AgroParisTech
INSTITUT DES SCIENCES ET INDUSTRIES DU VIVANT ET DE L'ENVIRONNEMENT
PARIS INSTITUTE OF TECHNOLOGY FOR LIFE, FOOD AND ENVIRONMENTAL SCIENCES

INRA
SCIENCE & IMPACT

NUEVO MERCADO DE LA REVALORIZACIÓN Y BIOSÍNTESIS PROTEICA

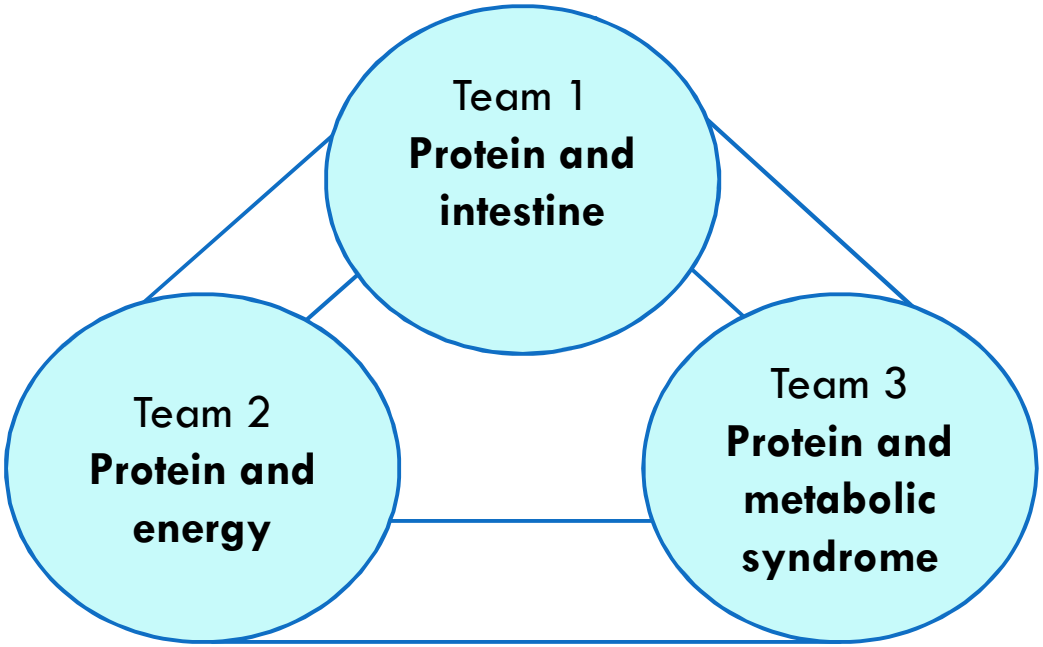
Tristan Chalvon Demersay, MSc

26/11

Encuentro AgroBiotech Innovacion

Presentation of the unit

- UMR914 – INRA/AgroParisTech. Physiology of Nutrition and feeding behaviour
- Created in 2002, 35 permanent members
- Unit attached to a clinical investigation center at the University Hospital Avicenne near Paris



Plan

- Protein metabolism
- Target populations for protein synthesis
- New perspectives on protein synthesis

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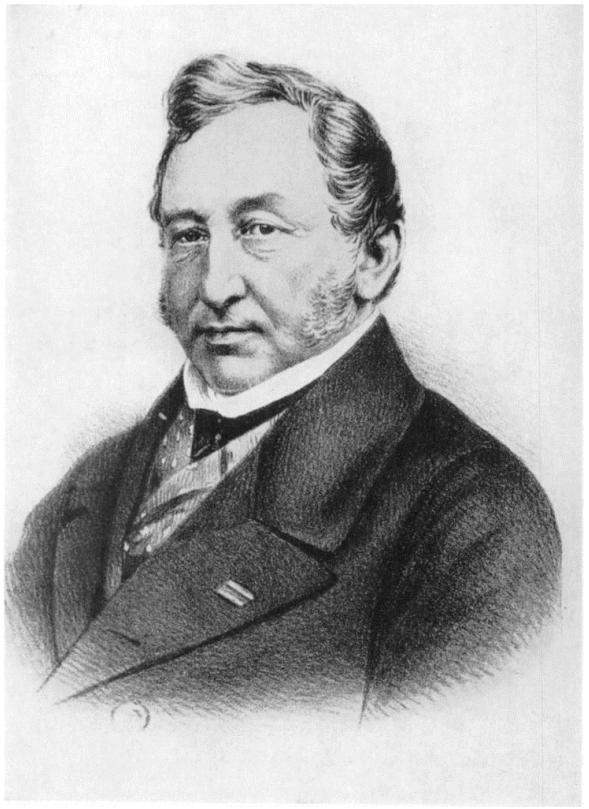
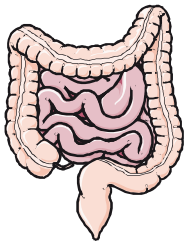
- New perspectives on protein synthesis

Protein metabolism

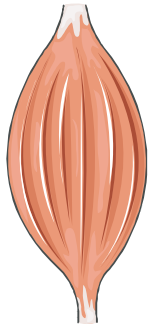
- Proteins were first identified by Gerrit Mulder in 1835 in Rotterdam
- Protein comes from the greek « prôtos » meaning « primary »
- Constitute nearly 60% of dry weight of cells



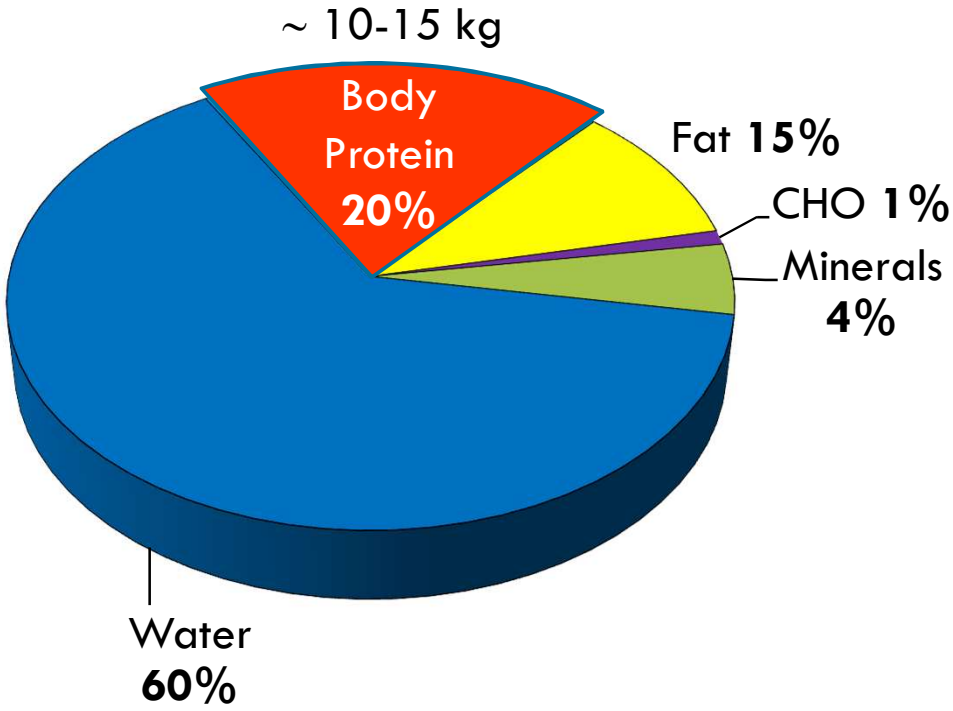
6 **Protein in the body** 26/11

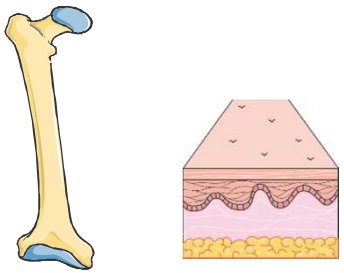


10% of total protein



42% of total protein





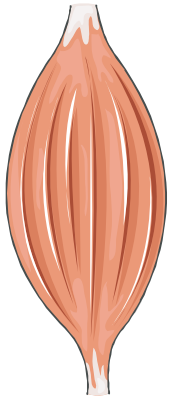
15% of total protein

- Proteins is the second most important component of the body, mainly concentrated in the liver, muscle, intestine and skin

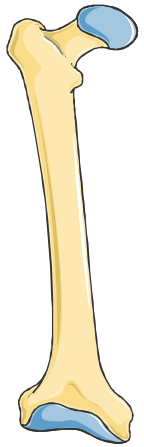
Protein metabolism

Body Protein 20%

Ex: hormones (insulin)

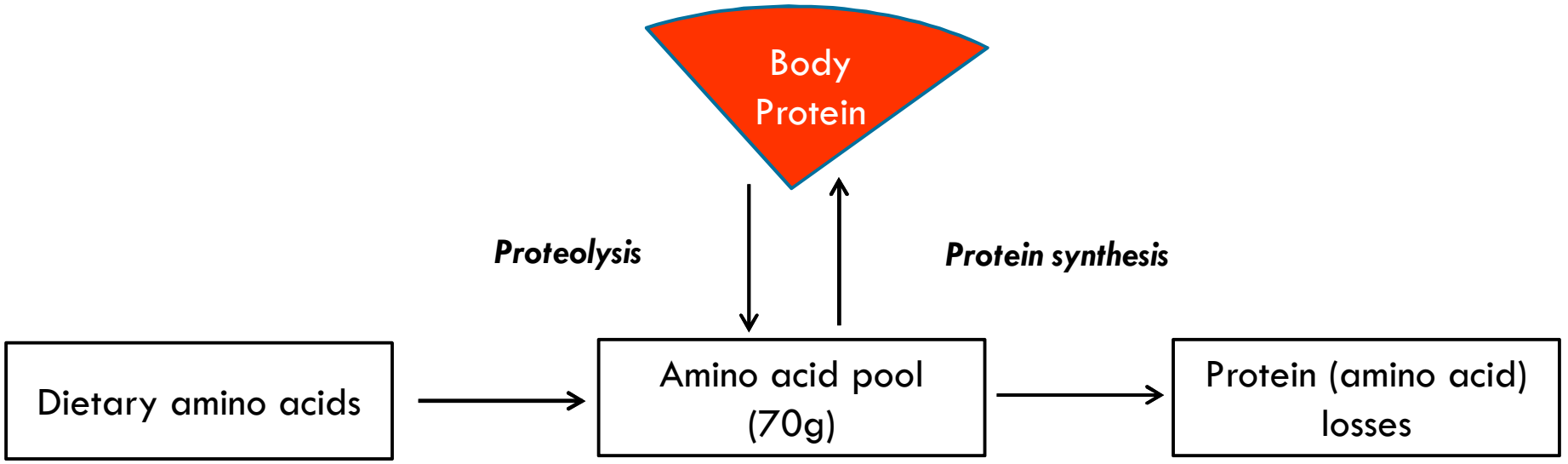


Ex: actine in muscles



Ex: collagen in bones

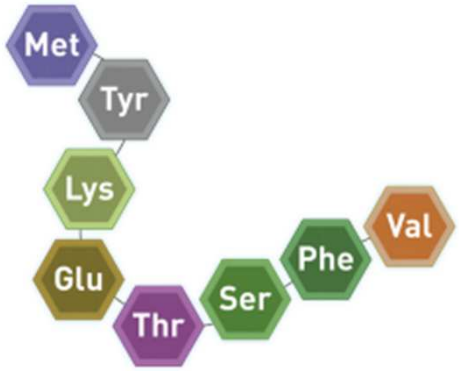
Protein metabolism

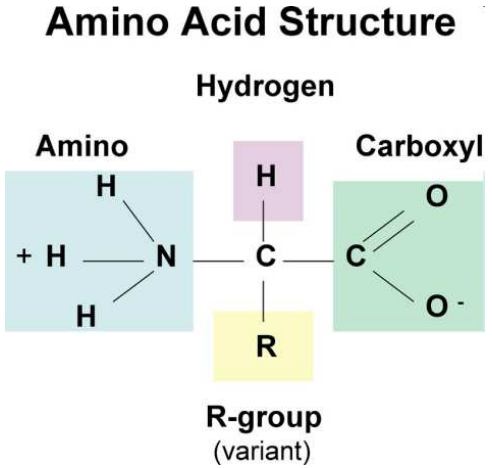


Proteins are synthetized from amino acids

Protein metabolism

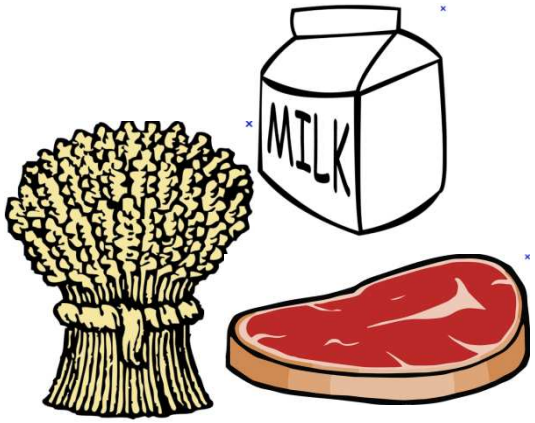
- Amino acids contain a carboxylic and amine functions and differs from their carbon radical
- 20 amino acids are proteinogenic

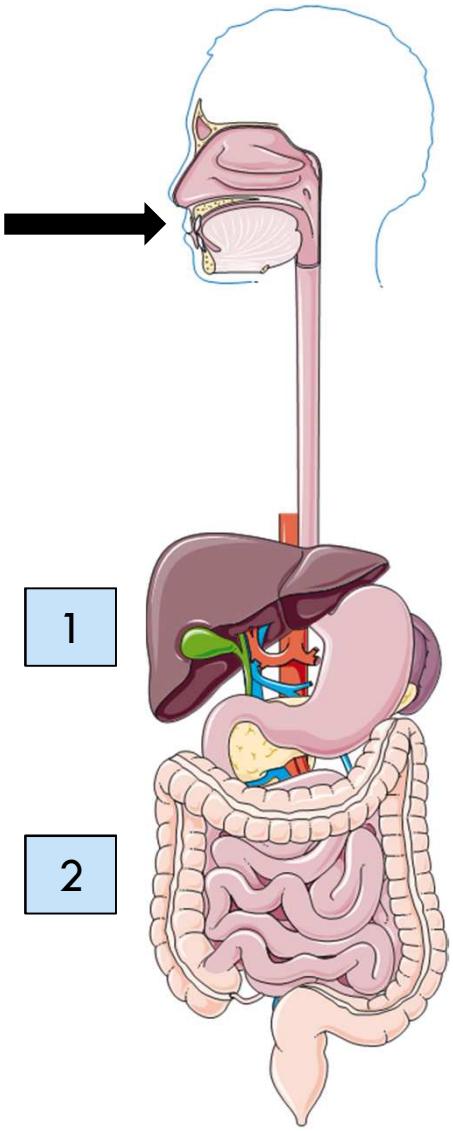




Alanine	Glutamic acid	Leucine	Serine
Arginine	Glutamine	Lysine	Threonine
Asparagine	Glycine	Methionine	Tryptophan
Aspartic acid	Histidine	Phenylalanine	Tyrosine
Cysteine	Isoleucine	Proline	Valine

Protein metabolism





Protein digestion and amino acid absorption in the gut

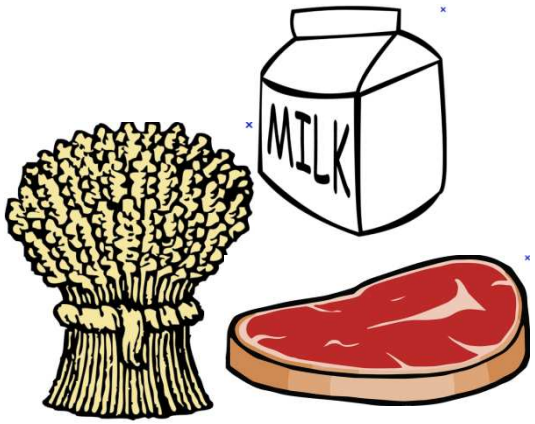
Gastric phase (stomach)

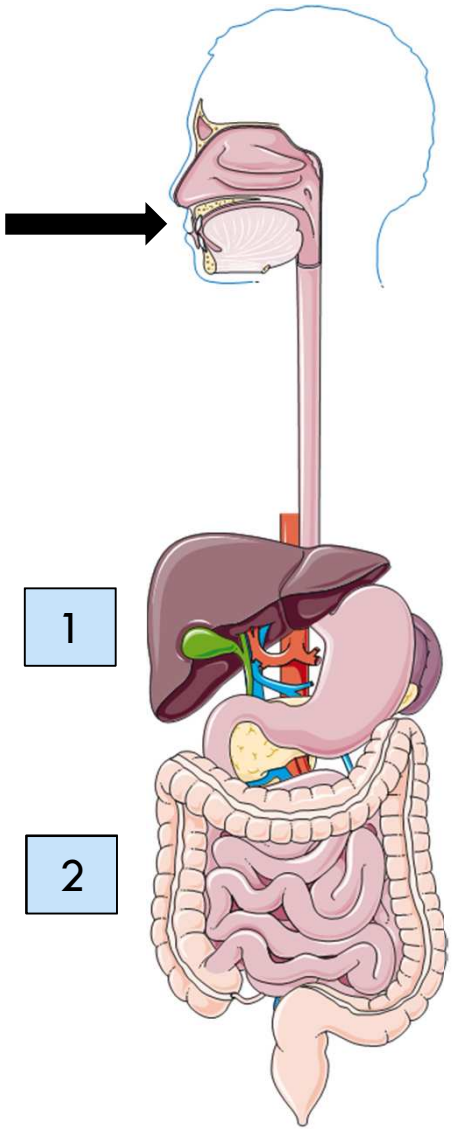
- Enzymes digest proteins into smaller fragments

Intestinal phase

- Fragments are broken down and free amino acid are absorbed

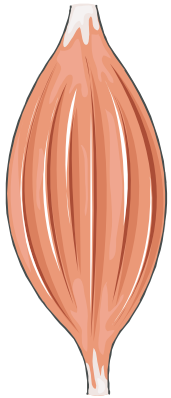
Protein metabolism



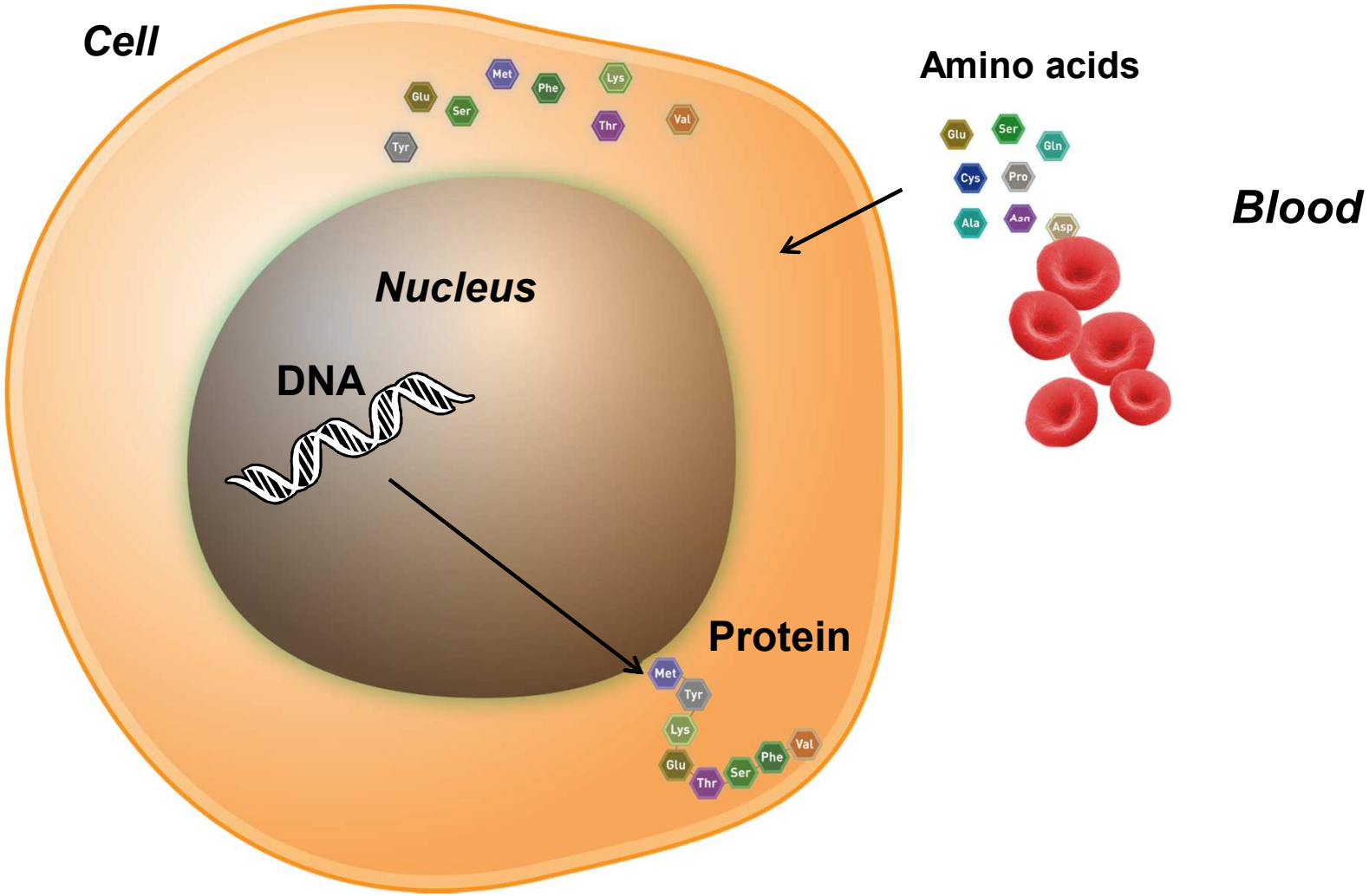


Peripheral organs

3



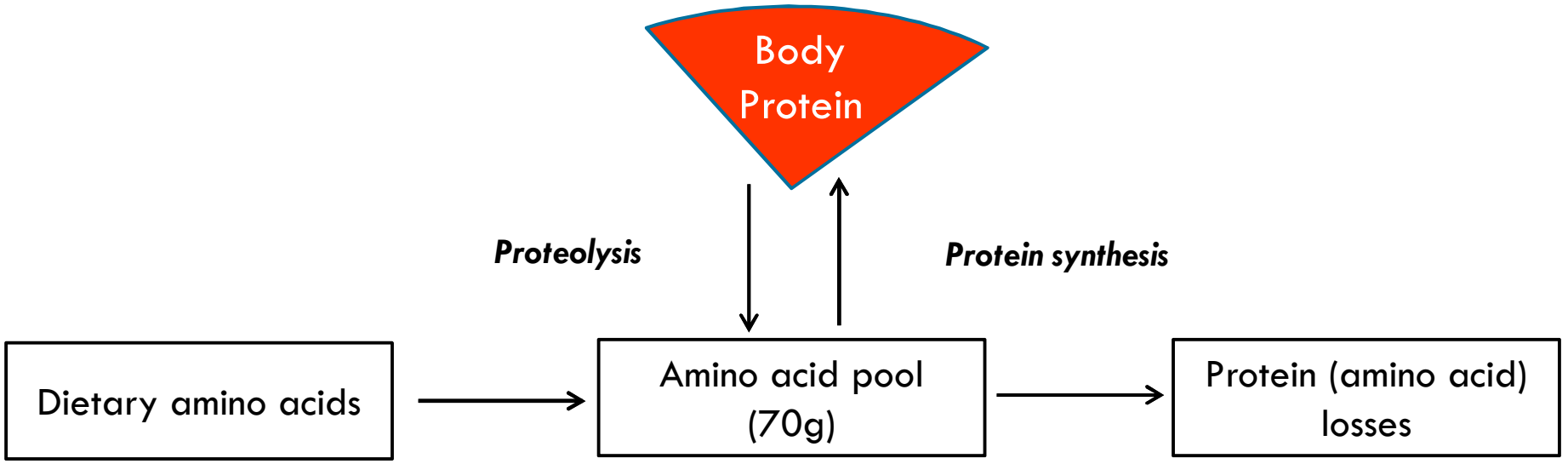
Protein metabolism



Protein metabolism

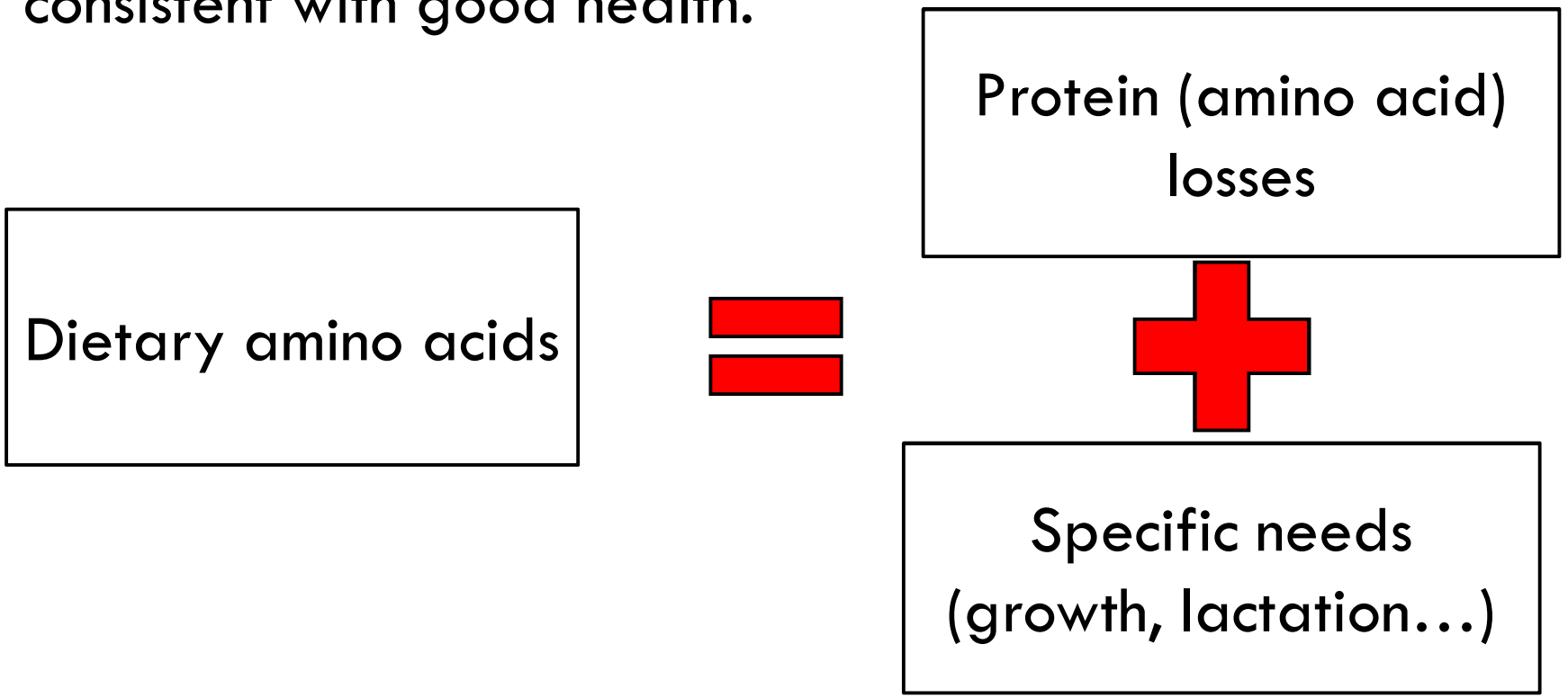
"**The protein requirement** of an individual is defined as the lowest level of dietary protein intake that will balance the losses of nitrogen from the body in persons maintaining energy balance at modest levels of physical activity." (WHO/FAO, 2007)

Protein metabolism



Protein metabolism

"In children and pregnant or lactating women, the protein requirement is taken to include the needs associated with the deposition of tissues or the secretion of milk at rates consistent with good health."



Protein metabolism

- The intake recommendation for healthy adult human protein is **0.83 g/kg/d** (WHO/FAO/UNU; 2007)
- Recommendation is higher for children due to growth
- **Specific needs for 9 essential amino acids**

Subject	Protein requirement (g/kg/d)
Heathy adults	0.83

Protein metabolism

- Essential amino have to be provided by alimentation
- Protein quality is determined by its content in essential amino acids

Alanine	Glutamic acid	Leucine	Serine
Arginine	Glutamine	Lysine	Threonine
Asparagine	Glycine	Methionine	Tryptophan
Aspartic acid	Histidine	Phenylalanine	Tyrosine
Cysteine	Isoleucine	Proline	Valine

Protein metabolism

- PDCAAS (Protein Digestibility-Corrected Amino Acid Score), famous method to assess protein quality (WHO/FAO, 1993)

	PD-CAAS (%)	Limiting amino acid(s)
Animal sources		
Egg	>1.0	-
Milk, cheese	>1.0	-
Meat, fish	>1.0	-
Vegetable sources		
Soy	~0.95	Met+Cys
Beans	~0.7-0.75	Met+Cys
Rice	~0.65	Lys
Wheat	~0.5	Lys
Maize	~0.5	Lys

- Replaced by DIAAS (Digestible Indispensable Amino Acid Score)

PDCAAS = *(mg of limiting amino acid in 1 g of test protein / mg of same amino acid in 1 g of reference protein) x true digestibility*

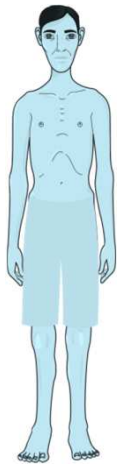
Plan

- Protein metabolism
- Target populations for protein synthesis
- New perspectives on protein synthesis

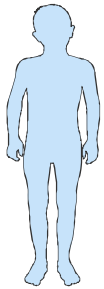
Target populations for protein synthesis

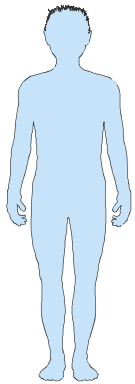
Athletes ↑

Weight loss ↓

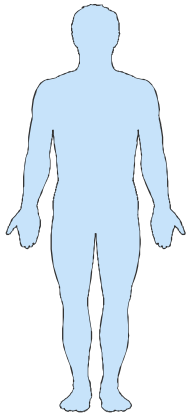


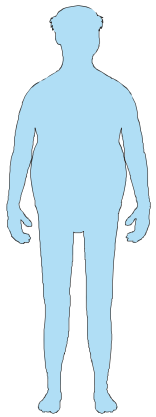
Cachexia ↓



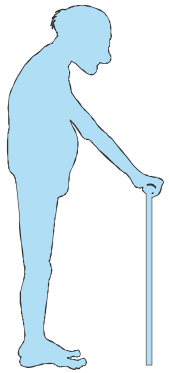


Growth ↑

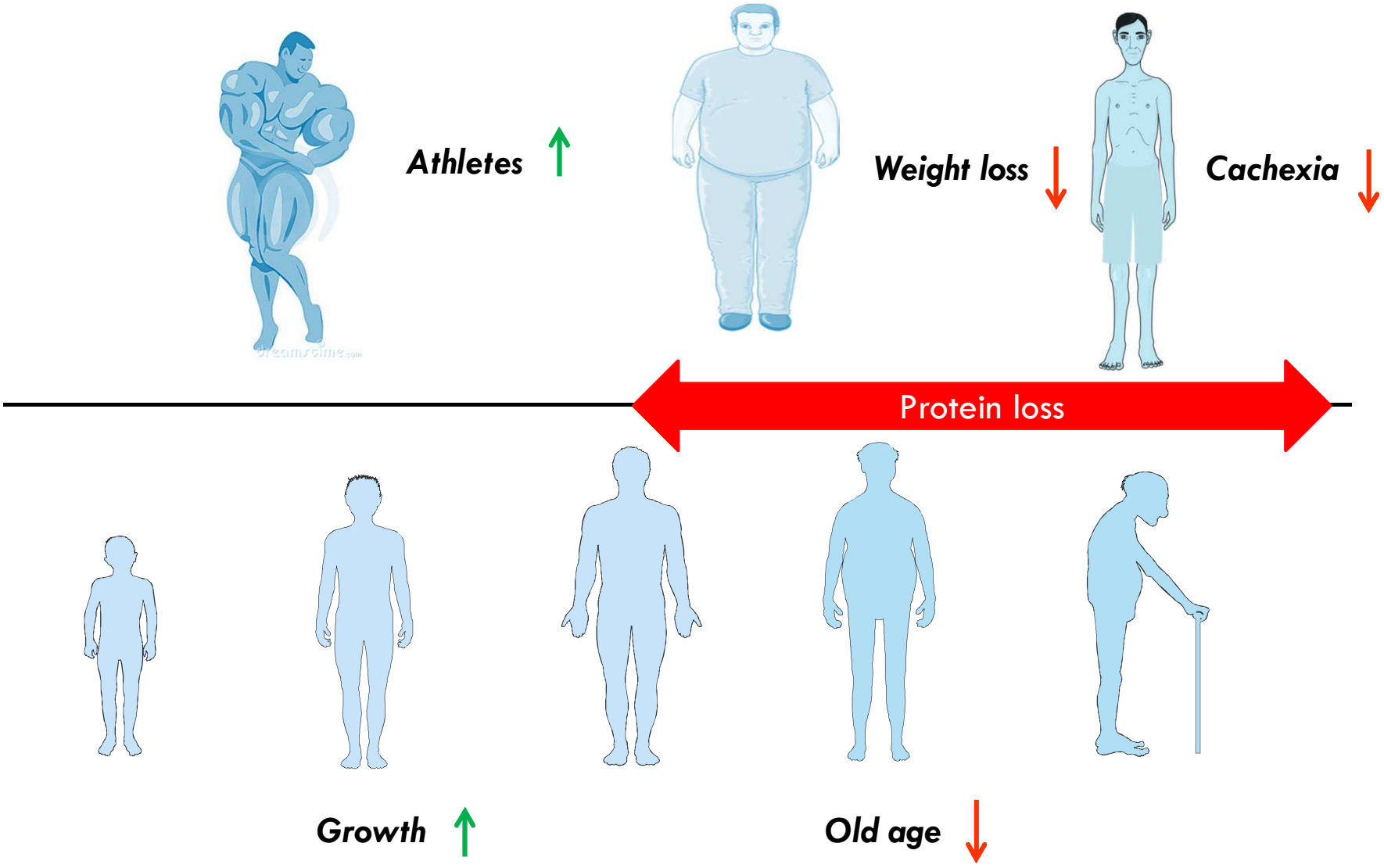




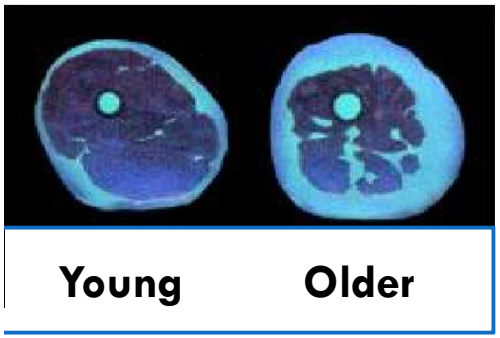
Old age ↓

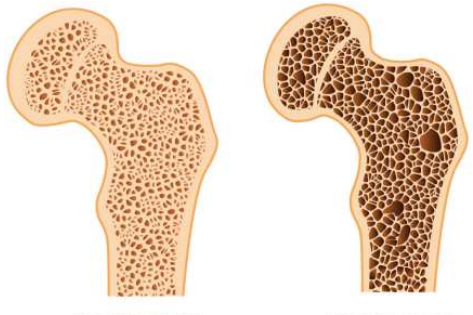


Target populations for protein synthesis

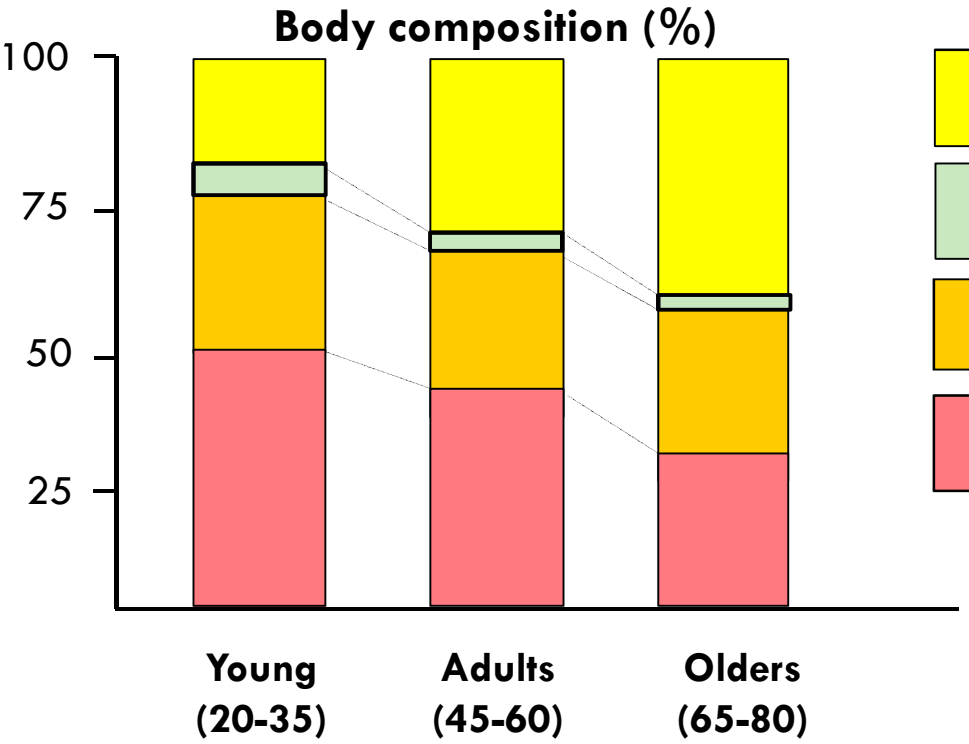


Target populations for protein synthesis

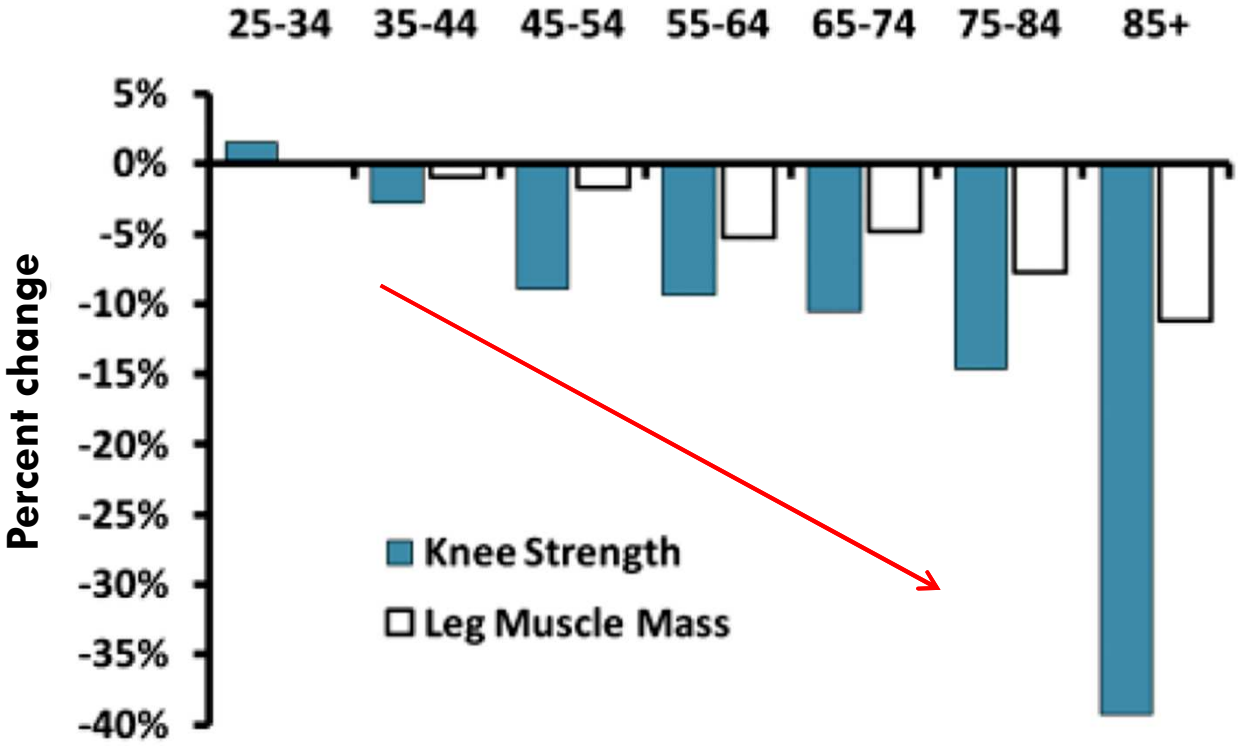




Muscle size is reduced and bone is honeycombed



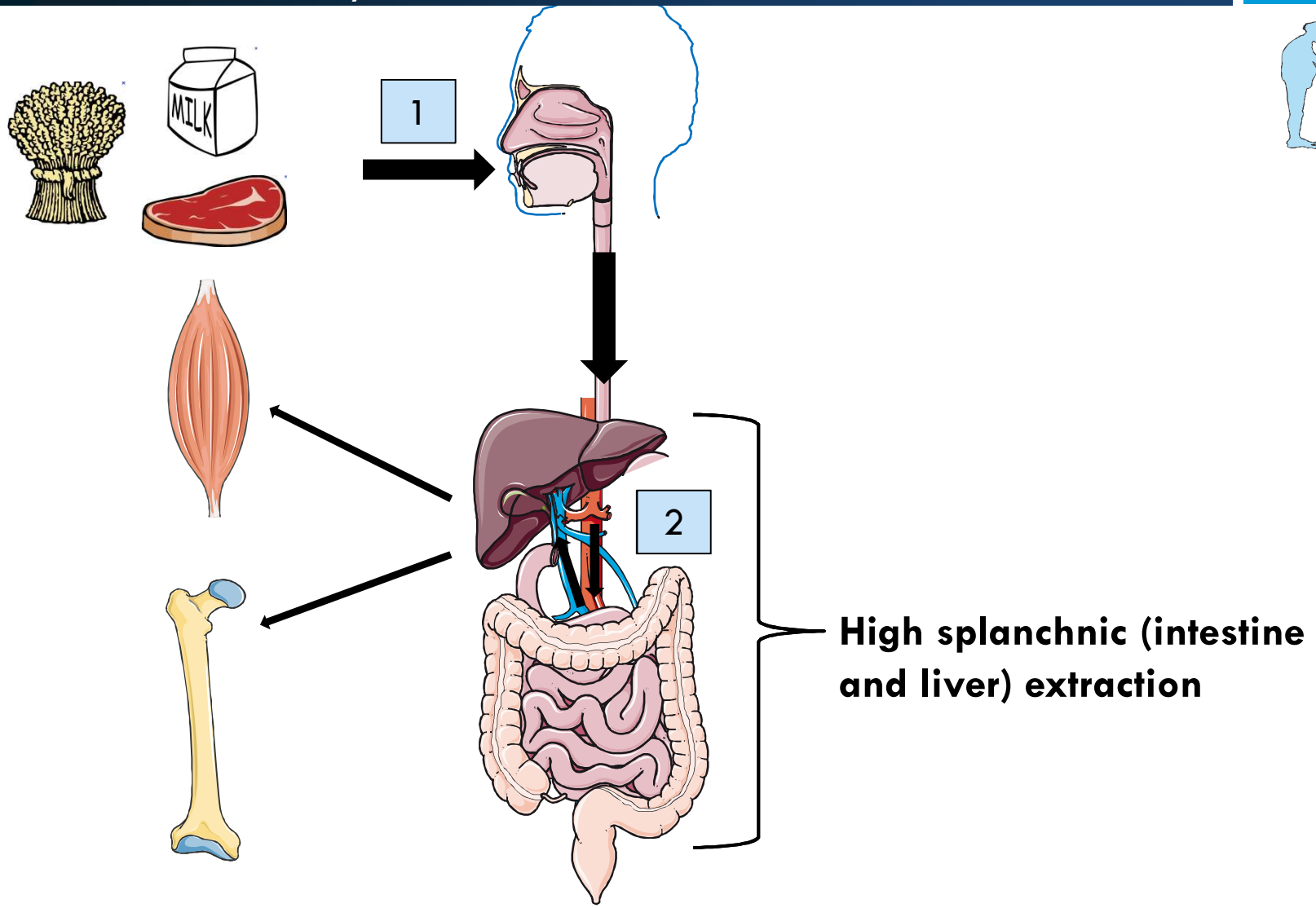
Target populations for protein synthesis



Ferrucci L et al. ***J Gerontol A Biol Sci Med Sci, 2012***

Between 20 and 80 years old, loss of muscle and bone mass and strength about 25%

Target populations for protein synthesis

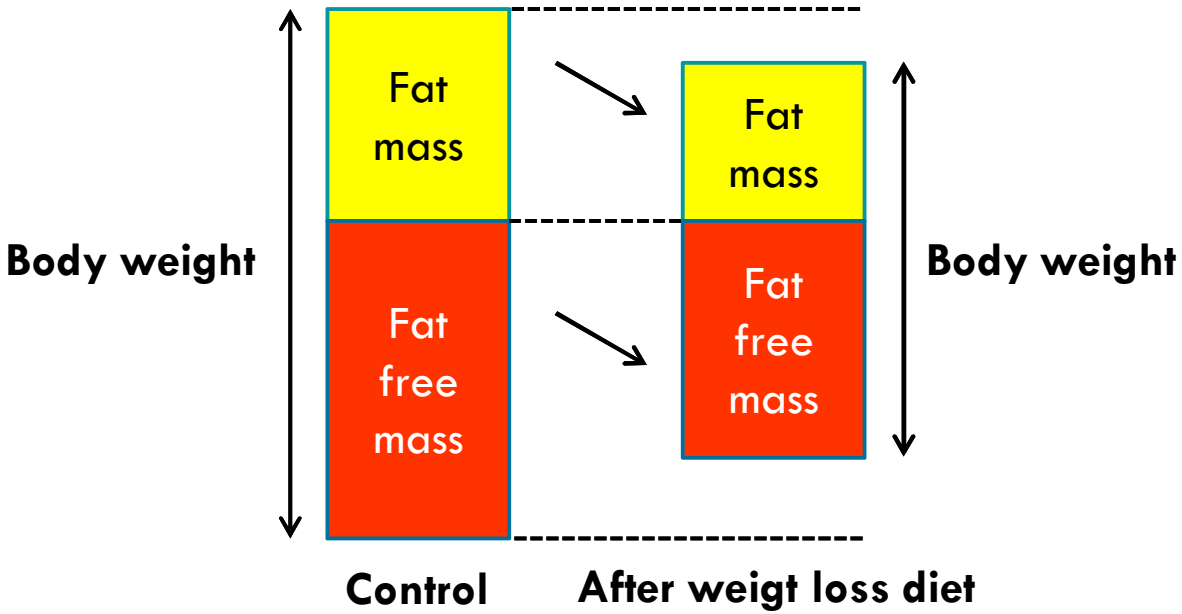


Target populations for protein synthesis

Have already followed a weight loss diet

86 % of women **13% of men**

Etude Nutrinet, **2009**

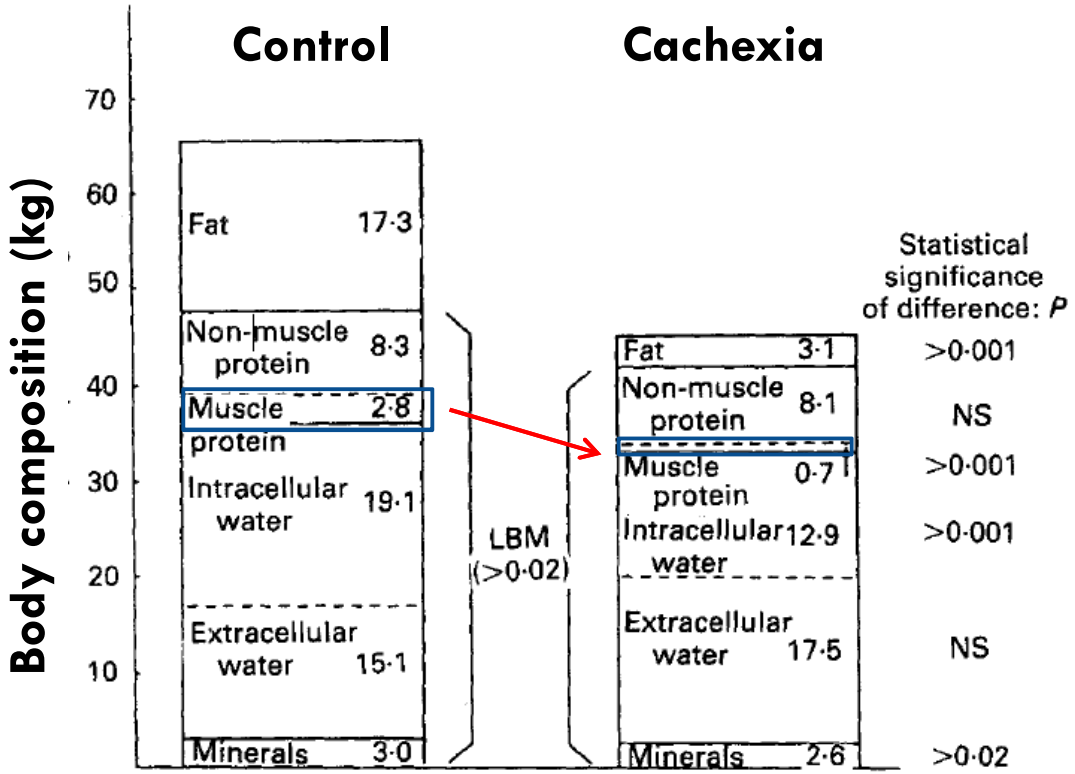


80% of people gain back their weight after one year (Anses, 2010)

Decrease in fat mass and fat-free mass

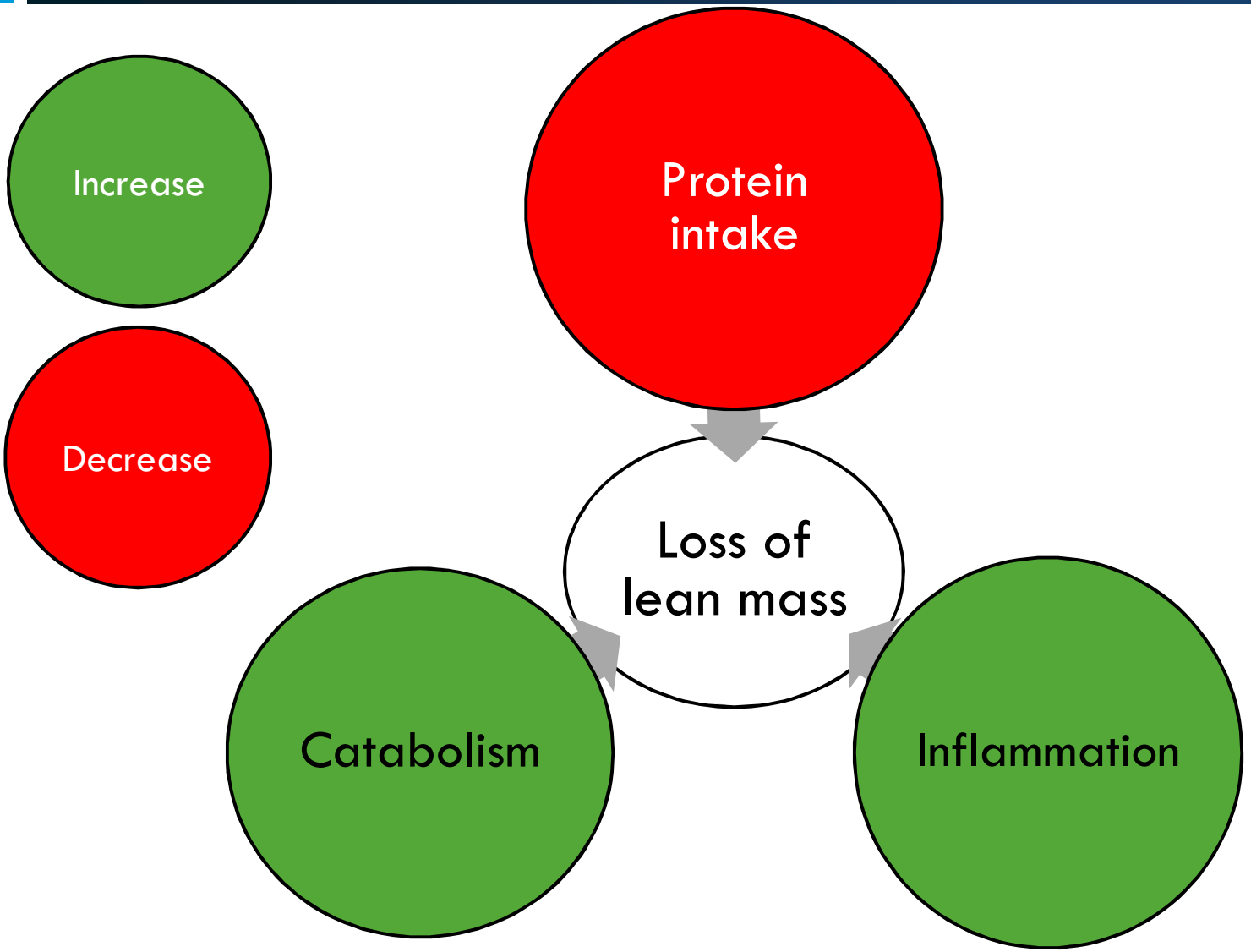
Target populations for protein synthesis

- Cachexia is a syndrome characterized by loss of body weight, particularly of lean body (muscle) mass
- Occurs in nearly 50% of patients with cancer

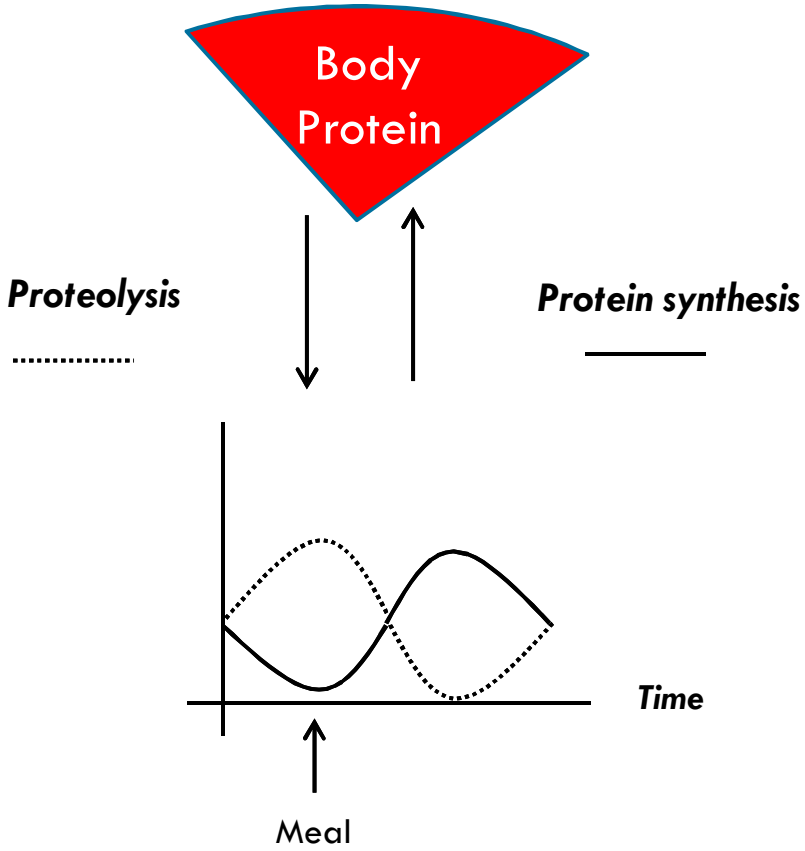


Cuthbertson et al. ***Proceedings of the Nutrition Society, 1992***

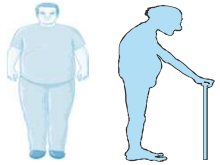
Target populations for protein synthesis

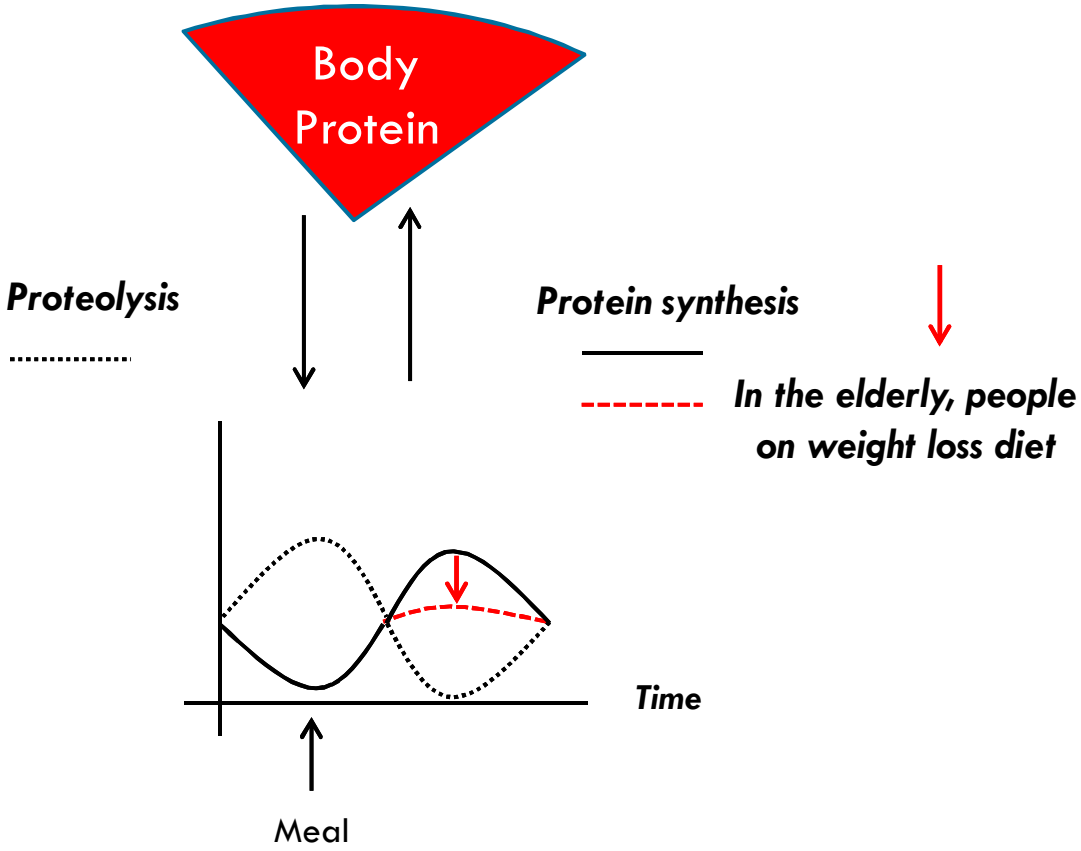


Target populations for protein synthesis



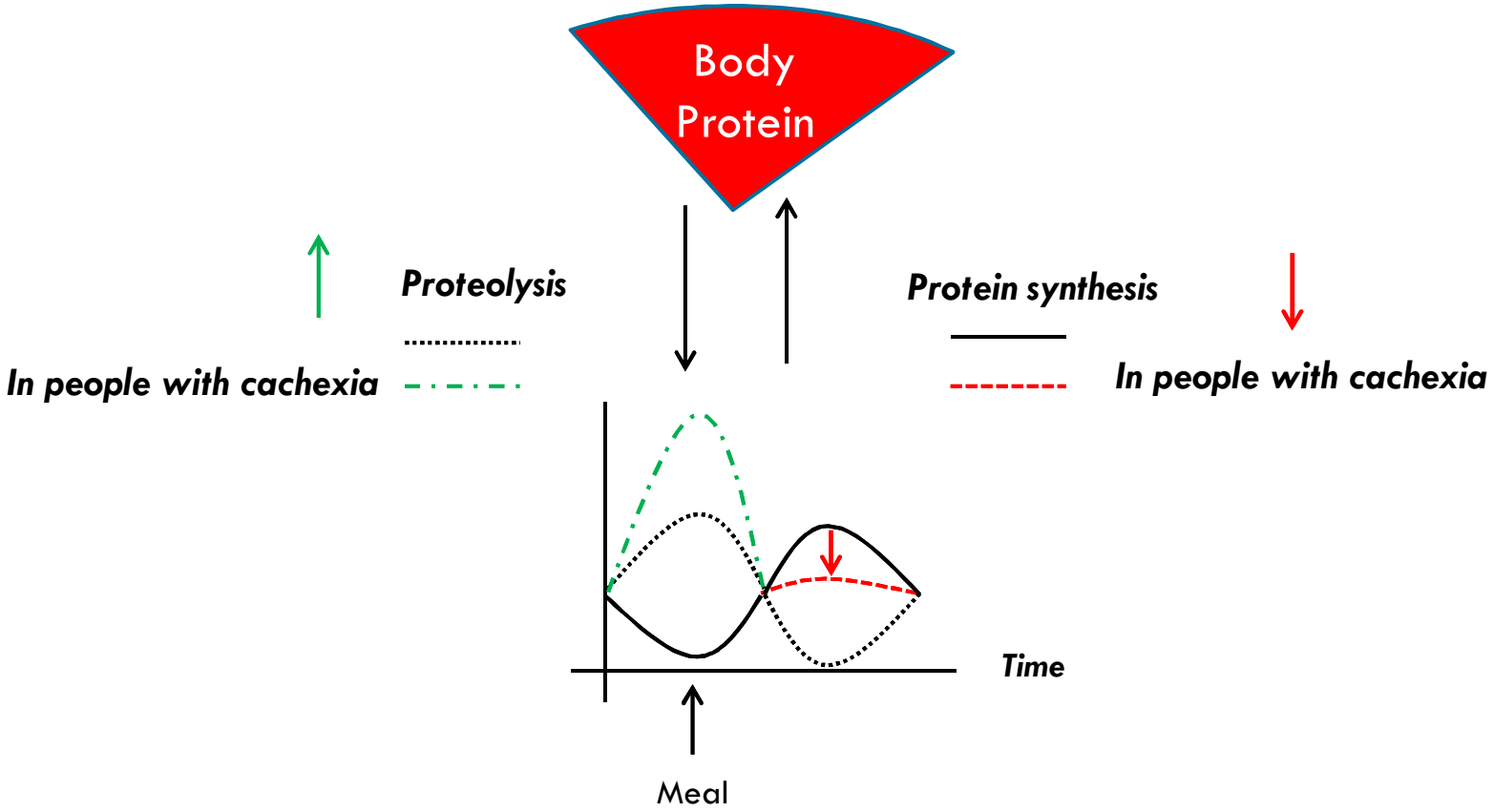
Target populations for protein synthesis





Lower response of protein synthesis

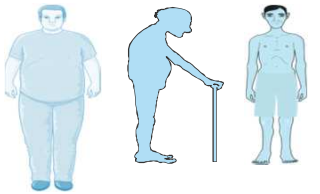
Target populations for protein synthesis

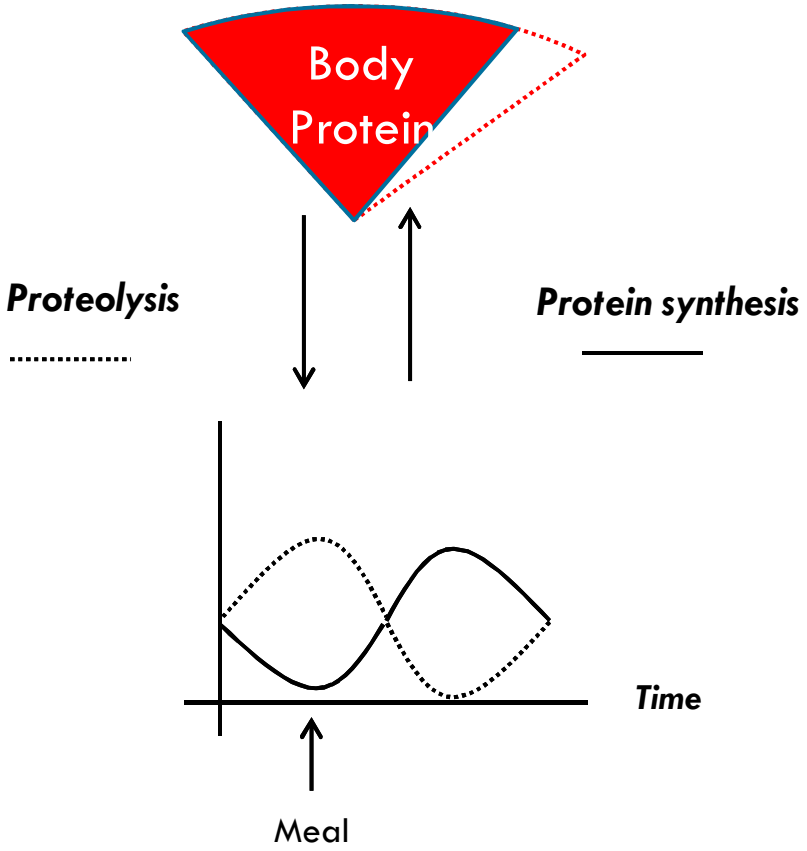


Lower response of protein synthesis and hypercatabolism

Target populations for protein synthesis

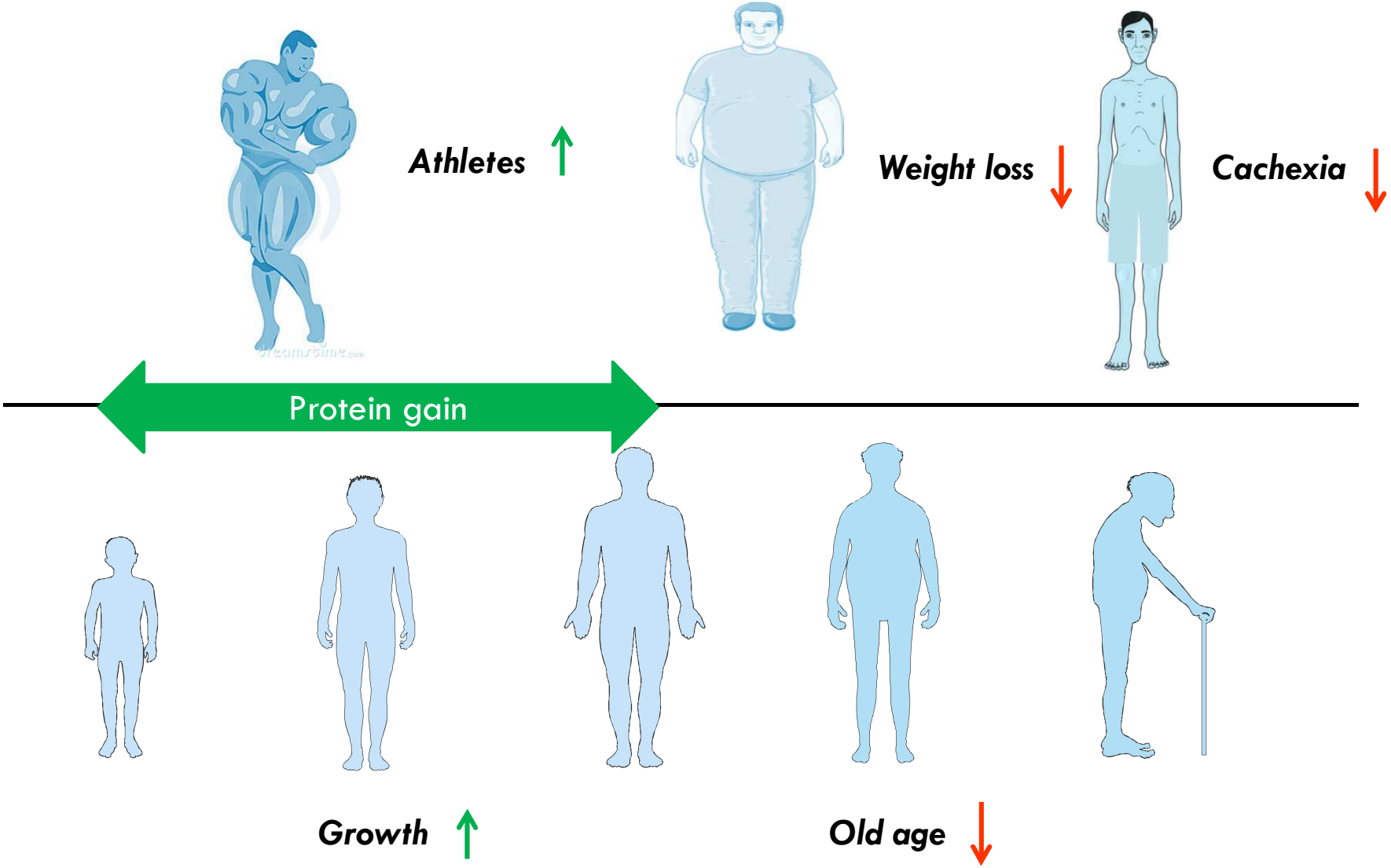
31 **Conclusion on people with protein loss** 26/11





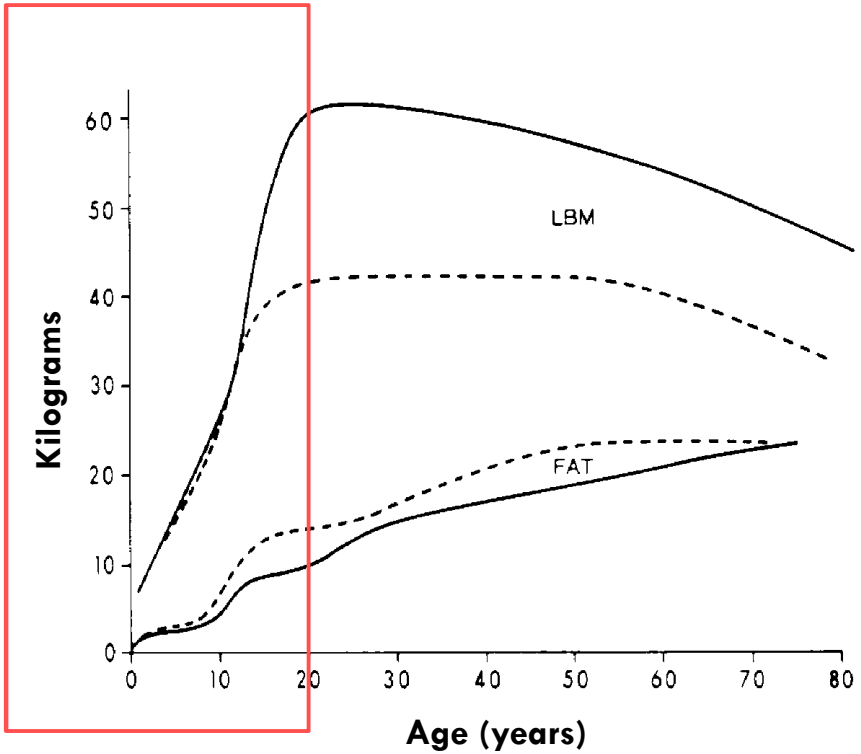
This results in a reduction of body protein

Target populations for protein synthesis



Target populations for protein synthesis

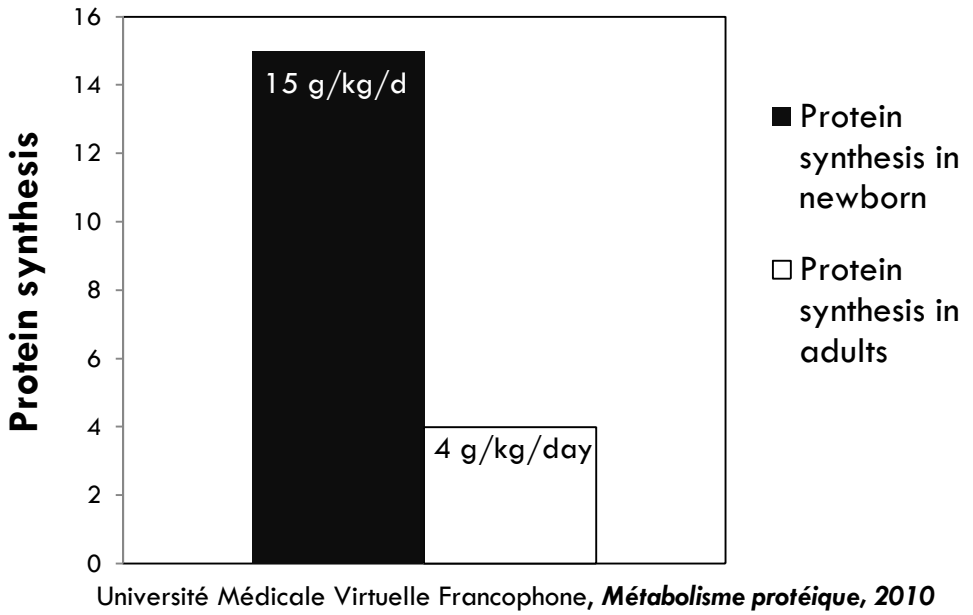
- Infancy is associated with a very high increase in lean body mass compared to other period of life



Forbes et al **Springer,** ***1987***

Target populations for protein synthesis

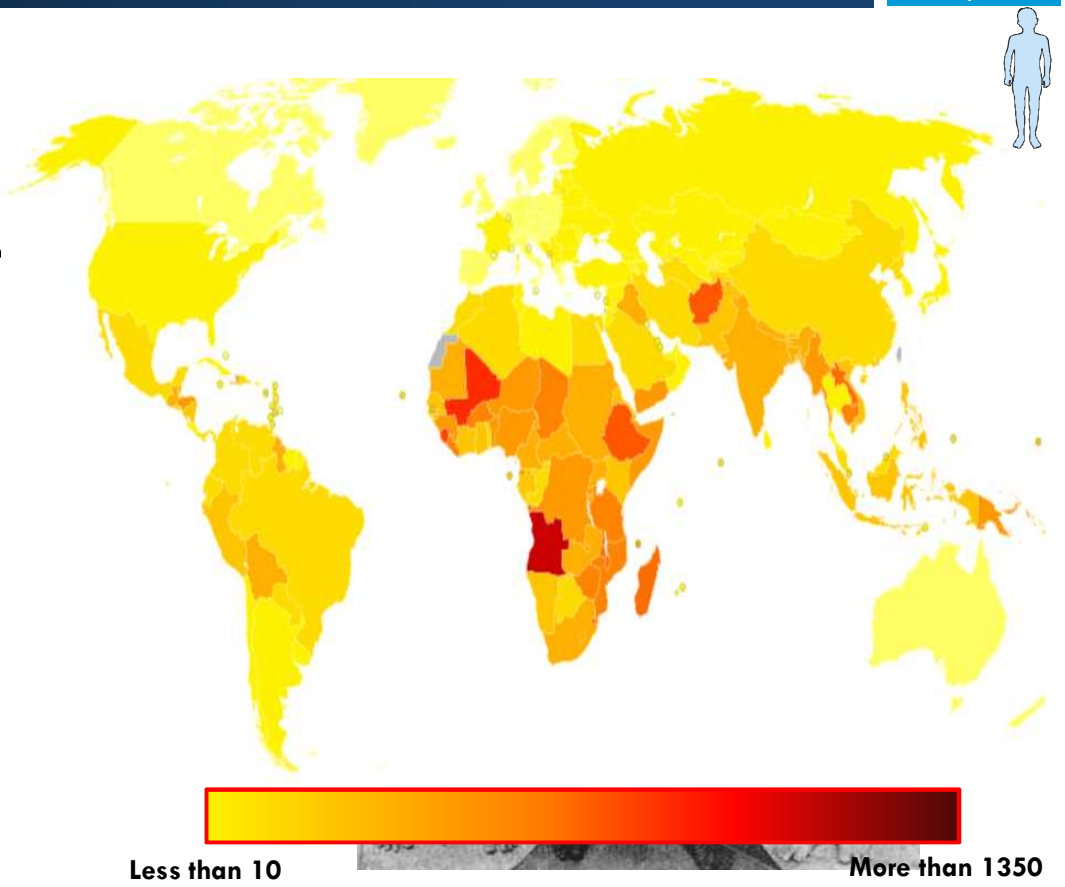
- Infancy is associated with a very high increase in lean body mass compared to other period of life
- This is due to a very high level of protein synthesis and deposition



Université Médicale Virtuelle Francophone, ***Métabolisme protéique, 2010***

Target populations for protein synthesis

- Deficit in protein intake during infancy can be associated with growth retardation
- Kwashiorkor is one a the most common manifestation of this protein malnutrition



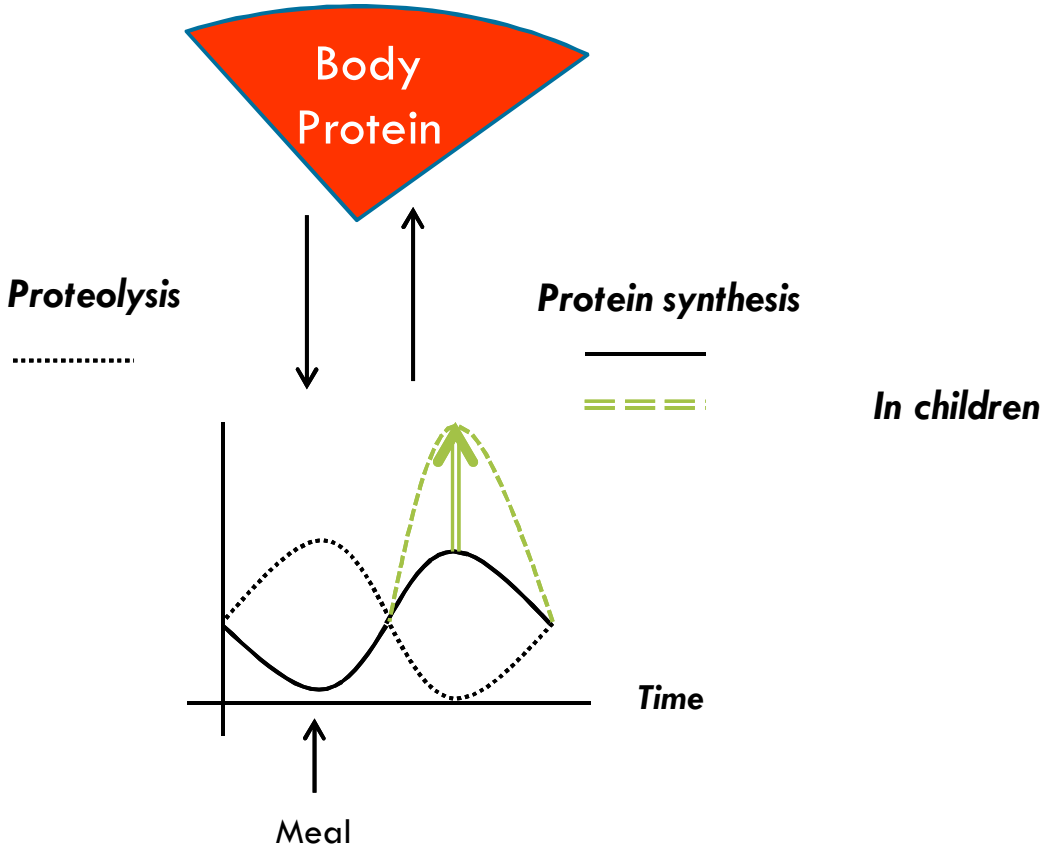
Protein–energy malnutrition per 100,000 inhabitants

FAO, **2004**

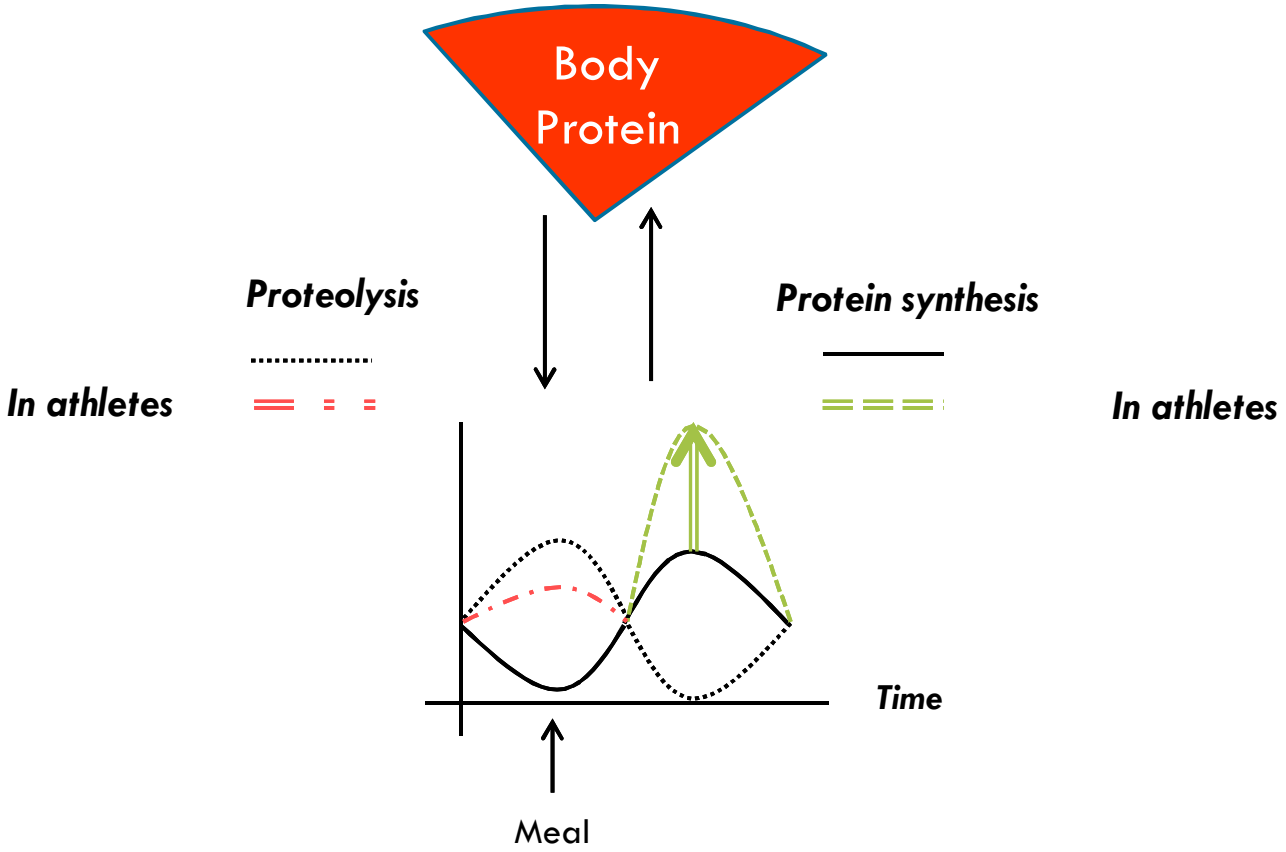
Target populations for protein synthesis

- Athletes can be divided as endurance athletes and strength athletes
- Use of food supplements
- Clinical studies suggest there is no apparent benefit at intakes above 2.0 g/kg per day but potential adverse effects

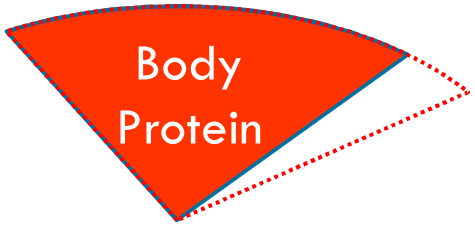
Target populations for protein synthesis



Target populations for protein synthesis

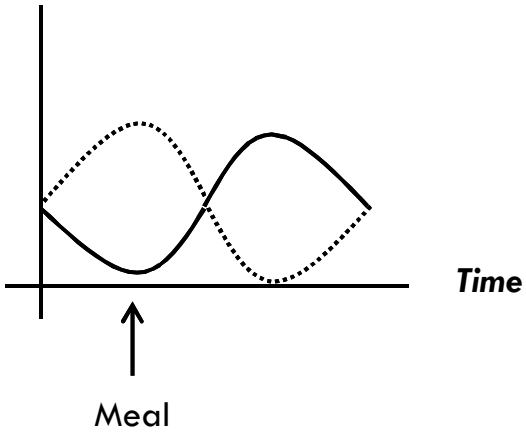


Target populations for protein synthesis



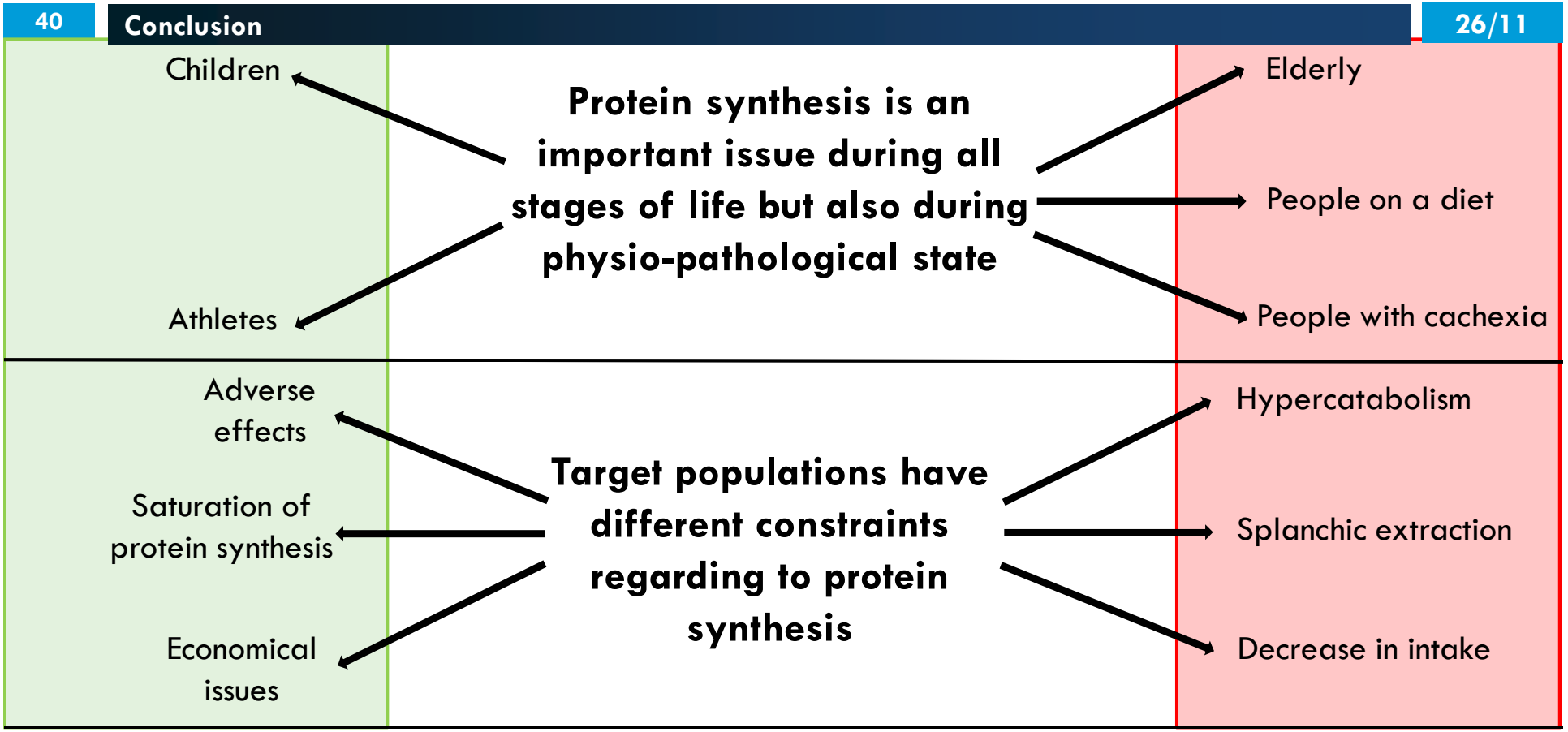
Proteolysis .....

Protein synthesis _____



This results in a reduction of body protein

Target populations for protein synthesis



Which strategy can be used to ensure high protein synthesis in these populations?

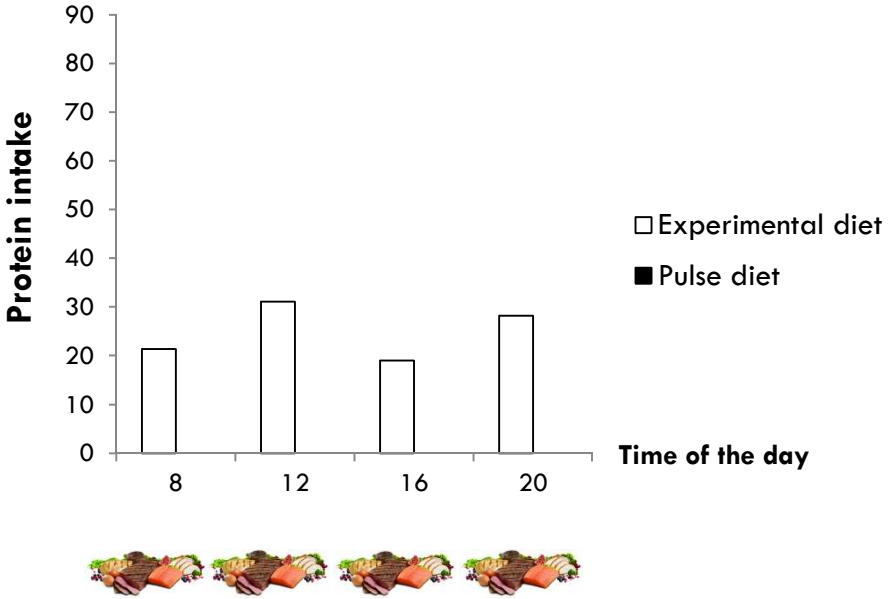
Plan

- Protein metabolism
- Target populations for protein synthesis
- New perspectives on protein synthesis

Target populations for protein synthesis

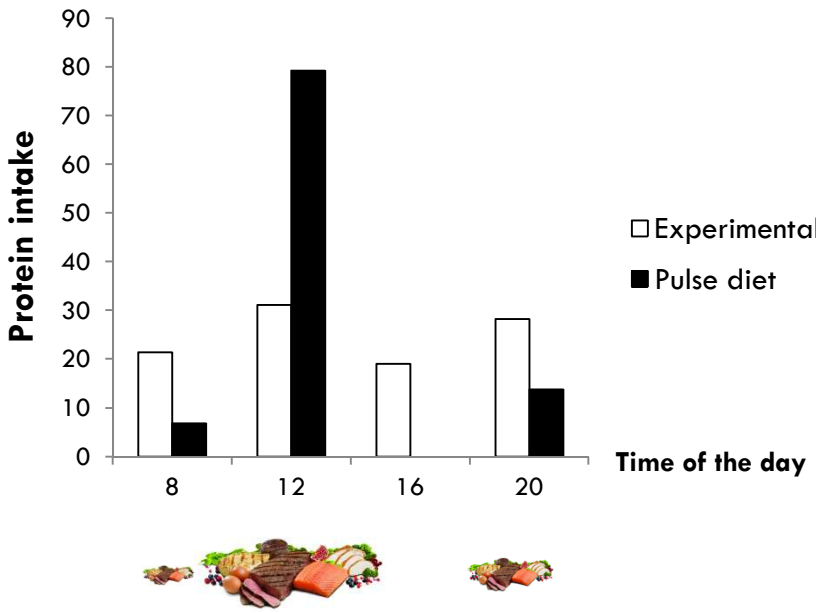
What should be the timing of protein intake during the day to ensure high protein synthesis?

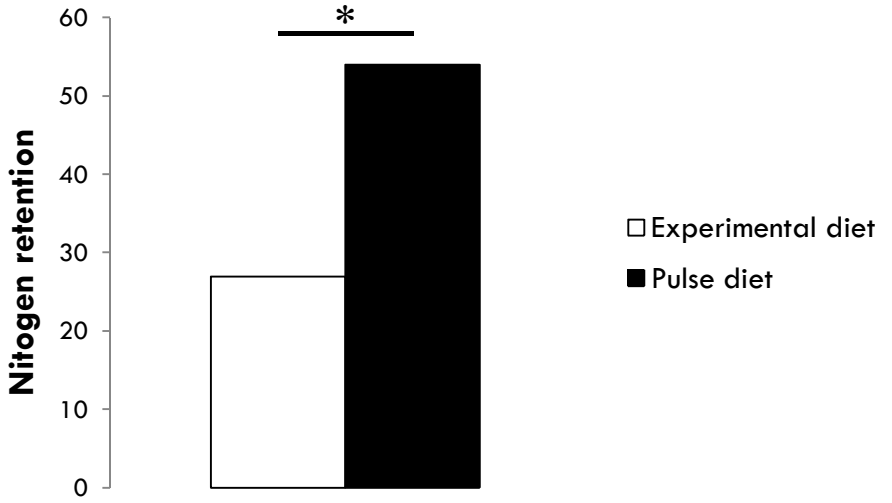
New perspectives on protein synthesis



In elderly women, Arnal et al., **Am J Clin Nutr 1999**

New perspectives on protein synthesis

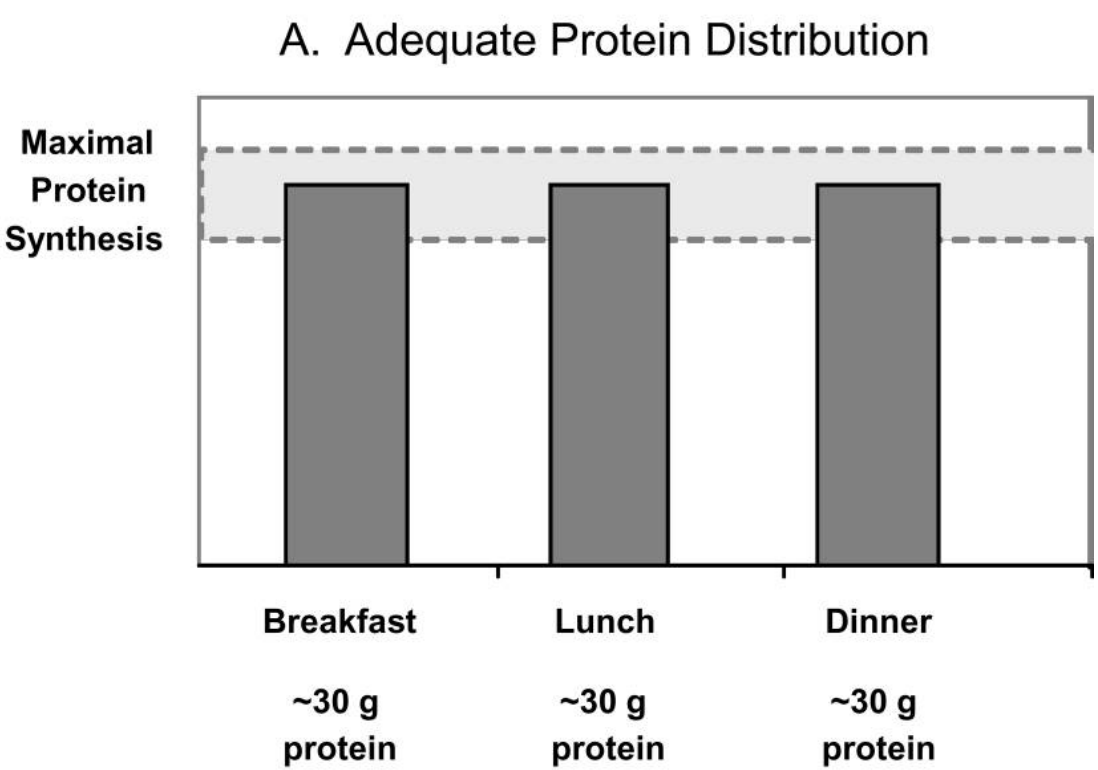




In elderly women, Arnal et al., **Am J Clin Nutr 1999**

Pulse diet allows saturation of splanchnic extraction and therefore amino acids to reach peripheral tissue for protein synthesis .

New perspectives on protein synthesis



In elderly, Paddon-Jones et al., **Curr Opin Clin Nutr Metab Care, 2010**

No consensus on the optimal protein pattern in the elderly.

New perspectives on protein synthesis

Proposed optimal protein meal pattern

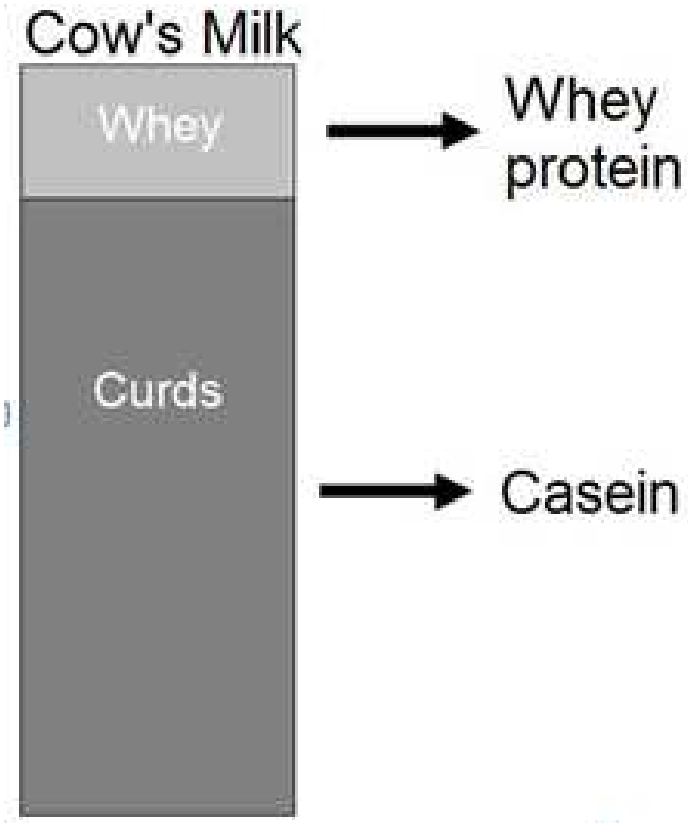
In men, Macnaughton et al. , **The Sport and Exercise Scientist, 2014**

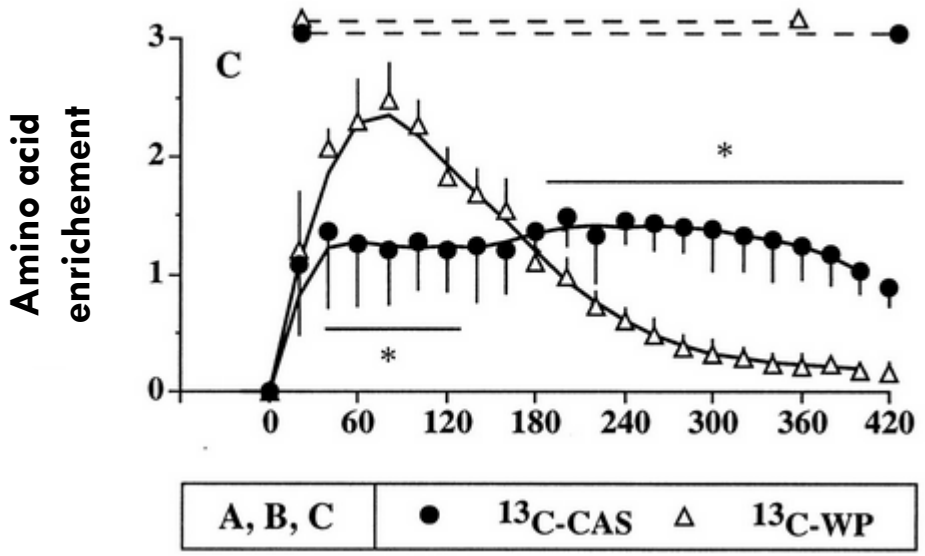
On the contrary to elderly, higher muscle hypertrophy occurs with balanced distribution of protein intake during the day.

New perspectives on protein synthesis

Which types of protein should be eaten to increase protein synthesis?

New perspectives on protein synthesis





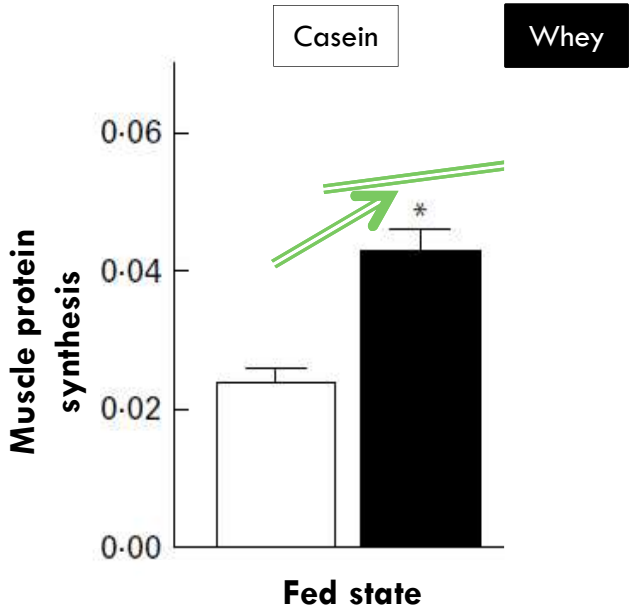
In men, Boirie et al., **Proc Natl Acad Sci, 1997**

Milk protein are composed of whey and casein proteins.

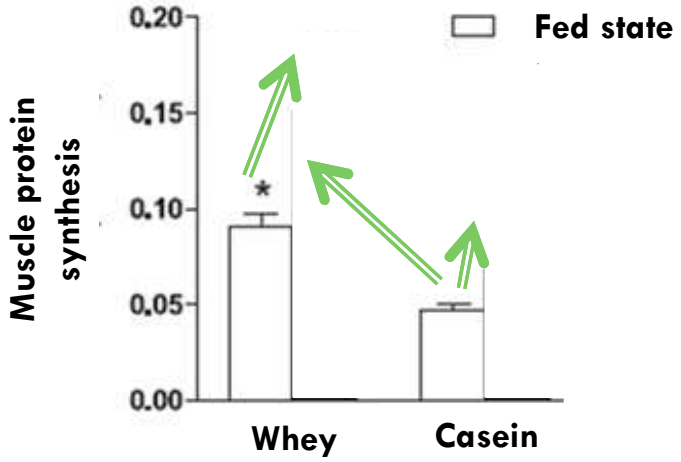
Whey and casein are digested at different kinetics.

New perspectives on protein synthesis

49 **Type of protein** 26/11



In elderly men, Burd et al., **Br J Nutr. 2012**



In men, Tang et al., **Journal of Applied Physiology, 2009**

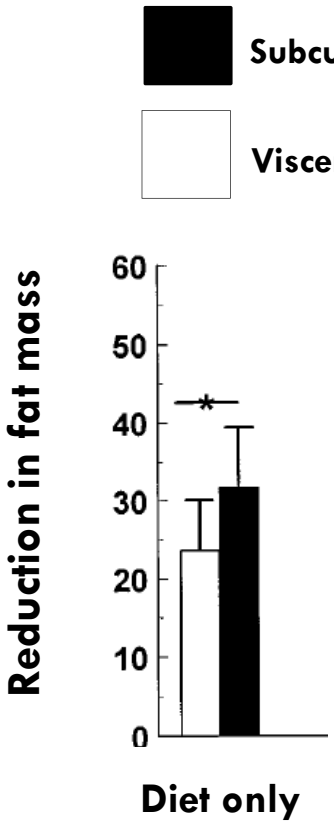
Whey allows higher protein synthesis than casein.

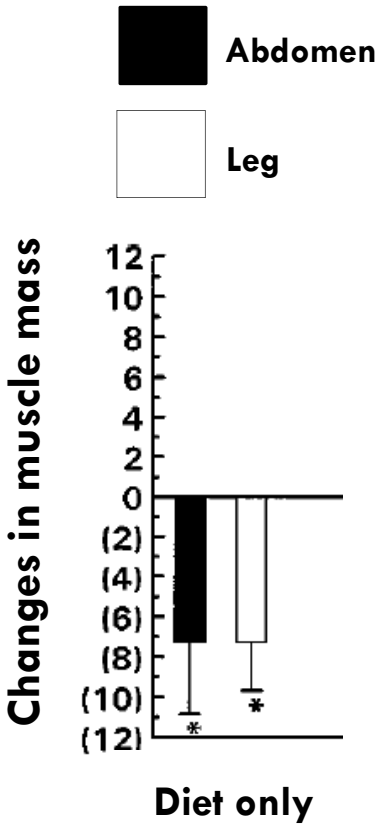
Exercise increases muscle protein synthesis

New perspectives on protein synthesis

Is exercise should be advised to maintain lean body mass?

New perspectives on protein synthesis

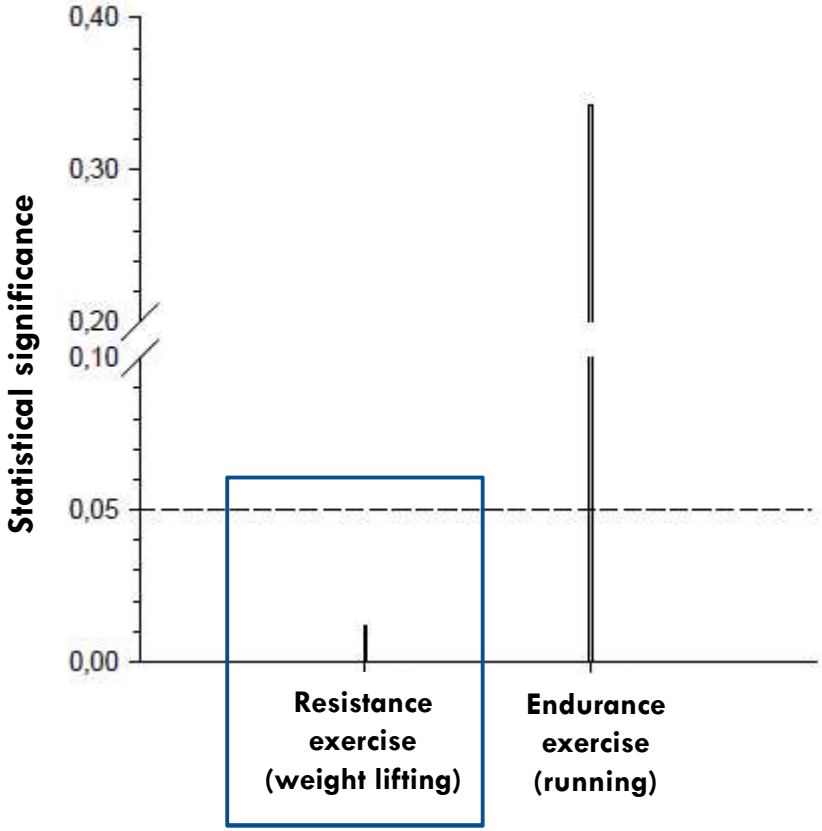




In obese men, Ross et al., **American Physiology society, 1996**

Exercise spares lean mass during weight loss diet

New perspectives on protein synthesis



- Muscle volume
- Muscle strength

- Muscle volume
- Muscle strength

In people with Cachexia, Perniconi et al., ***Basic Applied Myology*, 2008**

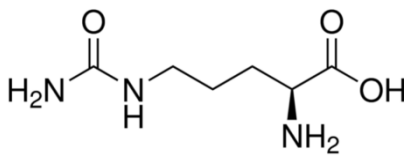
Resistance exercise spares lean mass in people with cachexia

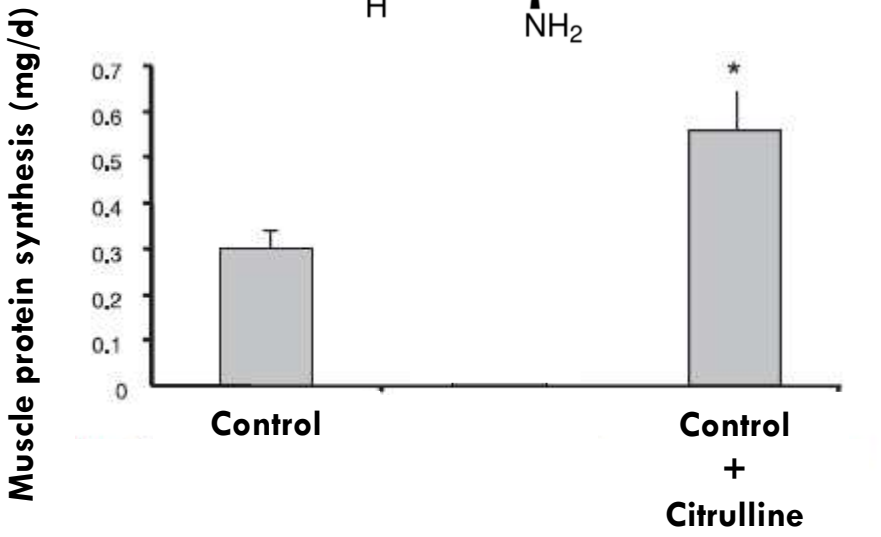
New perspectives on protein synthesis

Does amino acid supplementation increase protein synthesis?

New perspectives on protein synthesis

Citrulline

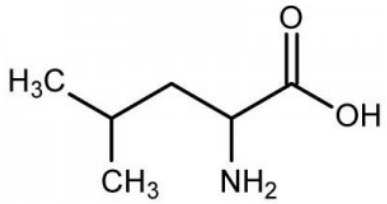


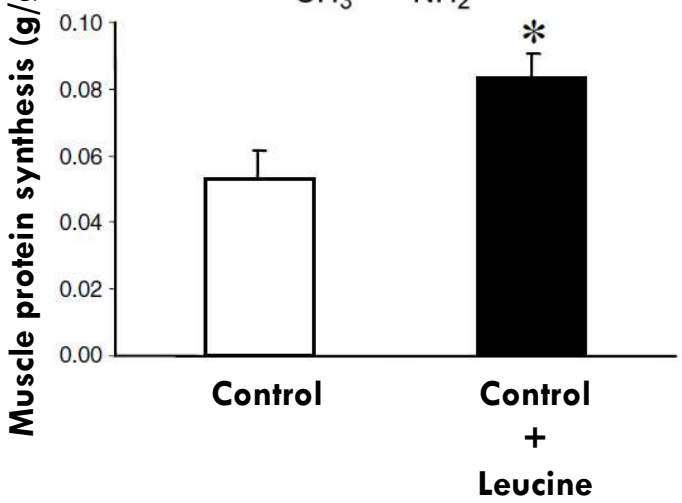


In old rats, Osowska et al., **AJP-Endo 2006**

- Non-proteinogenic, precursor of arginine
- Citrulline is not subject to splanchnic extraction
- Evidence in humans are scarce

Leucine

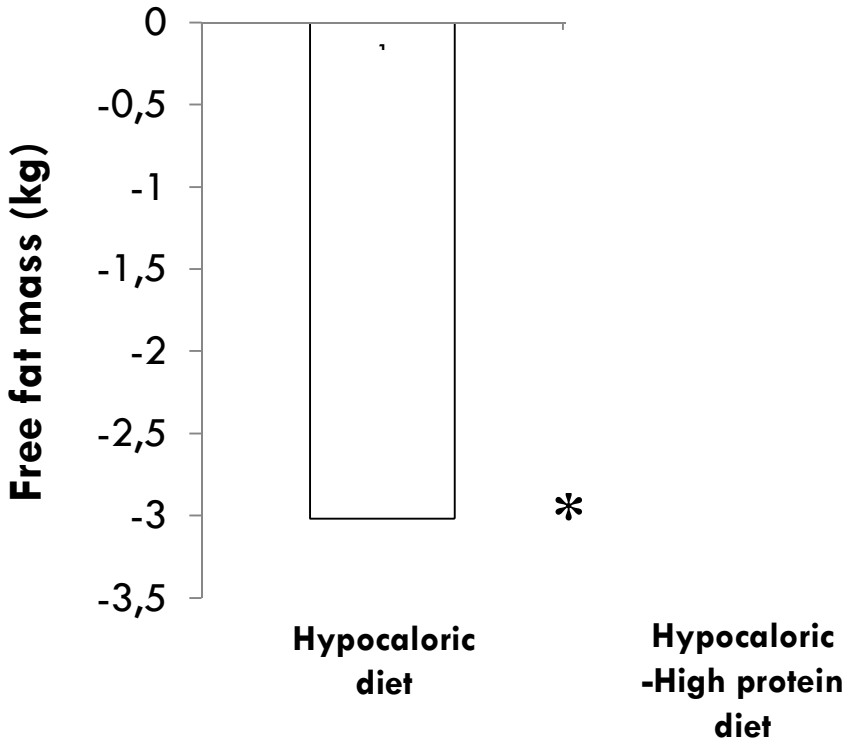




In elderly men, Rieu, **J. Phisiology 2006**

- Moderate splanchnic extraction
- High anabolic action (BCAA)

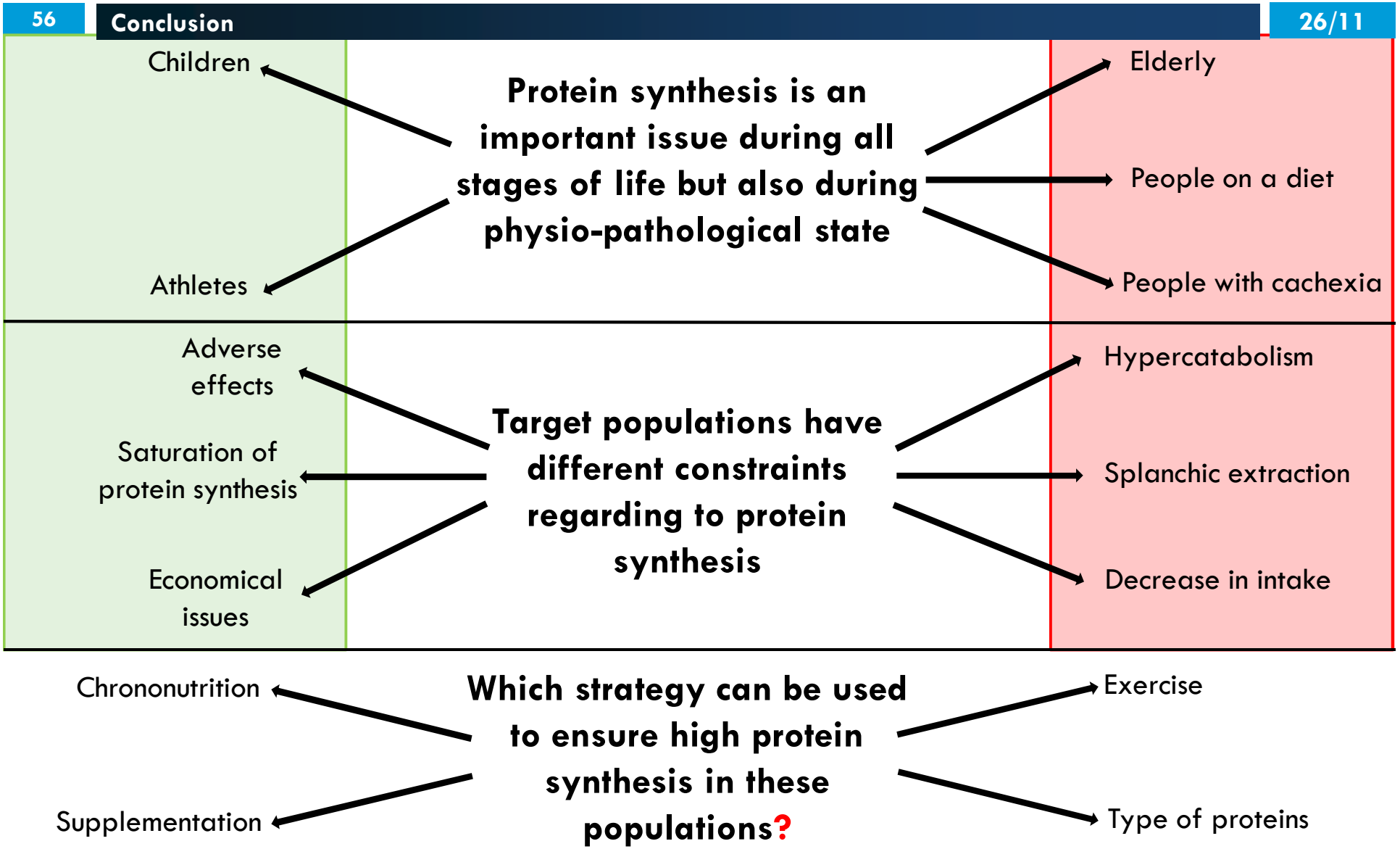
Target populations for protein synthesis



In women, Piatti et al., **Metabolism**, 1994

High protein diet spares lean mass during diet

Target populations for protein synthesis



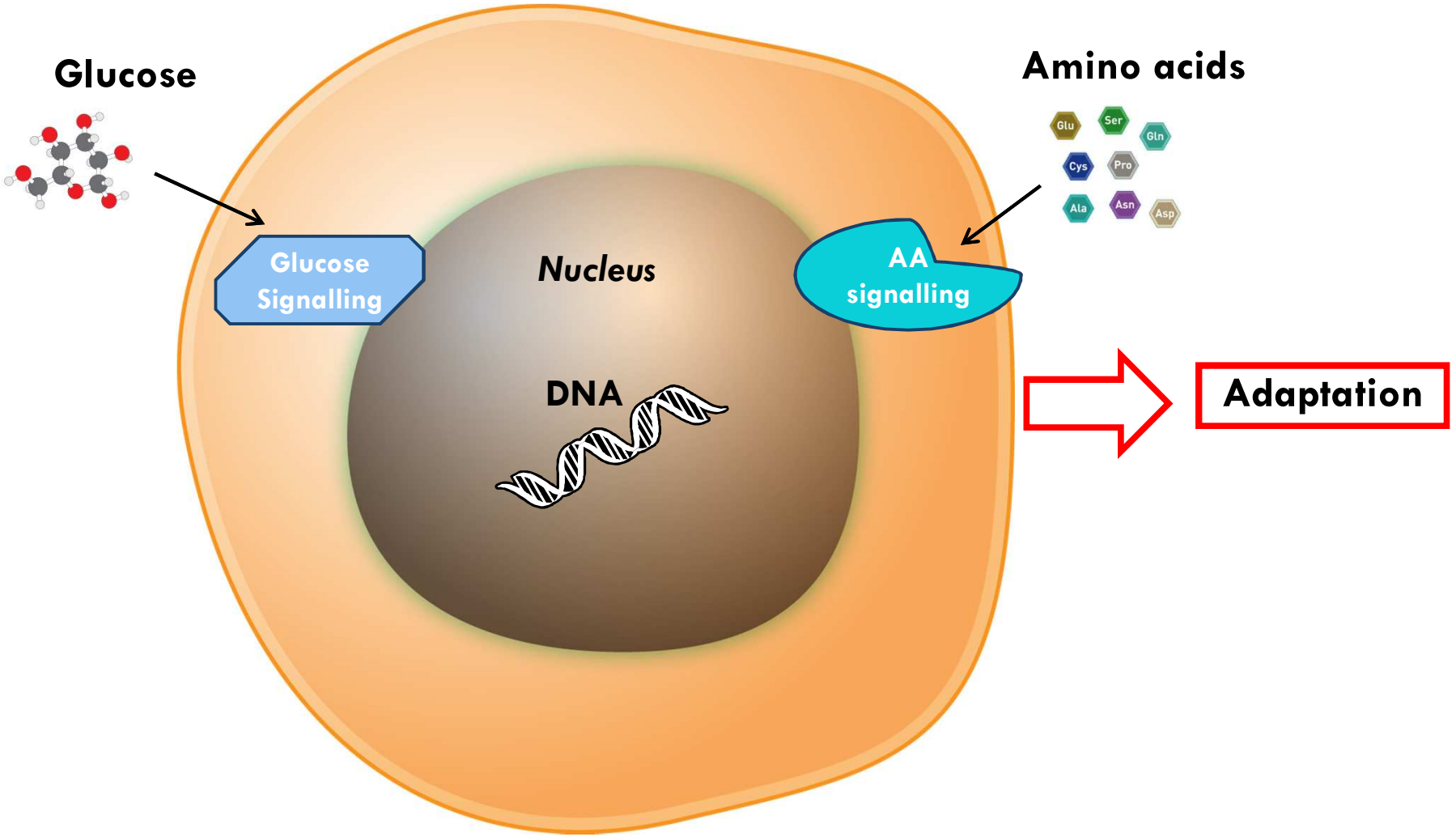
New perspectives on protein synthesis

Protein quality is calculated with PDCAAS or DIAAS

These methods have strong limitations

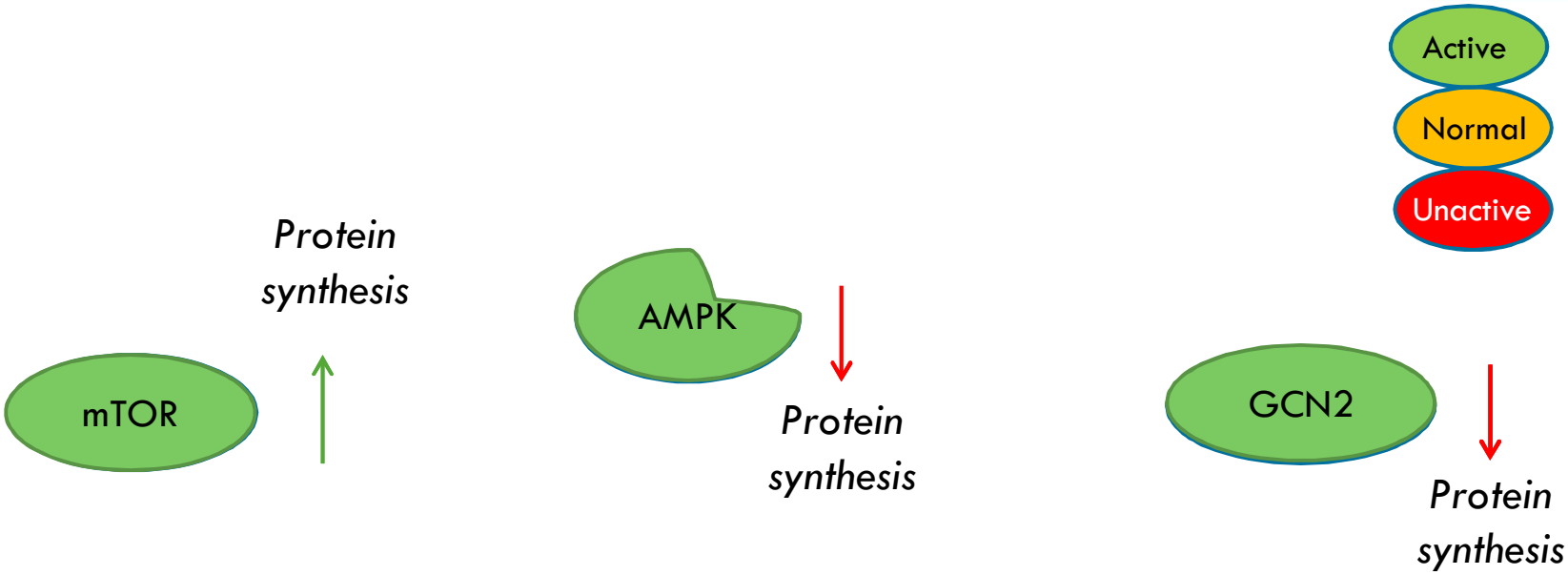
Are there physiological markers of protein quality in these different populations?

New perspectives on protein synthesis



New perspectives on protein synthesis

59 **Role of kinases in protein synthesis** 26/11

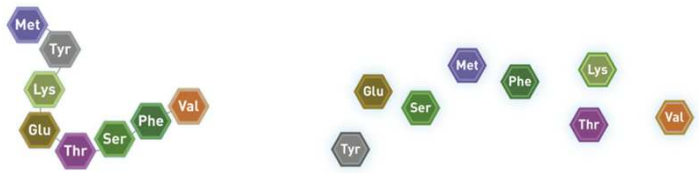


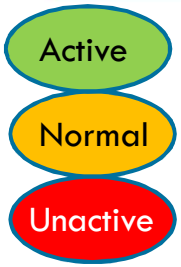
An activation of mTOR and a deactivation of AMPK and GCN2 allows protein synthesis.

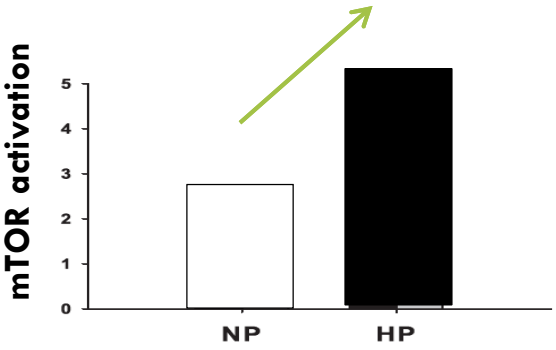
These proteins are also involved in amino acid signalling.

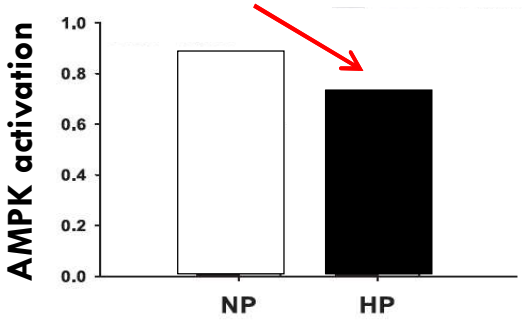
New perspectives on protein synthesis

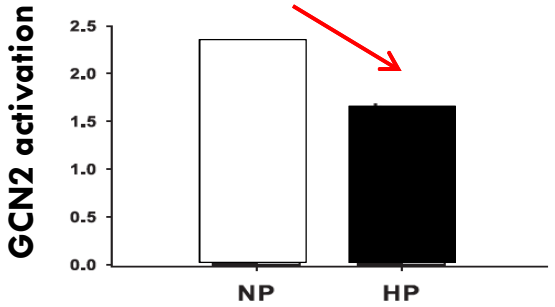
In the liver







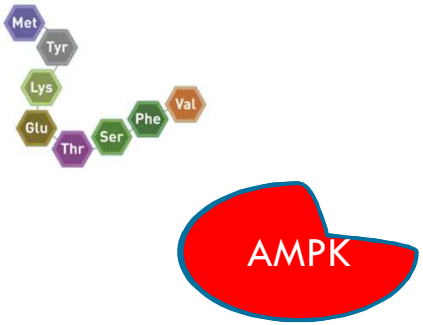


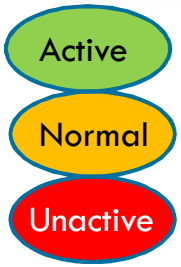


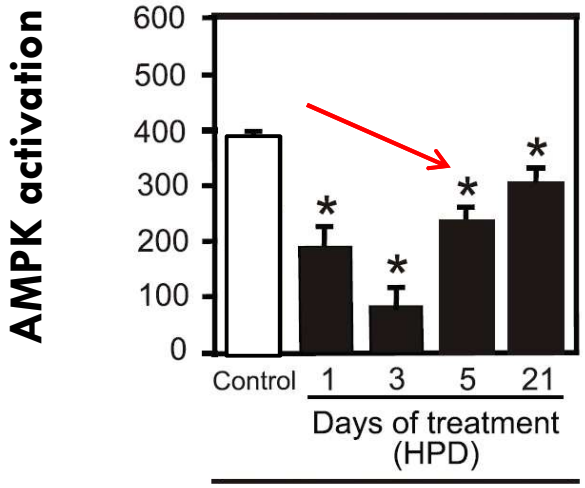
In rats, Chotechuang, **AJP-endo, 2009**

New perspectives on protein synthesis

In the brain



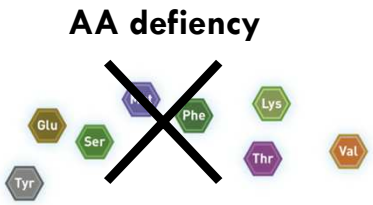


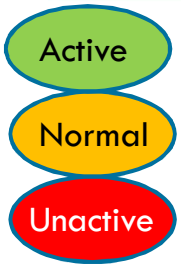


In rats, Ropelle et al. , **Diabetes, 2011**

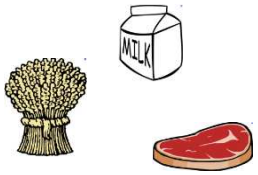
New perspectives on protein synthesis

In the liver



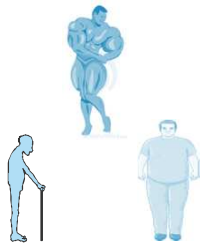


The ability of a meal or a protein to induce mTOR activity and to reduce GCN2 and AMPK activities could therefore indicate its capacity to stimulate protein synthesis.



Type of proteins

Period of the day



Physiopathological state

In rats, Xiao et al. , **Diabetes, 2011**

New perspectives on protein synthesis

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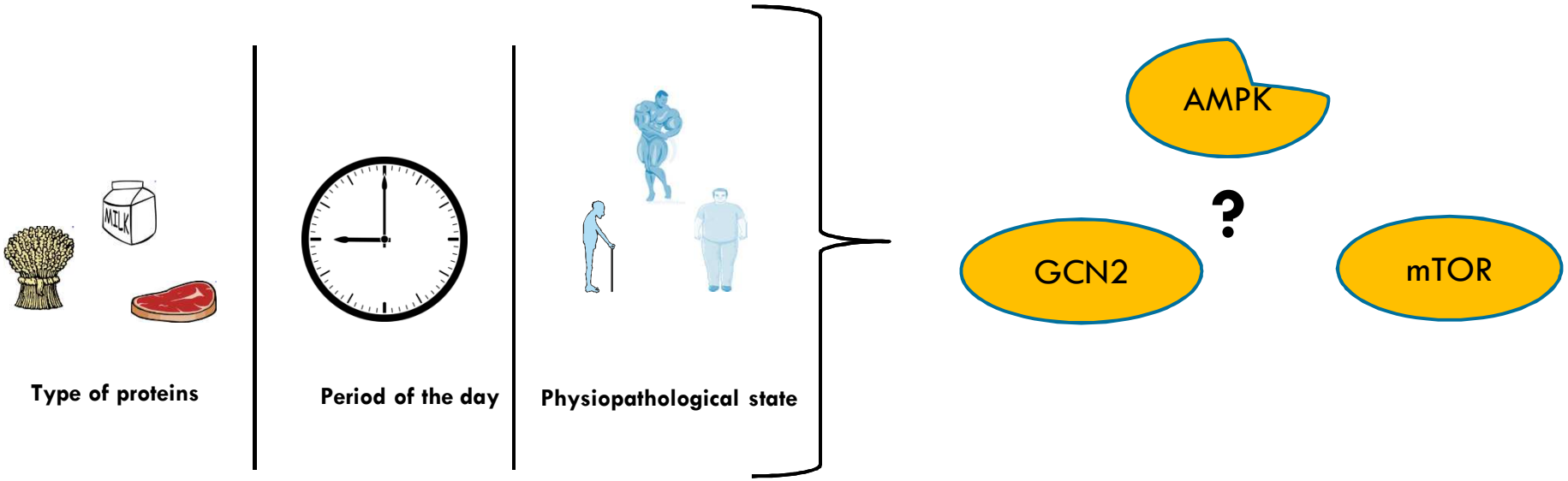

New perspectives on protein synthesis

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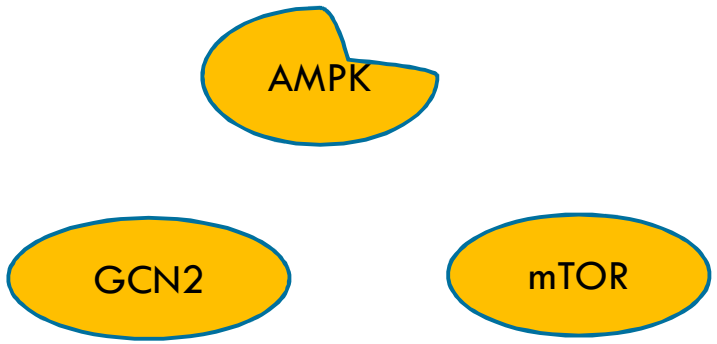
Are there physiological markers of protein quality in these different populations?

Signalling molecules



GRACIAS, ¿PREGUNTAS?

tristan.chalvon-demersay@agroparistech.fr