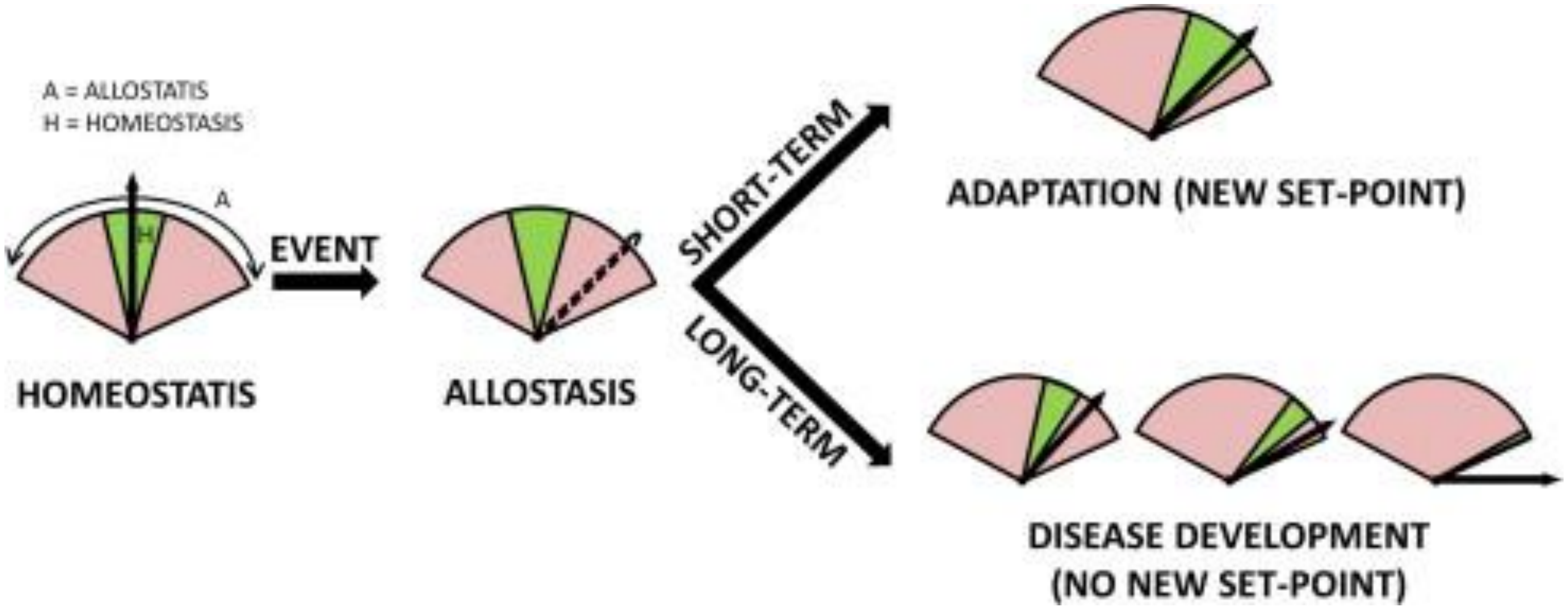
MUNI
MED

Energy metabolism

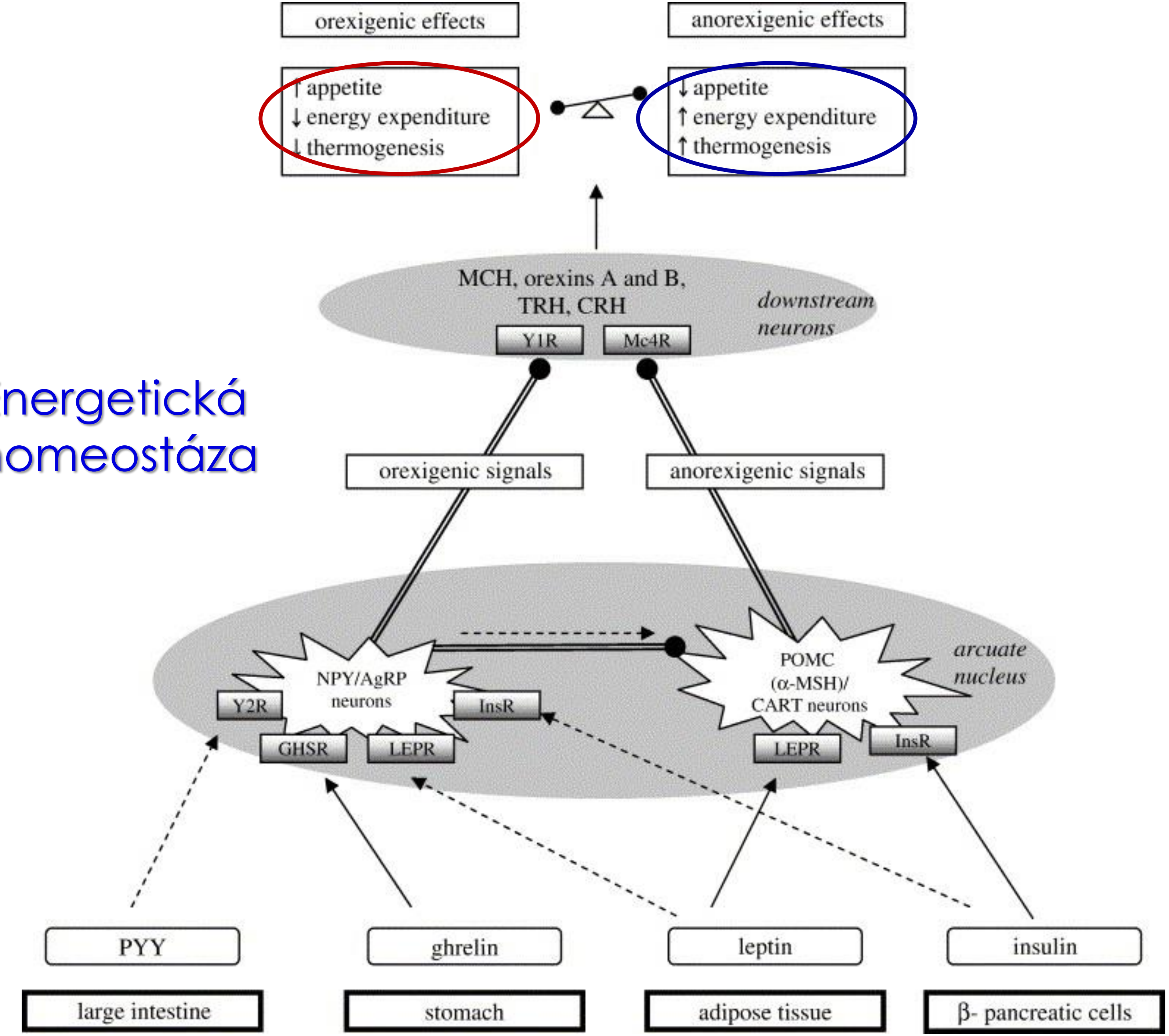
NiP-1
28. 2. 2025

 Prof. Anna Vašků



Bienertová-Vašků J, Zlámal F, Nečesánek I, Konečný D, Vasku A.
PLoS One. 2016 Jan 15;11(1)

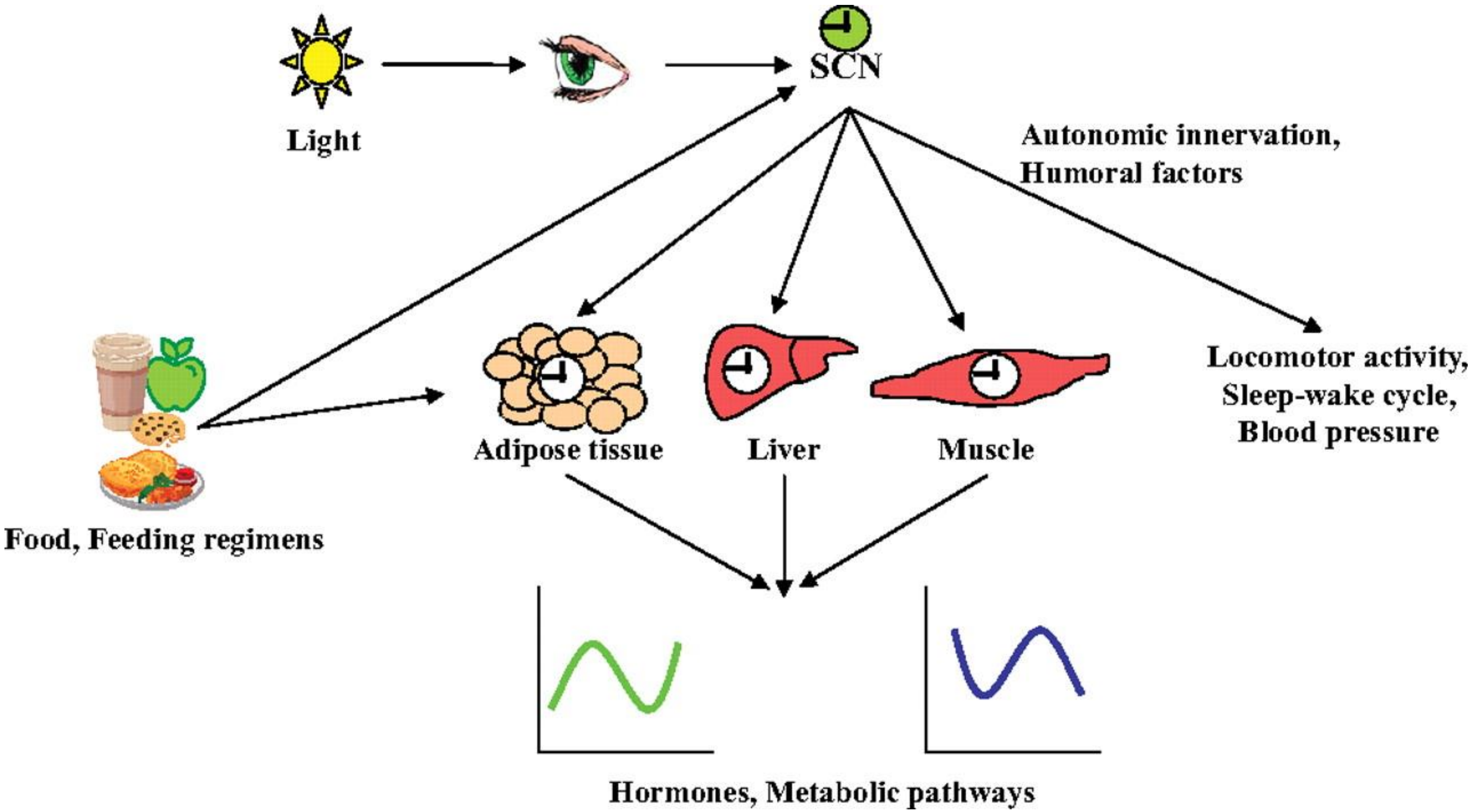
Energetická homeostáza



Energy metabolism

- \- most food compounds are used as a energy source
- 1g of sugars 17.22kJ
- 1g of lipids 39.06kJ
- 1g of proteins 23.73kJ

Resetting signals of the central and peripheral clocks.



Froy O Endocrine Reviews 2010;31:1-24

ENDOCRINE
REVIEWS

Regulation of metabolic processes

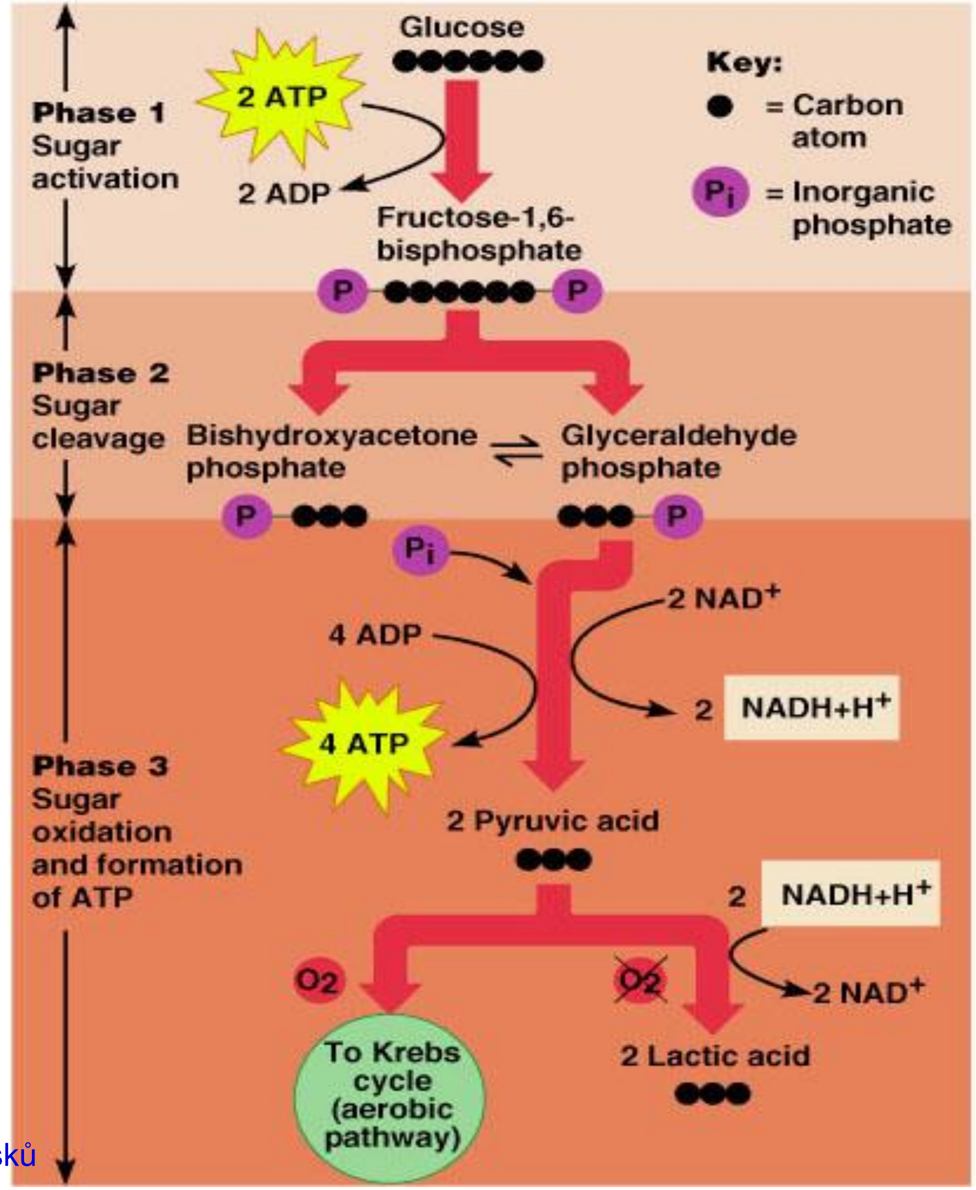
Neuro-immuno-endocrine regulation using hormones: (insulin, glucagon, growth hormone, glucocorticoids, T4 and T3, reproduction hormones:

- ✓ Liver
- ✓ Adipose tissue
- ✓ Skin
- ✓ Kidneys
- ✓ Respiratory and cardiovascular system

MUNI MED

Nutrient	Compound	Transcription factor
Macronutrients		
Fats	Fatty acids	PPARs, SREBPs, LXR, HNF4, ChREBP
	Cholesterol	SREBPs, LXRs, FXR
Carbohydrates	Glucose	USFs, SREBPs, ChREBP
Proteins	Amino acids	C/EBPs
Micronutrients		
Vitamins	Vitamin A	RAR, RXR
	Vitamin D	VDR
	Vitamin E	PXR
Minerals	Calcium	Calcineurin/NF-ATs
	Iron	IRP1, IRP2
	Zinc	MTF1
Other food components		
	Flavonoids	ER, NFκB, AP1
	Xenobiotics	CAR, PXR

Glycolysis



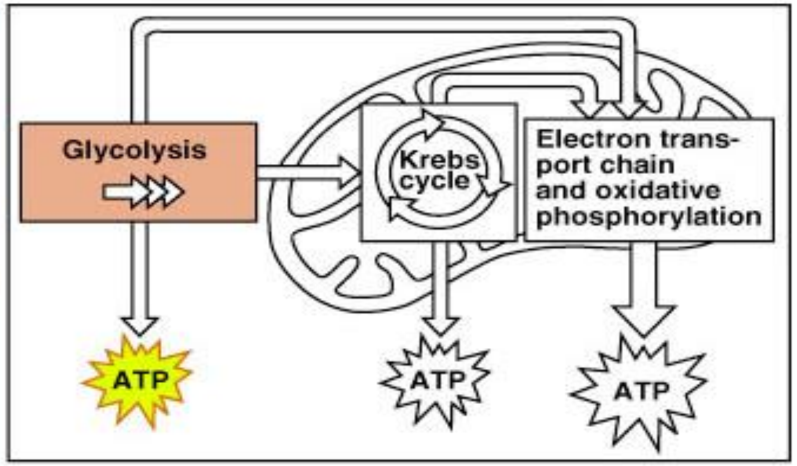
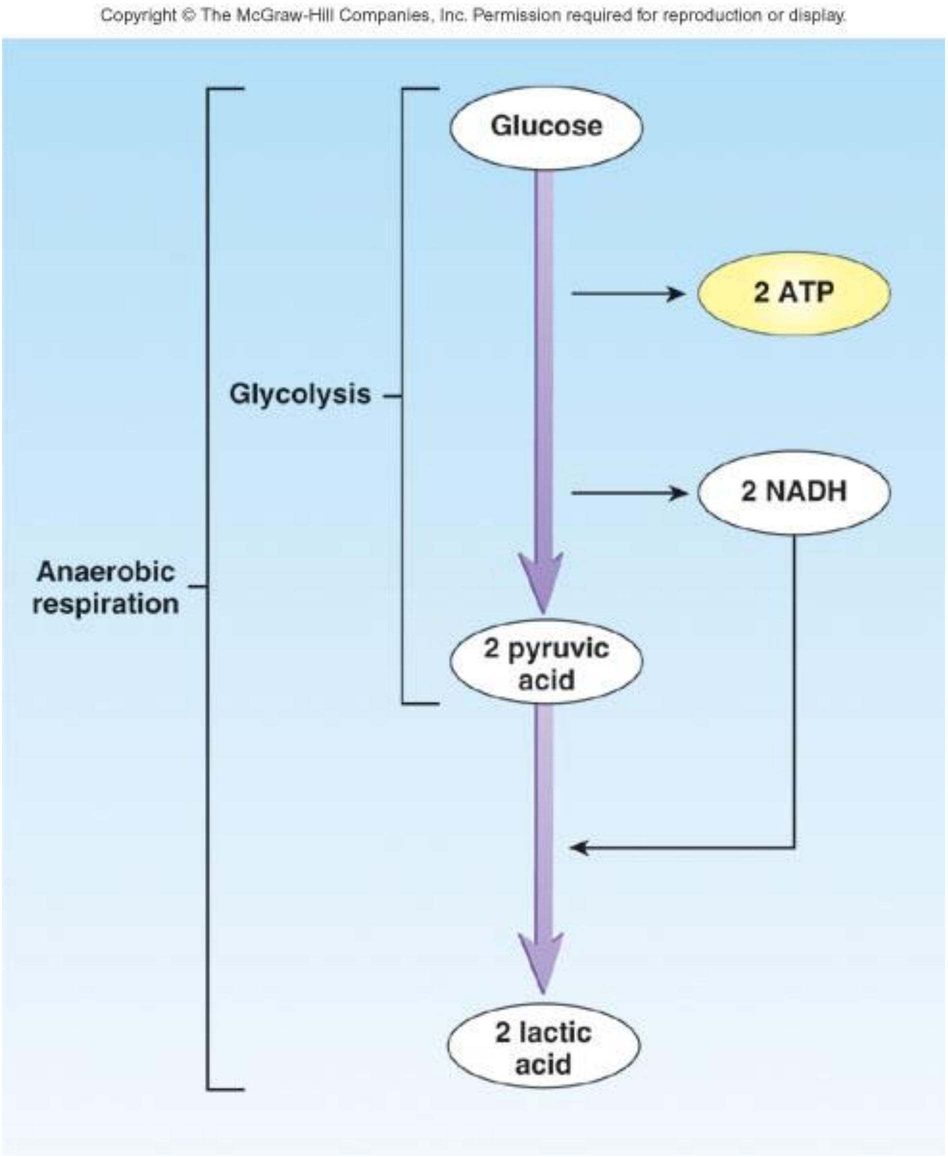
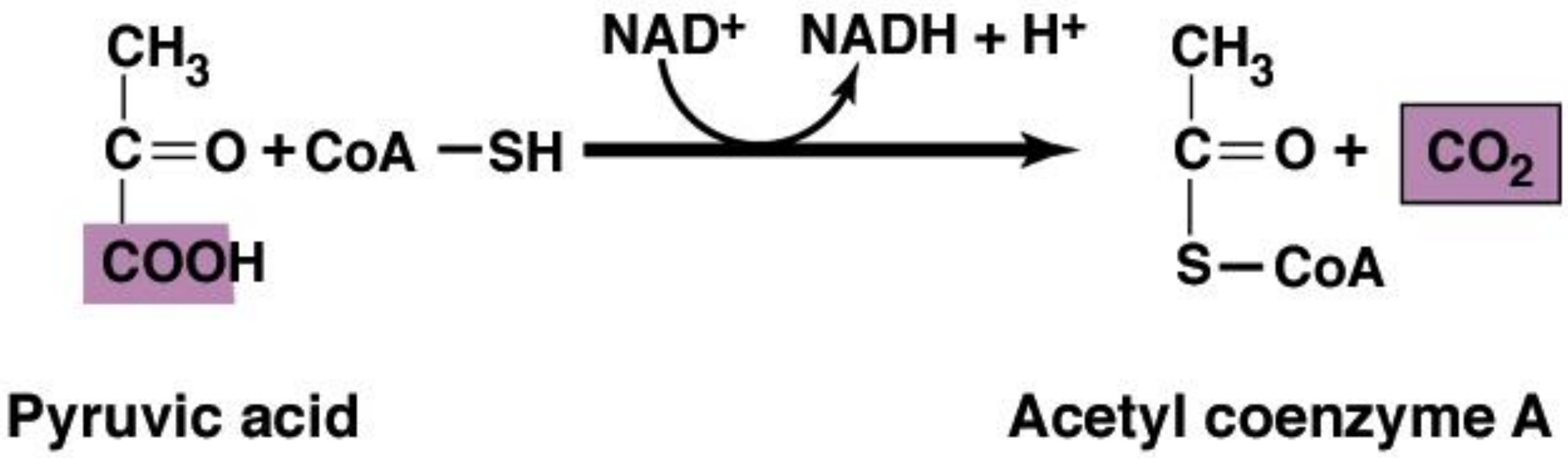


Figure 24.6

TABLE 3–8	Characteristics of Glycolysis
Entering substrates	Glucose and other monosaccharides
Enzyme location	Cytosol
Net ATP production	2 ATP formed directly per molecule of glucose entering pathway can be produced in the absence of oxygen (anaerobically)
Coenzyme production	2 NADH + 2 H^+ formed under aerobic conditions
Final products	Pyruvate—under aerobic conditions Lactate—under anaerobic conditions
Net reaction	
Aerobic:	Glucose + 2 ADP + 2 P_i + 2 NAD^+ $\longrightarrow$ 2 pyruvate + 2 ATP + 2 NADH + 2 H^+ + 2 H_2O
Anaerobic:	Glucose + 2 ADP + 2 P_i $\longrightarrow$ 2 lactate + 2 ATP + 2 H_2O

Anaerobic respiration





Each transition of pyruvate to acetyl coenzyme A yields one NADH and one CO_2.

The acetyl coenzyme A then enters the Krebs cycle.

Krebs cycle

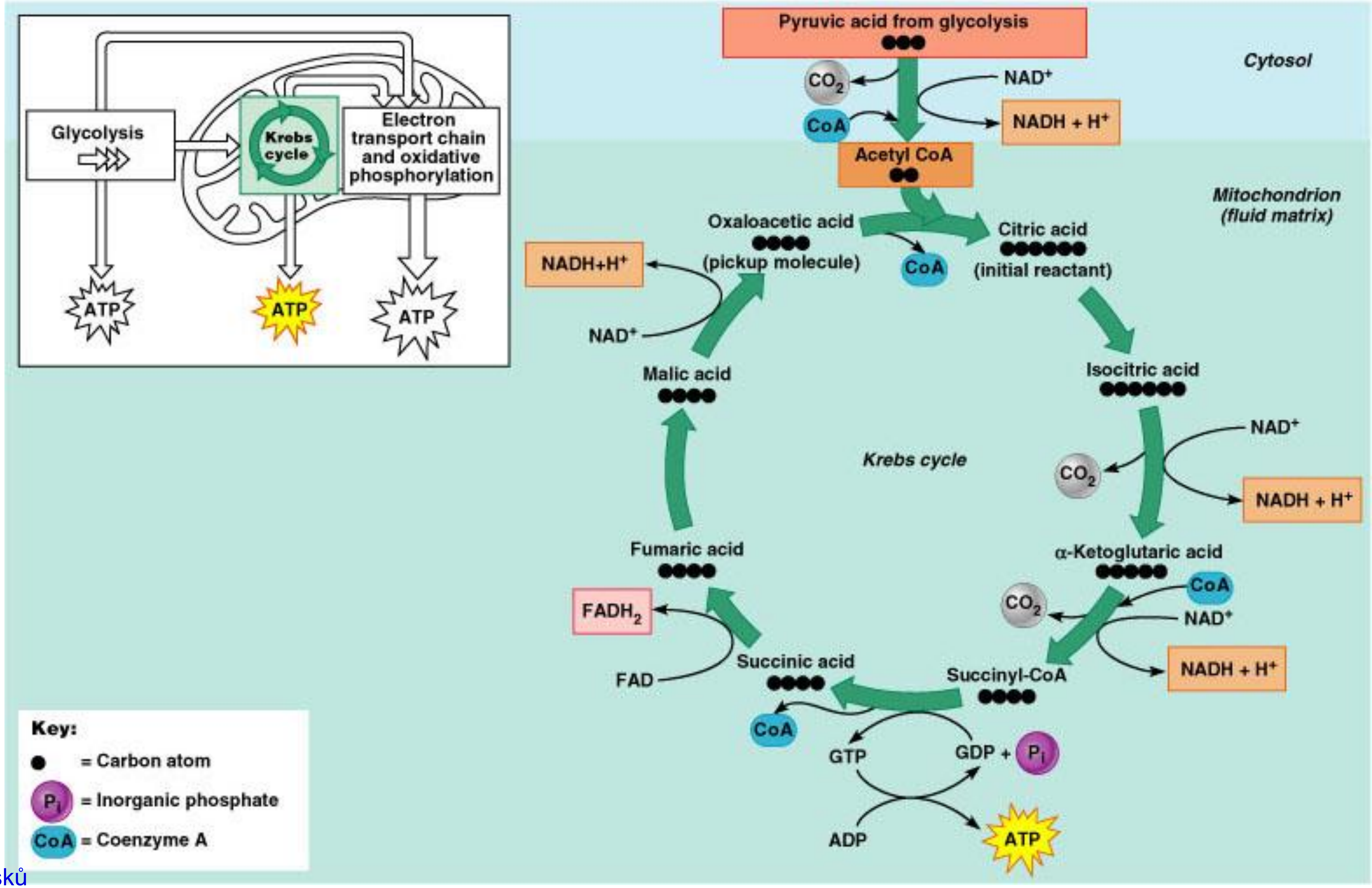
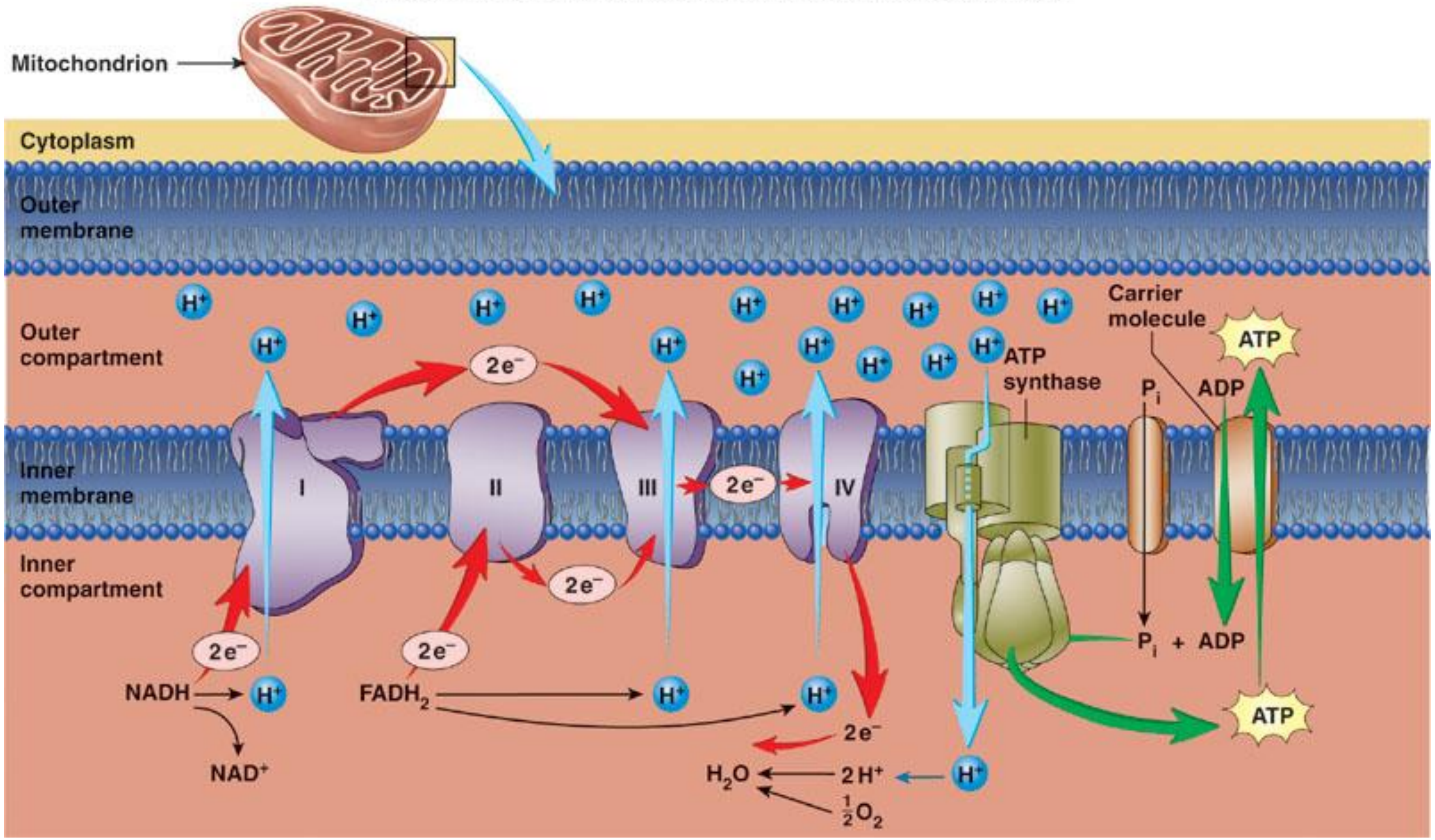


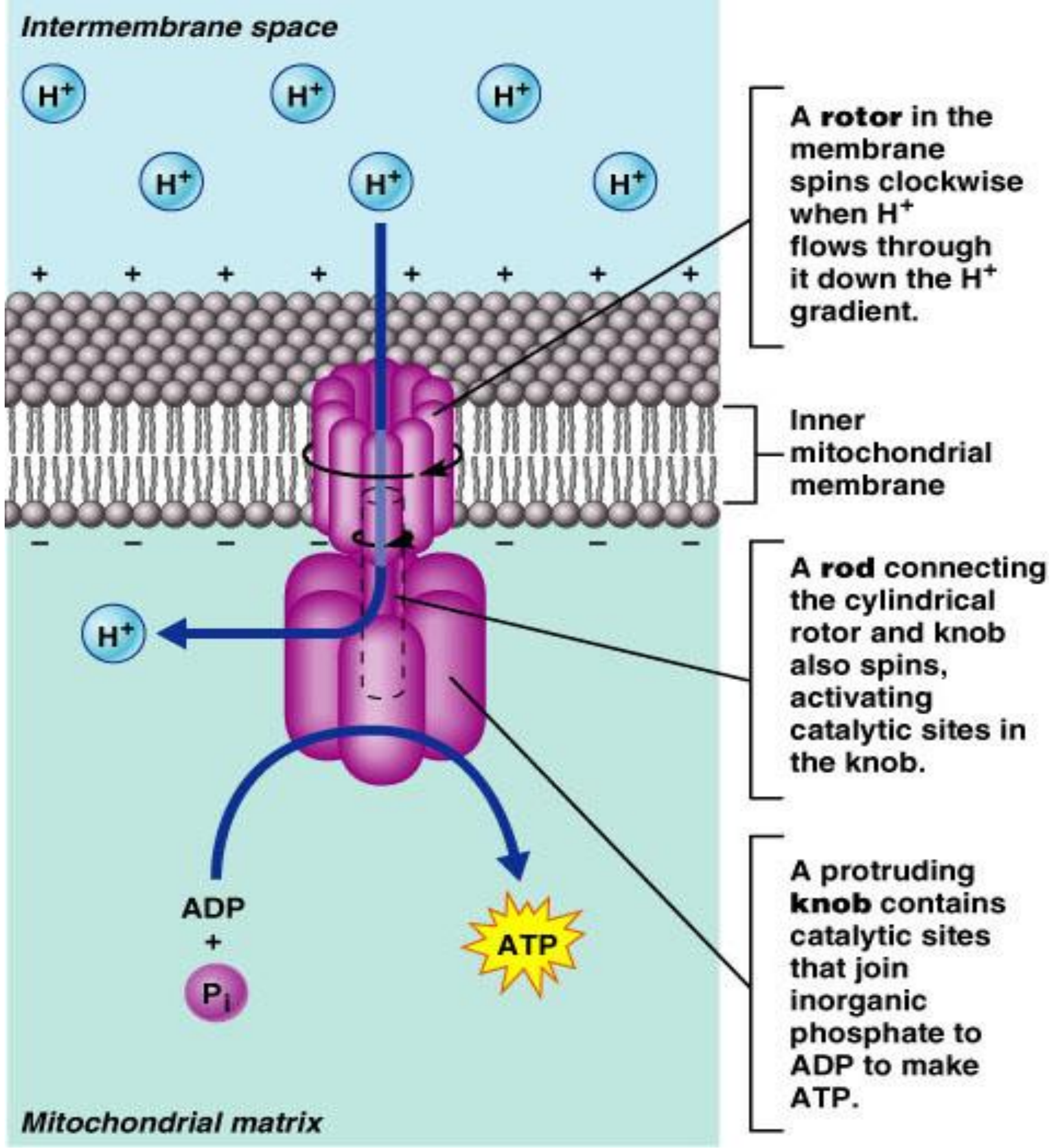
Figure 24.7

MUNI MED

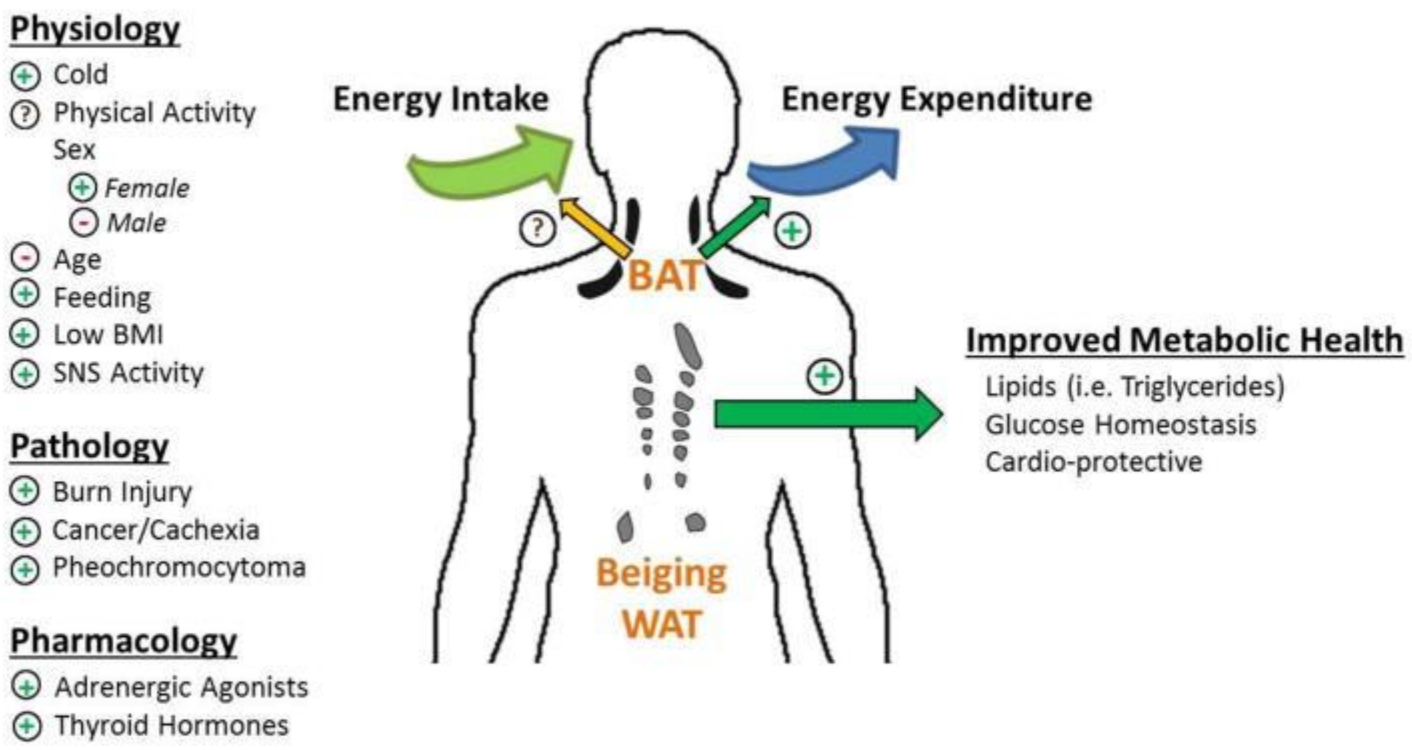
Oxidative phosphorylation



ATP synthase

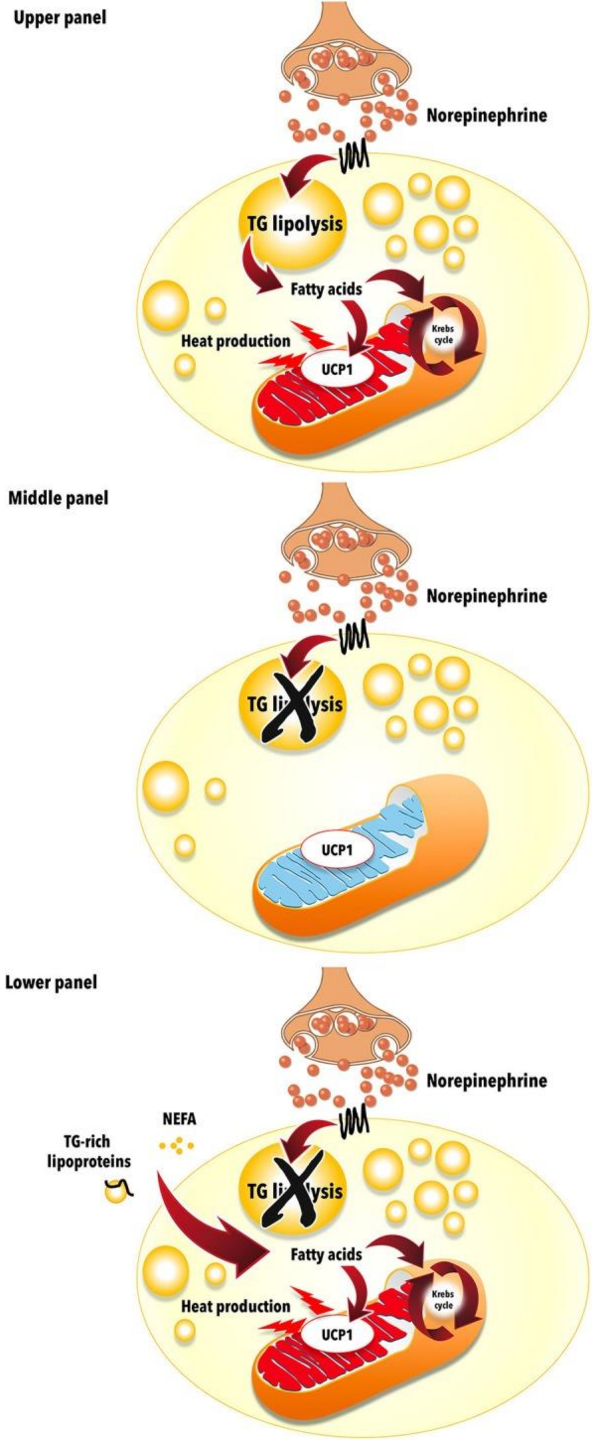


MUNI
MED



Mediators of BAT (or Beige) Amount/Activity and the Impact on Metabolism

There are several physiological, pathological, and pharmacological conditions that are known to mediate the amount of BAT and its activity (on the left). Specifically, "+" and "−" indicates that BAT is "stimulated" or "depressed" by the following condition or stimuli, respectively. On the right are the potential effects of BAT on energy intake, energy expenditure, and cardiometabolic health.



Uncoupling protein 1 (UCP1)-mediated brown adipose tissue thermogenesis.

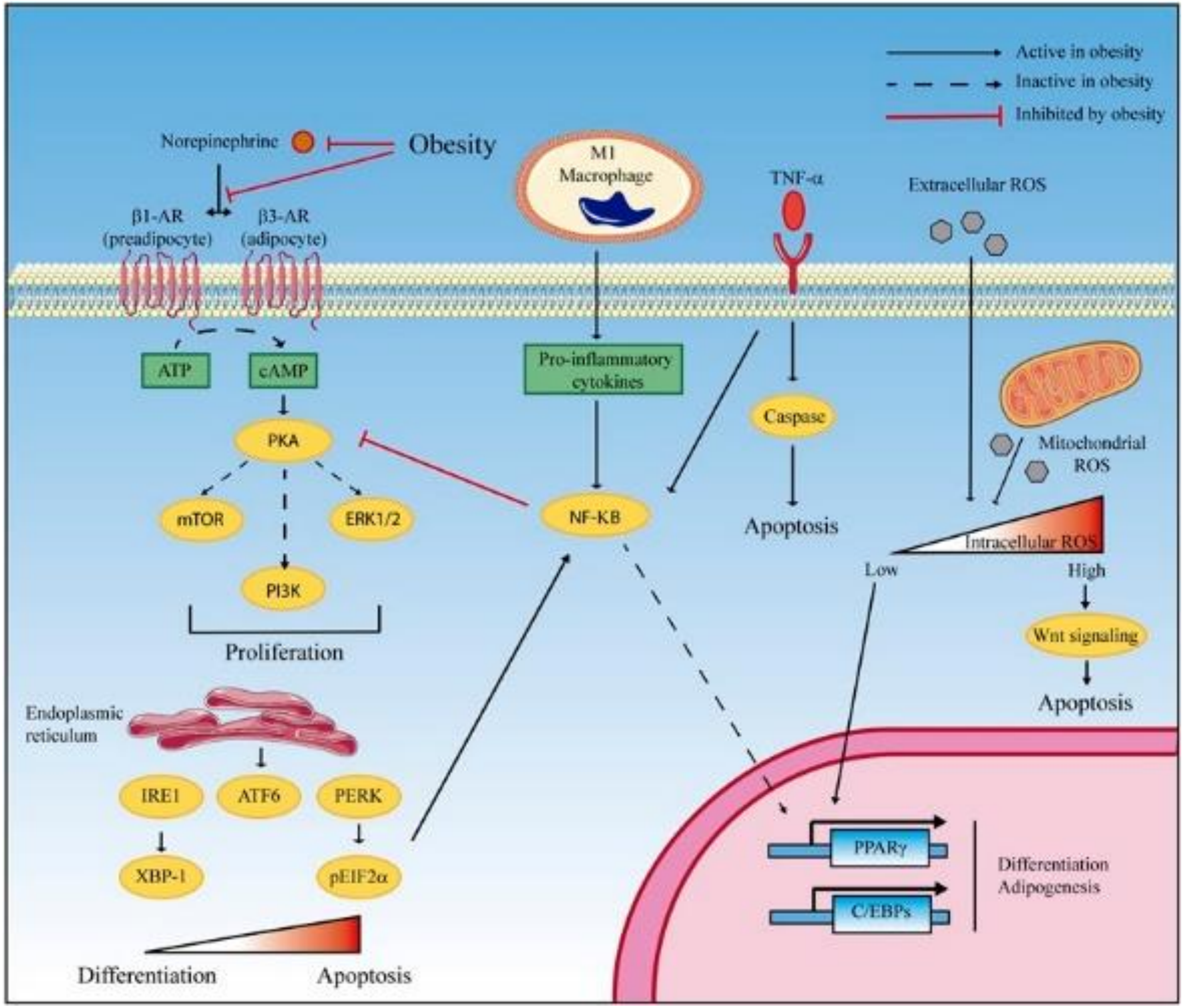
Upper panel: Brown adipose tissue UCP1-mediated thermogenesis is activated by fatty acids produced via norepinephrine-induced intracellular triglyceride (TG) lipolysis during cold exposure.

Middle panel: Acute pharmacological inhibition of intracellular TG lipolysis blunts brown adipose tissue thermogenesis via reduction of intracellular fatty acids availability.

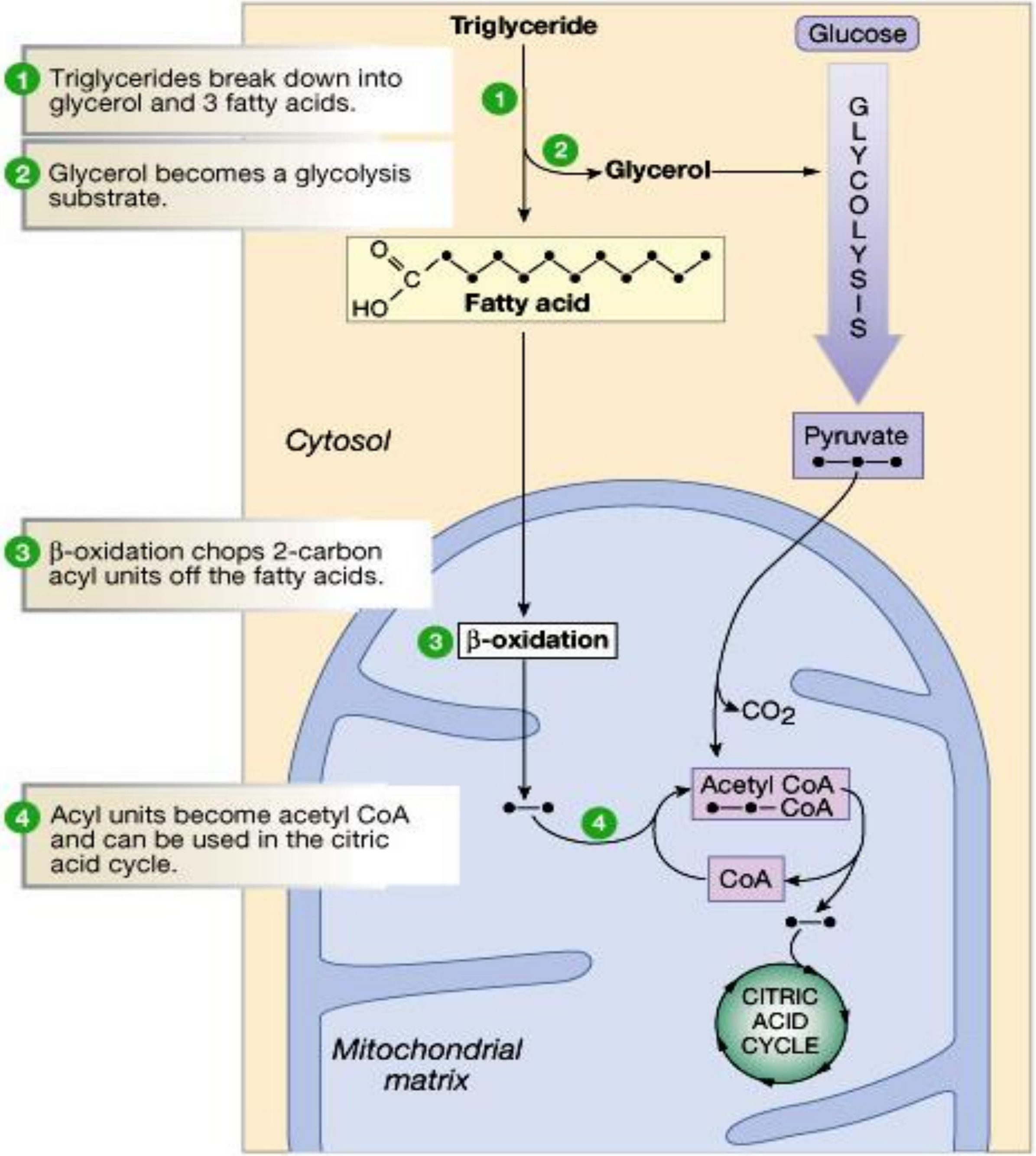
Lower panel: Genetic deletion-mediated issues leads to increased reliance on circulating nonepinephrine inhibition of intracellular TG lipolysis in brown adipose non esterified fatty acids (NEFA) and triglyceride (TG)-rich lipoproteins to sustain UCP1-mediated thermogenesis.

Front Endocrinol (Lausanne). 2018; 9: 447.

Depletion of BAT induced by obesity

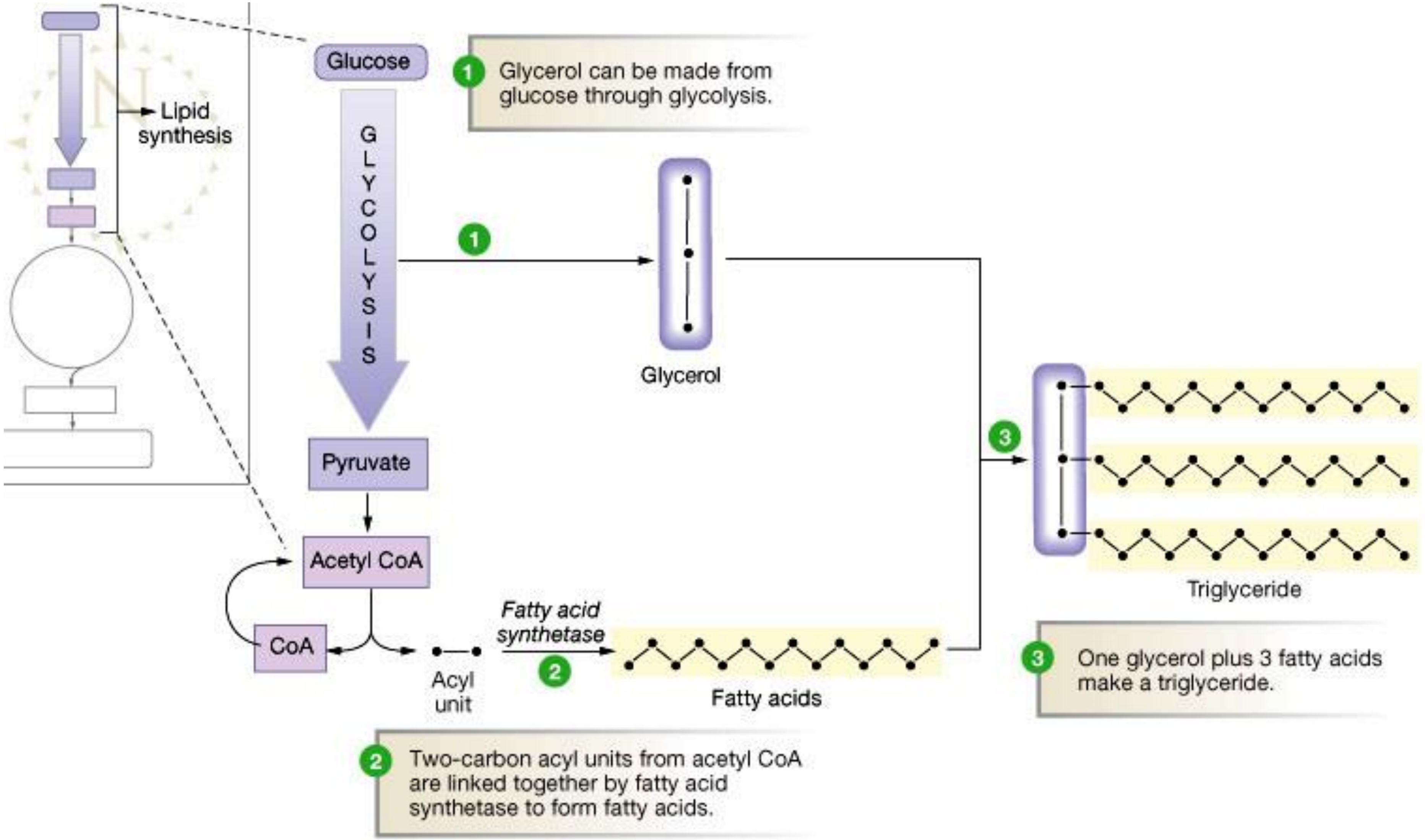


Lipolysis



MUNI MED

Synthesis of lipids



MUNI MED

Proteins

- Main building material of cells and tissues, enzymes, some hormones and compounds of pigments

- *Food sources:* animal(contain all AAs) and plant (not all contain essential AAs)proteins ⇨ digestion in stomach – pepsin (from pepsinogen, activated by HCL) and small intestine – trypsin, aminopeptidases (cleave N-terminal AAs), carboxypeptidases (cleave C-terminal AAs), dipeptidases (cleave dipeptides) – and AAs ⇨ absorption to v. portae in presence of vit. B6
- *Condition for adequate protein digestion- they must denaturized* (cooking)

MUNI
MED

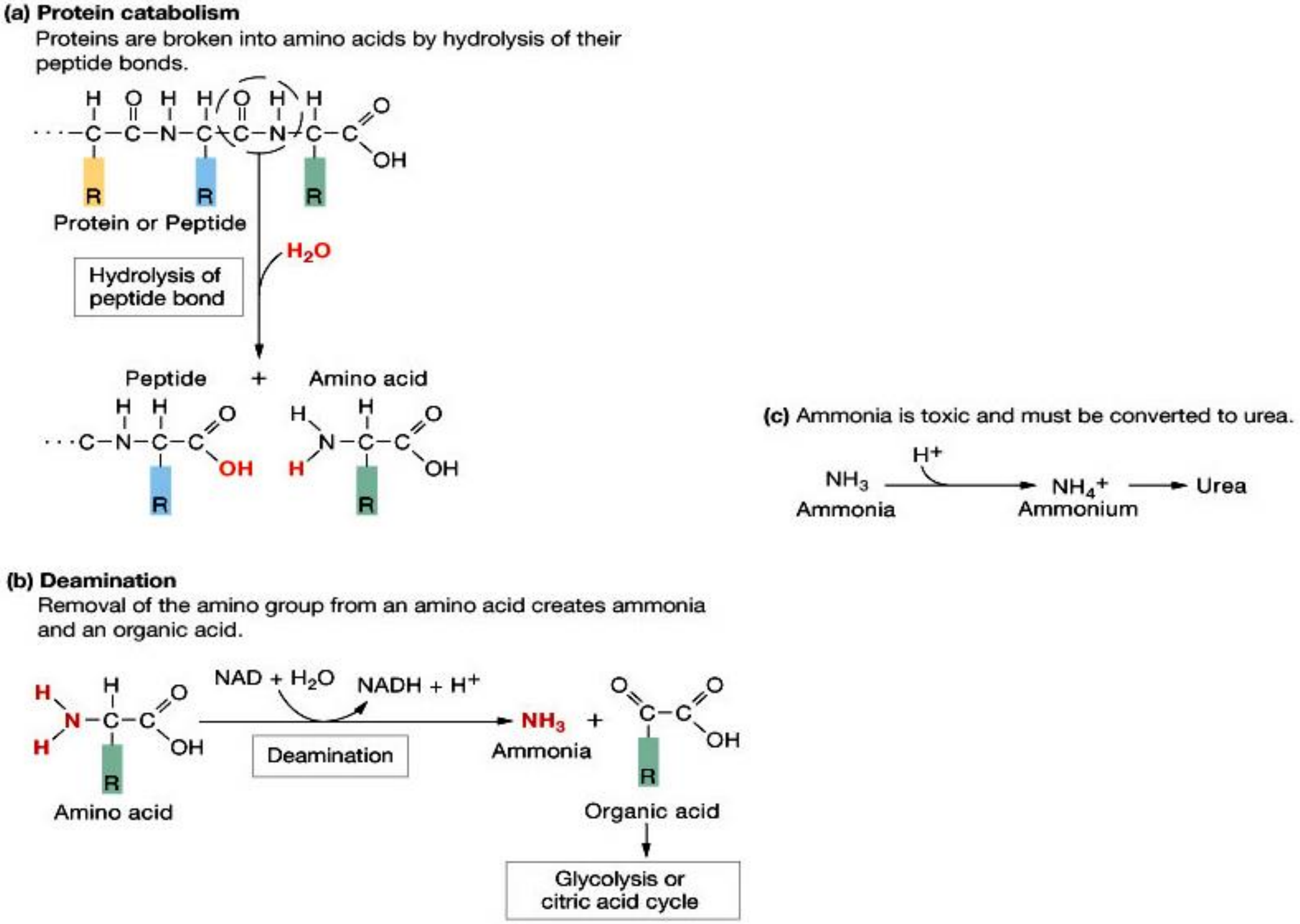
Protein metabolism

- Non essential amino acids can be formed by **transamination (=** transfer of amino acid group to keto acid).

- When using for energy formation, they undergo **oxidative deamination**. NH_3 and keto acids are side products of the reaction. NH_3 is changed to urea and excreted by urine.
- Amino acids are not stored in the body.

MUNI
MED

Catabolism of proteins



Summary: metabolic reactions of sugars

TABLE 24.4 Thumbnail Summary of Metabolic Reactions

Carbohydrates	
Cellular respiration	Reactions that together complete the oxidation of glucose, yielding CO_2, H_2O, and ATP
Glycolysis	Conversion of glucose to pyruvic acid
Glycogenesis	Polymerization of glucose to form glycogen
Glycogenolysis	Hydrolysis of glycogen to glucose monomers
Gluconeogenesis	Formation of glucose from noncarbohydrate precursors
Krebs cycle	Complete breakdown of pyruvic acid to CO_2, yielding small amounts of ATP and reduced coenzymes
Electron transport chain	Energy-yielding reactions that split H removed during oxidations to H^+ and e^- and create a proton gradient used to bond ADP to P_i, forming ATP

Table 24.2.1

Summary: metabolic reactions of lipids and proteins

TABLE 24.4 Thumbnail Summary of Metabolic Reactions

Lipids	
Beta oxidation	Conversion of fatty acids to acetyl CoA
Lipolysis	Breakdown of lipids to fatty acids and glycerol
Lipogenesis	Formation of lipids from acetyl CoA and glyceraldehyde phosphate
Proteins	
Transamination	Transfer of an amine group from an amino acid to α-ketoglutaric acid, thereby transforming α-ketoglutaric acid to glutamic acid
Oxidative deamination	Removal of an amine group from glutamic acid as ammonia and regenerating α-ketoglutaric acid (NH_3 is converted to urea by the liver)

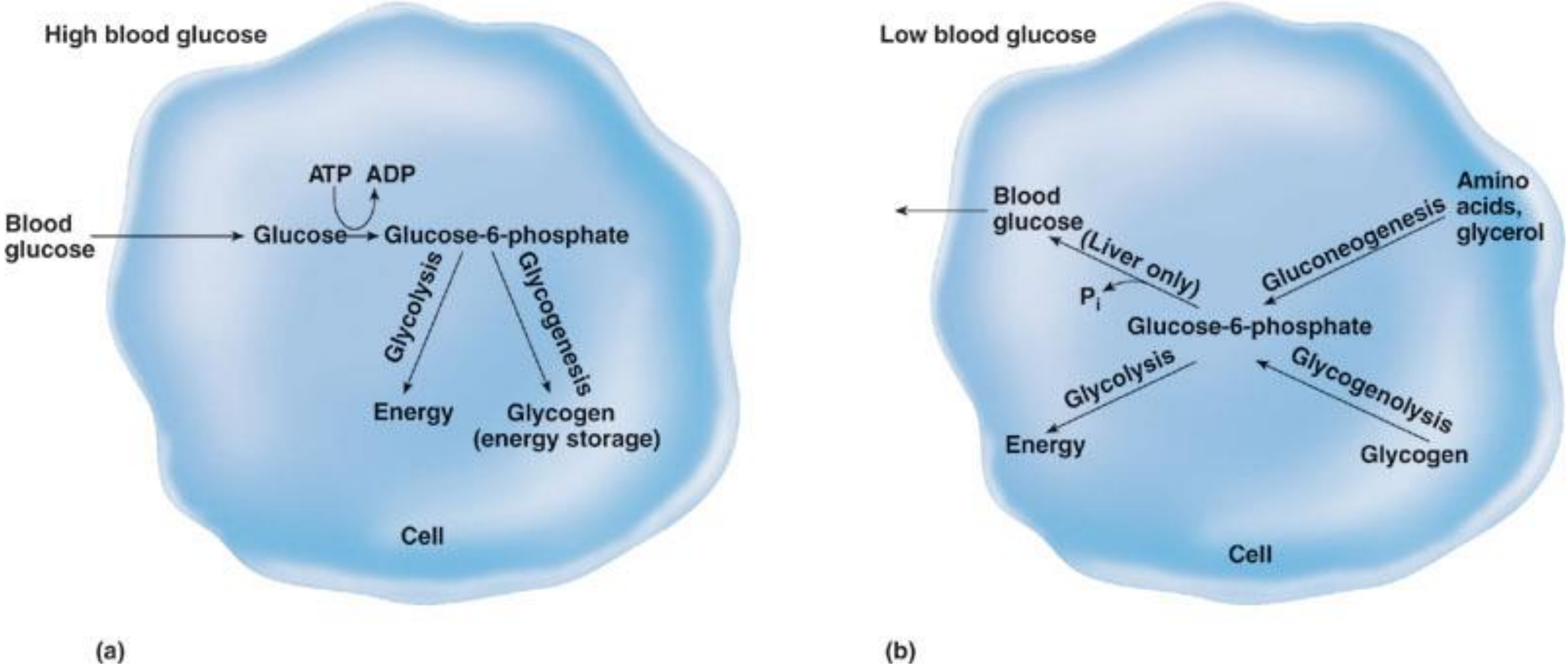
Table 24.2.2

Metabolism

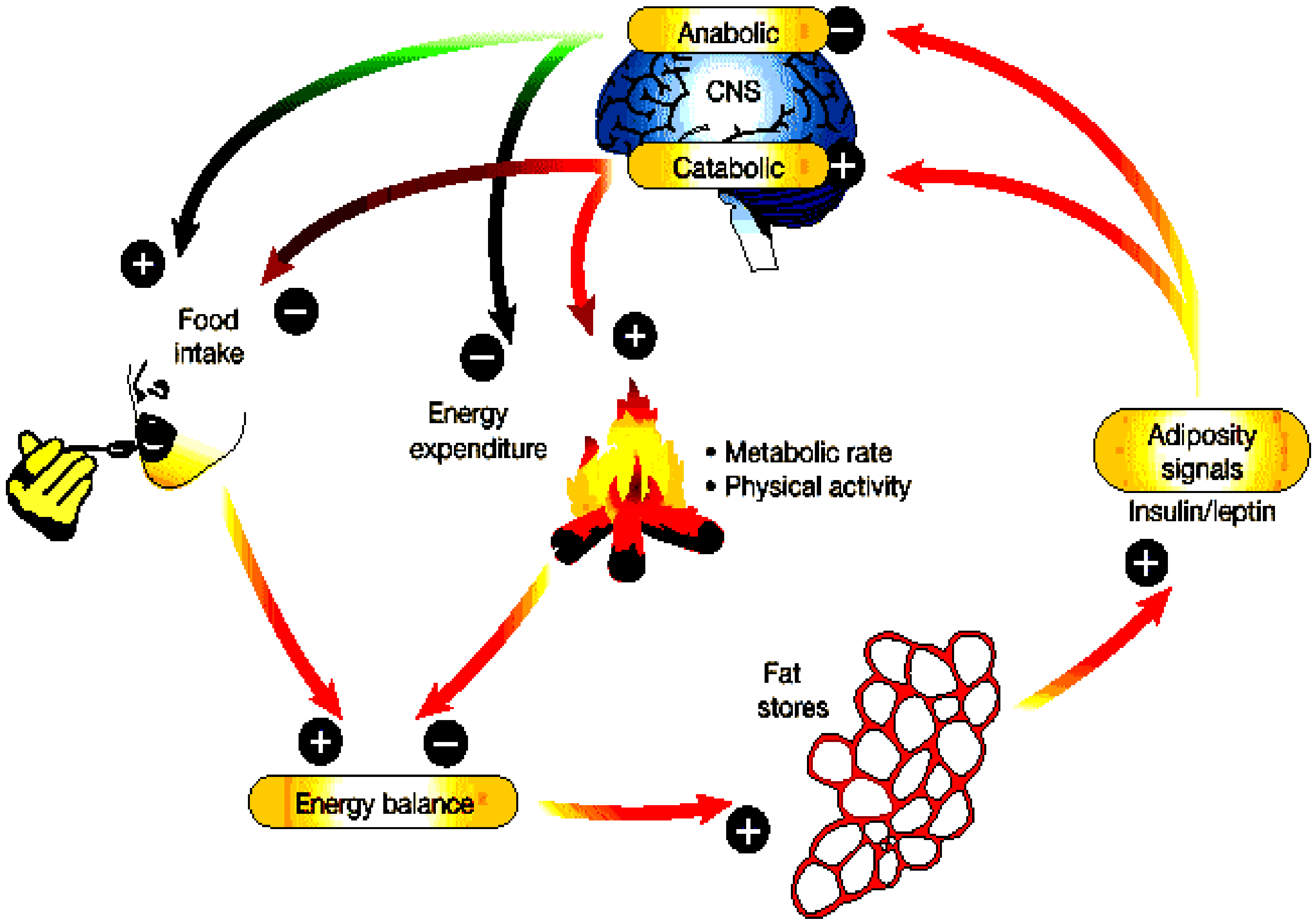
- Quantitative evaluation (energetic)
- Qualitative evaluation (sufficient and suitable proportion of proteins, lipids and sugars)

- Anabolism
- Catabolism

Internal changes of nutrition molecules



MUNI
MED


Anabolic
CNS
Catabolic
Food
intake
Energy
expenditure
• Metabolic rate
• Physical activity
Adiposity
signals
Insulin/leptin
Fat
stores
Energy balance

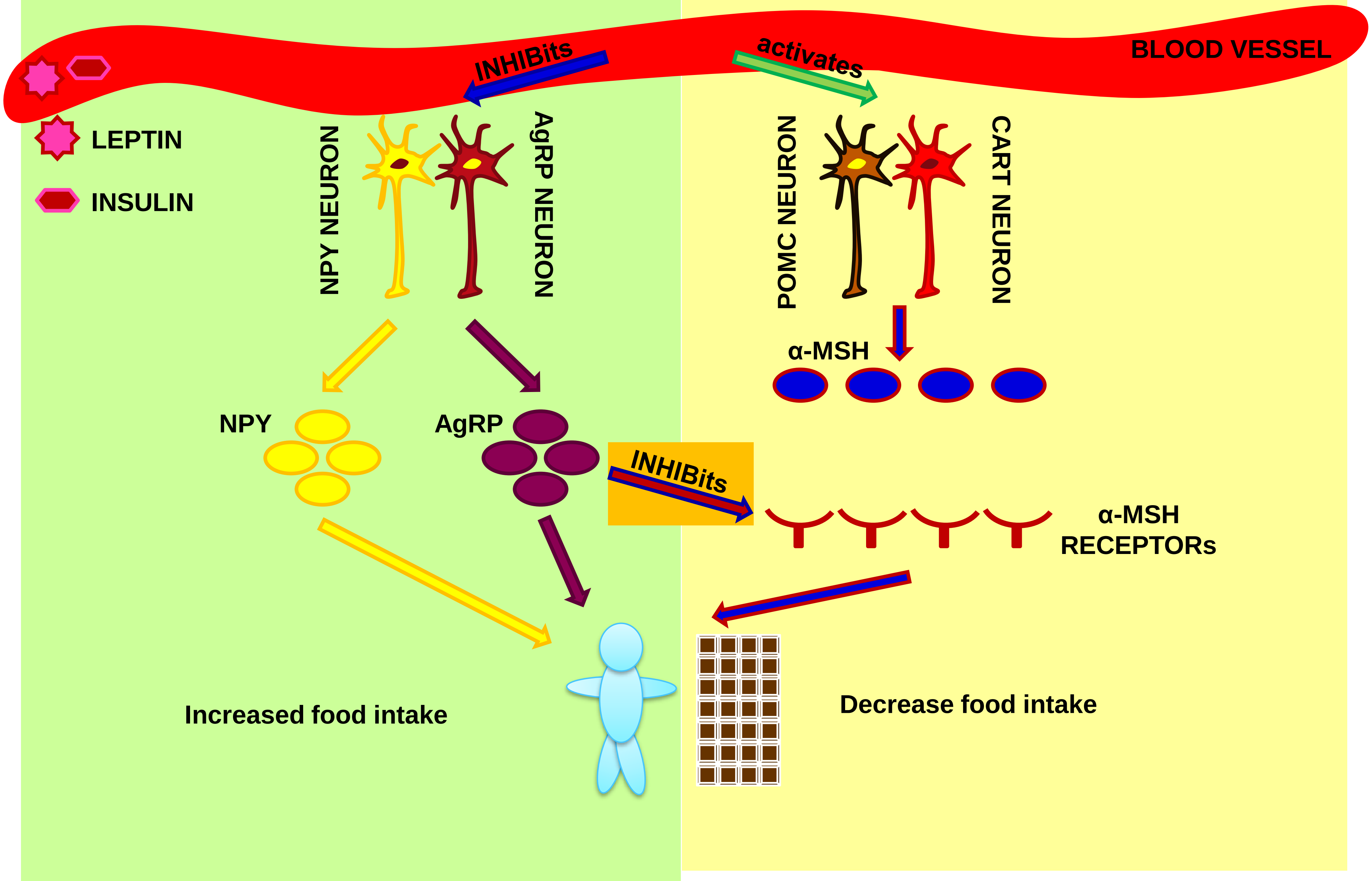
MUNI
MED

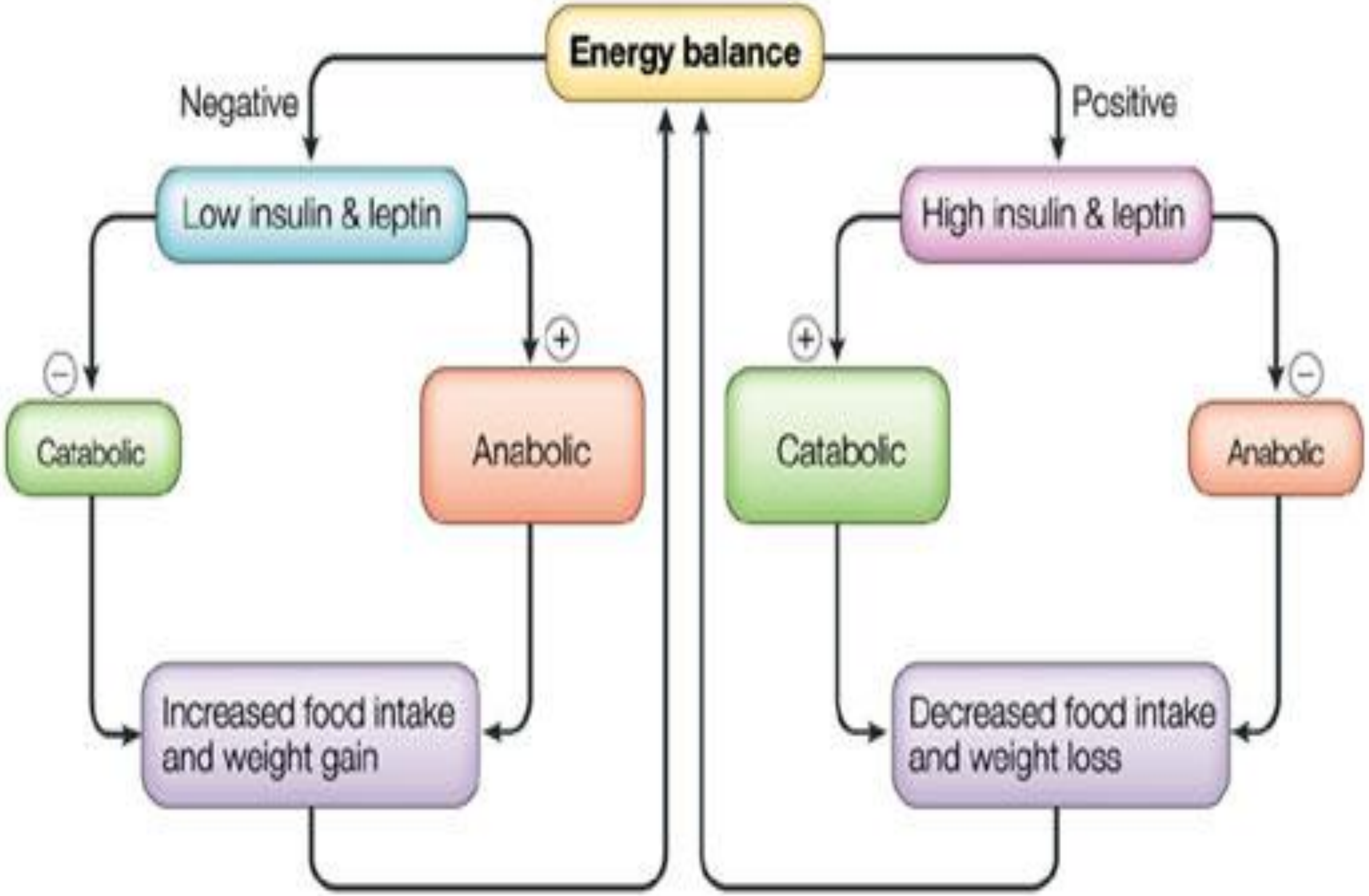
Metabolism of substance:

- -anabolism = more complicated products are synthetized from simple absorbed compounds (s.c. assimilation) – energy is used (endergonic reaction)
- -catabolism = portion of absorbed compounds is cleaved to simpler ones (dissimilation) – energy is released (exergonic reaction)

MUNI
MED

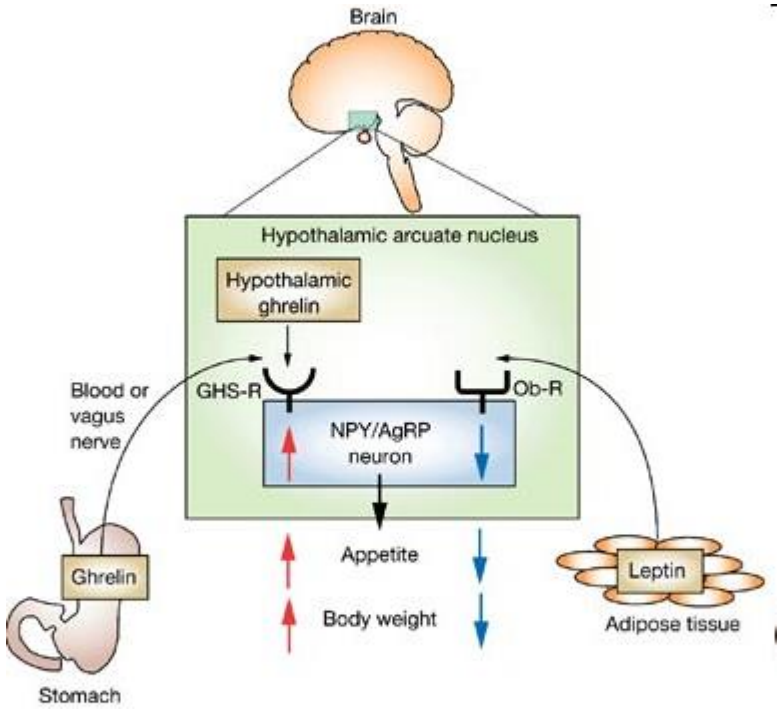
OREXIGENIC-ANOREXIGENIC PATHWAYS

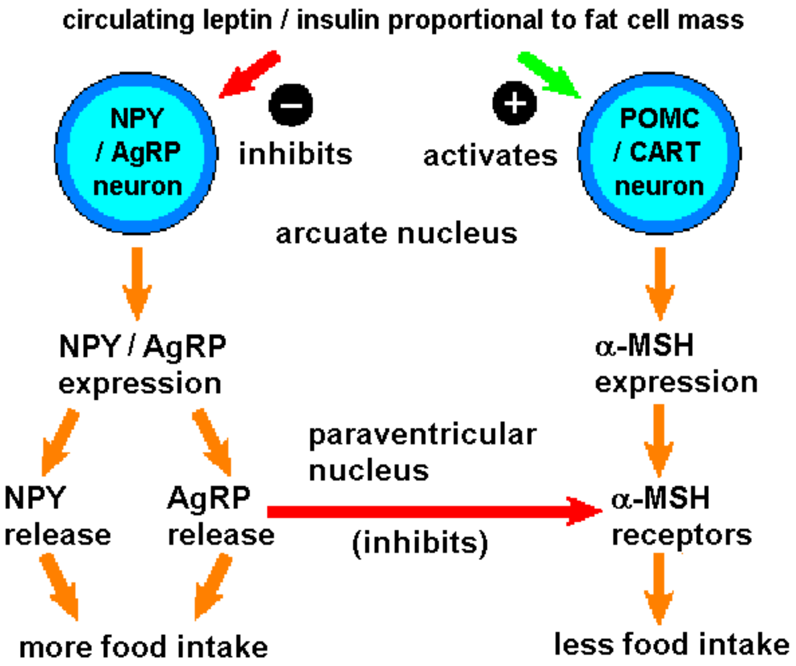




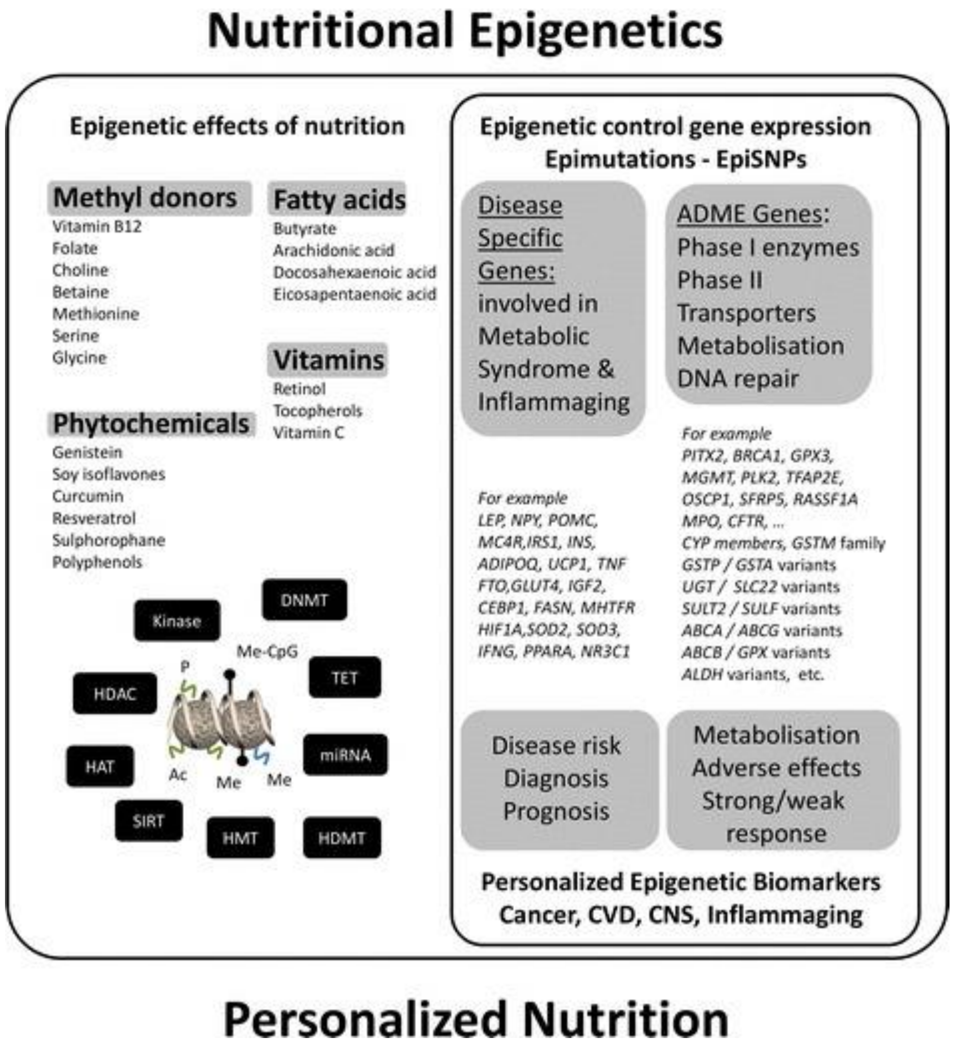
Nature Reviews | Neuroscience

Regulation of food appetite





Drug Insight: the functions of ghrelin and its potential as a multitherapeutic hormone
Masayasu Kojima and Kenji Kangawa
Nature Clinical Practice Endocrinology & Metabolism (2006) **2**, 80-88

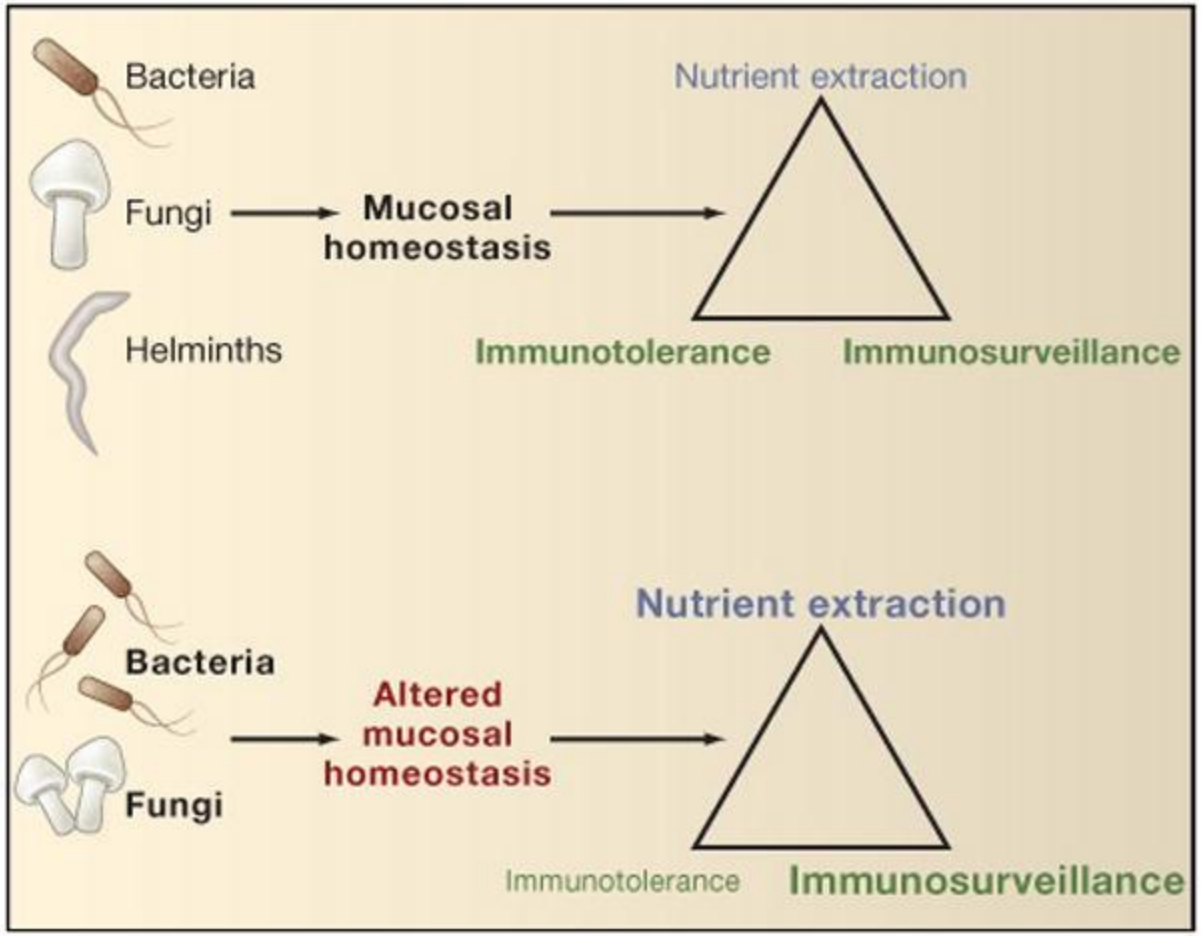


2015 Mar 25;7(1):33. doi: 10.1186/s13148-015-0068-2. eCollection 2015.

From inflammaging to healthy aging by dietary lifestyle choices: is epigenetics the key to personalized nutrition?

Vel Szic KS[1], Declerck K[1], Vidaković M[2], Vanden Berghe W[1].

Overview of the mechanisms and consequences of epigenetic regulation by nutritional compounds. Modulation of different classes of chromatin writers-erasers by phytochemicals (left panel). Genes encoding absorption, distribution, metabolism, and excretion (ADME) proteins can be epigenetically regulated and thereby determine individual nutritional responses. Epigenetic modification of disease-related genes can contribute to diagnosis (biomarker) as well as disease prevention or progression (right panel).



The loss of universal helminth infection as occurred in earlier human evolution may alter the numbers or types of bacterial and fungal commensals and thus affect normal mucosal tissue homeostasis. In susceptible or highly exposed individuals, such alterations might alter the balance between immunotolerance, immunosurveillance and nutrient extraction. This imbalance may contribute to the appearance of inflammatory systemic dysregulation at mucosal surfaces, resulting in increases in asthma and allergic diseases, particularly in the setting of environmental changes that have increased exposure to indoor allergens and pollutants, and even to increases in obesity, which can be a risk factor for severe asthma.

Catabolic states

Are induced by dysregulation of metabolic events by inflammation(cytokines), stress (A, GKs), chronic immobilization.

- *Acute severe diseases* (adaptation on starvation decreases, protein malnutrition can develop).
- *Cancer - cachexia* (cytokines TNF, IL-1 and IL-6).
- *Trauma, burns, fever, painful states, AIDS* (wasting syndrome).

MUNI MED

Organ changes in protein and energy deficits

- Loss of body weight (drop of 40% is leading to death).
- ECT volume is nor changing or relative expansion of ECT against ICT. When oncotic pressure was decreasing, edema could develop.
- Decreased cardiac output.
- Decreased function of respiratory system due to decreased contractility of respiratory muscles.
- Decreased stomach motility and stomach production of HCL
- Decreased exocrine function of pancreas
- Decrease liver mass with decrease proteins, lipids and glycogen in secondary malnutrition
- In primary malnutrition liver mass increased due to lipids infiltration and increased production of glycogen.

Organ changes in protein and energy deficits

- Kidney weight decreases.
- Increased ECT volume due to decreased osmotic gradient in the kidney.
- Increased secretion in endocrine system.
- Immunodeficiency state (decrease of non specific immune functions).
- Atrophy of the skin end GIT epithelia with functional lesions of barriers against external environment.
- Decreased wound healing in severe protein malnutrition.

MUNI
MED

The human starvation

- response is unique among animals in that human brains do not require the ingestion of glucose to function. During starvation, less than half the energy used by the brain comes from metabolized glucose. Because the human brain can use ketone bodies as major fuel sources, the body is not forced to break down skeletal muscles at a high rate, thereby maintaining both cognitive function and mobility for up to several weeks.

MUNI
MED

Human starvation

- This response is extremely important in human evolution and allowed for humans to continue to find food effectively even in the face of prolonged starvation.
- Initially, the level of insulin in circulation drops and the levels of glucagon, epinephrine and norepinephrine rise. At this time, there is an up-regulation of glycogenolysis, gluconeogenesis, lipolysis, and ketogenesis.
- The body’s glycogen stores are consumed in about 24 hours. In a normal 70 kg adult, only about 8,000 kilojoules of glycogen are stored in the body (mostly in the striated muscles).

MUNI MED

Human starvation

- The body also engages in gluconeogenesis to convert glycerol and glucogenic amino acids into glucose for metabolism.
- Another adaptation is the Cori cycle, which involves shuttling lipid-derived energy in glucose to peripheral glycolytic tissues, which in turn send the lactate back to the liver for resynthesis to glucose. Because of these processes, blood glucose levels remain relatively stable during prolonged starvation.

MUNI
MED

Human starvation

- However, the main source of energy during prolonged starvation is derived from triglycerides. Triglycerides are broken down to fatty acids via lipolysis. Epinephrine precipitates lipolysis by activating protein kinase A, which phosphorylates hormone sensitive lipase (HSL) and perilipin. These enzymes, along with CGI-58 and adipose triglyceride lipase (ATGL), complex at the surface of lipid droplets. The concerted action of ATGL and HSL liberates the first two fatty acids. Cellular monoacylglycerol lipase (MGL), liberates the final fatty acid. The remaining glycerol enters gluconeogenesis.

Malnutrition

– Malnutrition is a disorder in body composition in which inadequate macronutrient (protein, carbohydrate, and fat) or micronutrient (vitamins, minerals, and trace elements) intake results in decreased body mass, reduced organ mass, and most importantly, decreased organ function.

Nutrition: proteins

– Adequate intake of protein is one of the key nutritional factors to maintain independence, predominantly by preventing loss of muscle mass and strength (sarcopenia), frailty and associated comorbidities in later life.

Sarcopenia

– A gradual decline in muscle mass is observed from the third decade of life with a 30–50% decrease reported between the ages of 40 and 80. Muscle strength is correlated with muscle mass and rapidly declines after the age of 50. The beginning of the fourth decade of life might therefore be interpreted as the time when muscle ageing process begins and for this reason it is the optimal time for implementing appropriate dietary changes, to prevent or delay the onset of sarcopenia.

Type D behaviour

- is characterized by the joint tendency to experience negative emotions and to inhibit these emotions while avoiding social contacts with others. The observation that cardiac patients with type D personality are at increased risk for cardiovascular morbidity and mortality underlines the importance of examining both acute (e.g. major depression) and chronic (e.g. certain personality features) factors in patients at risk for coronary events.
- Both type D dimensions (negative affectivity and social inhibition) are associated with greater cortisol reactivity to stress. Elevated cortisol may be a mediating factor in the association between type D personality and the increased risk for coronary heart disease and, possibly, other medical disorders.

MUNI
MED

Personality type D („distressed“ personality)

- Type-D denotes the synergistic effect of negative affectivity (tendency to experience negative emotions) and social inhibition (tendency to inhibit self-expression).
- As a result, type-D patients experience more feelings of anxiety, depression, and anger, but inhibit self-expression in order to avoid disapproval by others.
- Type-D is associated with a four- to fivefold increased risk of death or myocardial infarction in cardiac patients.
- Type-D personality was positively associated with the **cortisol-awakening response**, independently of age, sex, and body mass.

MUNI
MED

Proteinuria as a cause of a loss of proteins

Table 1 | Types of proteinuria

Types	Characteristics
Glomerular	Most common form, up to 90% Feature of chronic kidney disease Loss of albumin and higher molecular weight proteins
Tubular	Low molecular weight proteins, such as β2-microglobulin
Overflow	Increased production, that is, light chains in multiple myeloma
Post-exercise	Transient benign Can be up to 10 g/day
Post-prandial	Transient physiological proteinuria Possibly through insulin action in podocytes
Infection-associated	Physiological response Mediated by toll-receptors Possibly involved in clearing pathogens from the circulation

Mundel P, Reiser J. **Kidney Int**. 2010 Apr;77(7):571-80.

Table 1. The principle genes involved in congenital nephrotic syndrome and in associated syndromes

Genes	Locus	Protein	Phenotype
AD			
WT1	11P13	Wilms tumor 1	IDMS, DDS, Frasier syndrome, WAGR syndrome, ISRNS
LMX1B	17q11	Lim homeobox transcription factor 1-β	Nail-patella syndrome
INF2	14q32.33	Inverted formin-2	FSGS
CD2AP	6p12	CD2-associated protein	FSGS (adult)
AR			
NPHS1	19q13.1	Nephrin	CNF
NPHS2	1q25-31	Podocin	Idopathic CNS, SRNS
LAMB2	3p21	Laminin $\beta 2$ chain	Pierson's syndrome
PLCE1	10q23	Phospholipse C epsilon 1	SRNS, DMS
PDSS2	6q21	Decaprenyl disphosphate synthase, subunit 2	NS with Leigh syndrome
ITGA3	17q21.33	Integrin $\alpha 3$	NS with intestitial lung disease
ARHGDIA	17q25.3	Rho GDP dissociation in inhibitor 2	Idiopathic CNS
SCARB2	4q21.1	Scuvenger receptor class B, number 2	Action myoclonus-renal failure syndrome
Unknown			Galloway-Mowat syndrome

AD: autosomal dominant; AR: autosomal recessive; IDMS: idiopathic diffuse mesangial sclerosis; DDS: Denys-Drash syndrome; WAGR: Wilm's tumor, aniridia, genitourinary abnormalities and mental retardation; FSGS: focal segmental glomerulosclerosis; CNS: congenital nephrotic syndrome; CNF: CNS of the Finnish type; SRNS: steroid-resistant nephrotic syndrome; DMS: Denys-Drash syndrome.

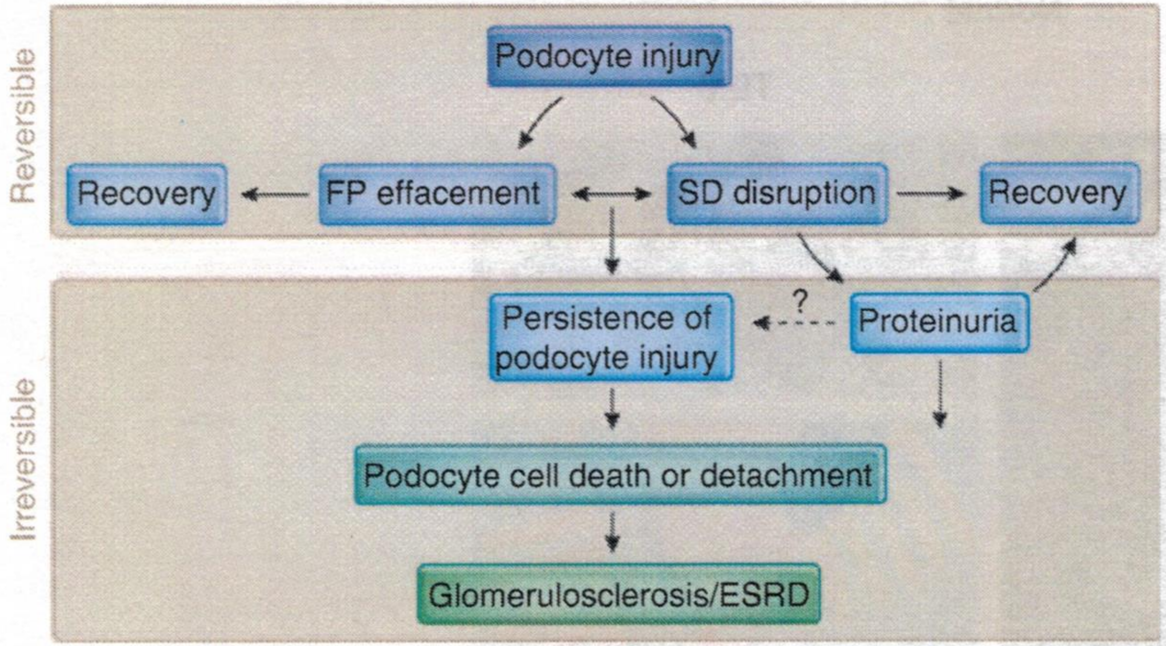


Figure 2 | Consequences of podocyte injury. Podocytes can be injured in many human and experimental glomerular diseases, leading to structural changes, such as foot processes (FP) effacement and slit diaphragm (SD) disruption that are reversible.[124] Persistence of podocyte injury can cause cell death or detachment of podocytes from the glomerular basement membrane (GBM).[72] The resulting loss of podocyte will ultimately lead to irreversible glomerulosclerosis and end-stage renal failure (ESRD).[73] The role of proteinuria in the progression of ESRD is a matter of debate. In some patients, nephrotic-range proteinuria can persist over years without progression to ESRD.

Mundel P, Reiser J. **Kidney Int**. 2010 Apr;77(7):571-80.

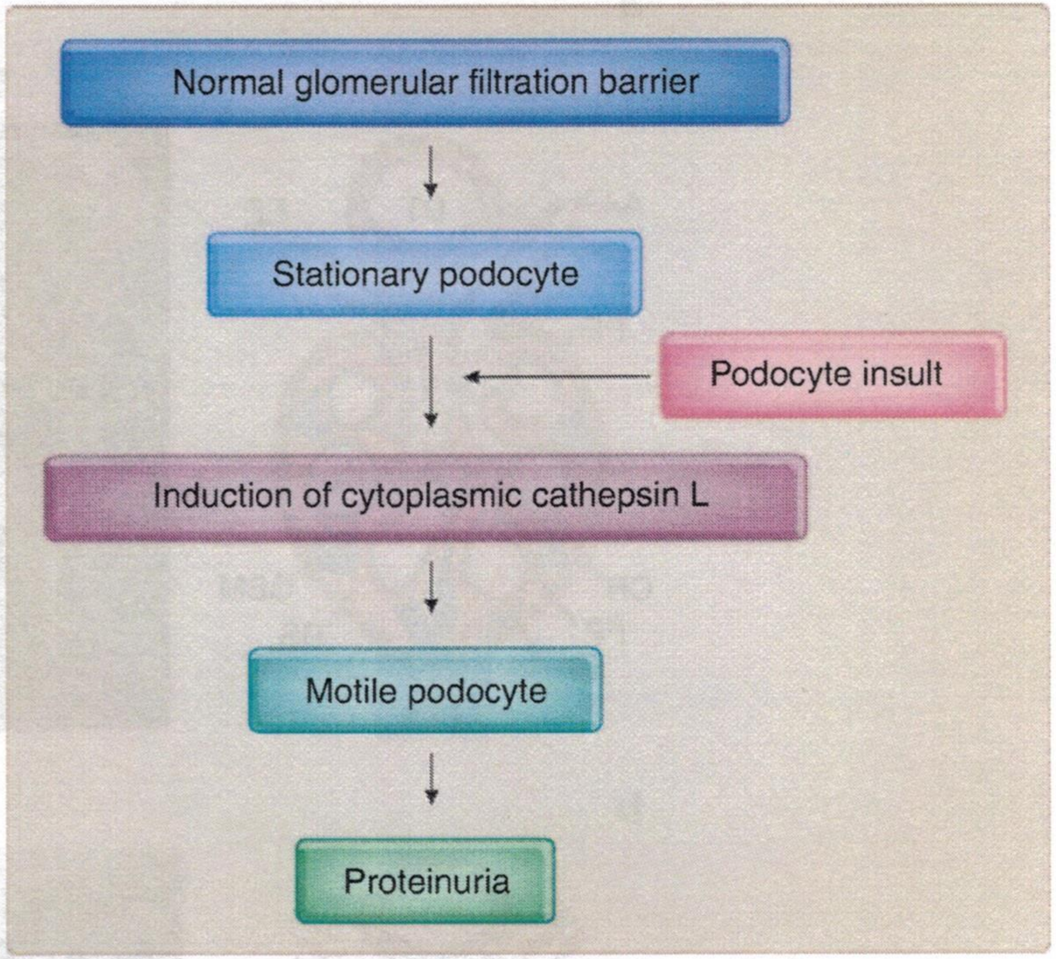


Figure 3 | Induction of cathepsin L in podocytes precedes FP effacement and proteinuria. Upon an insult, stationary podocytes upregulate cytoplasm cytosolic cathepsin L expression and activity and develop motile podocyte foot processes (FPs). This migratory response leads to FP effacement, slit diaphragm remodeling, and proteinuria.[58]

Mundel P, Reiser J. **Kidney Int**. 2010 Apr;77(7):571-80.

Other causes of hypoalbuminimia

- Chronic severe diseases of liver
- Enteropathy with loss of proteins
- Malnutrition

Děkuji vám za pozornost

MUNI

MED