คม 524 สารออกฤทธิ์ทางชีวภาพ (CH 524 Bioactive compounds) เนื้อหา หลักการเมตาบอลิซึม ส่วนที่ 2

โดย อ.ดร. เอกวิทย์ ตรีเนตร

ภาควิชาเคมี คณะวิทยาศาสตร์

Study of metabolic pathway

Major metabolic pathway (เทอม ที่ 2 ในรายวิชา คม 325)

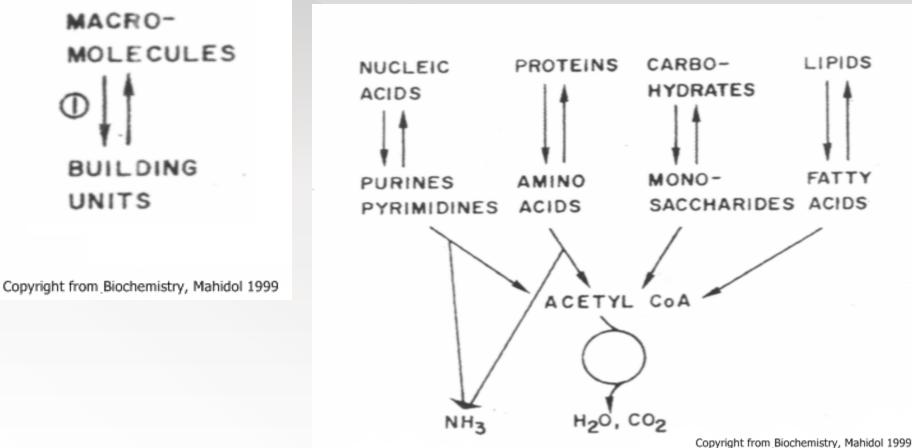
Specific metabolic pathway (ในบาง pathways ที่น่าสนใจ)

Main pathways (all living organisms) Glycolysis Aerobic respiration and/or Anaerobic respiration Citric acid cycle / Krebs cycle Oxidative phosphorylation Other pathways (most) : Fatty acid oxidation (β -oxidation) Gluconeogenesis Amino acid metabolism Urea cycle / Nitrogen metabolism Nucleotide metabolism Glycogen synthesis / Glycogen storage Pentose phosphate pathway (hexose monophosphate shunt) Porphyrin synthesis (or heme synthesis) pathway Lipogenesis HMG-CoA reductase pathway (isoprene prenylation chains, see cholesterol) Synthesis of energetic compounds from non-living matter: Photosynthesis (plants, algae, cyanobacteria)

Chemosynthesis (some bacteria)

Steps of Major Metabolic Pathway

Step 1. Change between biomolecule and building units



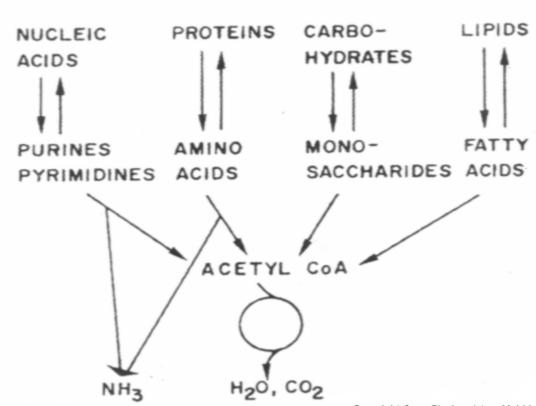
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Steps of Major Metabolic Pathway

Step 2. Change between building units and simple molecules

BUILDING UNITS 2 SIMPLE MOLECULES

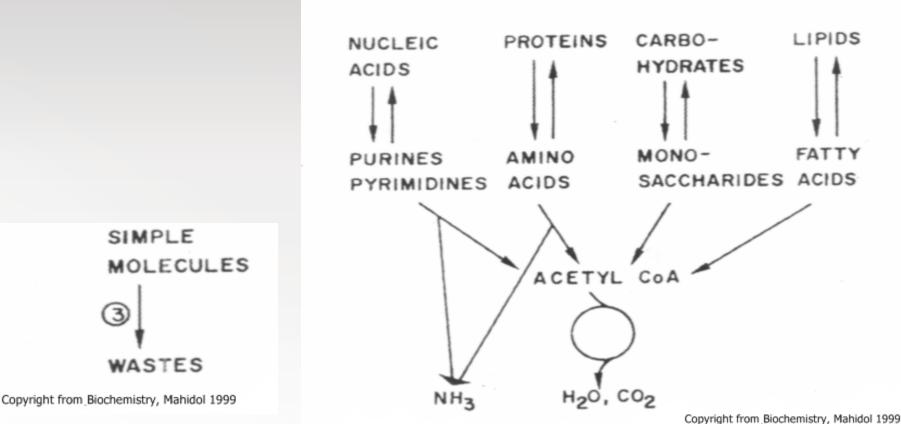
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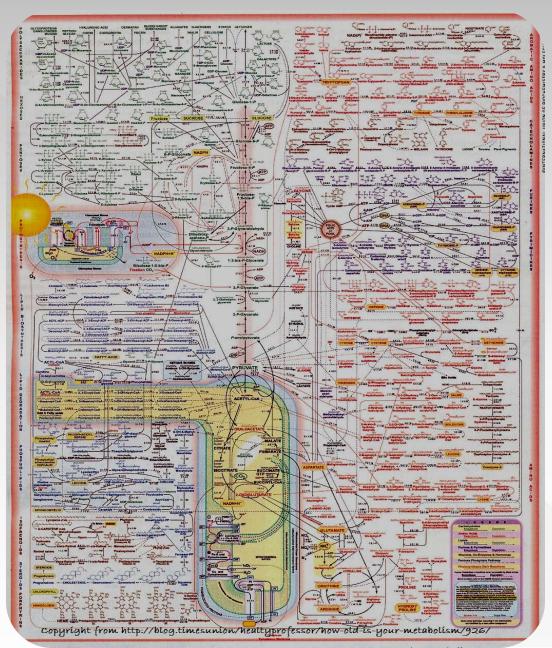
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Steps of Major Metabolic Pathway

Step 3. Change between simple molecules and wastes



Network of Major Metabolic Pathway



Types of Major Metabolic Pathway Glycolysis

Type 1. Linear sequence

B

C

ATP P: hexokinase glucose 6-phosphatase Glucose ADP H₂O 6-phosphate Fructose ATP 6-phosphate phospho fructose fructokinase-1,6-bisphosphatase Fructose ADP H₂O 1,6-bisphosphate Dihydroxyacetone Dihydroxyacetone phosphate phosphate D (2) Glyceraldehyde 3-phosphate (2) Pi - \rightarrow (2) P; (2) NAD⁺ (2) NAD⁺ (2) NADH + (2) H⁺ < (2) NADH + H⁺ (2) 1,3-Bisphosphoglycerate (2) ADP -> (2) ADP (2) ATP < (2) ATP Copyright from http://www.t3portal.org/ (2) 3-Phosphoglycerate T3 Portal v1/!SSL! /WebHelp/ales_vancura/ Gluconeogenesis and metabolism of glycogen.htm (2) 2-Phosphoglycerate (2) GDP (2) Phosphoenol-**PEP carboxykinase** (2) ADP pyruvate - (2) GTP pyruvate kinase (2) Oxaloacetate

(2) Pyruvate

(2) ATP

Glucose

Gluconeogenesis

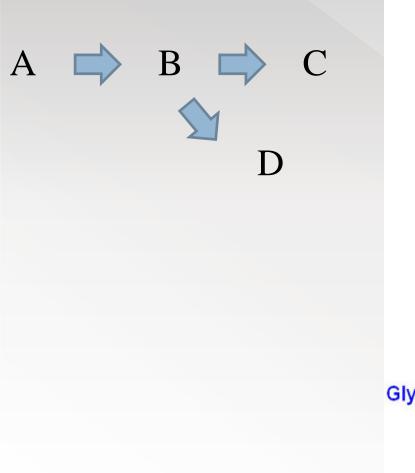
(2) ADP

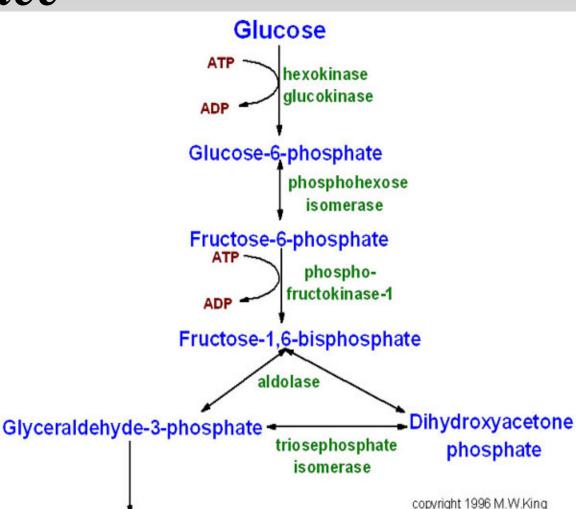
(2) ATP

pyruvate carboxylase

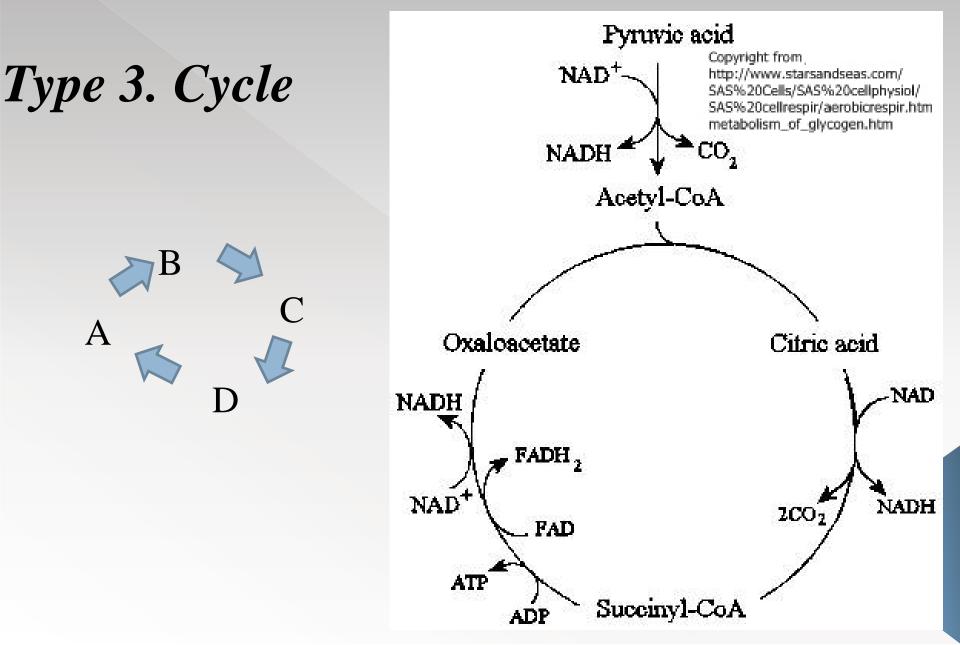
Types of Major Metabolic Pathway

Type 2. Branched sequence

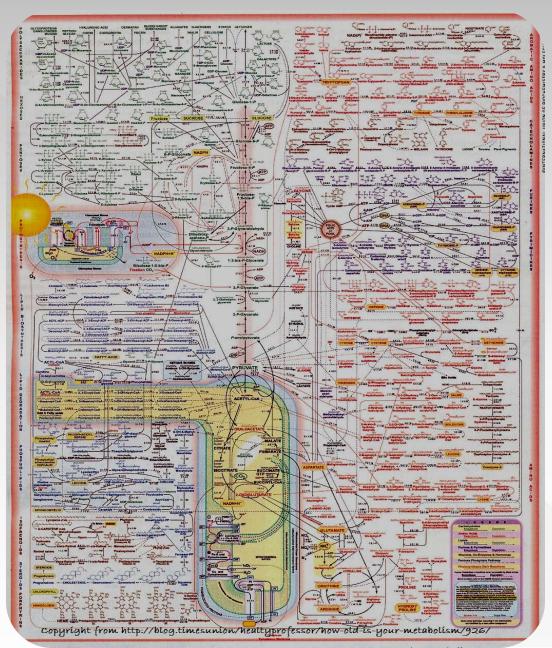




Types of Major Metabolic Pathway



Network of Major Metabolic Pathway



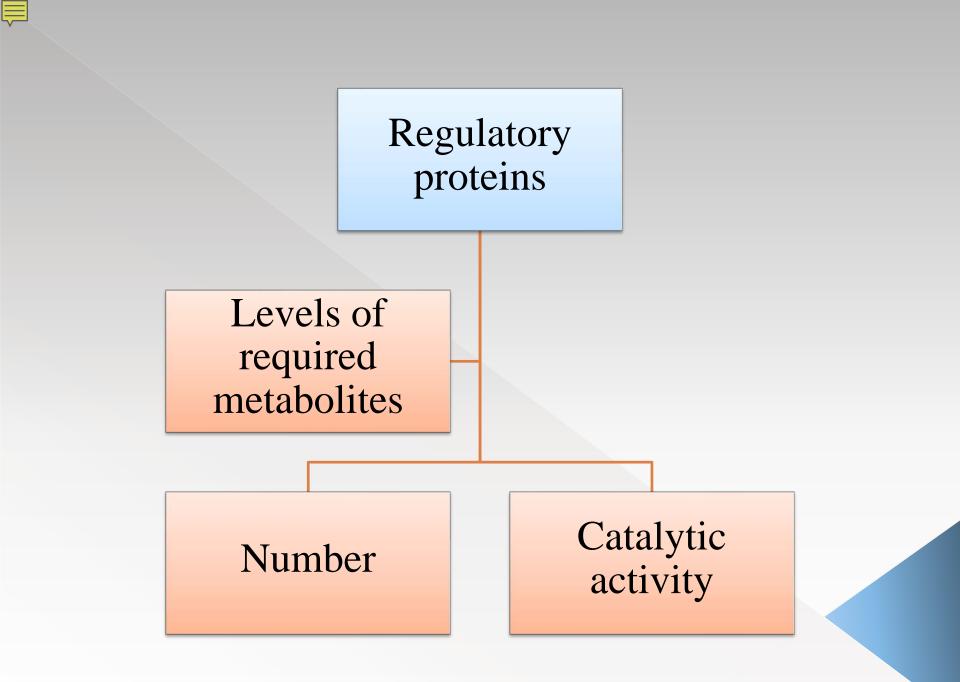
สภาวะสมดุล (Homeostasis)

 ทุกสิ่งมีชีวิตจะรักษาสภาวะสมดุล ด้วยการรักษาระดับปริมาณของ สารเมทาบอไลท์ให้อยู่ในระดับที่คงที่
(การสร้างเมทาบอไลท์ = การสลายเมทาบอไลท์)

$S \xrightarrow[v_1]{v_1} M \xrightarrow[v_2]{v_2} P$

ระดับที่คงที่ ถูกรบกวน → การเกิดโรค

Regulatory protein (4000 ยืนส์ ประมาณ 12% ของ
ยืนส์ในมนุษย์→เป็นตัวควบคุมหลักให้เกิดสภาวะสมดุล

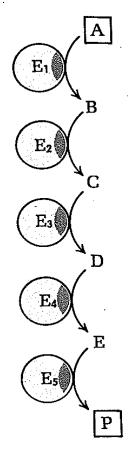


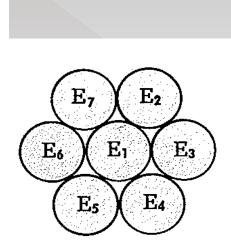
Control models of Major Metabolic Pathway Model 1. Rate-limiting reaction

 $A \equiv B \Longrightarrow C \equiv D \equiv E \equiv F$ A 茾 F $A \underset{B}{\Longrightarrow} B \longrightarrow C \underset{D}{\Longrightarrow} D \underset{E}{\Longrightarrow} E \underset{F}{\Longrightarrow} F$ A ----- F $A \equiv B \equiv C \equiv D \equiv E \equiv F$ $A \equiv F$ $A \underset{B}{\Longrightarrow} B \underset{C}{\Longrightarrow} C \underset{D}{\Longrightarrow} D \underset{E}{\Longrightarrow} E \underset{F}{\Longrightarrow} F$ A == F

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Model 2. Modulation at enzyme ENZYMES THAT WORK TOGETHER IN A PATHWAY CAN BE



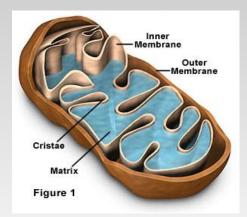


Covalently bound in complex E_2

Eı

Membrane

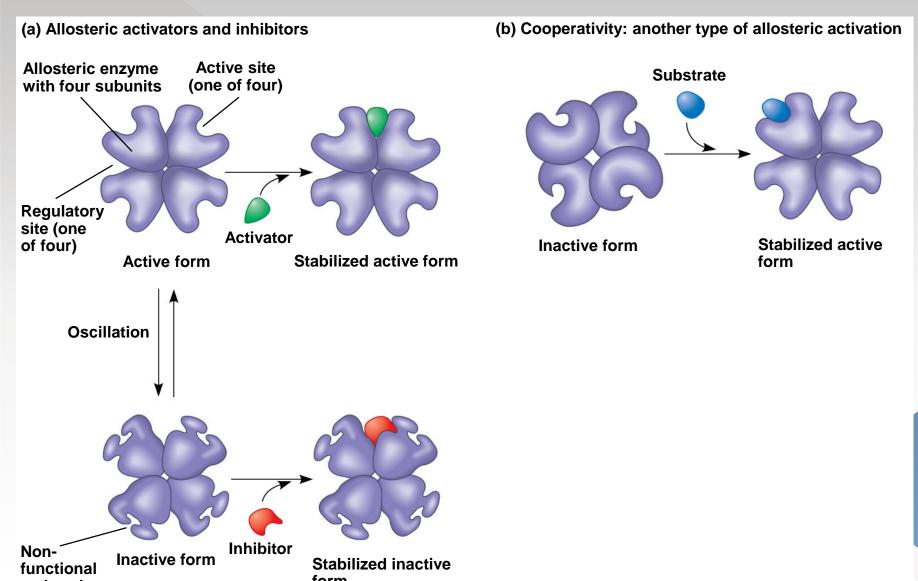
Attached to a membrane in sequence



Concentrated in specific location

Soluble with free floating intermediates Biochemistry Lehninger

Model 2. Modulation at enzyme Model 2.1. Modulation at enzyme site

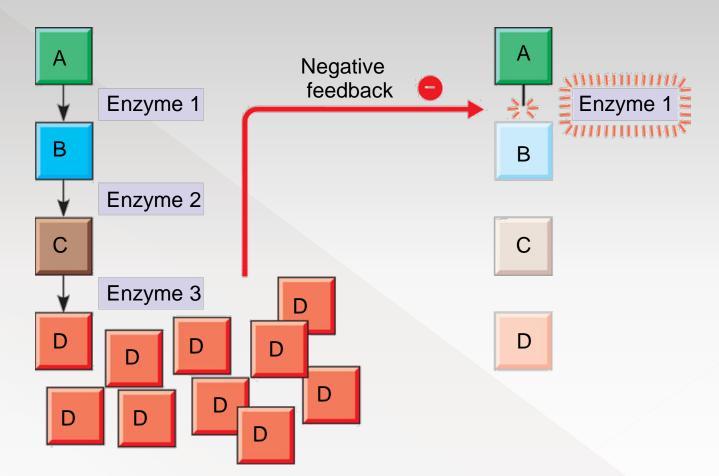


Feedback Inhibition

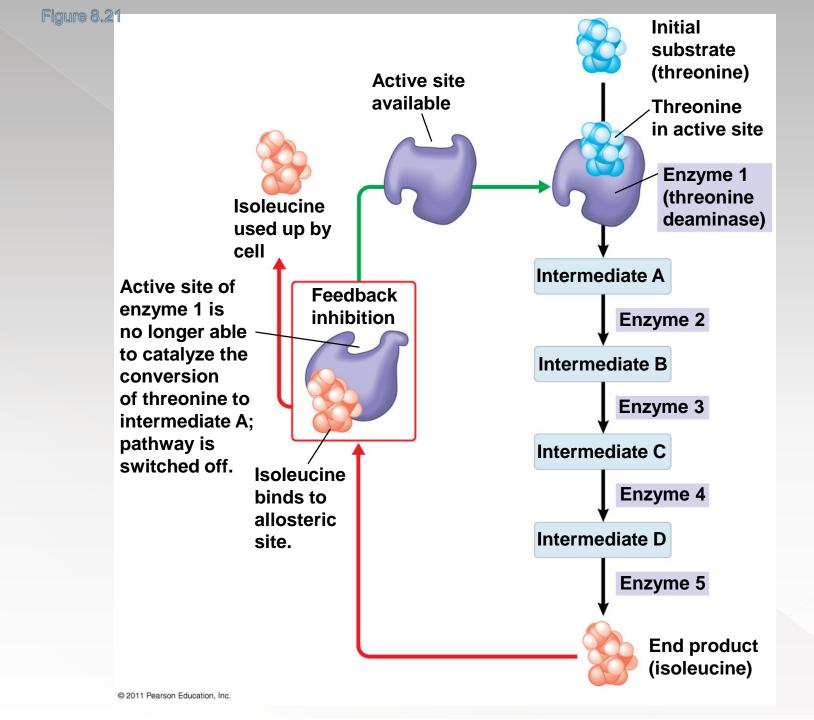
- In feedback inhibition, the end product of a metabolic pathway shuts down the pathway
- Feedback inhibition prevents a cell from wasting chemical resources by synthesizing more product than is needed

NEGATIVE FEEDBACK

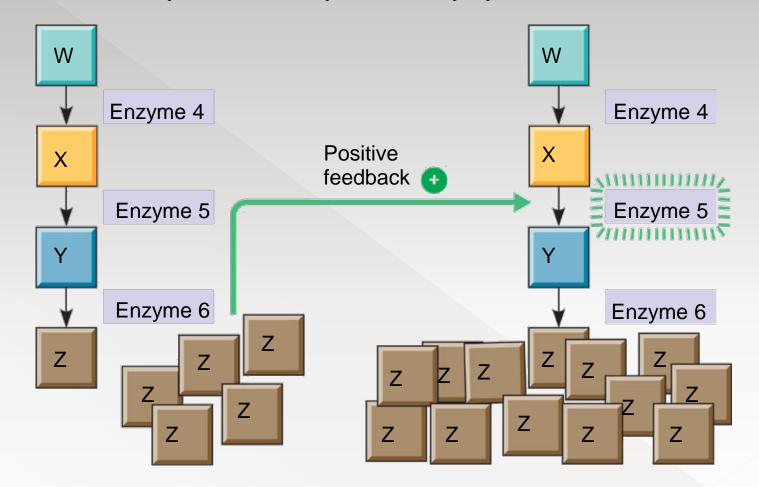
An accumulation of an end product slows the process that produces that product



Example: sugar breakdown generates ATP; excess ATP inhibits an enzyme near the beginning of the pathway

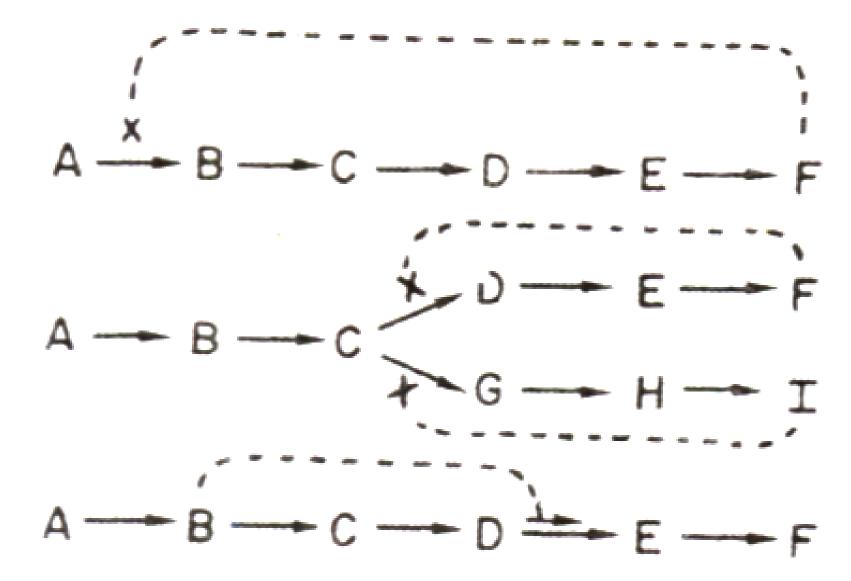


POSITIVE FEEDBACK (less common) The end product speeds up production



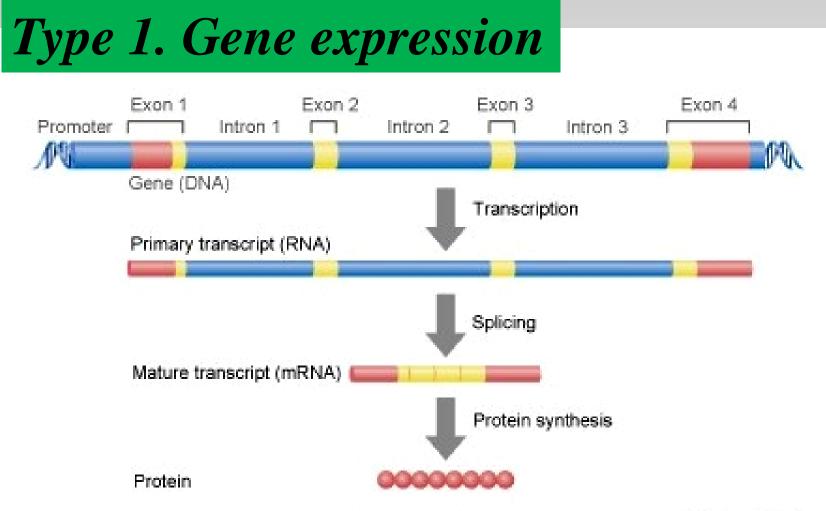
EXAMPLE: Chemicals released by platelets that accumulate at injury site, attract MORE platelets to the site.

Modulation at enzyme



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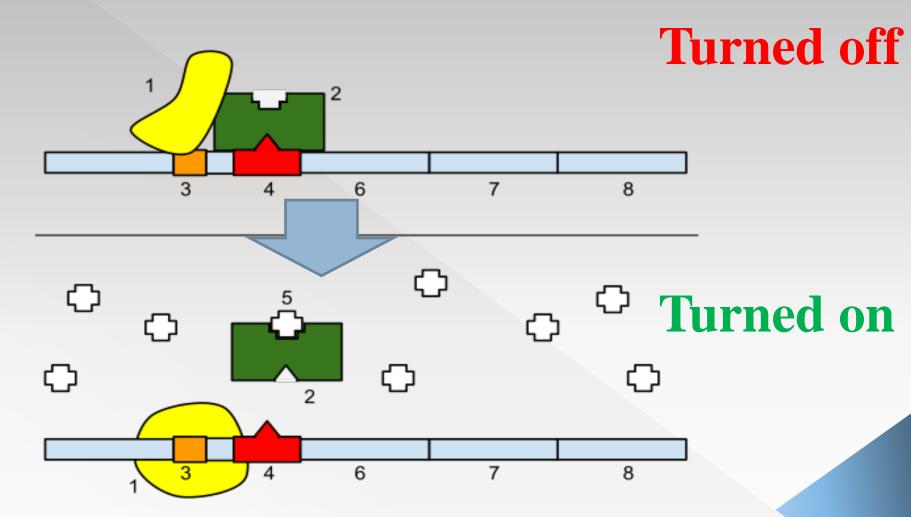
Model 2. Modulation at enzyme Model 2.2. Modulation at enzyme numbers



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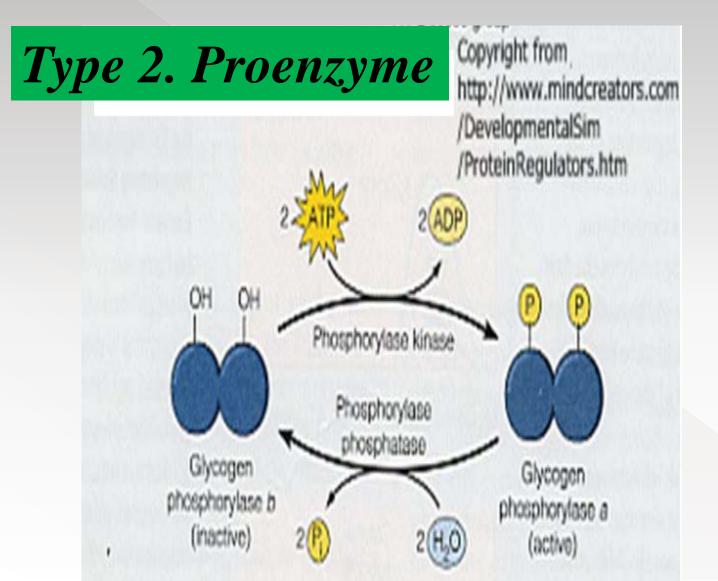
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ตย. Type 1. Gene expression

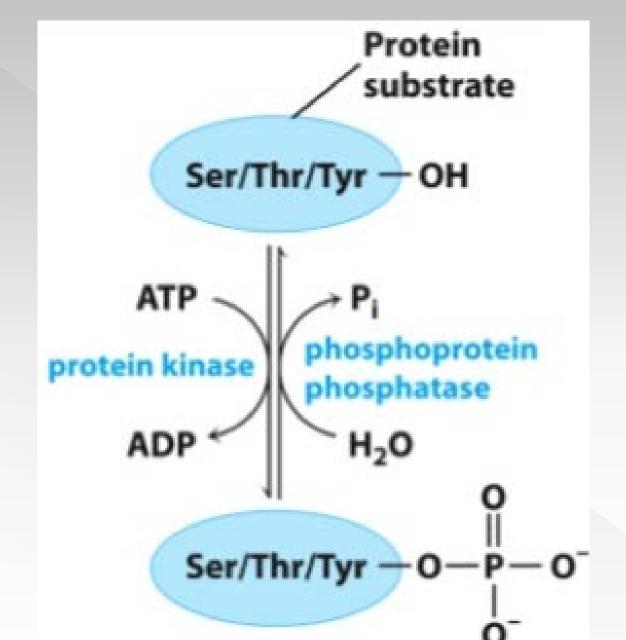


1: RNA Polymerase, 2: Repressor, 3: Promoter, 4: Operator, 5: Lactose, 6: lacZ, 7: lacY, 8: lacA.

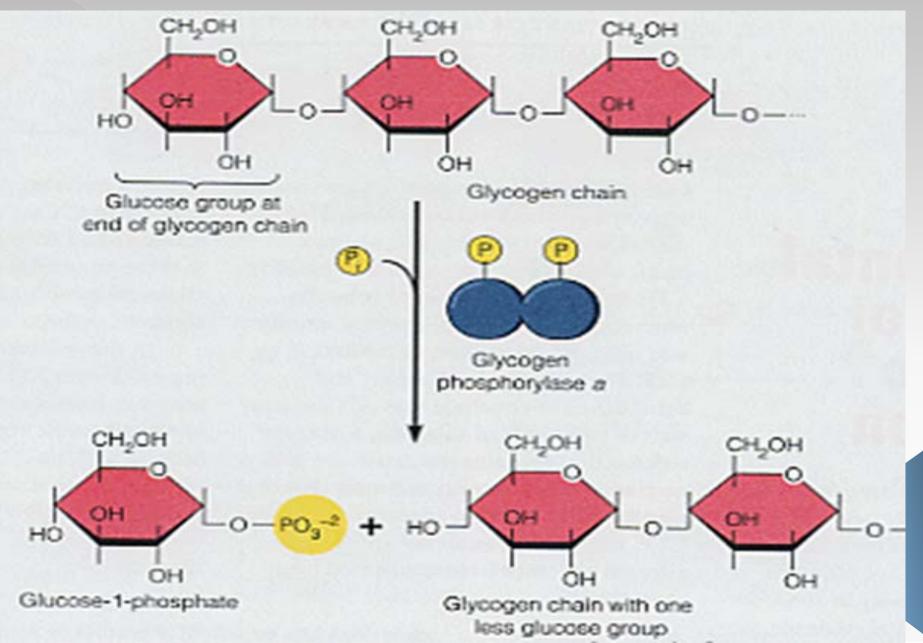
Model 2. Modulation at enzyme Model 2.2. Modulation at enzyme numbers



Phosphorylation of Enzyme affects their activity



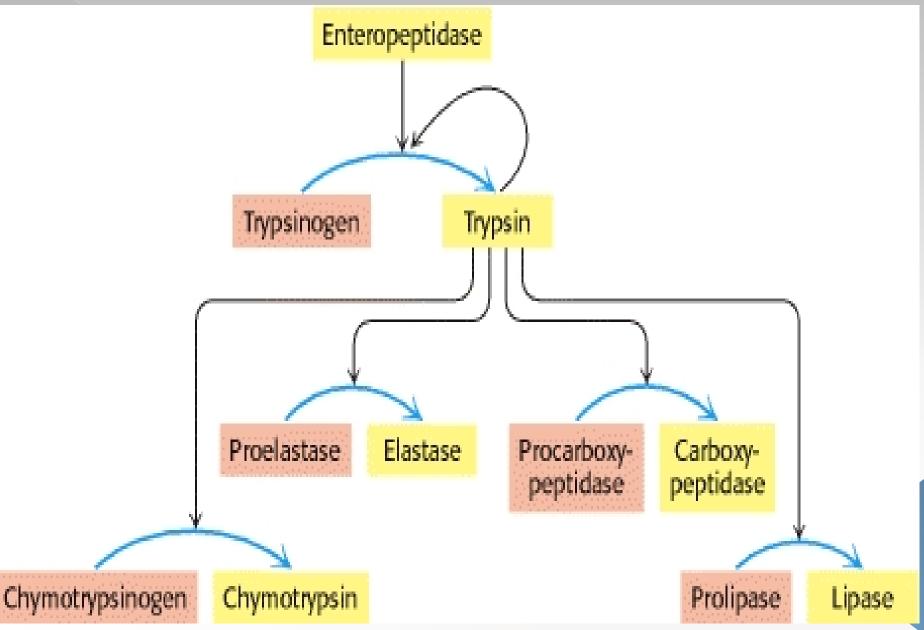
Proenzyme with phospholytic activation



Proenzyme with proteolytic activation

Site of **Active enzyme** Zymogen synthesis **Stomach** Pepsinogen Pepsin **Chymotrypsin Pancreas** Chymotrypsinogen **Pancreas** Trypsinogen **Trypsin** Carboxypeptidase **Procarboxypeptidase Pancreas Elastase Pancreas Proelastase**

Proteolytic Activation of Digestic Enzyme



Thank You For Your Atten