the editing file

Aerobic and anaerobic metabolism in muscle

Color Index:

- Original content
- Important
- Dr's Notes
- Extra info
- Only in girls' slides
- Only in boys' slides

Biochemistry team 438

Objectives:

Slide No. 4 1. Recognize the importance of ATP as energy source in skeletal muscle

Slide No. 3 2. Compare three systems of energy transfer in the body

Slide No. 9 3. Differentiate between energy metabolism in red and white muscle fibers

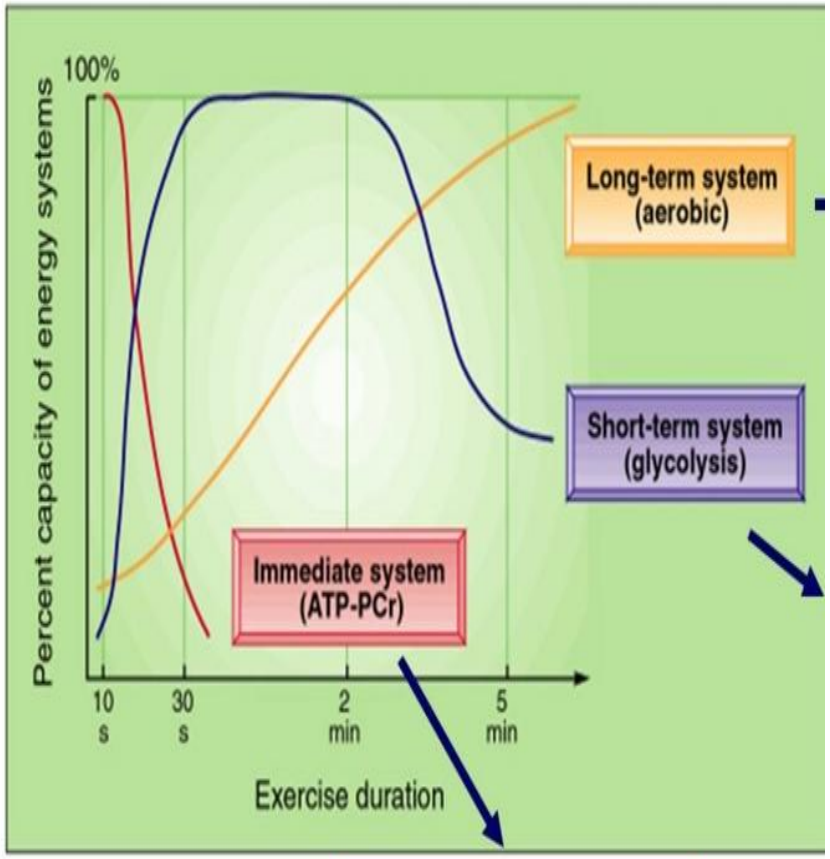
Slide No. 11 4. Understand how skeletal muscles derive ATP from aerobic and anaerobic metabolism

Slide No. 12 5. Discuss the importance of Cori and glucose-alanine cycles in energy metabolism

Three systems of energy transfer:

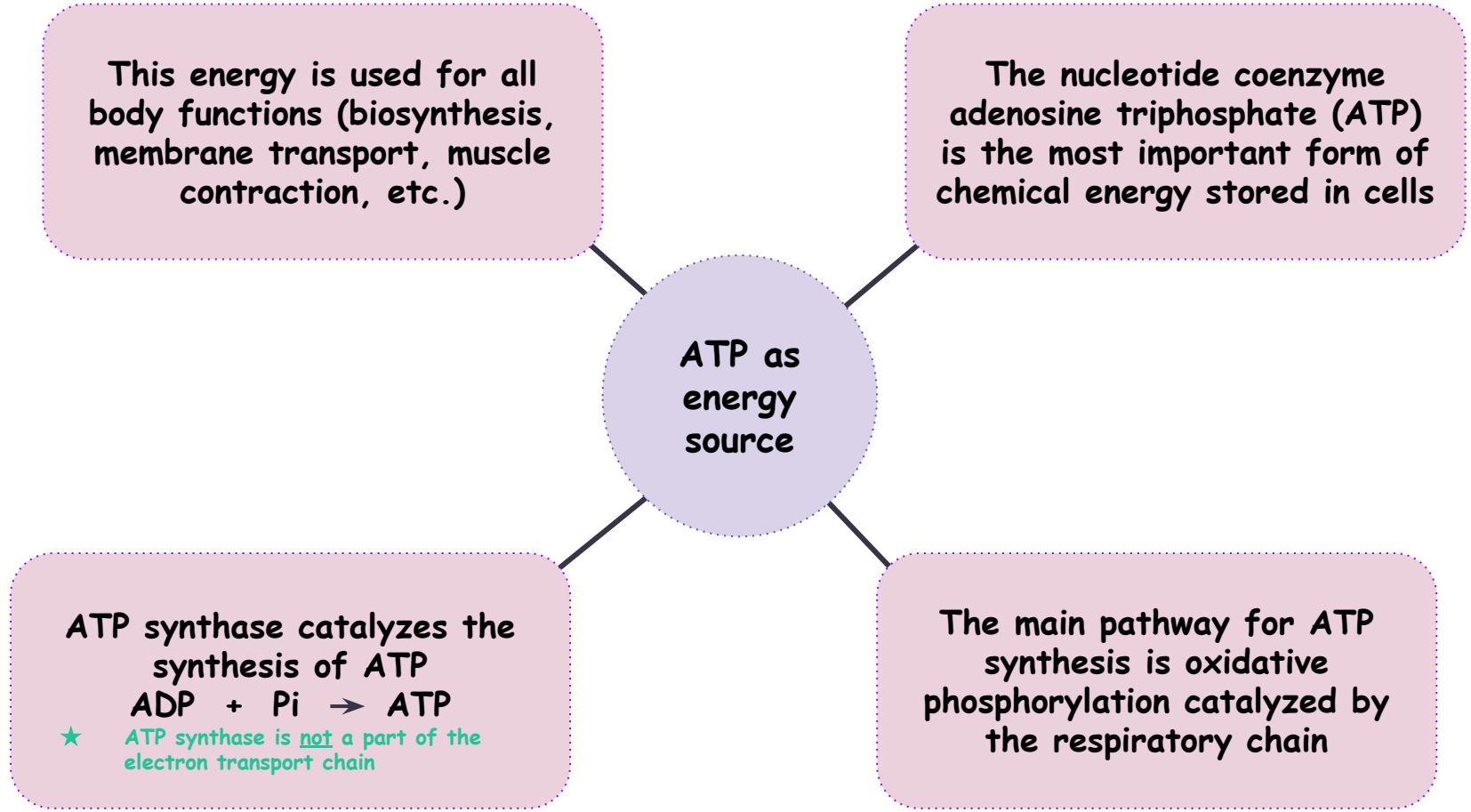
The three systems are overlapping
في الخلية الطاقة دائمًا متوفرة من خلال أن هذه الانظمة تنتج الطاقة بشكل مستمر

Type of system:	Immediate system (ATP-PCr)	Short term system (glycolysis)	Long term system (aerobic)
Type of metabolism:	Anaerobic	Aerobic	Aerobic
main energy source:	Phosphocreatine (PCr)	Glucose "glycogen as the first substrate"	Fatty Acids, Glucose, proteins ..etc
Type of exercise:	High intensity exercise	High intensity exercise Fast, strong contraction e.g. weight lifting	Continuous exercise Prolonged effort e.g. running for long time (moderate)
Duration:	3-15 sec (4-6 in normal people) (8-10 in athletes)	15 sec to 2min	Hours
Final product		lactate "causes fatigue"	CO_2 & H_2O "doesn't cause fatigue"



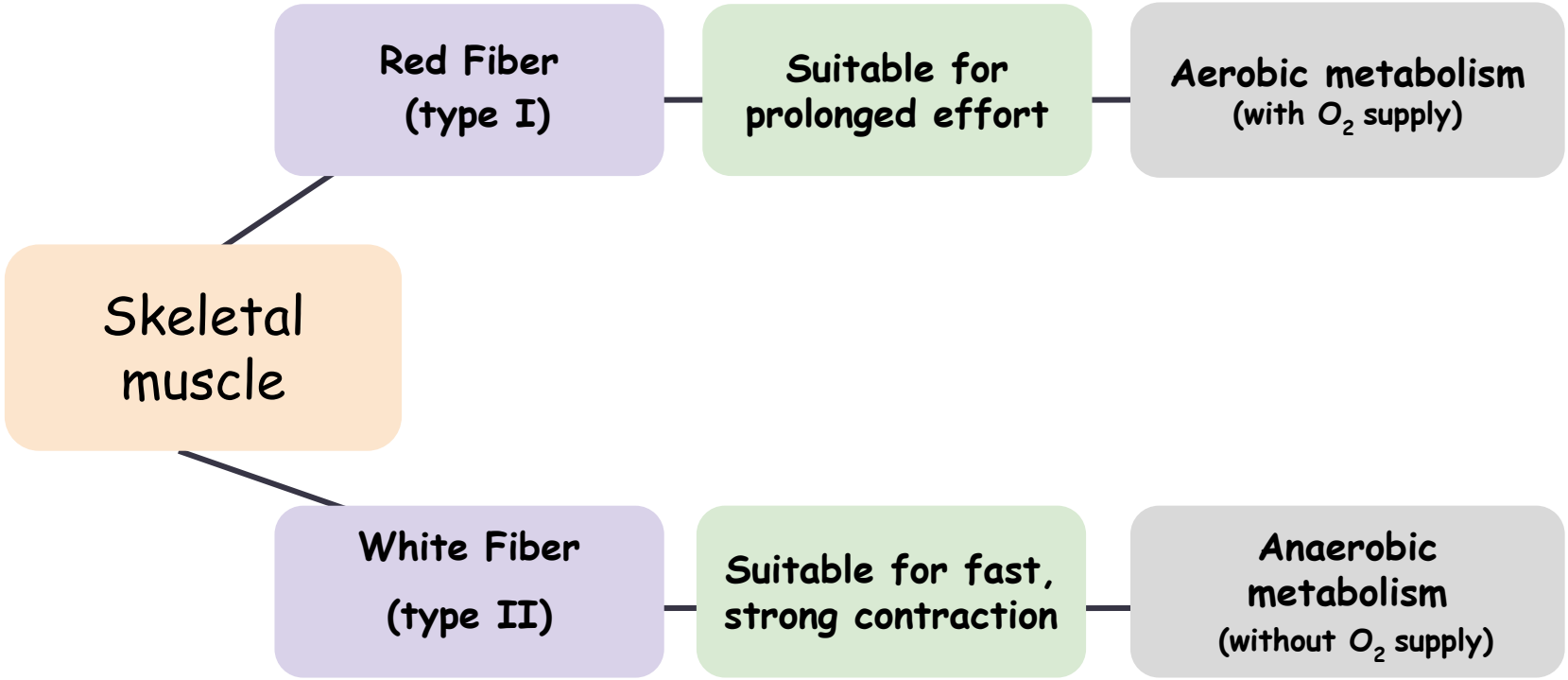
ATP as energy source:

Breakdown of ATP into ADP+PO_4 releases energy



Energy metabolism in muscle

- Muscle contraction requires high level of **ATP** consumption.
- Without constant resynthesis, the amount of ATP is used up in **less** than 1 sec. of contraction



★ The muscle can't store energy for more than 1-2 sec, so they need constant re synthesis

★ in humans the type of muscle is mixed "pink"

Overview of energy metabolism

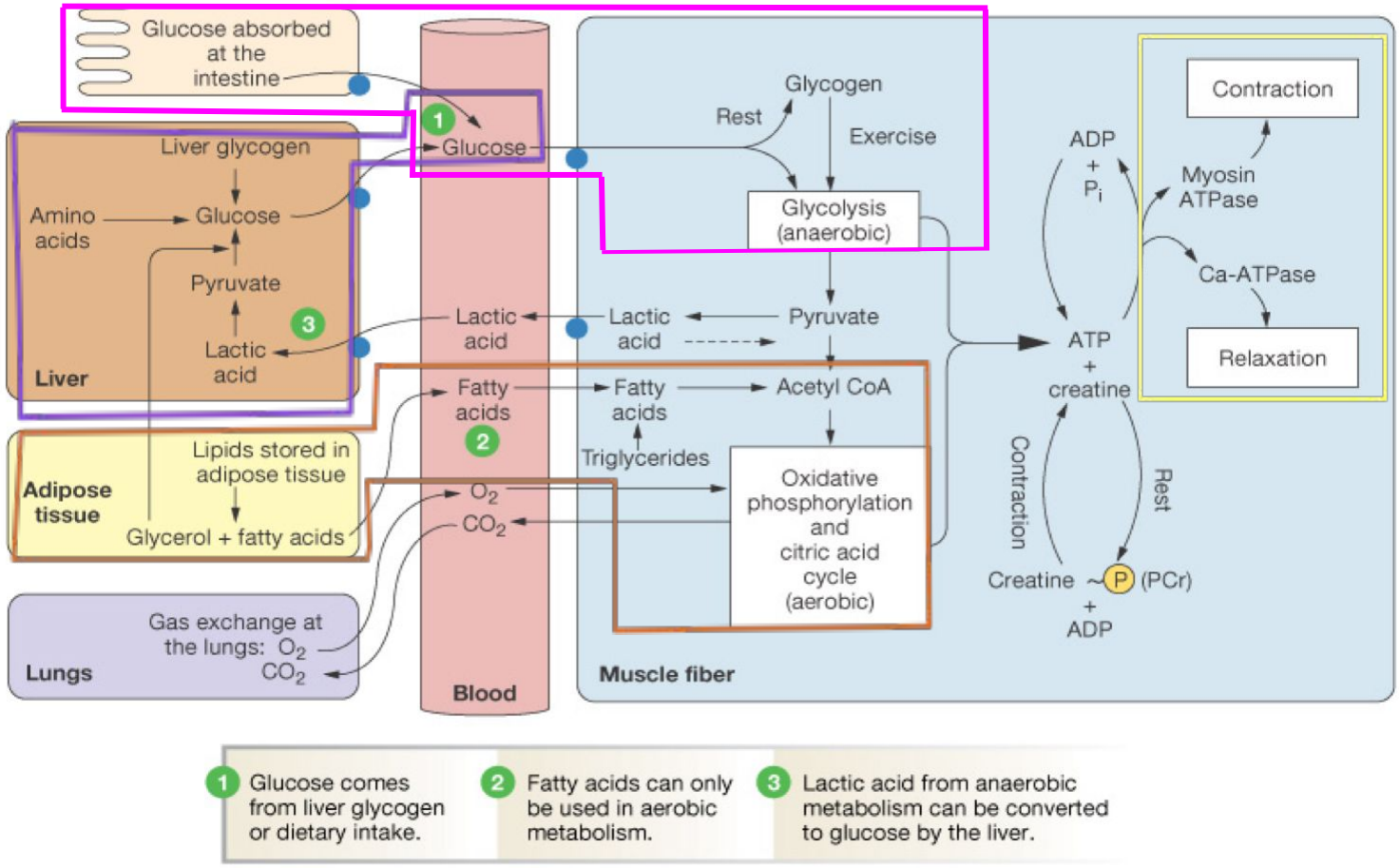
When we eat ,
glucose is absorbed in the intestine -> goes to bloodstream -> goes to the muscle.

- Inside to muscle fibers:

- at rest:
its stored as glycogen.

-During exercising:
it undergoes glycolysis (anaerobic pathway) to give ATP

Gas exchange happens in the lungs
- when exercising, breathing increases for more O2 supplying.



The produced ATP will be used for contraction and relaxation.
-myosin ATPase
(for **contraction**)

-Ca-ATPase
(for **relaxation**)

Liver also can give glucose from
1) its stored glycogen (glycogenolysis)
2) using amino acids, fatty acid, pyruvate (gluconeogenesis).

-glucose then will go to blood stream then to the muscle fibers.

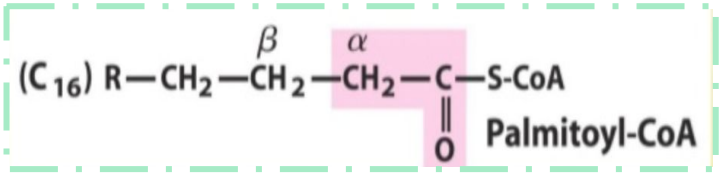
★ in prolonged exercise
adipose tissue will give fatty acid -> goes to bloodstream -> goes to muscle fibers -> get converted into 6 Acetyl CoA (by β-oxidation) -> undergoes oxidative phosphorylation + O_2 produced from the lung (aerobic pathway) to give ATP

Red muscle fibers (Aerobic metabolism)

- Red muscle fibers are suitable for prolonged muscle activity
  الرياضيون يمتلكون هذا النوع من العضل بسبب الممارسة المستمرة للرياضة
- Their metabolism is mainly Aerobic and "**Depends on adequate supply of O_2**"
- They obtain ATP mainly from fatty acids
  عشان كذا لما الشخص يبي ينحف يسوي تمارين هوائية لأنها تستخدم الدهون
- Fatty acids are broken down by β-oxidation which will produce Acetyl CoA (A process in which the fatty acids are degraded and energy is Produced), Krebs cycle, and the respiratory chain.

★ why it's called β-oxidation ?

The process of beta oxidation is named after the carbon atom in the beta position of the fatty acyl-CoA which becomes the most oxidized during the cyclic redox reactions that remove C2 units in form of acetyl-CoA from the fatty acyl chain. **(a pathway that converts fatty acid to Acetyl COA)**



Why they're called RED fibers ? **"Important Question"**

- **Red colour is due to the rich of myoglobin**, mitochondria and capillaries

Myoglobin

- has higher O2 affinity than hemoglobin

*O2 can't be released easily -> in absence of O_2 muscles undergo anaerobic metabolism

- It releases O2 when its level drops .

- Each one **myoglobin** binds to **ONE** molecule of O2 ,while **hemoglobin** bind with **4** O2

continued in NEXT SLIDE

Red muscle fibers (Aerobic metabolism)

There are 4 ways for muscle fibers to get ATP :

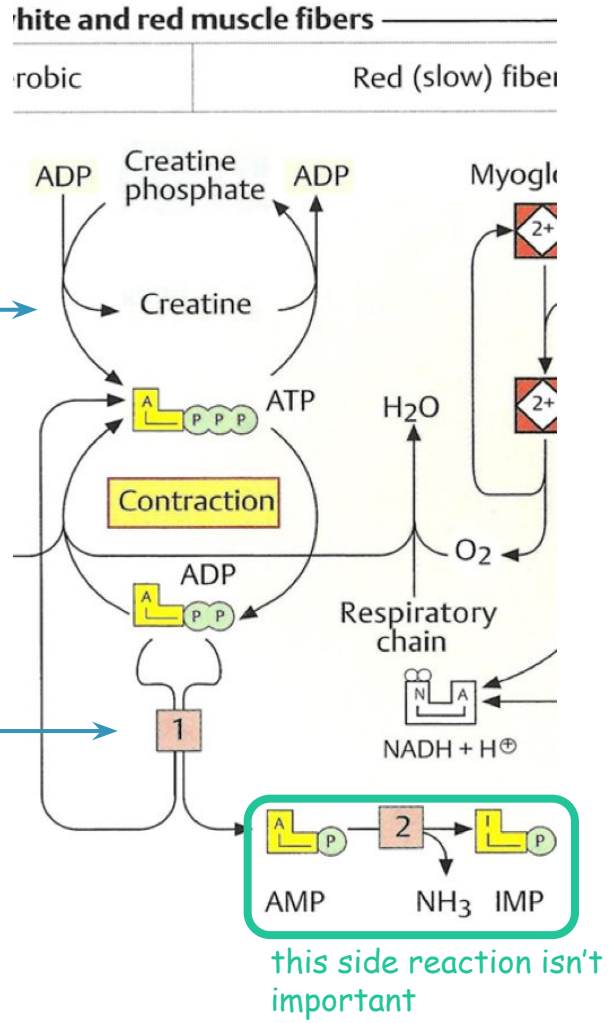
1. aerobic by red fibers
2. anaerobic by white fibers
3. creatine phosphate
4. by the enzyme **adenylate cyclase**;

   * it's mechanism:

   2 ADP -> 1 ATP + 1 AMP

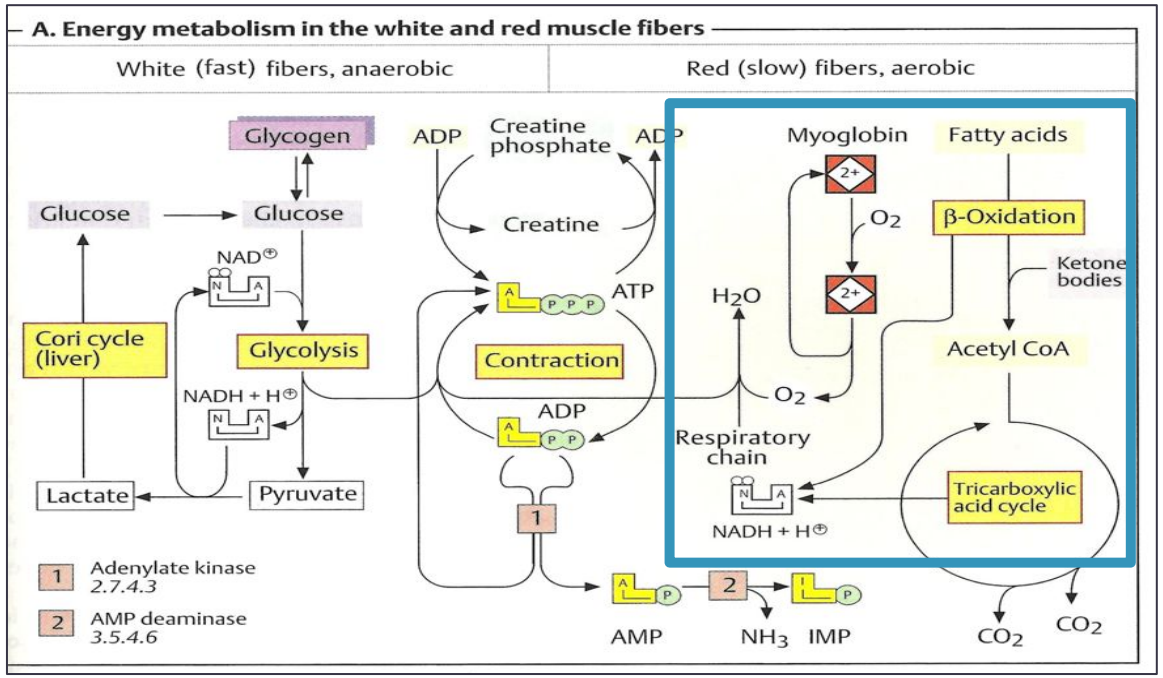
What do we need the ATP for?
It is used in both contraction and relaxation of the muscle.

العضلة في حالة الراحة راح تخزن اي تي بي على صورة كرياتين فوسفيت و جلايكوجين بمجرد ما يصير في حركة تبدأ تستهلك اي تي بي المخزن فيها



this side reaction isn't important

ATP metabolism in red muscle fibers:



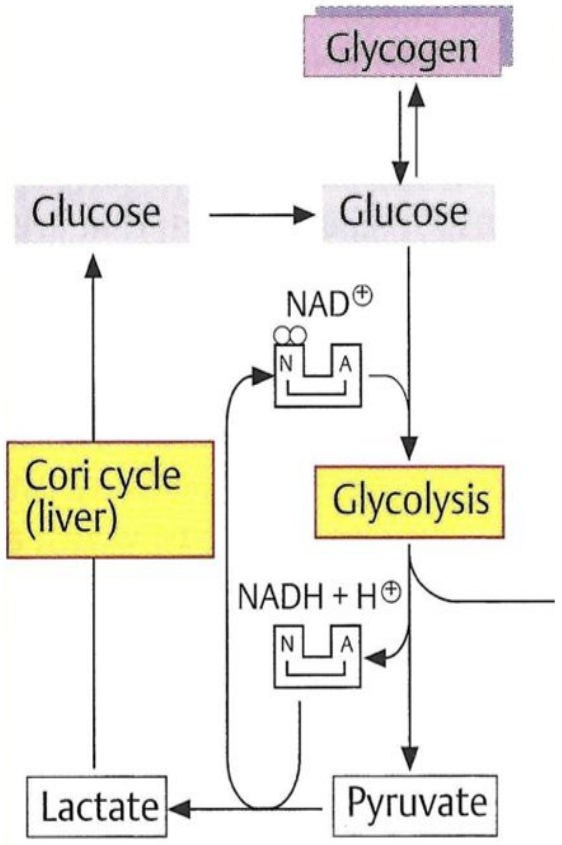
Fatty acids are oxidized to acetyl coA → Acetyl coA enters the krebs cycle → Krebs cycle will give NADH → NADH goes to respiratory chain in presence of O_2 given by myoglobin → Production of ATP

White muscle fibers (anaerobic)

- ★ White muscle fibers are suitable for fast, strong contractions
- ★ They mainly obtain ATP from **anaerobic glycolysis**.
- ★ During intense muscle activity (weightlifting, etc.) O_2 supply from blood quickly drops, then the muscle will use anaerobic glycolysis
- ★ They have supplies of glycogen that is catabolized and undergoes glycolysis.

- They are white because they have less mitochondria, capillaries and myoglobin
- They make energy from glycogen breakdown fast

Anaerobic Pathway:



glycogen phosphorylase

Glycogen ⟶ **glucose-1-PO_4** + free glucose (8:1)

-> glucose-6-PO_4 -> glycolysis -> ATP

- anaerobic glycolysis
  - ATP is produced, $NADH^+H^+$ is re-oxidized to maintain glucose degradation and ATP formation
  - pyruvate will be converted into lactate

Lactate is resynthesized into glucose in the liver by Cori cycle

Cori cycle functions:
Lactic acid to glucose
NADH to NAD+

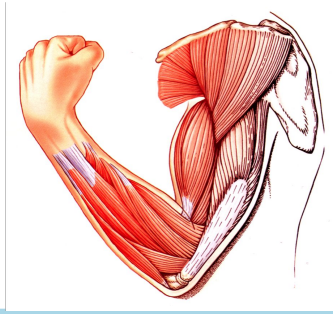
Why skeletal muscles can't produce new glucose from lactate?

Because:

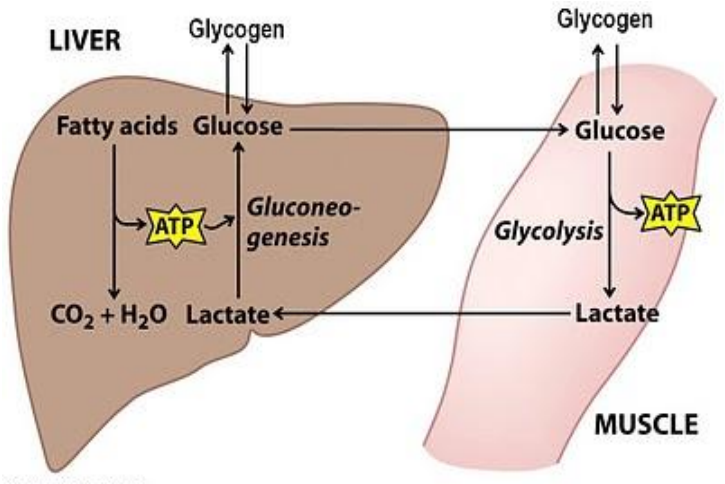
1- Gluconeogenesis (energy consuming) requires much more ATP than is supplied by glycolysis in muscle

2- O_2 deficiencies do not arise in the liver even during intense exercise

➔ **Therefore, liver always has sufficient ATP for gluconeogenesis**



The Cori Cycle



In anaerobic glycolysis, the glucose is converted to lactate

Lactate in muscle is released into blood

Then, transported to the liver

Liver converts lactate into glucose via gluconeogenesis

The newly formed glucose is transported to muscle to be used for energy again

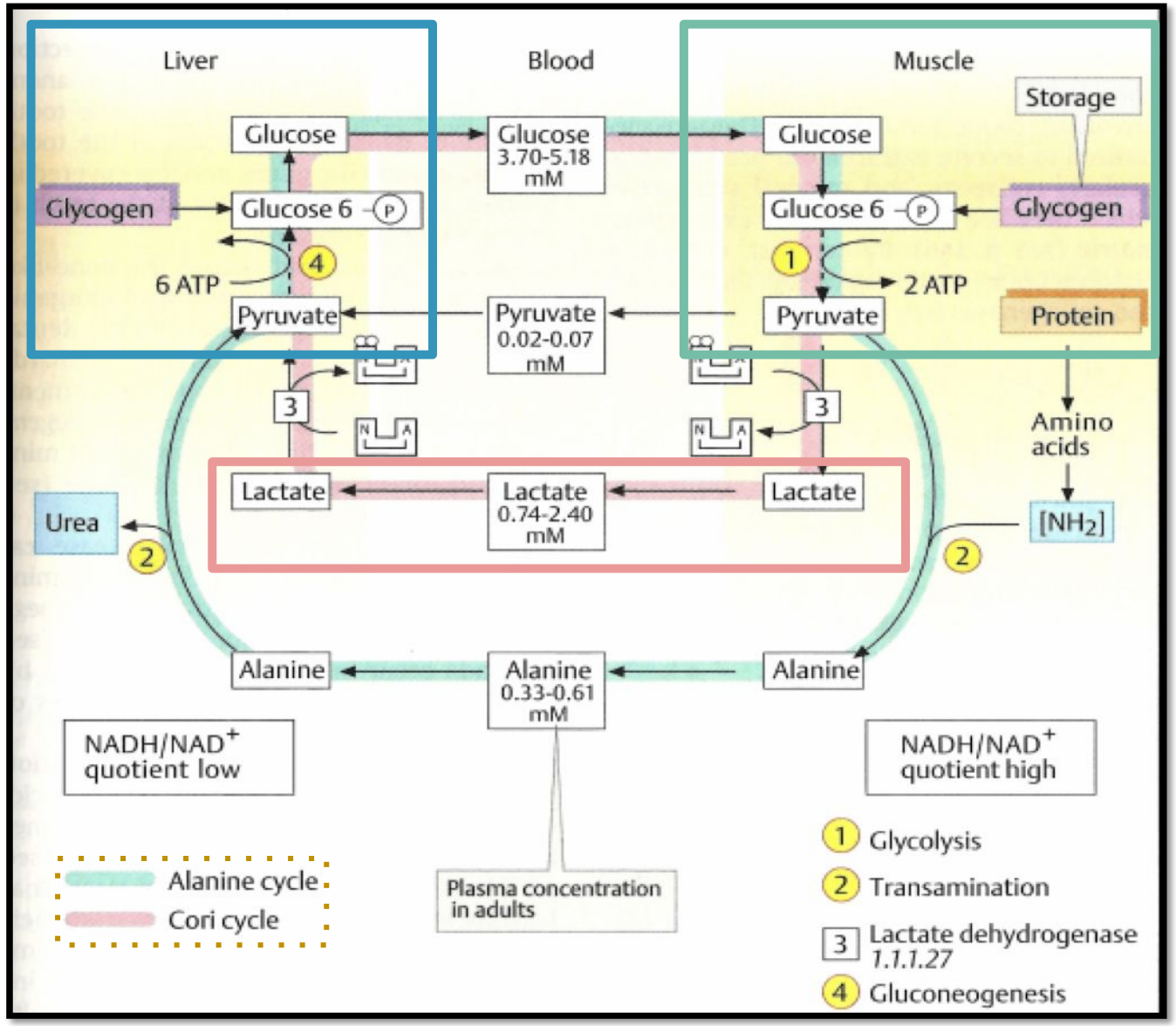
Important

Cori cycle

★ In the liver:

- Liver produces glucose via gluconeogenesis or glycogenolysis.

the newly formed glucose is transported to muscle to be used for energy again
" **complete cycle** "



★ In the Muscle:

- white muscle fibers (Fast & Strong contraction) obtain ATP from Anaerobic glycolysis.

In Anaerobic glycolysis glucose is converted to lactate.

★ In the blood:

- Lactate in muscle is released into blood.
- Transported to the liver.

Objective : Discuss the importance of Cori and glucose-alanine cycles in energy metabolism

The glucose-alanine cycle

The glucose-alanine cycle products

1 In muscle

- Pyruvate from glycolysis during exercise
- Amino nitrogen (NH_2) from normal protein degradation

Pyruvate (with NH_2) is converted to alanine :
* Pyruvate + NH_2 = Alanine

2

ALANINE IS TRANSPORTED FROM THE MUSCLE BY THE BLOOD INTO THE LIVER

3 In liver

- Liver converts **alanine** back to **pyruvate**:
Alanine – NH_2 = Pyruvate
(NH_2 is Converted to urea which is excreted later.)

- pyruvate is used in gluconeogenesis to form glucose

- The newly formed **glucose** is transported to **muscle** to be used for **energy** again.

*Recall that it's different from the liver "opposite"

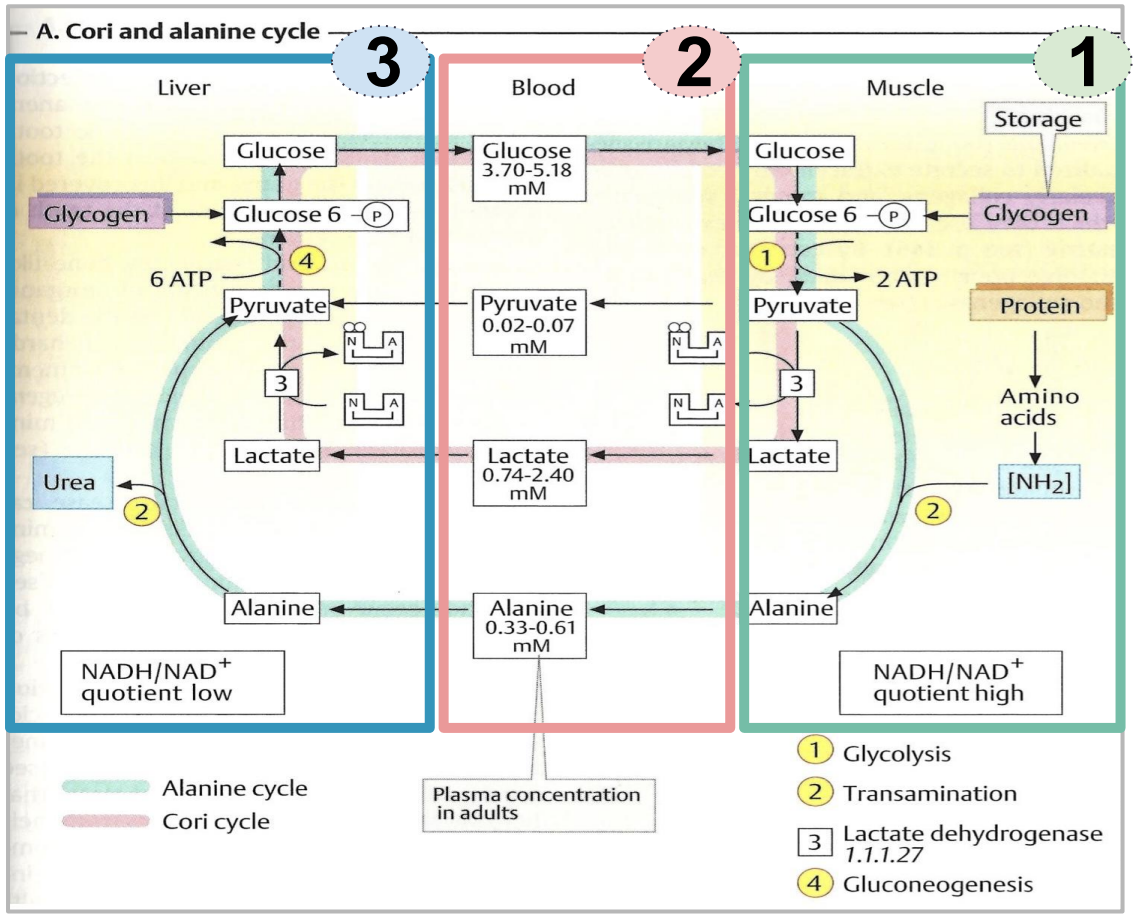
ليش تحصل هذي السايكل ؟
عند الفترة الطويلة للصيام العضلات الحركية تبدأ تتكسر والناتج لتكسر البروتينات اللي في العضلة مادة اسمها (أمينو نيتروجين) ترتبط مع البيروفيت ويصير اسمهم (الألانين) ويدخل هذي السايكل عشان يزودنا بالطاقة

NOTES:

- ★ The alanine cycle in the liver doesn't only provide alanine as a precursor for gluconeogenesis, but also transports to the liver the amino nitrogen arising in muscles during protein degradation. In the liver, it's incorporated (يختلط) into urea for excretion.
- ★ Alanine is the second important form of transport for amino nitrogen in the blood. And the first transport form is glutamate.

Objective : Discuss the importance of Cori and glucose-alanine cycles in energy metabolism

The glucose-alanine cycle



1- In skeletal muscles:

- **glycolysis** produces pyruvate.

- Pyruvate can be transaminated to alanine. (producing an amino group)

2- In the blood:

The alanine then enters the **bloodstream** and is transported to the **liver**.

★ Alanine is returned to the liver for **gluconeogenesis**.

3- in the liver:

- Within the liver, alanine is converted back to pyruvate by deamination (The removal of amino group).

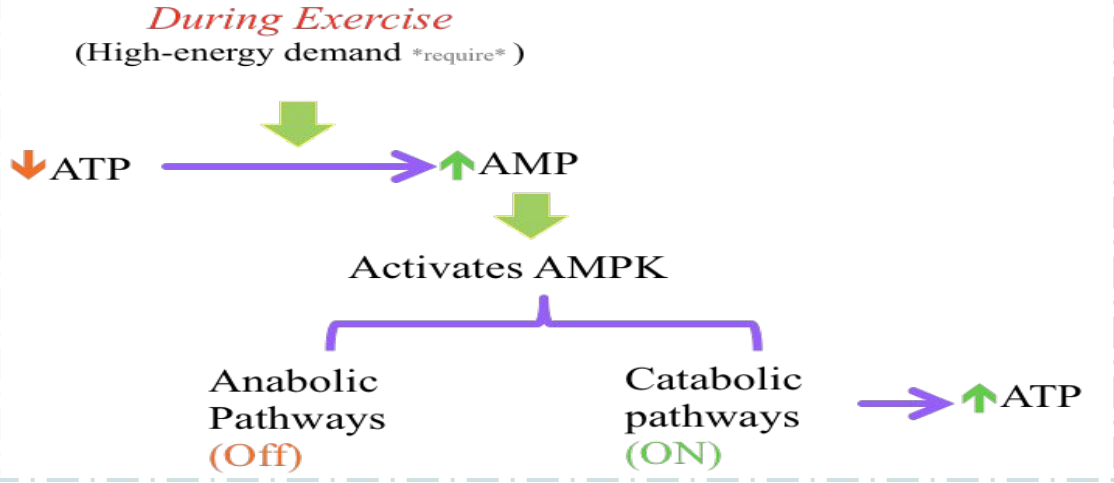
- Pyruvate is available for **gluconeogenesis** and the glutamate supplies the urea cycle.

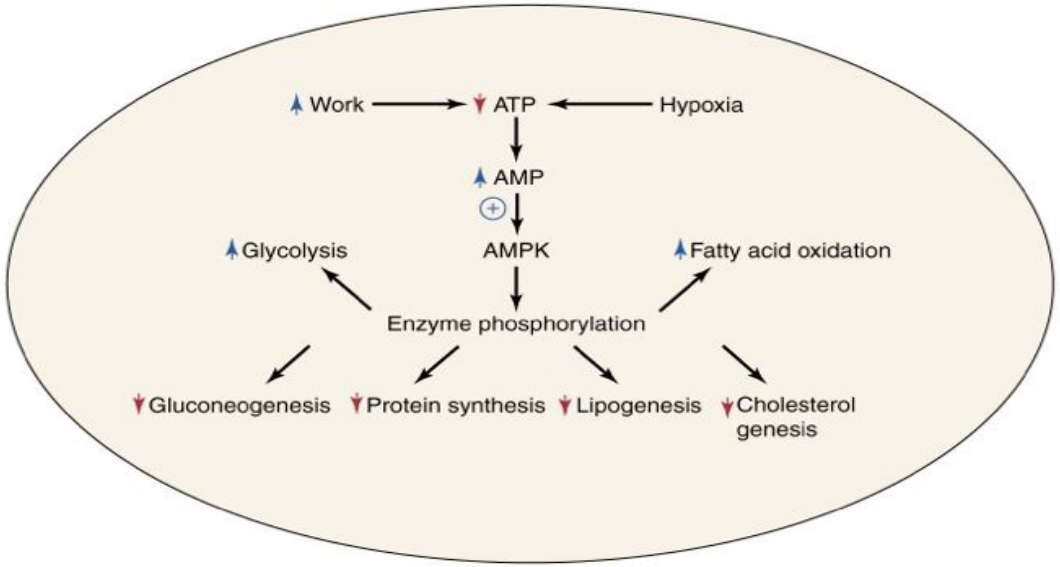
- **Gluconeogenesis** converts pyruvate to form glucose.

- The newly formed glucose can then enter the blood for delivery back to the muscle.

Objective : Discuss the importance of Cori and glucose-alanine cycles in energy metabolism

Exercise and AMPK





- In exercise, the **metabolic** enzymes are **regulated** thru **phosphorylation** by **AMP-activated protein kinase (AMPK)**

*EXTRA : By this process the body try to save energy .

❑ Explanation :

- During exercise **ATP** level goes **down** at the same time **AMP** level goes **up** .

- When **AMP** level goes **up** it activates the **AMPK** enzyme .

- The activation of **AMPK** enzyme will

1) **shut down** the **anabolic** pathway (ATP requiring processes)
★ to save energy

2) **stimulates catabolic** pathway (ATP producing processes)
★ to produce energy.

Objective : Discuss the importance of Cori and glucose-alanine cycles in energy metabolism

Muscle fatigue and endurance in athletes

Muscle fatigue:

Inability of muscles to maintain a particular strength of contraction over time.

Causes:

Muscle **damage** & **accumulation** of lactic acid "decrease PH in tissues".

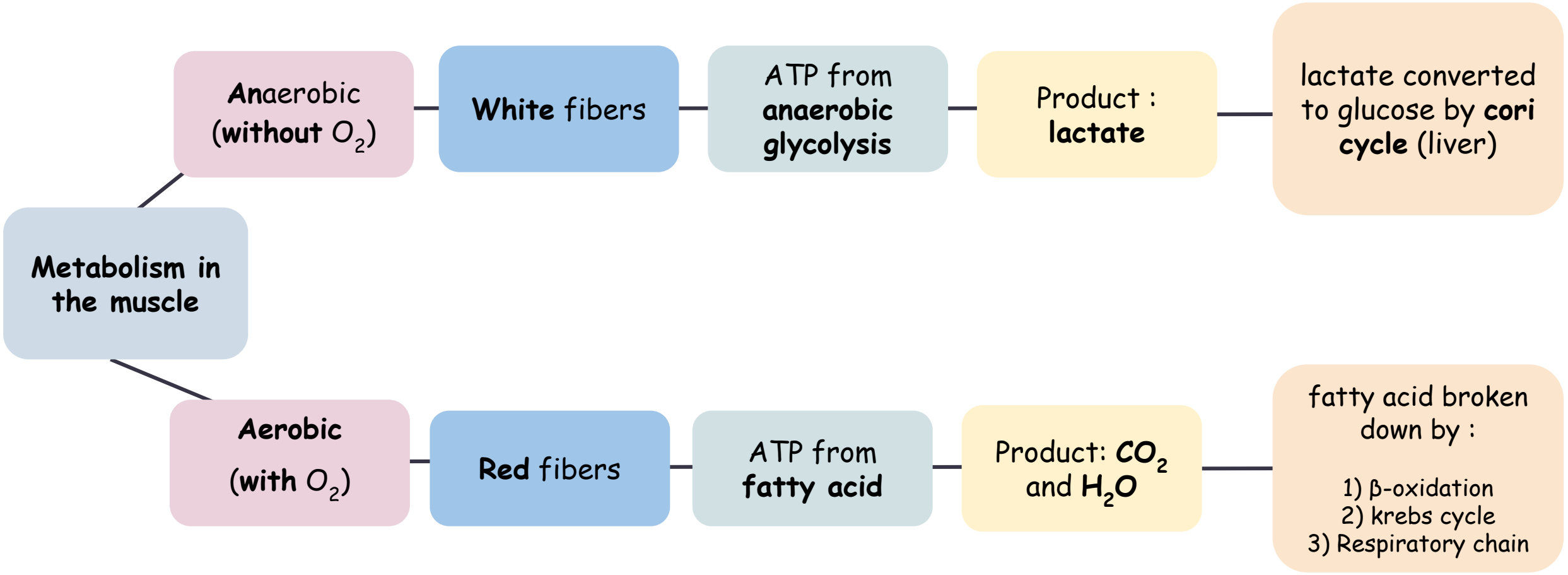
- **Athletes** are able to change the proportions of red and white* muscle fibers **by** targeted training.
- The expression of muscle proteins can also change during the course of training.

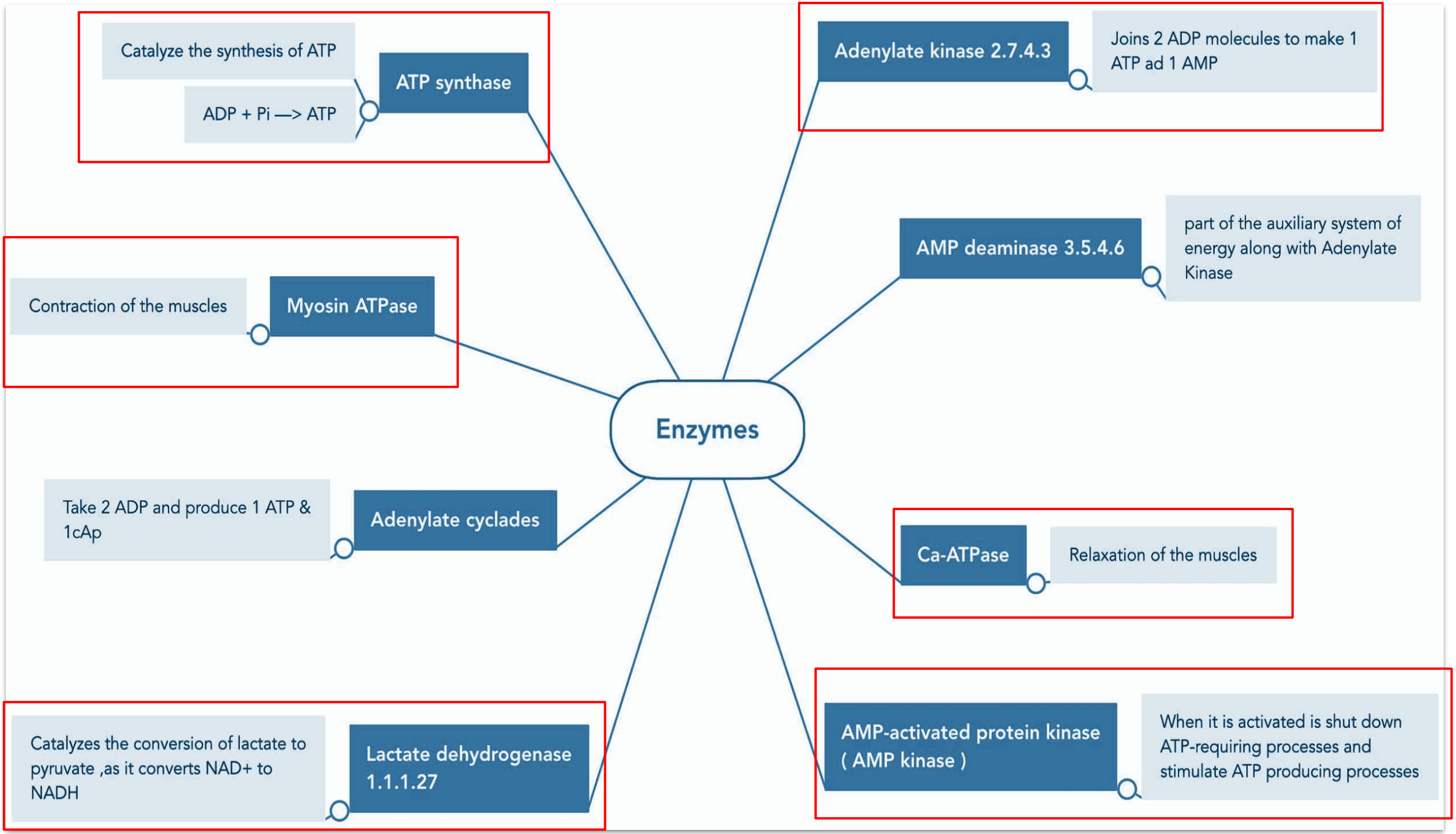
This provides them with

1. High endurance during muscle activity.
2. Efficient energy production and consumption.
3. Delayed fatigue.

* The **red** muscle fibers are **better** for them because it is suitable for **prolonged** effort + it is an **aerobic** which doesn't cause lactic acid formation which leads to muscle fatigue .

Review


Metabolism in the muscle
Anaerobic (without O_2)
White fibers
ATP from anaerobic glycolysis
Product : lactate
lactate converted to glucose by cori cycle (liver)
Aerobic (with O_2)
Red fibers
ATP from fatty acid
Product: CO_2 and H_2O
fatty acid broken down by :
1) β-oxidation
2) krebs cycle
3) Respiratory chain


Enzymes
ATP synthase
Catalyze the synthesis of ATP
ADP + Pi —> ATP
Adenylate kinase 2.7.4.3
Joins 2 ADP molecules to make 1 ATP ad 1 AMP
AMP deaminase 3.5.4.6
part of the auxiliary system of energy along with Adenylate Kinase
Myosin ATPase
Contraction of the muscles
Adenylate cyclades
Take 2 ADP and produce 1 ATP & 1cAp
Ca-ATPase
Relaxation of the muscles
Lactate dehydrogenase 1.1.1.27
Catalyzes the conversion of lactate to pyruvate ,as it converts NAD+ to NADH
AMP-activated protein kinase (AMP kinase)
When it is activated is shut down ATP-requiring processes and stimulate ATP producing processes

Take home message

- ATP is an important source of chemical energy needed by the cells to perform body functions
- Muscular activity requires constant supply of ATP for energy either from aerobic or anaerobic metabolism
- Cori and glucose-alanine cycles play an important role in regenerating glucose for energy
- Athletes are able to change proportions of their red and white muscle fibers with appropriate training

Overview

★ Three systems of energy transfer
★ ATP as energy source
★ Aerobic metabolism: red muscle fibers
Anaerobic metabolism: white muscle fibers
★ Cori cycle
★ Glucose-alanine cycle
★ Muscle fatigue and endurance in athletes

MCQs

Q1:During exercise **ATP** level goes down and the AMP level gose?			
A)Down	B)Up	C)Remain the same	D)Down and up in the same time
Q2:How many O2 molecule can myoglobin take?			
A)1	B)2	C)3	D)4
Q3:What is the enzyme that converts two ADP to produce 1 ATP & 1 AMP			
A)Myosin ATPase	B)adenylate cyclase	C)Lactate dehydrogenase	D)Adenylate kinase
Q4: the first step of ATP metabolism in red muscle fibers			
A) Acetyl coA enters the krebs cycle	B) Production of ATP	C) Fatty acid is oxidized to acetyl COA	D) Krebs cycle will give NADH
Q5: in the White Muscle Fibers; they mainly obtain ATP from…			
A) aerobic glycolysis	B) anaerobic glycolysis	C) Krebs cycle	D) electron transport
Q6: Liver converts lactate into glucose via			
A) glycolysis	B) glycogenesis	C) gluconeogenesis	D) glucogenesis
Q7:during exercising, the metabolic enzymes are regulated through phosphorylation by:			
A) ATPK	B) AMPK	C) GAPk	D) GMPk
Q8: In muscle, Pyruvate (with NH_2) is converted to			
A) guanine	B) lysine	C) Alanine	D) Valine

Answer key:

1) B
2) A
3) D
4) C
5) B
6) C
7) B
8) C

SAQs

Q1: List 3 ways to get ATP in the muscles?

1. aerobic by red fibers
2. anaerobic by white fibers
3. creatine phosphate degradation

Q2: What is the definition of muscle fatigue?

Inability of muscles to maintain a particular strength of contraction over time

Q3: Why skeletal muscles can't produce new glucose from lactate?

Because Gluconeogenesis requires much more ATP than is supplied by glycolysis in muscles and O_2 deficiencies do not arise in the liver even during intense exercise

Q4: Explain the mechanism of ATP metabolism in red muscle fibers?

Fatty acids are oxidized into acetyl coA after that acetyl coA enters the krebs cycle to give NADH which will go to the respiratory chain in presence of O_2 given by myoglobin to start production of ATP

❖ Team leaders:

Deema Almaziad **Raed Alojairi**

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- ➔ **Elaf Almusahel**
- ➔ **Noura Alturki**
- ➔ **Nouf Alhumaidhi**
- Reem Alqarni
- Taif Alotaibi
- Noura almazrou
- Lina alosaimi
- Nouran Arnous
- Ajeed Alrashoud
- Abeer Alkhodair
- Alwateeen albalawi
- Shahd Alsalamh

❖ Boys team:

- ➔ **Omar alghamidi**
- Saad Dammas
- Mohannad alqarni
- Rakan alfaifi
- Nayef alsaber
- Alkaseem Binobaid

★ إن الرياح إذا اشتدّت عواصفها فليس تُردي سِوى العالي من الشجر

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