« وَلَا تَحْسَبَنَّ اللَّهَ غَافِلًا عَمَّا يَعْمَلُ الظَّالِمُونَ »

Mays Aljundi ✓

Biochem ✓

رُبما على حاء الحيرة

- نقطة لا تراها -

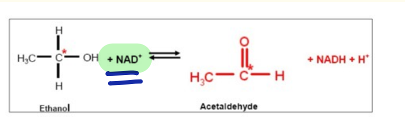
ENZYMES CLASSES

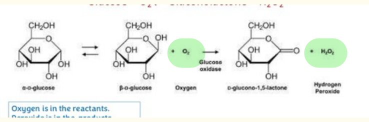
✱ Enzymes are classified into 6 groups :

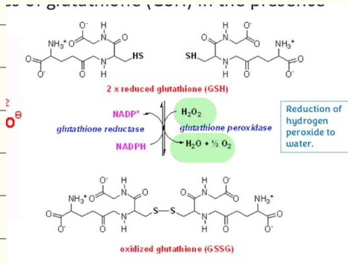
① Oxidoreductases (Largest group):

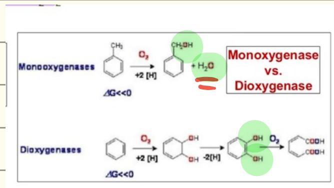
- Catalyze oxidation / reduction reactions involving the transfer of H atoms or e^-
- They can be devided into 4 groups :

Dehydrogenases	oxidases	peroxidases	Oxygenases
• Removing H from Substrate • Need to have coenzymes : ① NAD^+ / NADH ② FAD / $FADH_2$	• O_2 considered as substrate • H_2O_2 product	• oxidation by H_2O_2 • H_2O_2 surves as a substrate → عكس يصير لـ H_2O_2 reduction لـ H_2O	• Introducing O_2 into the substrate • Reduced product is H_2O





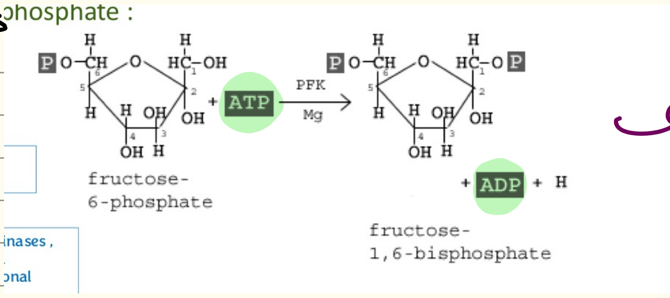




② Transferases :

- These enzymes transfer a functional group from one substrate to acceptor molecule
- Kinases are example (transferred group is phosphate)

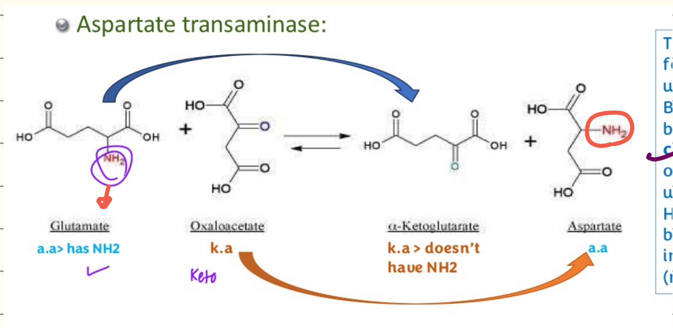
Kinases



① you can see ATP
② Addition of phosphate group

← هون أخذنا فوسفات من الـ ATP يعني دخلت بالـ rxn

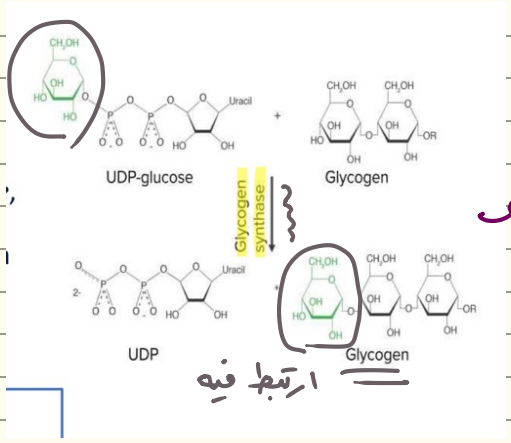
transaminases



① Transfer an amino functional group from amino acid to keto acid

((الـ amino acid راح يصير keto acid, والعكس))

Synthases



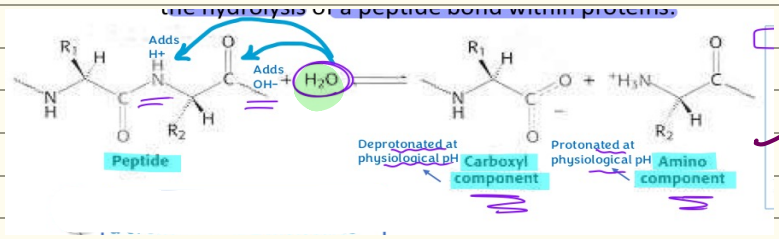
ارتبط فيه

① The compound is physiologically IMP

بنفرق بينه وبين الـ Synthase تبع الـ lyases :
« ما بتشوف double bond جديدة أو ما بتشوف تحول
ring أو ما بتشوف single bond لـ double bond »

③ Hydrolases :
- Catalyze cleavage reactions using water
- Such as: proteases, esterases, lipases, digestive enzymes

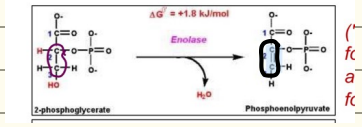
like: Trypsin, Chemotrypsin, elastase



① H_2O substrate

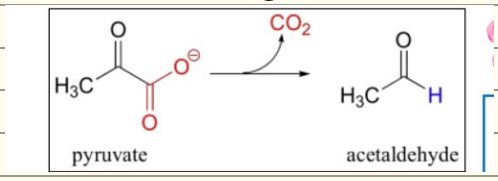
④ Lyases: « Without H_2O, coenzymes, isomers etc »
- Cleave C-C, C-O, C-N and other bonds leaving double bonds or rings
- Such as :

Dehydrases



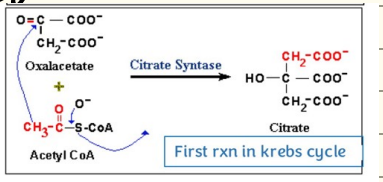
⇒ Removing H_2O from the substrate to give double bond

Decarboxylases



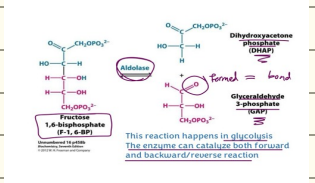
⇒ Replacement of carboxyl group by H

Syntheses



⇒ Addition of small molecules to a double bond

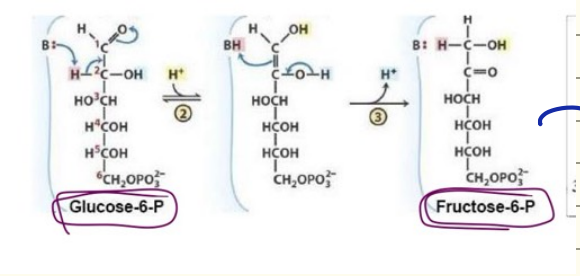
Special: Aldolase



⇒ Breaks down the substrate into 2 products and forms double bond

⑤ Isomerases:

- Convert an isomer into another
- They dont require energy
- They rearrange the bond structure of a compound



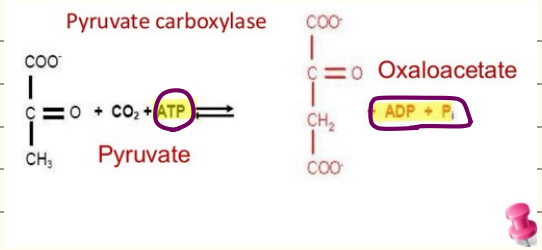
تغيرت أماكن الـ bonds فتحول لـ isomer
لـ isomer ثاني

⑥ Ligases:

- Join C-C, C-O, C-N bonds
- connect 2 molecules together
- use energy derived from ATP

ATP Substrate
ADP product

ما تاخذ من functional group إنتبهي ♥ ATP



Ligase هي phosphate الـ transfer ما في

الله يوفقكم وييسر لكم أموركم ♥

" اللهم إني فوضت أمري إليك فَاكفني،

واصرف عني ما يقلقني، وتولني بفضلِك يا الله "

ENZYMES REGULATION

* عشان نتحكم في الـ amount للـ enzyme :

Slow mechanisms ←
- gene level
- proteases
- synthesis for isosymes

* التقسيم (compartmentalization) بيعمل :

هدول التنين بيتحكموا فيها non specific regulation مع Temperature + pH

limit diffusion rate to produce higher collision rate
Such as: lysosomal + fatty acid metabolism
- synthesis: cytosol
- degredation: Mitochondrial

* الـ limit بتعمل نفس اللي فوق enzyme complexing

(oxidoreductases) ex: pyruvat dehydrogenase
- decarboxylase (3C) ← E1 subunit
- oxidation (2C)
- Transfer (1C)

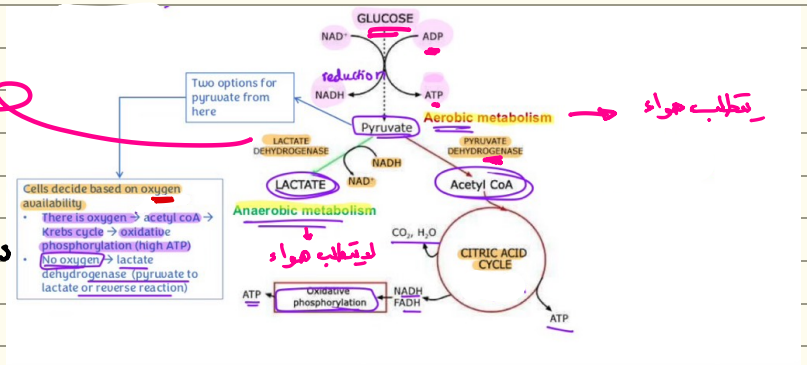
بتحول من 3C, pyruvate إلى 2C, CoA

* الـ isoZymes اتعرفت من :
- diff genes
- diff tissues
- diff V_{max} & Km

هدول نفس الـ isoforms بتختلف enzymes/gene ← They catalyse same rxn

---

* Aerobic vs Anaerobic metabolism :



* تتحكم بتعمل عكس الـ rxn وهو (reversible) tetramer وهو عنده 5 من isoZymes وهم :

H4, H3M1, H2M2, H1M3, M4
- H4: Heart
- H3M1: RBC
- H2M2: lungs
- H1M3: kidney
- M4: liver + muscles

LDH1 prefers to:
Lactate → pyruvate
High efficiency towards pyruvate

LDH5 prefers to:
pyruvate → Lactate
High efficiency towards lactate

allosteric isozymes

NOTE: When glucose is phosphorylated it wont cross pM cuz of phosphate

* Differences between ① Hexokinases + ② Glucokinases:

① Hexokinase:

- A RBC + skeletal muscles enzyme → High efficiency to trap glucose
- Allosteric isozyme (phosphorylates glucose to glucose-6-phosphate)

> **1. Allosteric Enzymes:**
>
> - **Definition**: Allosteric enzymes are enzymes that can be regulated by molecules binding to sites other than their active sites. These alternative binding sites are called **allosteric sites**.

- It is inhibited by glucose-6-phosphate → favors T state
- Low Km, High affinity, low Vmax

② Glucokinases:

- A Liver enzyme → low efficiency
- It is activated by insulin and inhibited by glucagon
- High Km, low affinity

Regulation of enzymatic activity

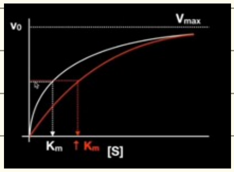
INHIBITORS

جد ولنشرحوا تحت ال
Regulation of enzymatic activity

Inhibitors: ←
عنا نوعين إله:
- Reversible → Competitive / NON Competitive → All physiological inhibitor
- Irreversible → Covalent / Transition state analog / Heavy metals → low concentration of active enzyme (Synthetic inhibitors)

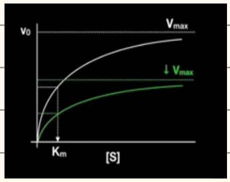
Reversible

- Competitive inhibition:



- لما Sub يصيرلها compete مع enzyme.
- عشان نتغلب على الـ inhibition بنزيد كمية الـ sub.
- Vmax نفسها بس Km بتصير أعلى لما يكون عندي competitive

- Non-competitive inhibition:



- لما E أو ES يرتبط بمكان غير الـ catalytic site
- Km نفسها والعكس Vmax أقل لـ non competitive

Irreversible

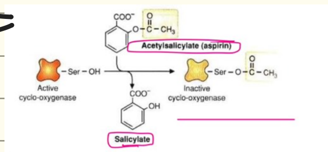
- Covalent inhibitors:

- يكونوا روابط covalent أي tight
- They modify the active site chemically

① Example: di-isopropyl fluorophosphate (DFP) i...
The nerve gas sarin

it inhibits acetylcholinesterase → الي بعمل degredation لل acetylcholin → acetyl + choline
→ بيصير في تجمع لـ acetylcholine وبعمل شلل (paralysis)

② Aspirin (acetylsalicylic acid)
cyclooxygenase Which inhibits th...



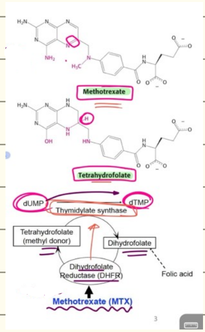
بيشبه الـ precursor prostaglandin
بضيف acetyl group

Transition State analogs :

- بيربط مع Sub و بيعلق
- بيعدل من ال enzyme كامل على عكس asprin
- بيربط Tightly وبشرط covalent
- ال drugs مابنقدر نصممها بحيث تحاكي ال transition state

• Substrate and transi...
Suicide inhibitors
هيك اسمهم

① • Methotrexate



- synthetic inhibitor بيعالج ال cancer, rheumatoid
- بيعتبر Structural analog لل folat
- بيعتبر Sub للانزيم dihydrofolate بس يثبط تكوين Nucleotide base من خلال تثبيط الانزيم الي
- بيعتبر coenzyme لل thymidylate يمنع deoxyTMP

② • Penicillin
The first antibiotic to be discovered.

- نفس structure تبع alanyl-alanine
- بيعمل تثبيط لـ transpeptidase glycopeptidy → مسؤول لحل ال bacteria cell wall
- serine هو بيجي و بيعمل attachment مع penicillin و بيفكك الحلقة تبعت β-lactam و بتصير مفتوحة

Heavy metals :

- بتحسر على nonspecific doses عالية
- ال Hg بيربط مع Sulfhydryl ، بيبعدهم عن ال active site
- ال pb بتحل محل Ca^{+2}, Fe^{+2}, Mn^{+2} عن طريق irreversible mechanism
- toxic

Regulation through conformational changes

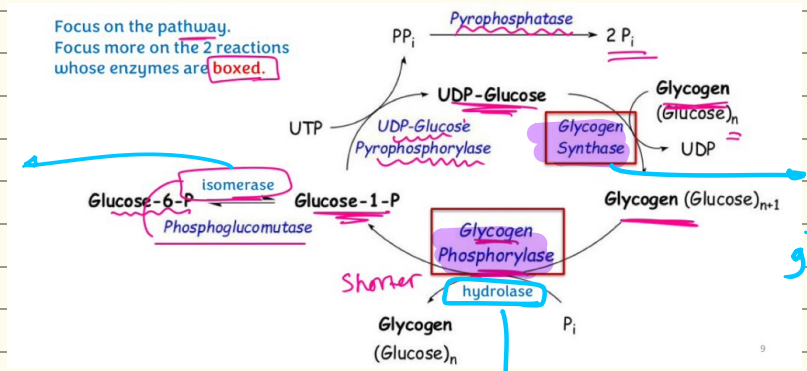
through changing of the enzyme structure.

Regulation: conformational changes

- These regulatory mechanisms include
  - Allostery
  - Covalent modulation
  - Protein-protein interactions between regulatory & catalytic subunits or between two proteins;
  - Proteolytic cleavage

* glycogen الـ metabolism :

- يحدث كله (Synthesis) او (degredation) يتأثر على عكس Cytosol في fatty acids metabolism



glucose 1P الى glucose 6P يحول

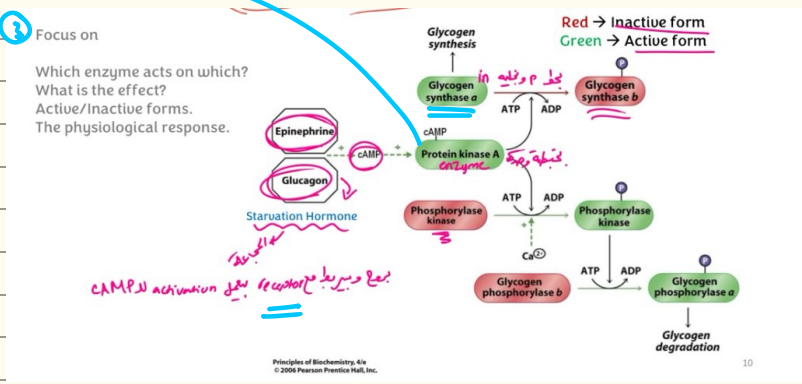
يحول من glucose 1P الى glycogen

يحول من glycogen الى glucose 1P

* Regulation by phosphorylation *

When inactive
- 2 catalytic
- 2 Regulator — Quaternary ①
- Serine / threonine ②
- (4 cAMP are needed) ③ يحتاج cAMP ربط فيه بيتحفز

adenyly cyclase من



هدول بالبروتينات
Reversible covalent modification

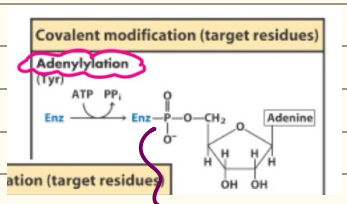
• Reversible covalent modification
- Rapid
- ATP بتعتبرها phosphoryl donor
- phosphorylation بتزيد فوسفات بين dephosphorylation بتشيل فوسفات بـ hydrolysis

لو عندي بروتينات لبعض بدك اياهم تتصغرب Kinases والثانية phosphatases
بتعمل Amplification

- أمثلة :

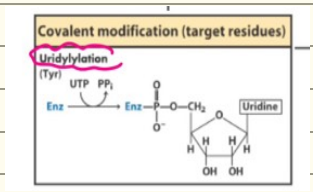
Adenylylation | Uridylylation | ADP-ribosylation | Methylation | Acetylation

• Addition of adenylyl group

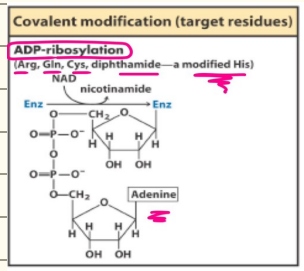


phosphodiester linkage بصير في

• Addition of uridyly group

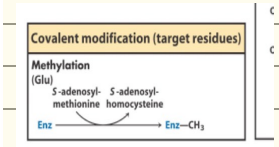


• Addition of adenosine diphosphate ribosyl group



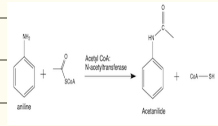
• Addition of methyl group

• Masking (-) charges



• Addition of acetyl group $CH_3-\overset{O}{\overset{\|}{C}}-$ بـ

• Masking (+) charges



allostery يشرح تحت

: Glycogen phosphorylase ✱

allosteric –

–

– يوجد بـ 4 حالات :

active ← R & T → inactive

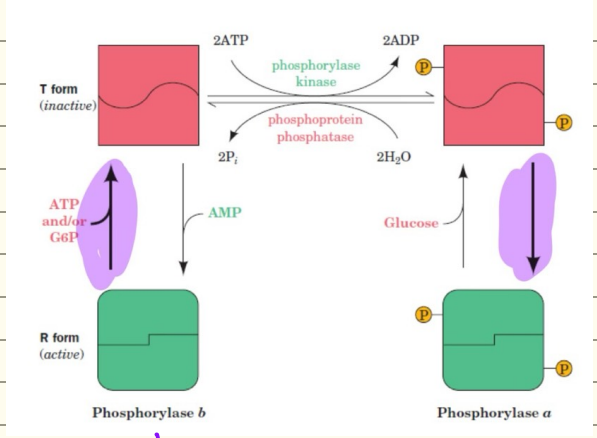
phosphorylation a & b

active ← a

b → inactive

(Negative allosteric) ATP favors T State

(positive allosteric) AMP favors R State



phosphorylase a ← وبنفس الشي لـ

usually inactive cuz the equilibrium favors T state

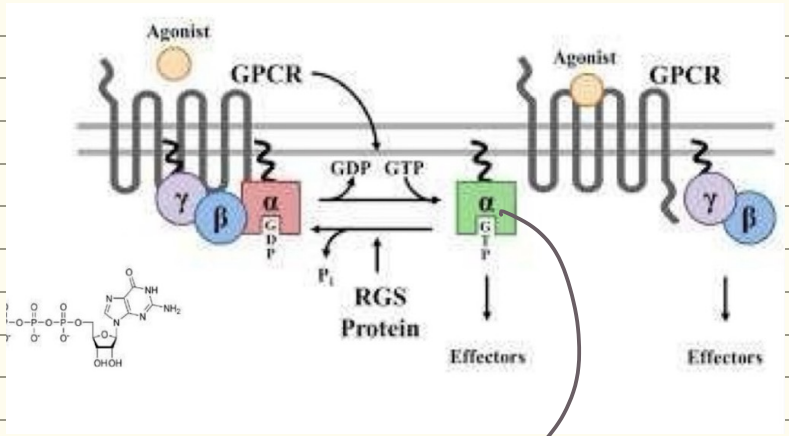
لانه بشكل عادي يكون R State

بتذكير شوي

protein-protein interactions between regulatory & catalytic subunits or between 2 proteins

G proteins :

- Trimeric ← α, β, γ
- يوصلوا الرسائل من Signals محددة عبر G protein-coupled receptors
- مهمين لـ Smell, taste, vision, hearing
- عندهم 7 transmembrane domains receptors
- لما يحس في replacement من GDP لـ GTP active
- لما يقيس في hydrolysis من GTP لـ GDP inactive



ممكن تربط مع cAMP واللي بربط بعدين مع PKA

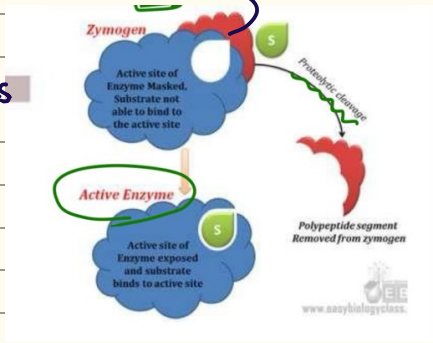
يتم عن طريق proteolytic cleavage : (proteolytic activation) Irreversible covalent modification *

: (Trypsinogen) Zymogens

They are proenzymes that require proteolysis (lysis/cleavage of specific regions of their protein structure) in order to be active. *

6 amino acids لـ نشيل منها أول

pro region
present at N terminus

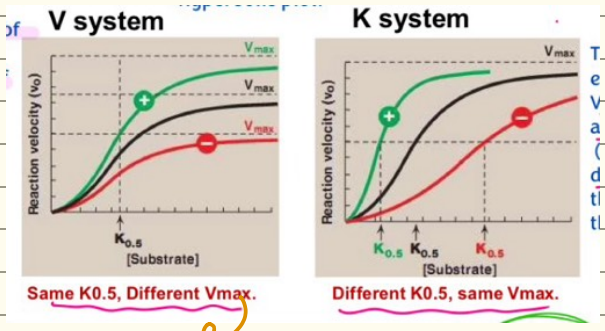


موجود بـ pancreas *

Allosteric regulation

✱ Allosteric enzymes :

- multi-Subunit proteins هم
- Quaternary
- The binding of regulatory molecules triggers conformational changes in active site
- allosteric site بيربطوا ب

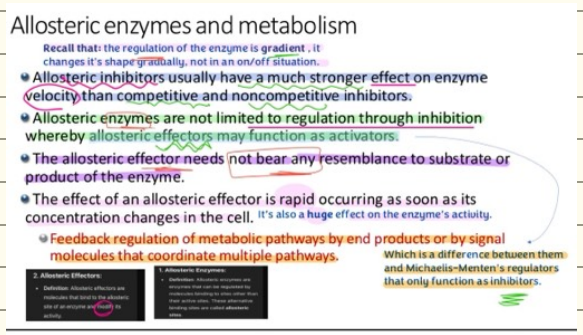


Vmax يأثر على

Km يأثر على

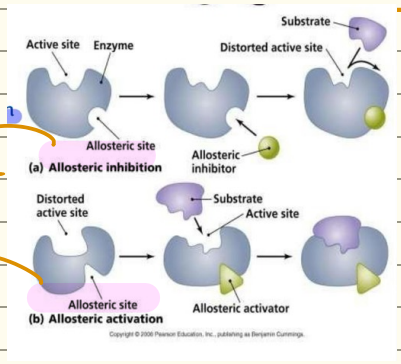
Positive cooperativity means that the binding of one substrate to the active site of one subunit, makes it easier for another substrate to bind to the active site of another subunit.

Notes :



Less active ← Substrate won't fit

more active ← Substrate will fit



(ATPase) : Aspartate transcarbamoylase

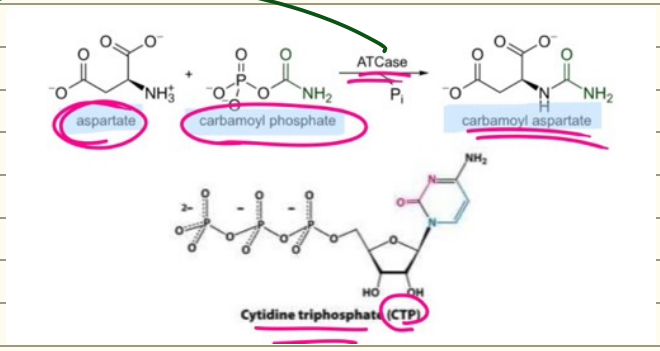
- هو responsible لأول خطوة للـ pyrimidine ← CTP
- فيه 12 polypeptide chains

6 catalytic ← 6 regulatory

- موجود بـ 2 forms

R form ← T form

inhibited by CTP




أليس الله بكاف عبده
@ishaiookh