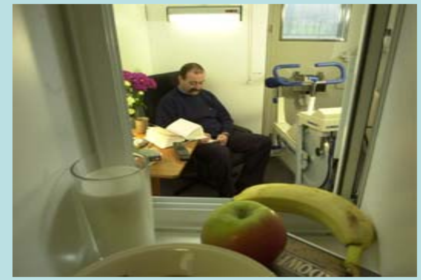
Conclusions

- Insulin sensitivity altered by CHO, AA and EFA supply
- Glucose utilisation affected by AA – at liver and muscle
- Signals override energy balance
- mTOR may be common regulator

General P:E Interactions

Appetite

Efficiency

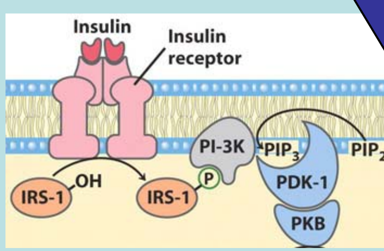


Bioenergetics

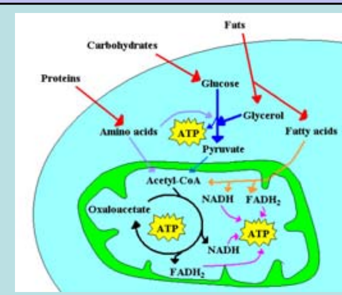
Epi-genetics

P **E**

Metabolic fuels



Hormonal sensitivity



Metabolite interconversion