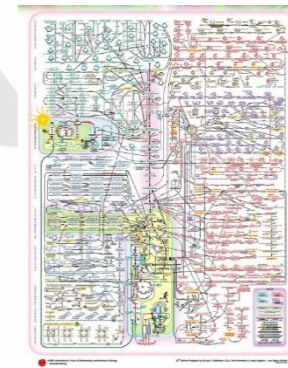


Regulação metabólica

Interferência direta ou indireta nas reações químicas que compõe o organismo.

Aumentando ou diminuindo a velocidade das reações (aumento de substratos ou de metabólitos).

Efeito propagado por todas as vias metabólicas.



Regulação Metabólica

Alterações das atividades enzimáticas

1. Regulação alostérica
2. Modificações covalentes
3. Regulação hormonal

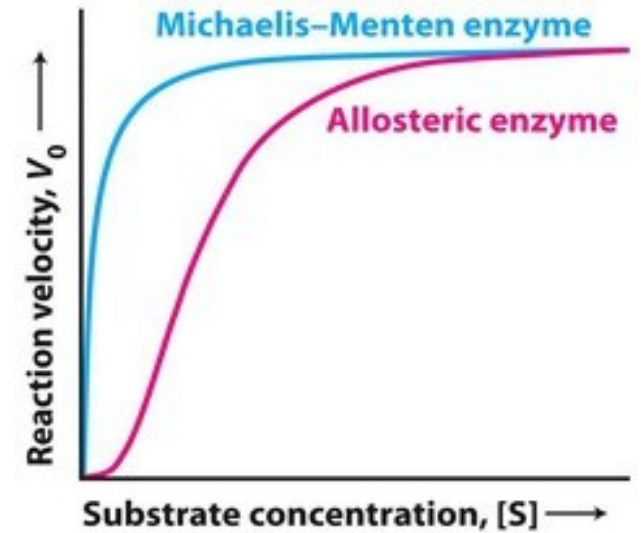
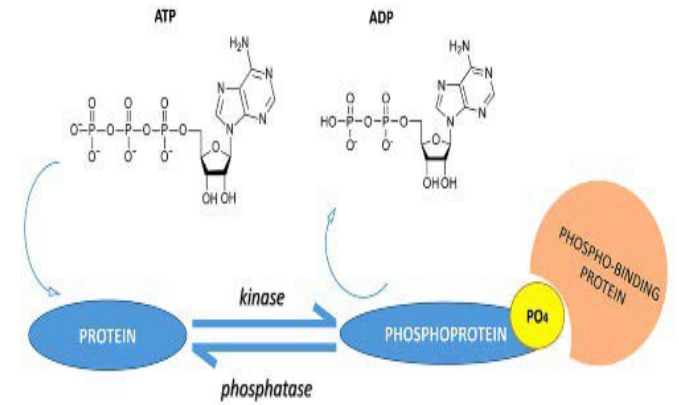
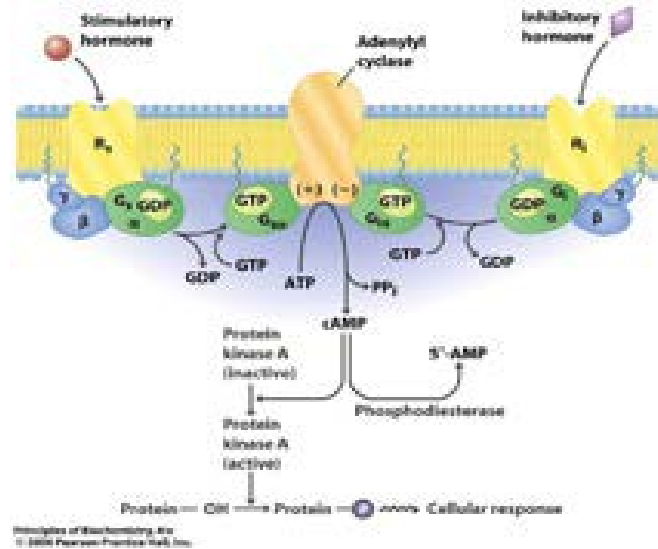


Figure 7.8
Biochemistry: A Short Course, Second Edition
© 2013 W. H. Freeman and Company



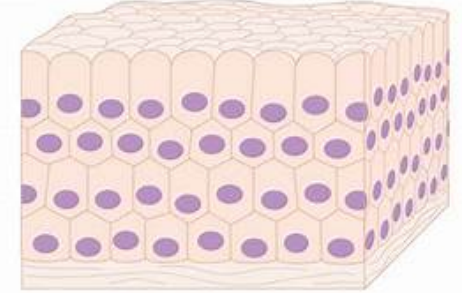
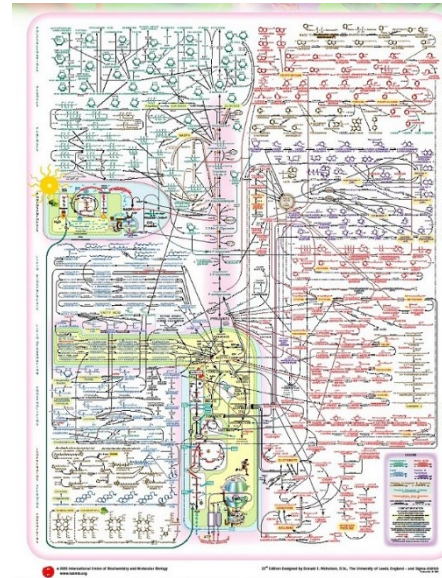
Integração Metabólica

-Respostas do organismo diante da abundância e escassez de nutrientes.

-Adaptações às oscilações diárias das concentrações de nutrientes.

-Adaptações às necessidades fisiológicas.

Integração a nível celular e do organismo com um todo é feita por hormônios.



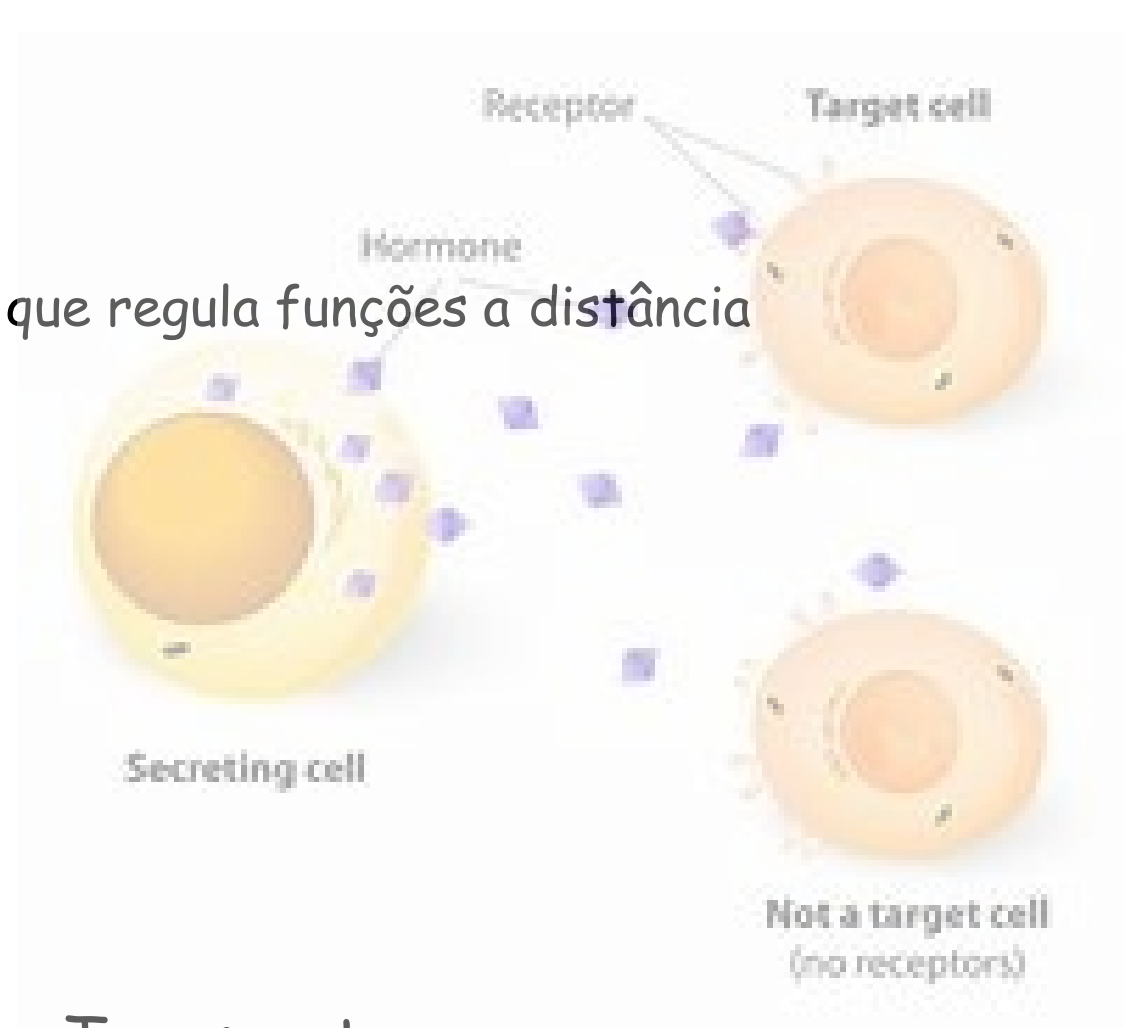
O que são hormônios?

<https://youtu.be/-SPRPkLoKp8>



Hormônios

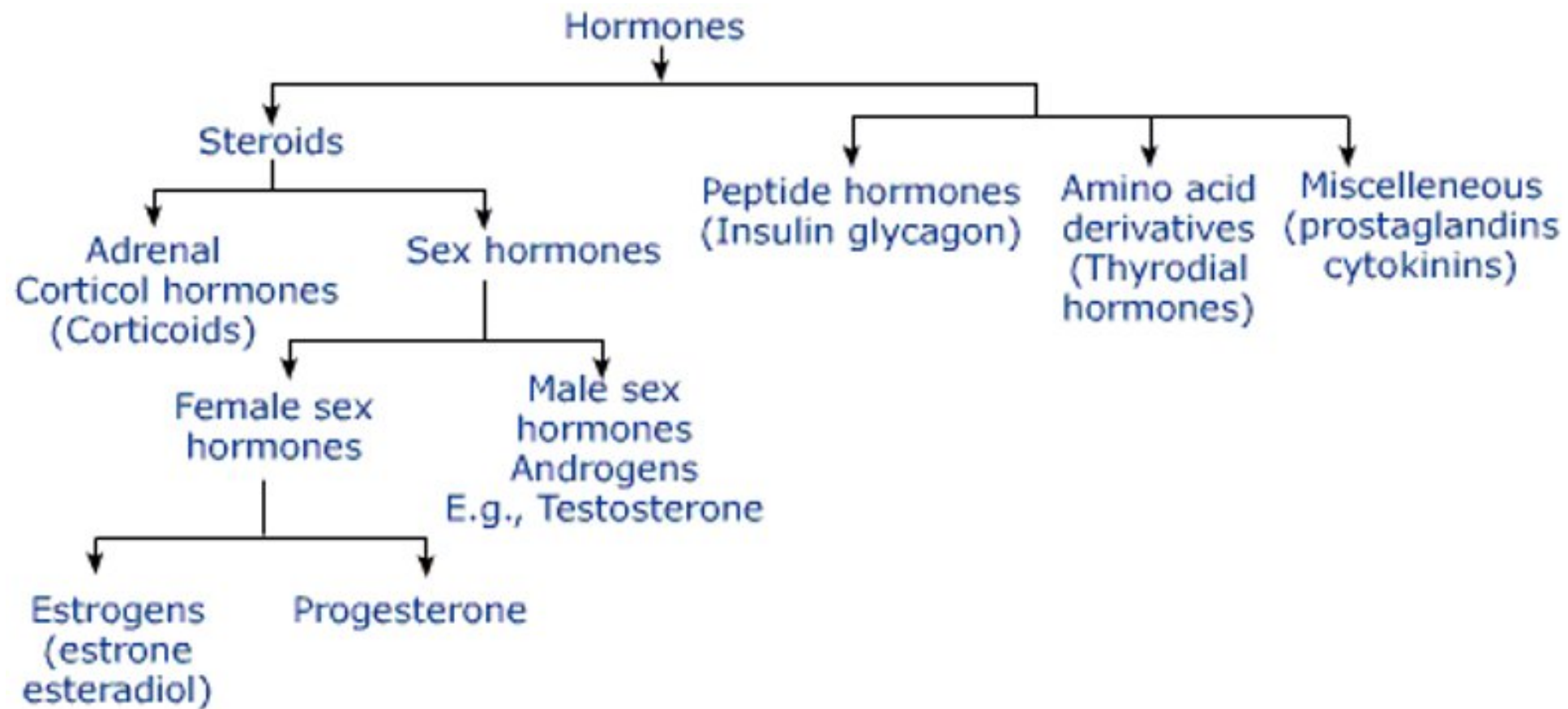
- Biomoléculas produzidas em uma parte do corpo que regula funções a distância
- Agem em baixas quantidades
- Essenciais para organismos multicelulares
- Agem por meio de receptores na célula-alvo



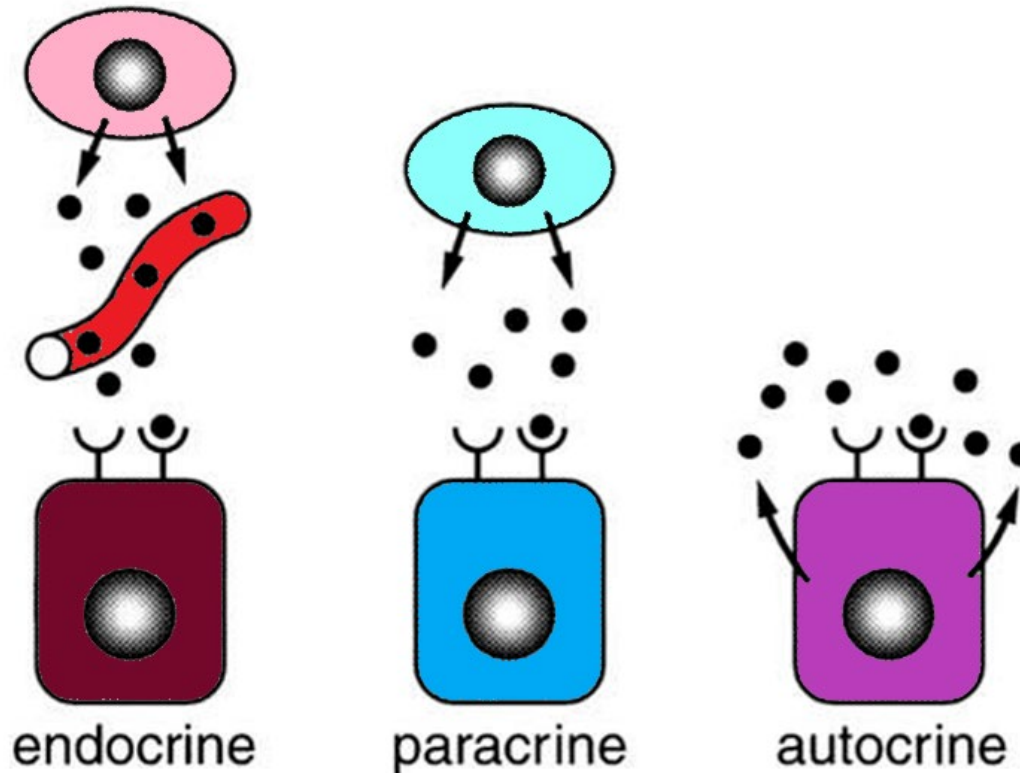
Regulação

Biossíntese → Estocagem → Secreção → Transporte →
Reconhecimento → Resposta → Degradação

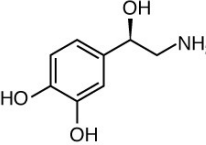
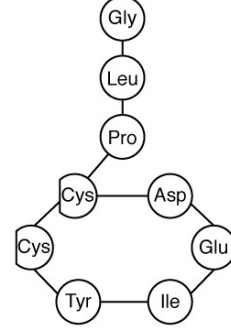
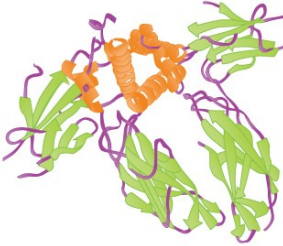
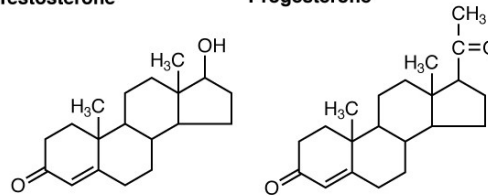




Hormônios podem ser classificados pela maneira na qual são transportados de uma célula para outra

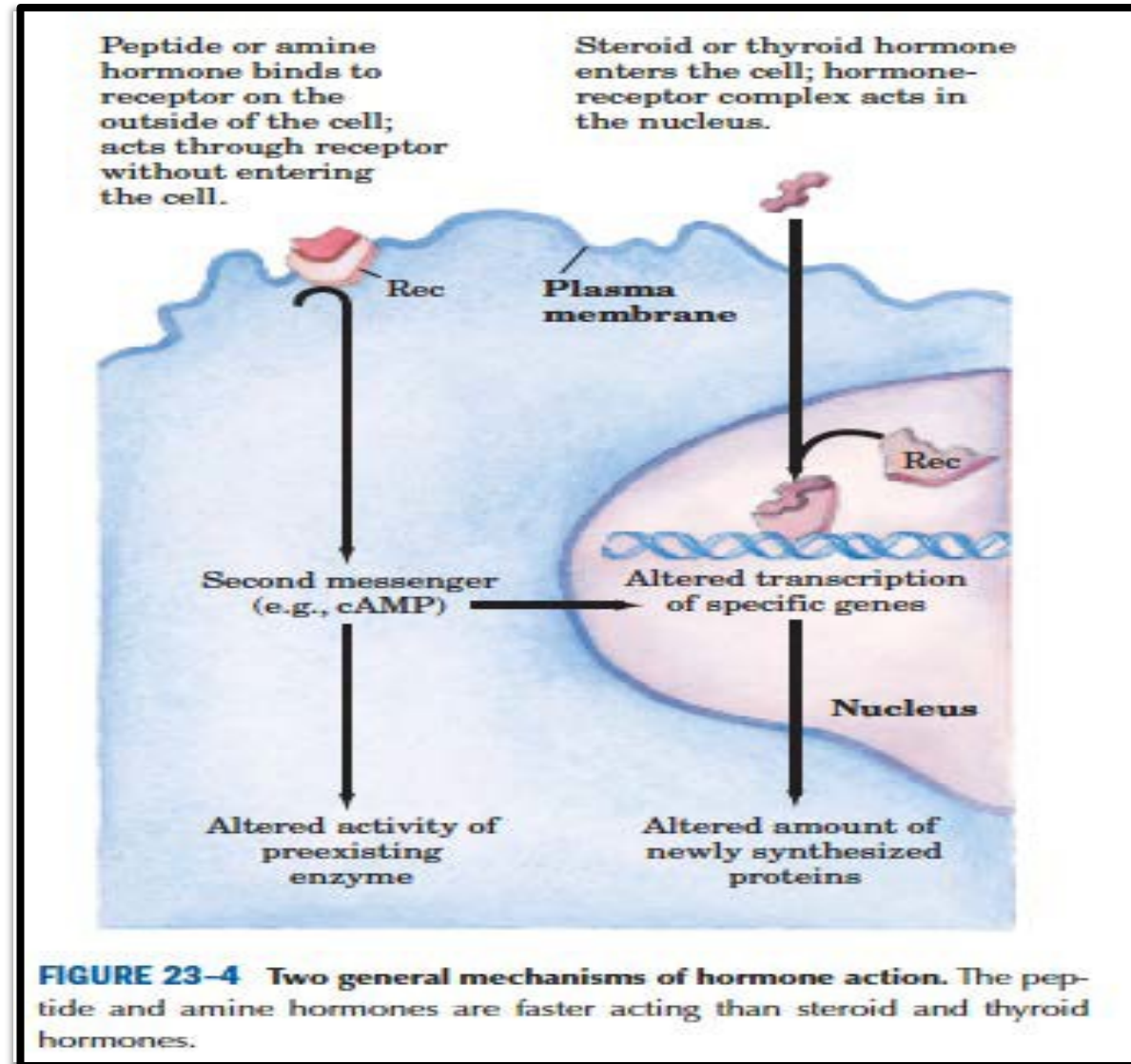


Hormônios podem ser classificados de acordo com sua estrutura química

Hormone Class	Components	Example(s)
Amine Hormone	Amino acids with modified groups (e.g. norepinephrine's carboxyl group is replaced with a benzene ring)	<p>Norepinephrine</p> 
Peptide Hormone	Short chains of linked amino acids	<p>Oxytocin</p> 
Protein Hormone	Long chains of linked amino acids	<p>Human Growth Hormone</p> 
Steroid Hormones	Derived from the lipid cholesterol	<p>Testosterone Progesterone</p> 

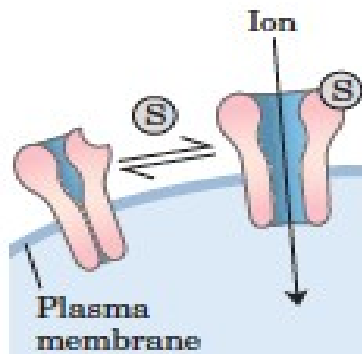


Todos os hormônios agem através de receptores de alta afinidade

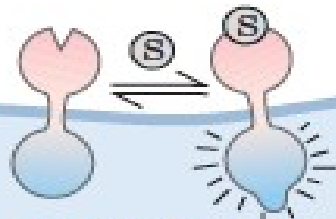


Tipos de transductores de sinal

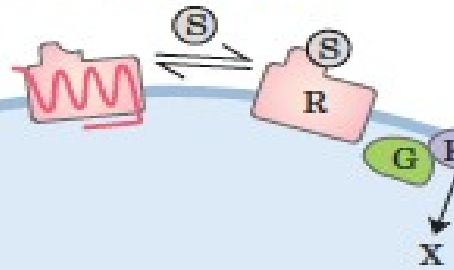
Gated ion channel
Opens or closes in response to concentration of signal ligand (S) or membrane potential.



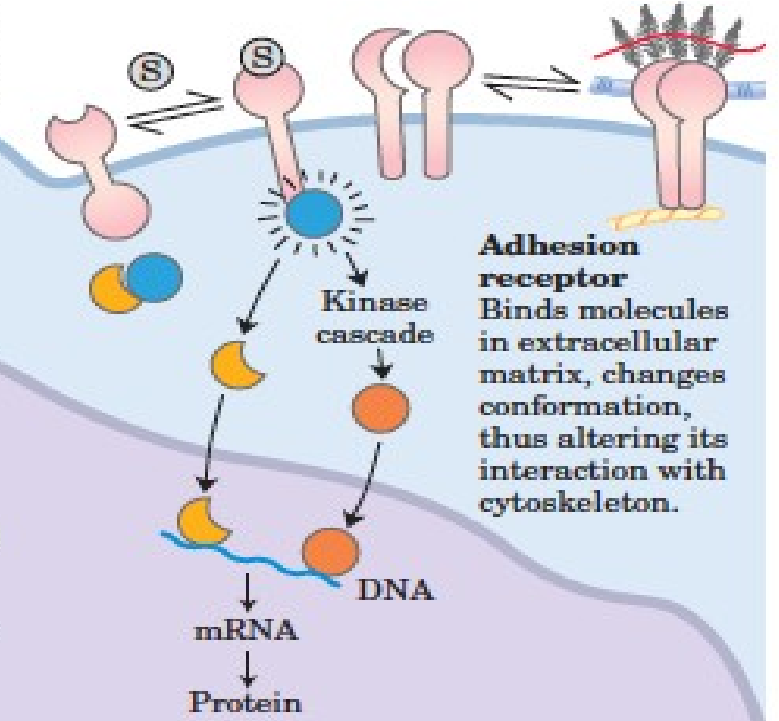
Receptor enzyme
Ligand binding to extracellular domain stimulates enzyme activity in intracellular domain.



Serpentine receptor
External ligand binding to receptor (R) activates an intracellular GTP-binding protein (G), which regulates an enzyme (Enz) that generates an intracellular second messenger, X.



Receptor with no intrinsic enzyme activity
Interacts with cytosolic protein kinase, which activates a gene-regulating protein (directly or through a cascade of protein kinases), changing gene expression.



Adhesion receptor
Binds molecules in extracellular matrix, changes conformation, thus altering its interaction with cytoskeleton.

Steroid receptor
Steroid binding to a nuclear receptor protein allows the receptor to regulate the expression of specific genes.

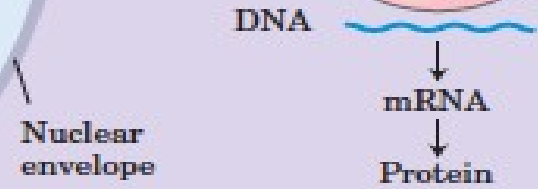
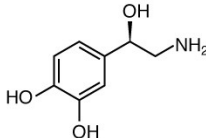
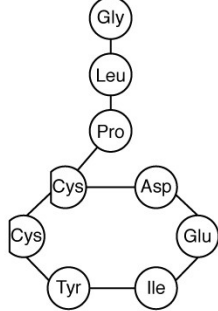
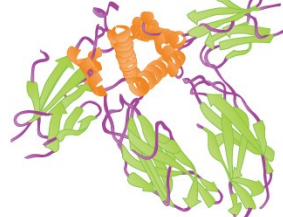
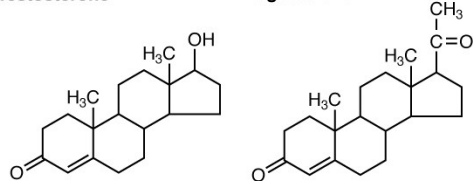


FIGURE 12-2 Six general types of signal transducers.

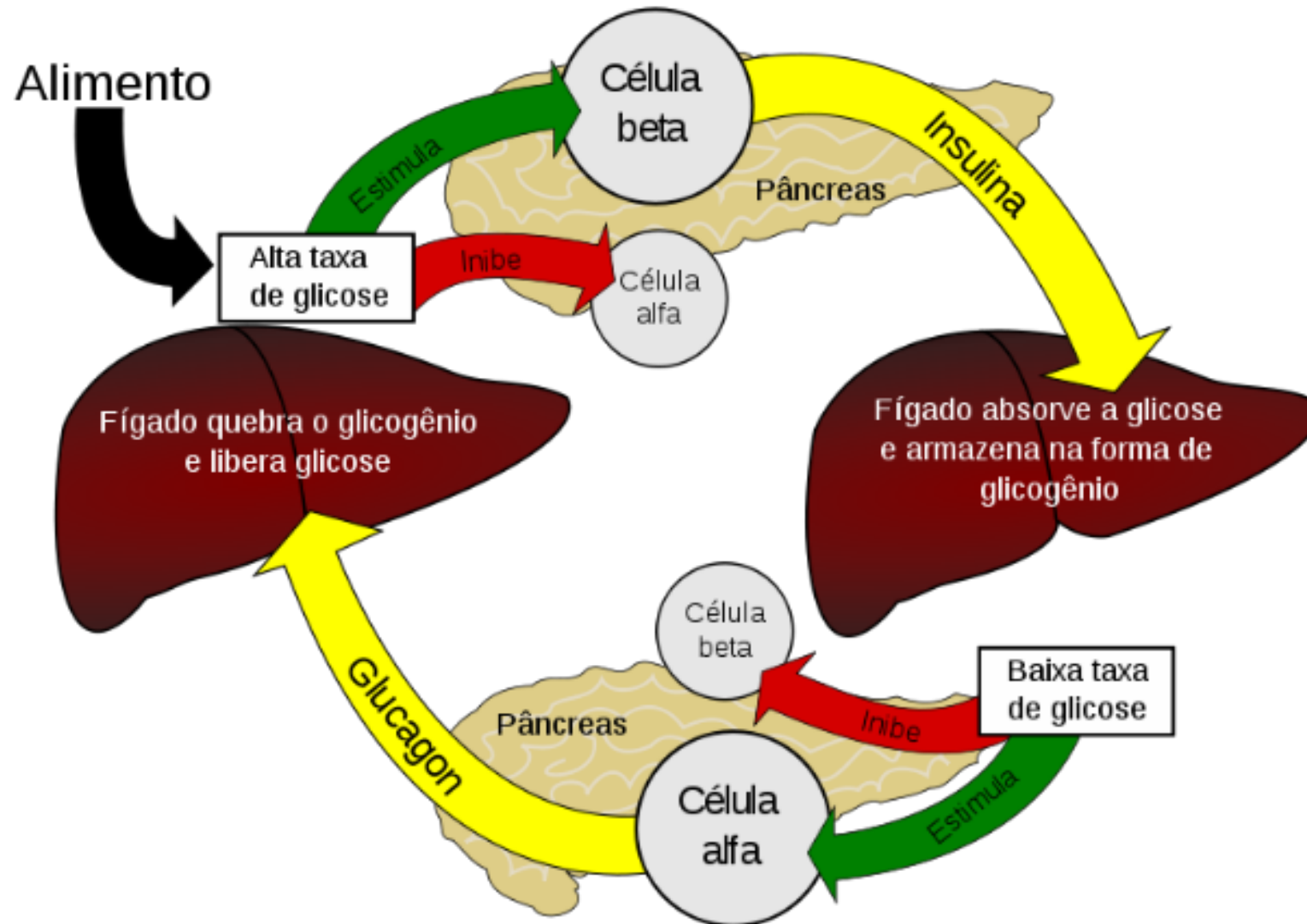


Hormônios Peptídicos

Hormone Class	Components	Example(s)
Amine Hormone	Amino acids with modified groups (e.g. norepinephrine's carboxyl group is replaced with a benzene ring)	<p>Norepinephrine</p> 
Peptide Hormone	Short chains of linked amino acids	<p>Oxytocin</p> 
Protein Hormone	Long chains of linked amino acids	<p>Human Growth Hormone</p> 
Steroid Hormones	Derived from the lipid cholesterol	<p>Testosterone Progesterone</p> 



Insulina e Glucagon



Hormônios peptídicos/proteicos sofrem processamento pós-traducional

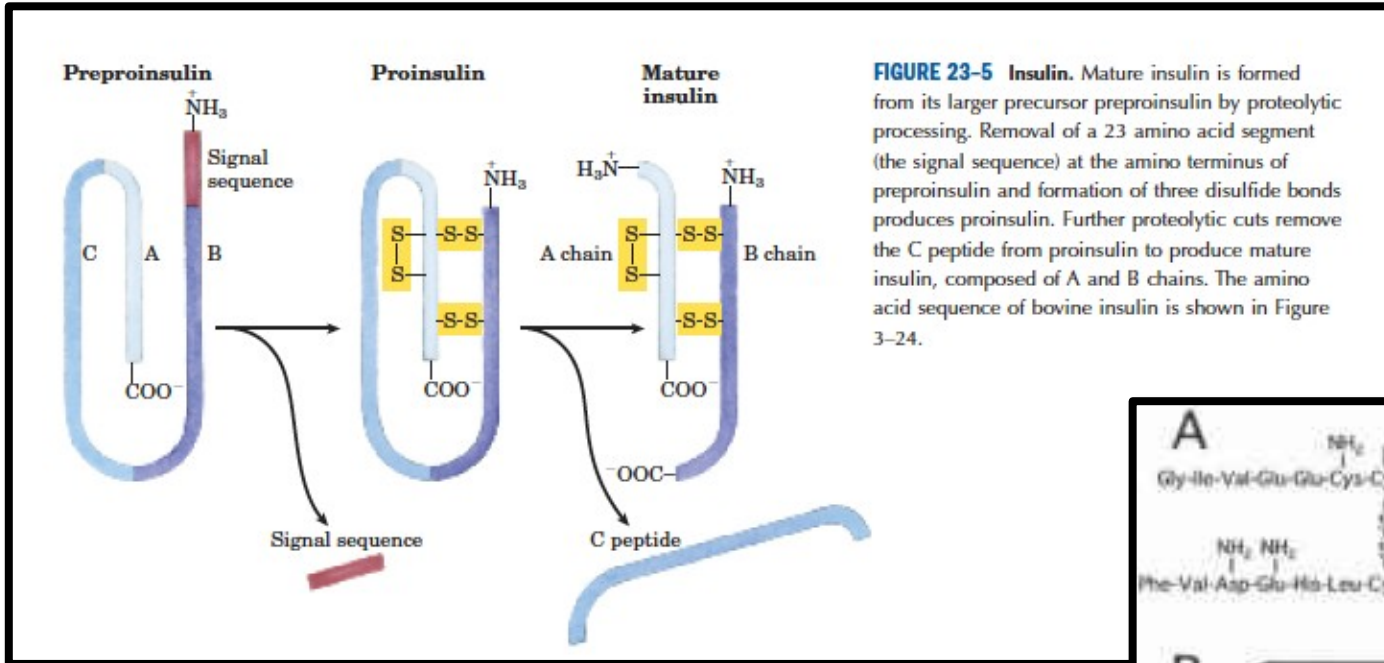
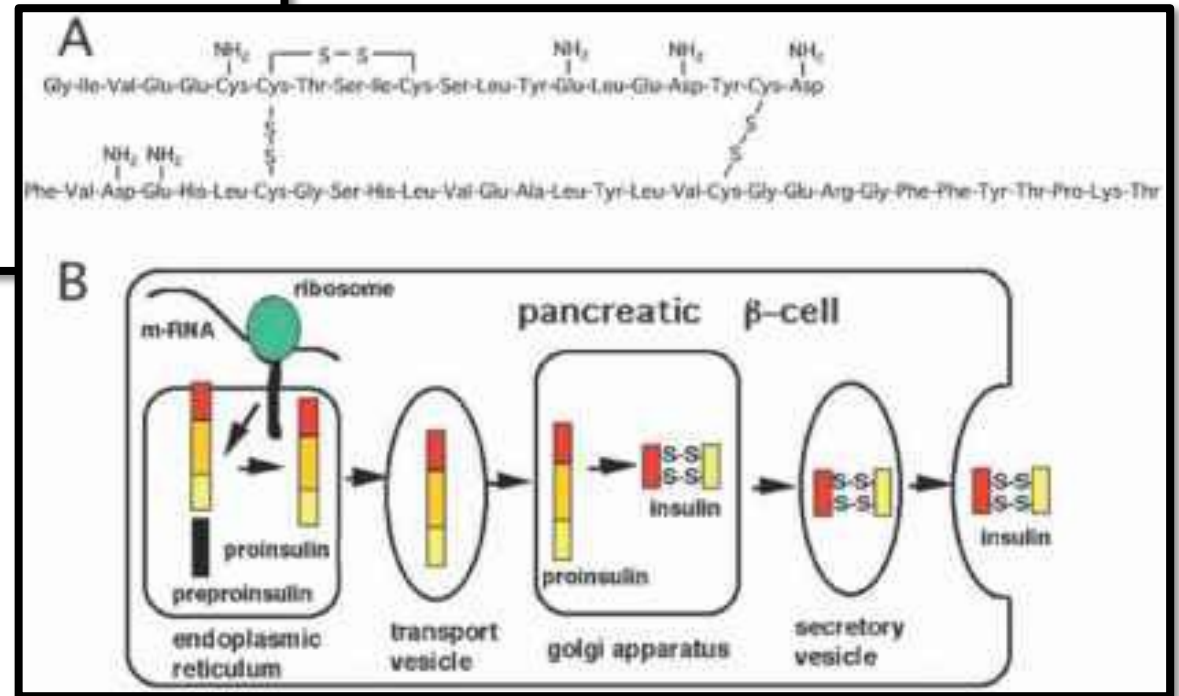


FIGURE 23-5 Insulin. Mature insulin is formed from its larger precursor preproinsulin by proteolytic processing. Removal of a 23 amino acid segment (the signal sequence) at the amino terminus of preproinsulin and formation of three disulfide bonds produces proinsulin. Further proteolytic cuts remove the C peptide from proinsulin to produce mature insulin, composed of A and B chains. The amino acid sequence of bovine insulin is shown in Figure 3-24.



Discovery of Insulin

“insulin”= Latin for “island”

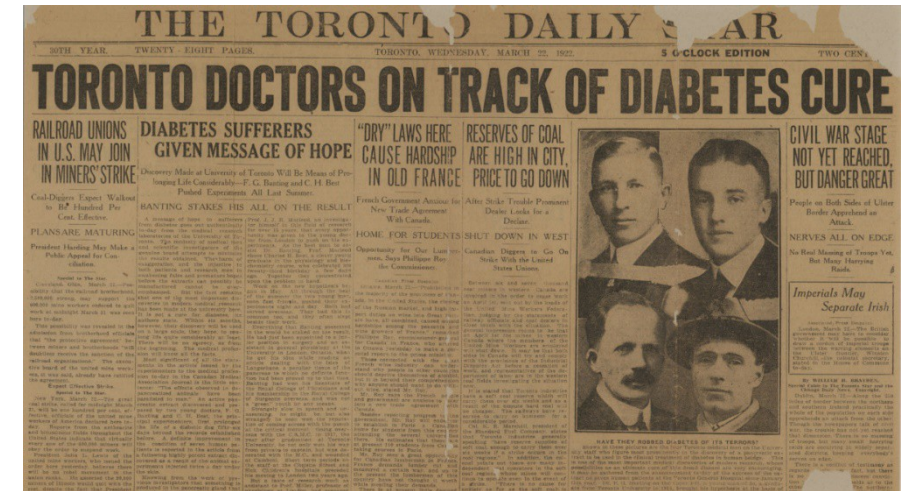
- 1889;
1st removal of pancreas from a dog to determine the effect of an absent pancreas by Oskar Minkowski
- 1921;
discovery of insulin
successful treatment of de-pancreatized dog with insulin
- 1922;
1st tested in a 14-year-old boy of diabetes in Toronto
- 1923;
Nobel Prize in Physiology & Medicine



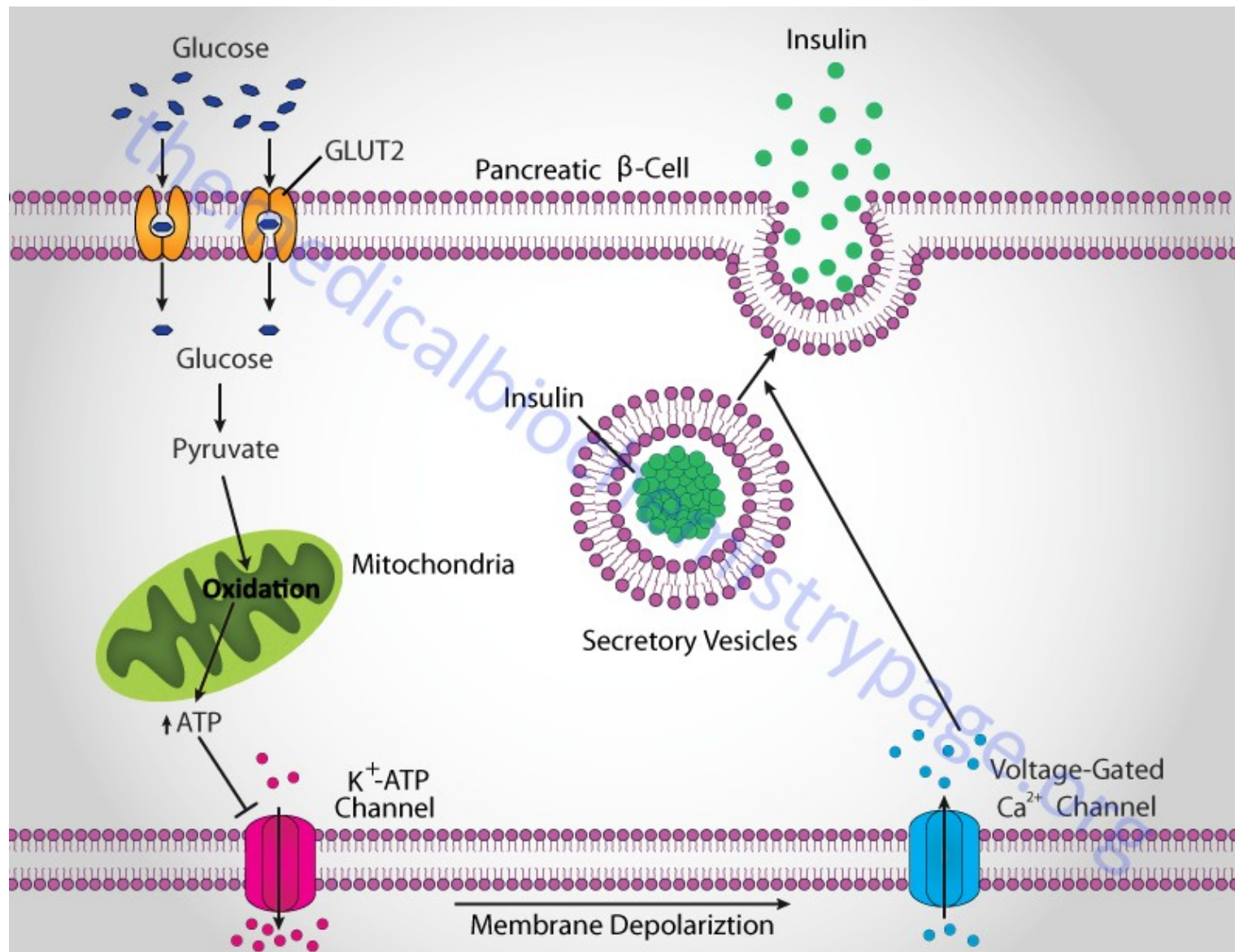
Frederick
Banting
(1891-1941)



Charles
Best
(1899-1978)



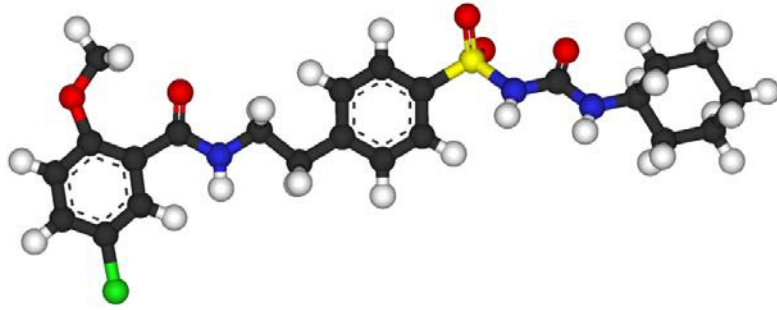
Regulação da Secreção da Insulina



- Células β possuem GLUT2
- Células β possuem glicoquinase
- \uparrow glicemia = \uparrow ATP
- ATP inibe canais para K^+
- Despolarização
- Ativação da entrada de Ca^{2+}
- Secreção de insulina
- Síntese de insulina



Sulfoniluréias no Tratamento da DM II



- Inibem canais para K^+ sensíveis a ATP
- Aumentam secreção de insulina
- Eficazes em resistência periférica a insulina



Compre3
Pague2

Glibenclamida 5 mg com 30 Comprimidos - Ems - Genérico

Produto com a qualidade Ems Genérico | código: 4637 - [105908]

Frete Grátis
Consulte*

- 1 un. +

De R\$ 10,15

Por R\$ **1,95** cada

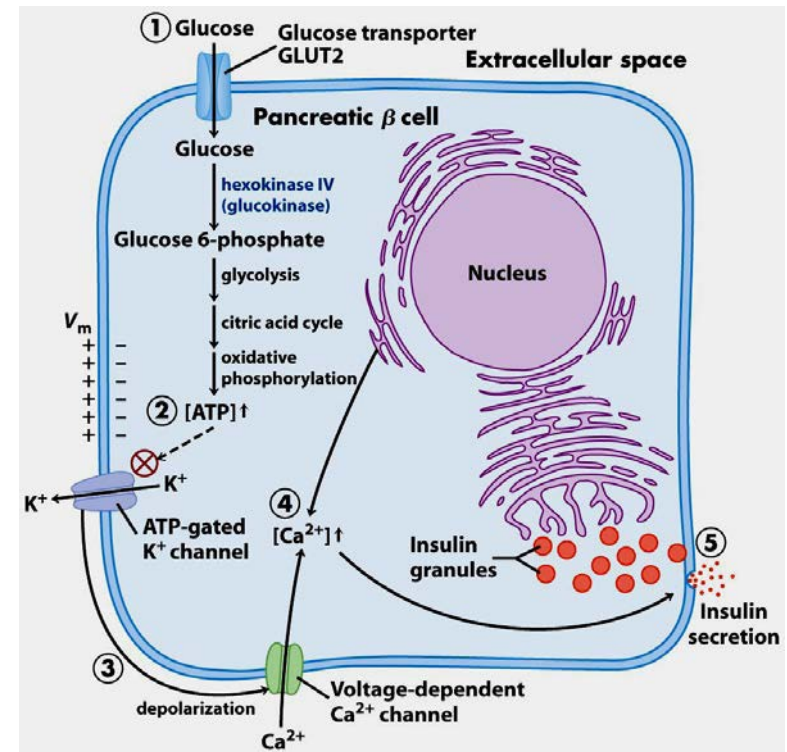
Economize já: R\$ 8,20

♥ Adicionar na minha lista

Comprar unidade

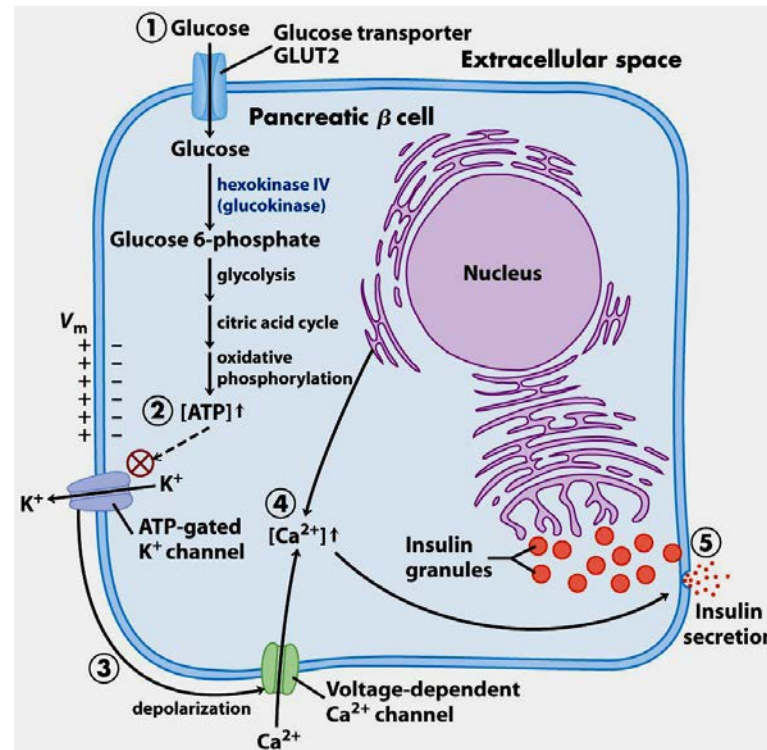
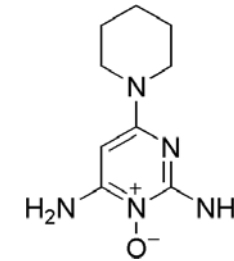
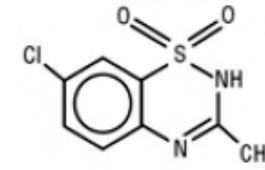
Comprar Kit

Compre 3 Pague 2



Agonistas de K_{ATP} s na Hiperinsulinemia

- Insulinomas levam a hiperinsulinemia e hipoglicemia
- Tratamento definitivo = remoção cirúrgica
- Tratamento medicamentoso = ativadores de K_{ATP} s



Vias de síntese e degradação de glicogênio

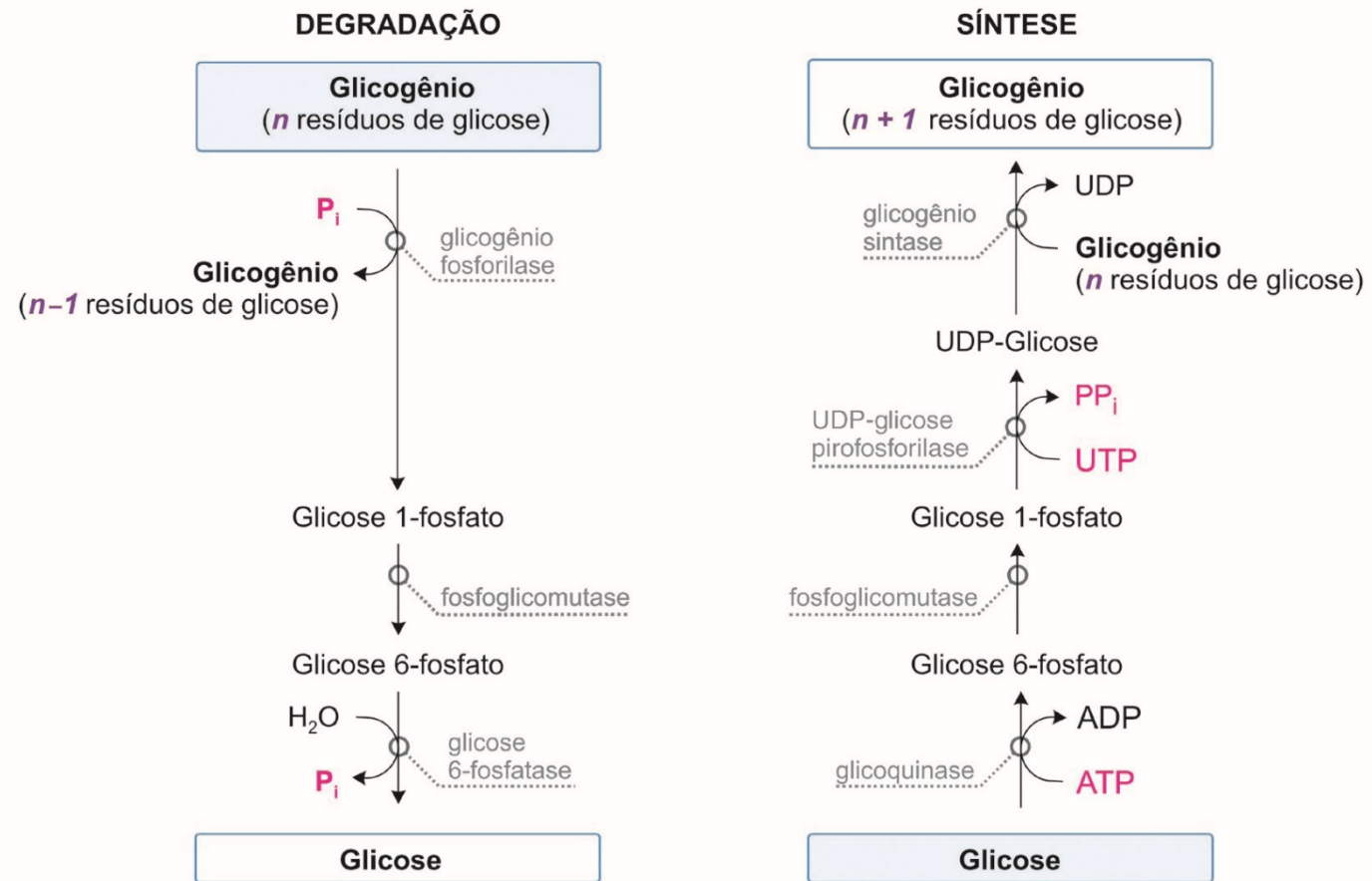
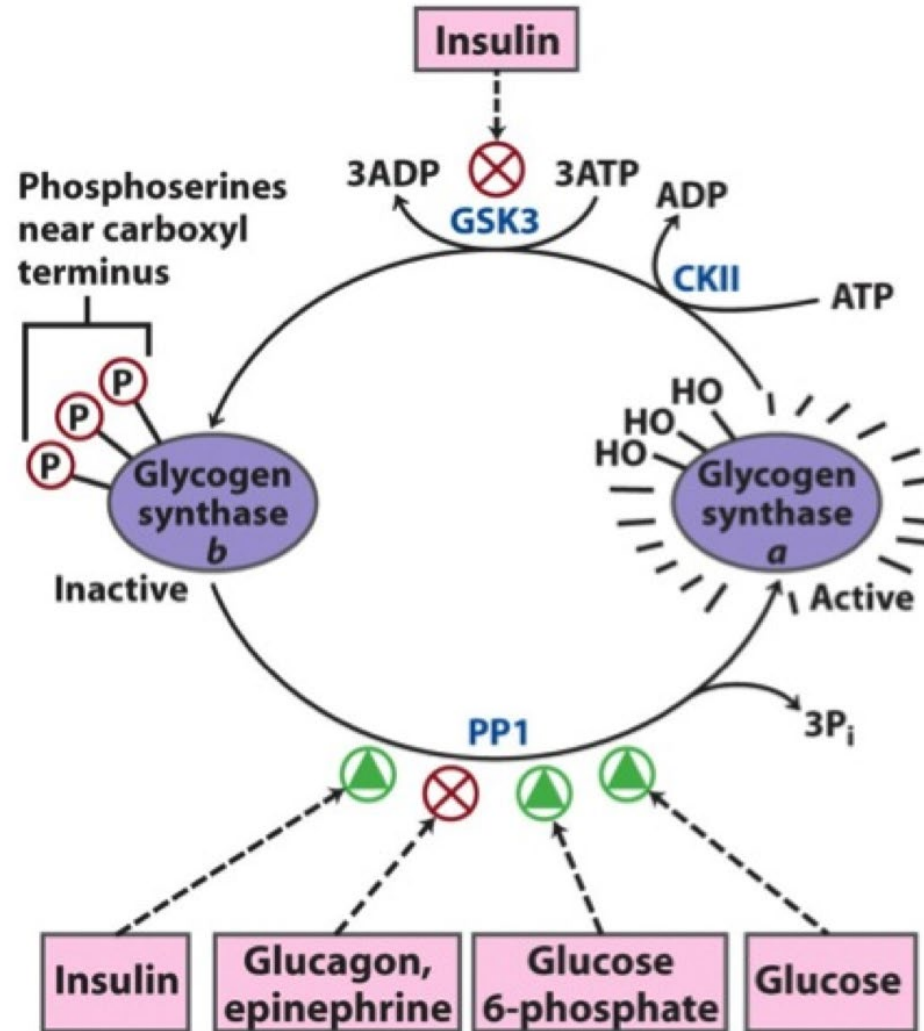


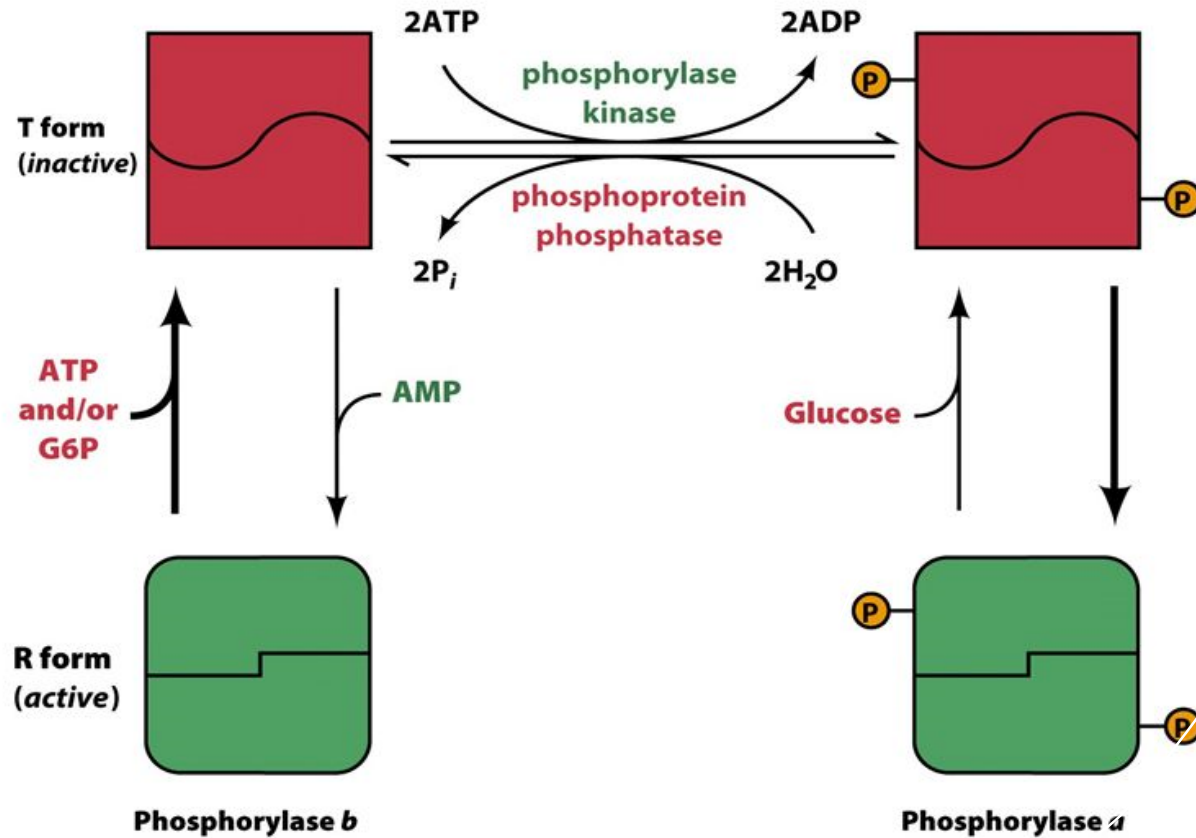
Fig. 13.5 Esquema geral da degradação e síntese de glicogênio no fígado.



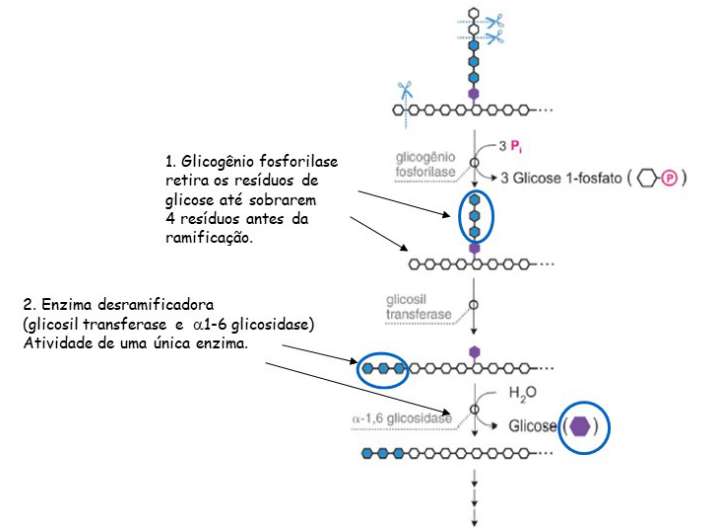
Regulação do metabolismo do glicogênio



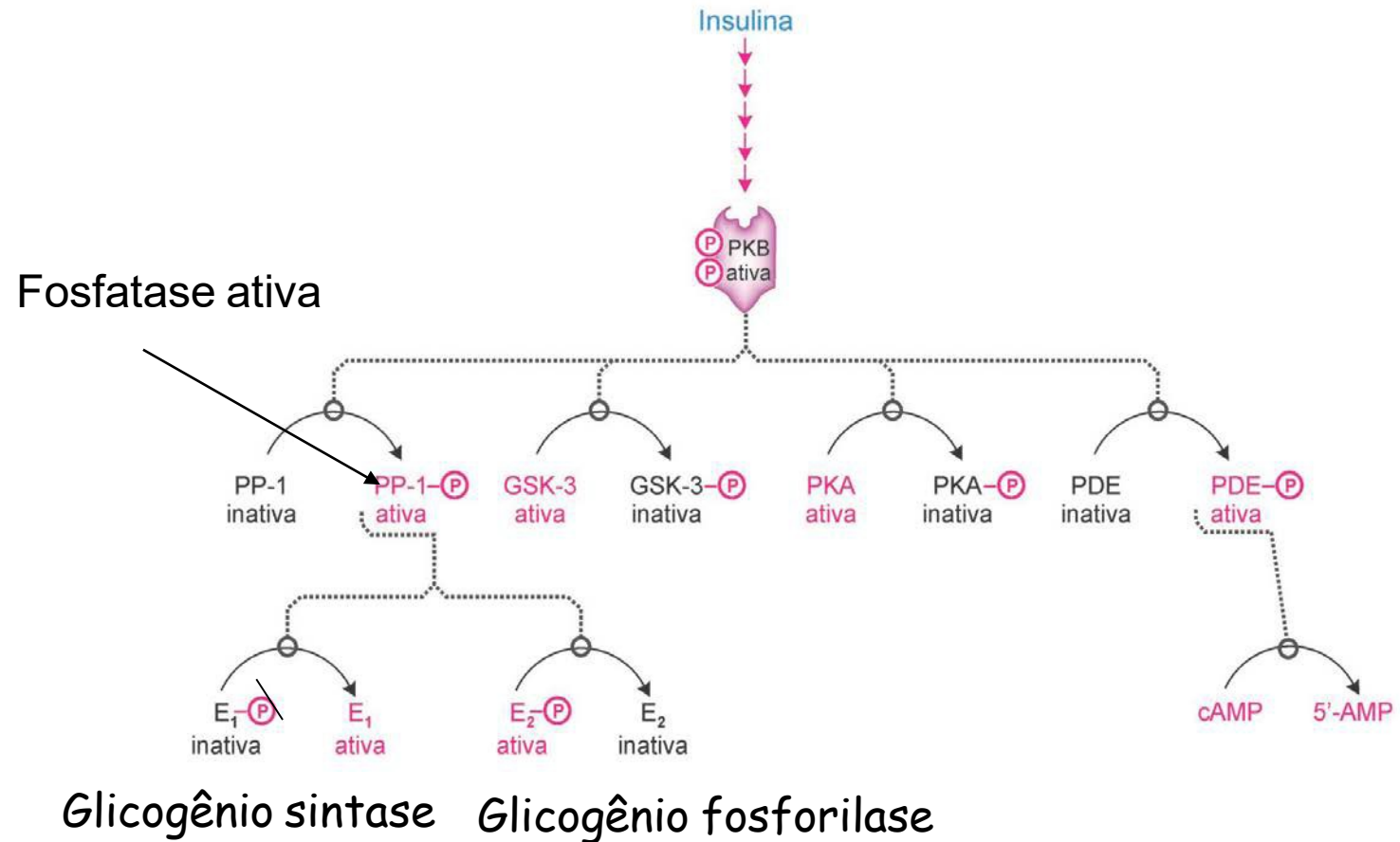
Regulação da glicogênio fosforilase (degradação do glicogênio)



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Regulação do metabolismo do glicogênio



Síntese de glicogênio



Regulação do metabolismo pela Insulina

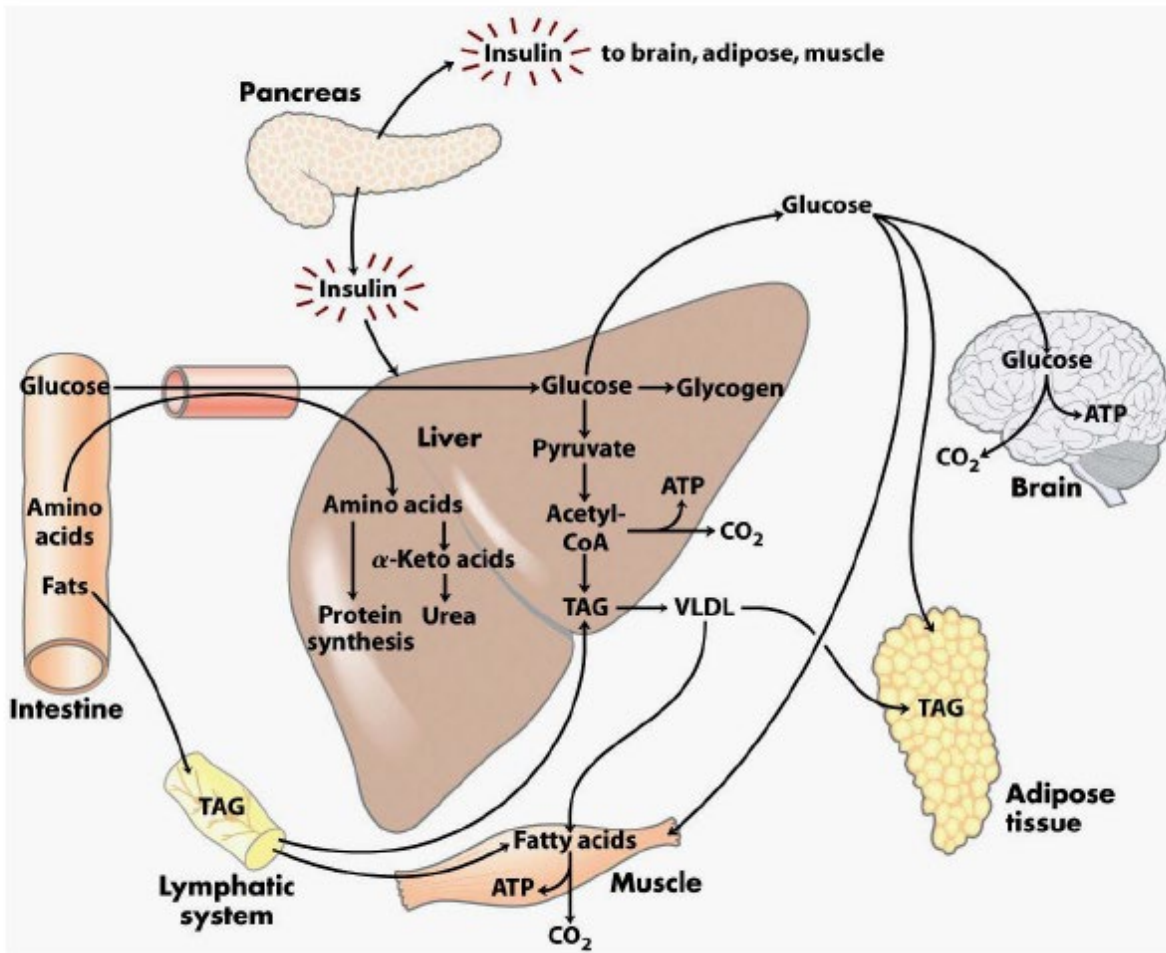
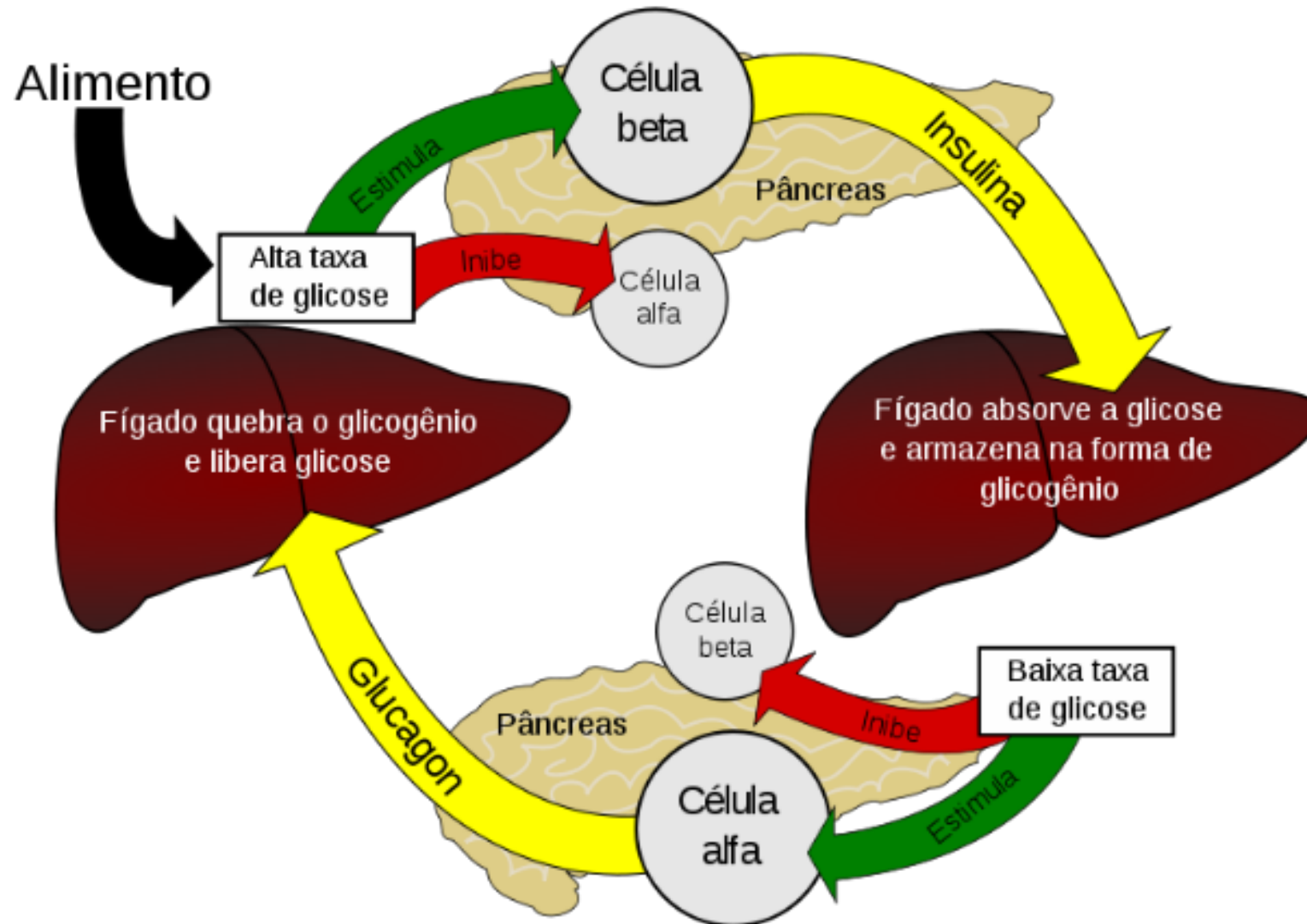


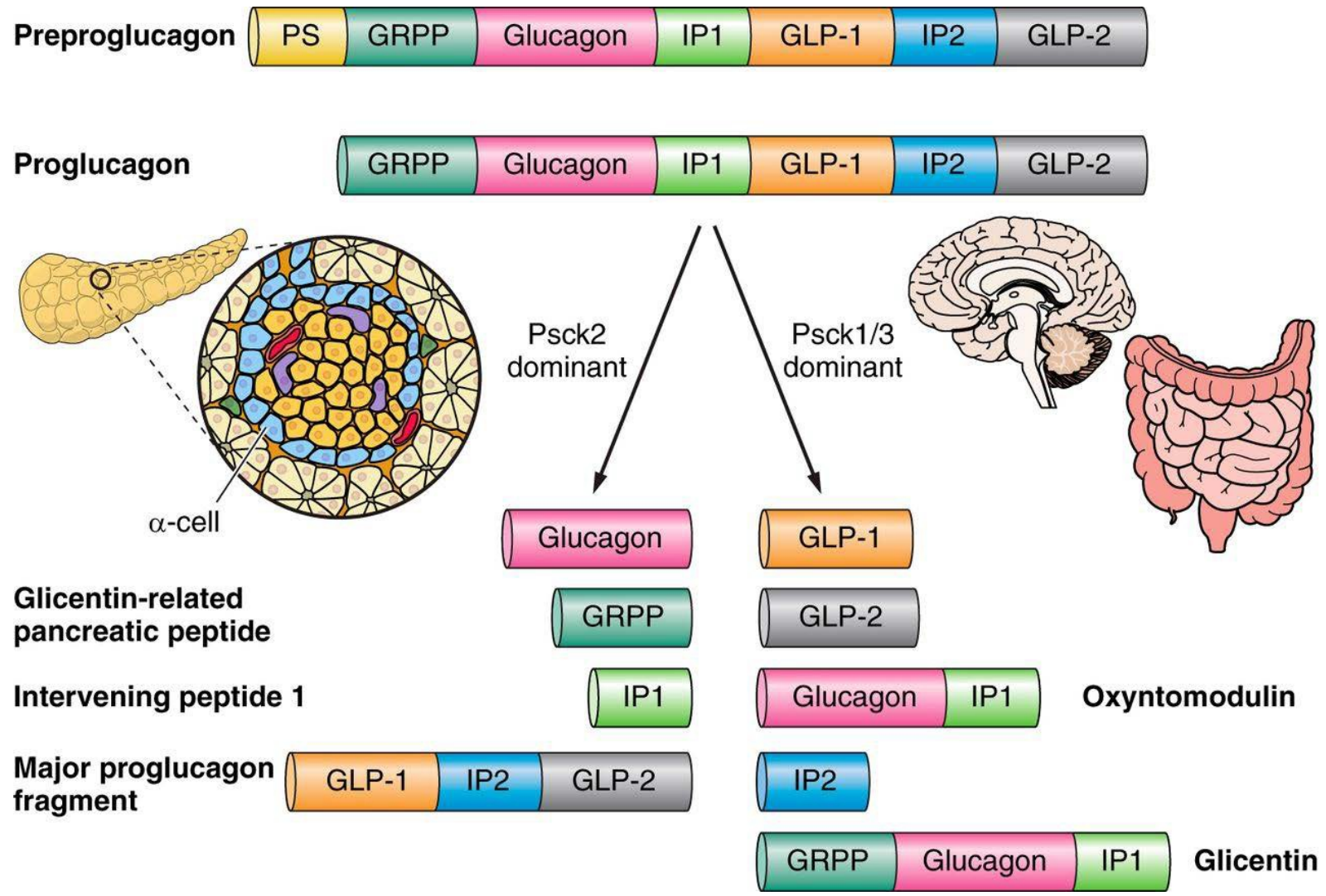
TABLE 23-3 Effects of Insulin on Blood Glucose: Uptake of Glucose by Cells and Storage as Triacylglycerols and Glycogen

<i>Metabolic effect</i>	<i>Target enzyme</i>
↑ Glucose uptake (muscle, adipose)	↑ Glucose transporter (GLUT4)
↑ Glucose uptake (liver)	↑ Glucokinase (increased expression)
↑ Glycogen synthesis (liver, muscle)	↑ Glycogen synthase
↓ Glycogen breakdown (liver, muscle)	↓ Glycogen phosphorylase
↑ Glycolysis, acetyl-CoA production (liver, muscle)	↑ PFK-1 (by ↑ PFK-2)
	↑ Pyruvate dehydrogenase complex
↑ Fatty acid synthesis (liver)	↑ Acetyl-CoA carboxylase
↑ Triacylglycerol synthesis (adipose tissue)	↑ Lipoprotein lipase

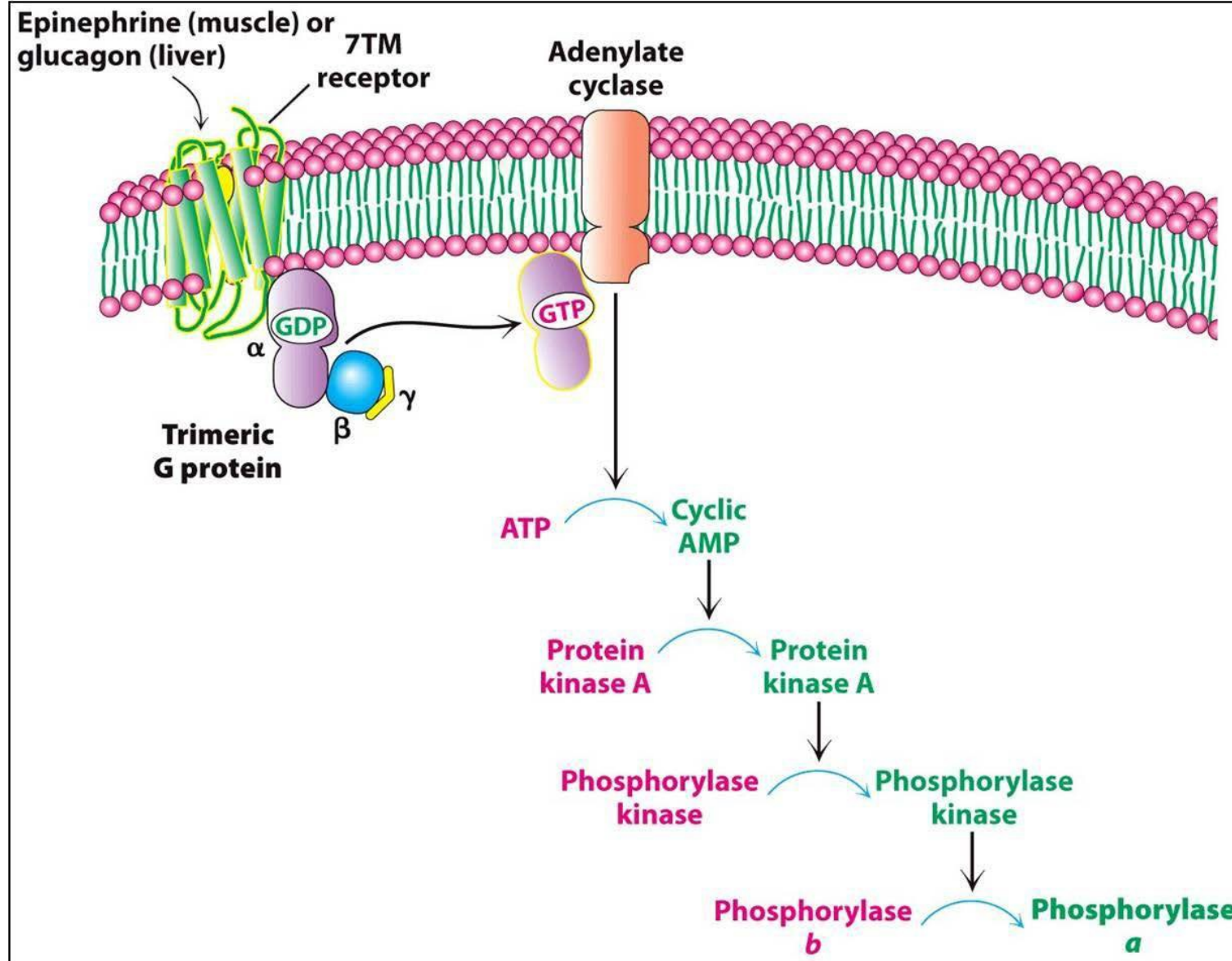


Insulina e Glucagon





Sinalização do Glucagon



Regulação do metabolismo pelo Glucagon

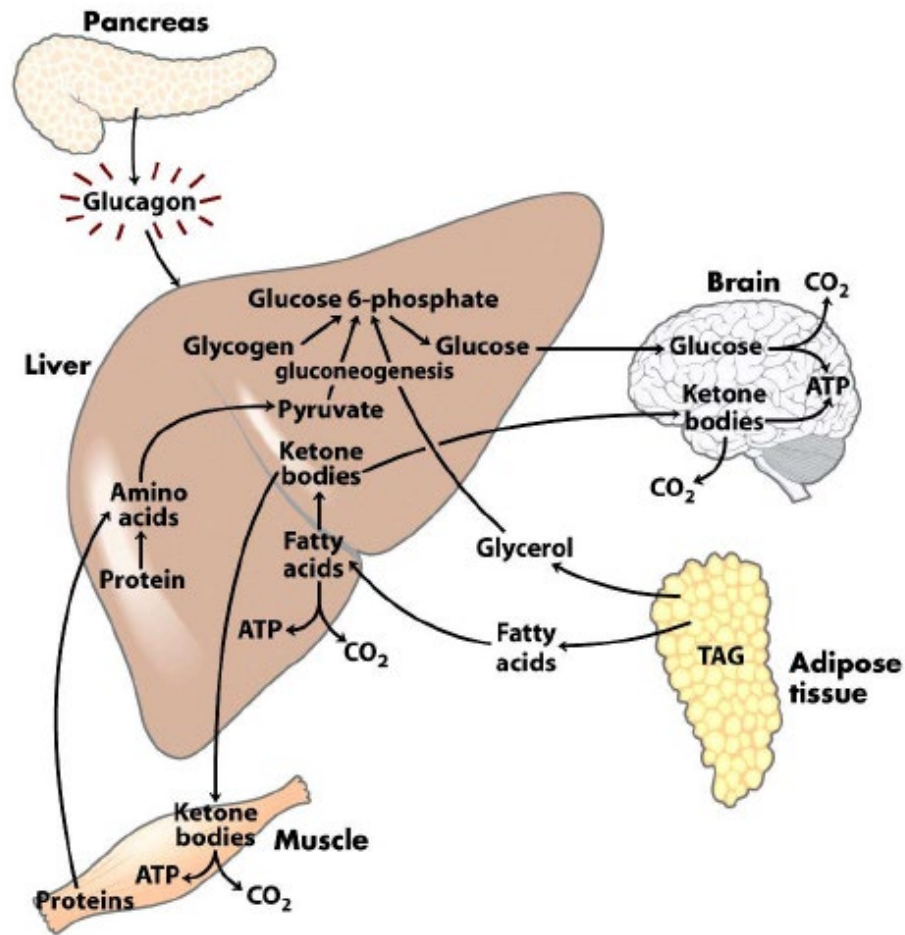
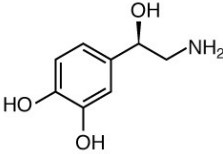
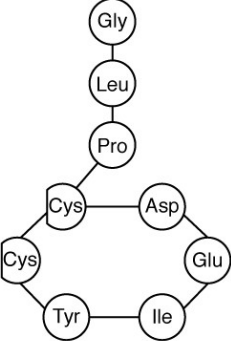

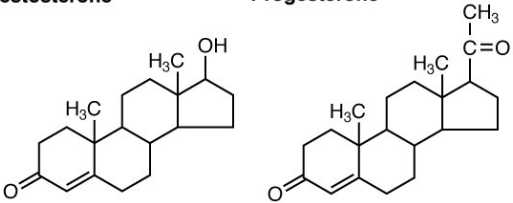


TABLE 23-4 Effects of Glucagon on Blood Glucose: Production and Release of Glucose by the Liver

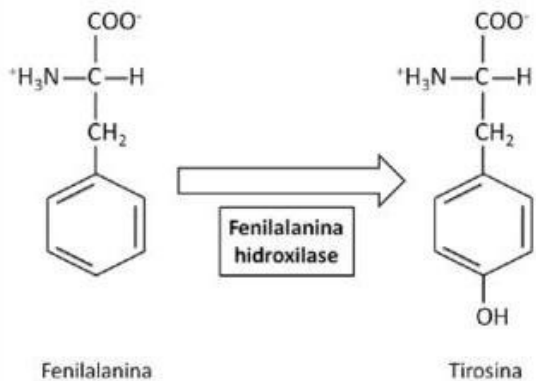
Metabolic effect	Effect on glucose metabolism	Target enzyme
↑ Glycogen breakdown (liver)	Glycogen → glucose	↑ Glycogen phosphorylase
↓ Glycogen synthesis (liver)	Less glucose stored as glycogen	↓ Glycogen synthase
↓ Glycolysis (liver)	Less glucose used as fuel in liver	↓ PFK-1
↑ Gluconeogenesis (liver)	Amino acids } → glucose Glycerol } Oxaloacetate }	↑ FBPase-2 ↓ Pyruvate kinase
↑ Fatty acid mobilization (adipose tissue)	Less glucose used as fuel by liver, muscle	↑ PEP carboxykinase ↑ Triacylglycerol lipase Perilipin phosphorylation
↑ Ketogenesis	Provides alternative to glucose as energy source for brain	↑ Acetyl-CoA carboxylase



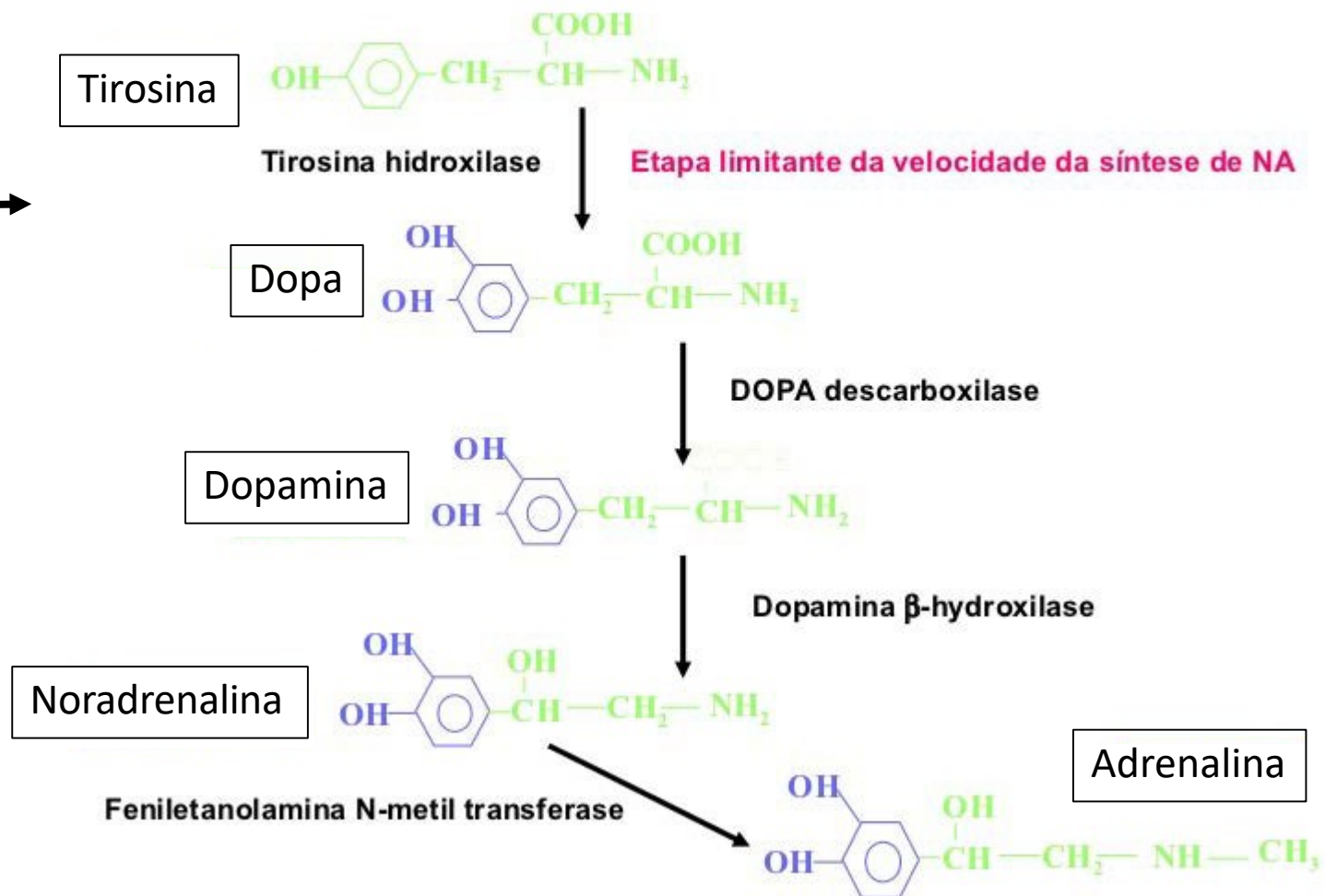
Hormônios Amino

Hormone Class	Components	Example(s)
Amine Hormone	Amino acids with modified groups (e.g. norepinephrine's carboxyl group is replaced with a benzene ring)	<p>Norepinephrine</p> 
Peptide Hormone	Short chains of linked amino acids	<p>Oxytocin</p> 
Protein Hormone	Long chains of linked amino acids	<p>Human Growth Hormone</p> 
Steroid Hormones	Derived from the lipid cholesterol	<p>Testosterone Progesterone</p> 





BIOSSÍNTESE DAS CATECOLAMINAS



Adrenalina e Noradrenalina sintetizados pela supra-renal funcionam como neurotransmissores (sinapse no cérebro e no músculo) e como hormônios que regulam o metabolismo no (fígado e no músculo).



Sinalização de epinefrina: resposta a um estresse ambiental/metabólico

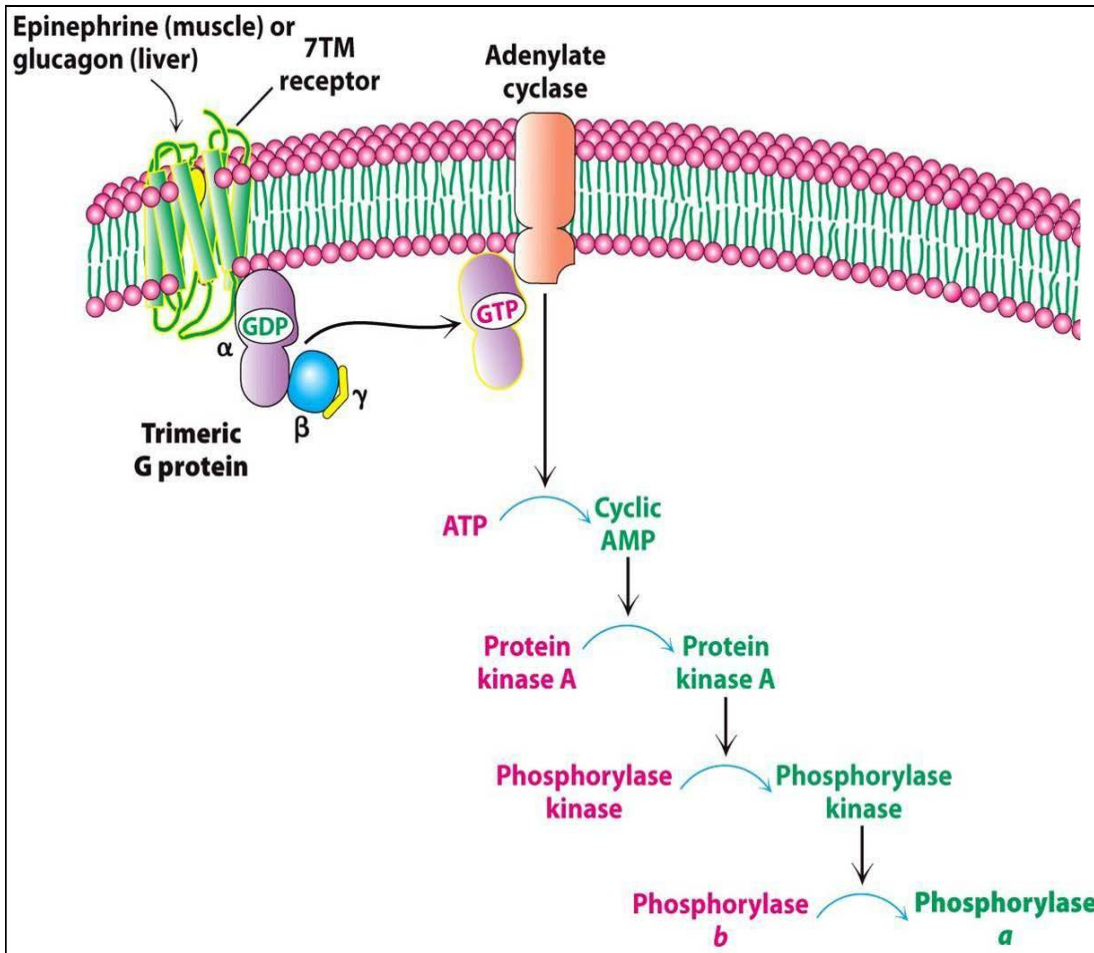
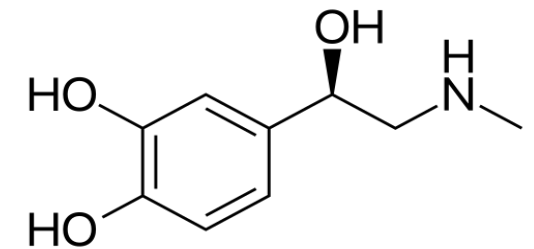


TABLE 23-6 Physiological and Metabolic Effects of Epinephrine: Preparation for Action

Immediate effect	Overall effect
Physiological ↑ Heart rate ↑ Blood pressure ↑ Dilation of respiratory passages	Increase delivery of O ₂ to tissues (muscle)
Metabolic ↑ Glycogen breakdown (muscle, liver) ↓ Glycogen synthesis (muscle, liver) ↑ Gluconeogenesis (liver)	
↑ Glycolysis (muscle) ↑ Fatty acid mobilization (adipose tissue)	
↑ Glucagon secretion ↓ Insulin secretion	Increases ATP production in muscle Increases availability of fatty acids as fuel Reinforce metabolic effects of epinephrine

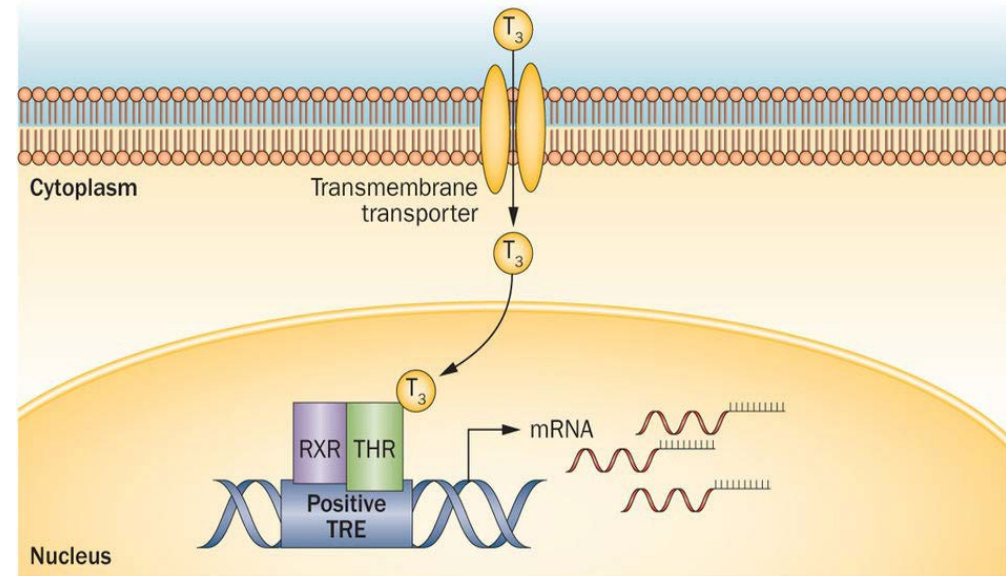
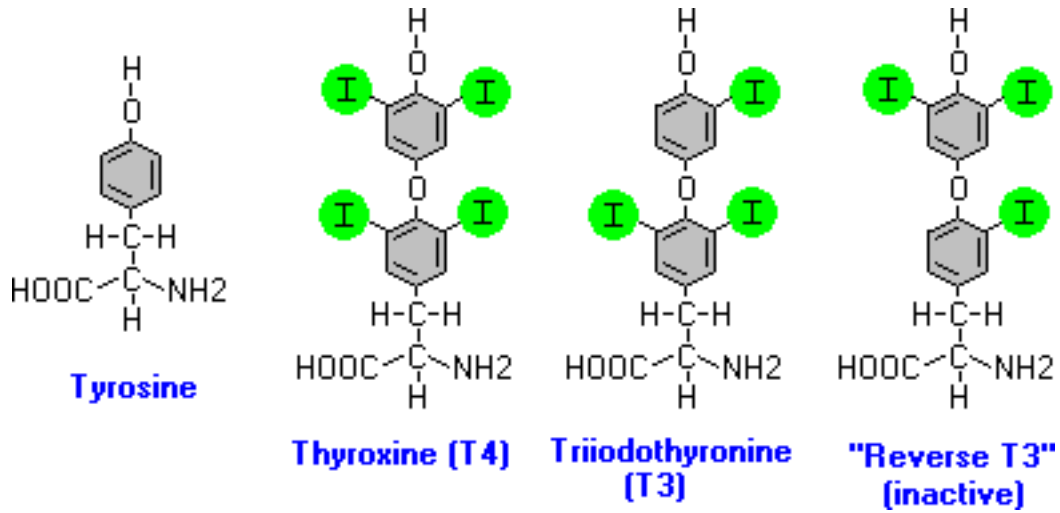
- Usado clinicamente em parada cardíaca, choque, anafilaxia



By Roland Mattern - Roland1952, Public Domain,
<https://commons.wikimedia.org/w/index.php?curid=5902493>



Hormônios Tireoidianos



- **thyroxine** (also known as T4 or L-3,5,3',5'-tetraiodothyronine)
- **triiodothyronine** (T3 or L-3,5,3'-triiodothyronine)



Hormônios Tireoidianos

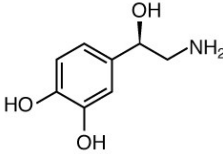
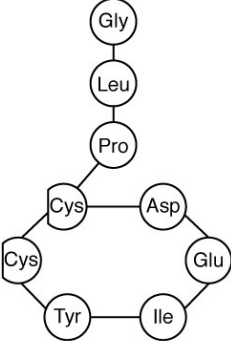

Parameter	↓ T₃, T₄	↑ T₃, T₄
Basal metabolic rate	↓	↑
Carbohydrate metabolism	↓ Gluconeogenesis ↓ Glycogenolysis Normal serum [glucose]	↑ Gluconeogenesis ↑ Glycogenolysis Normal serum [glucose]
Protein metabolism	↓ Synthesis ↓ Proteolysis	↑ Synthesis ↑ Proteolysis Muscle wasting
Lipid metabolism	↓ Lipogenesis ↓ Lipolysis ↑ Serum [cholesterol]	↑ Lipogenesis ↑ Lipolysis ↓ Serum [cholesterol]
Thermogenesis	↓	↑

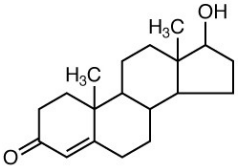
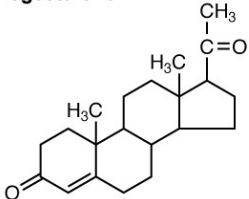
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Table 48-1, Boron & Boulpaep



Hormônios Esteroides

Hormone Class	Components	Example(s)
Amine Hormone	Amino acids with modified groups (e.g. norepinephrine's carboxyl group is replaced with a benzene ring)	<p>Norepinephrine</p> 
Peptide Hormone	Short chains of linked amino acids	<p>Oxytocin</p> 
Protein Hormone	Long chains of linked amino acids	<p>Human Growth Hormone</p> 

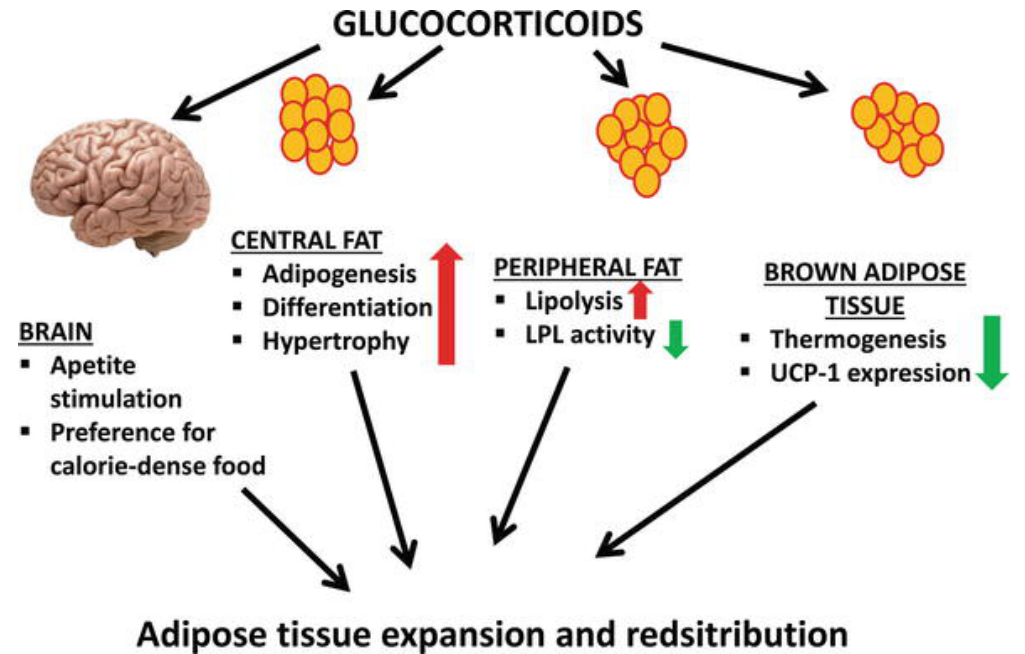
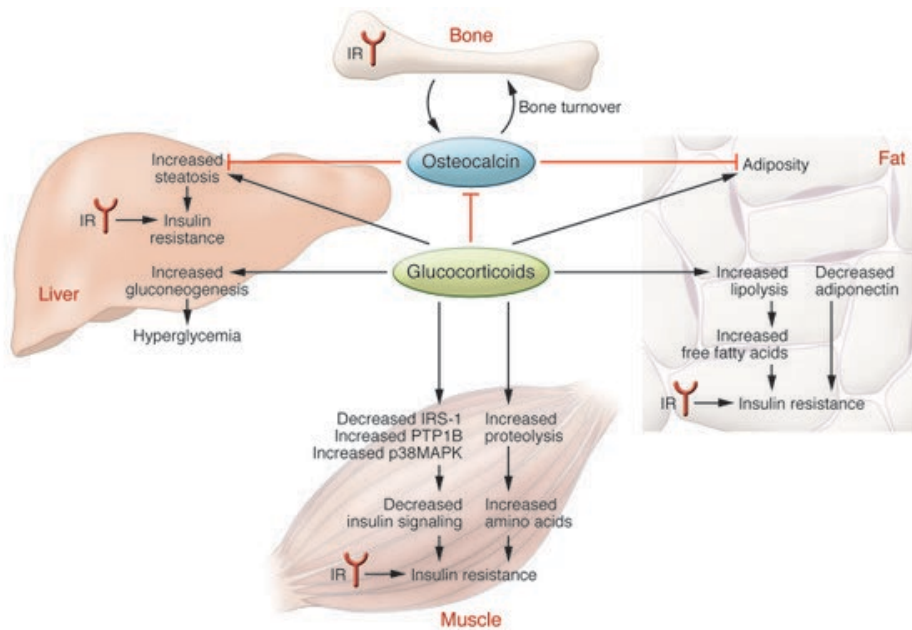
Steroid Hormones	Derived from the lipid cholesterol	<p>Testosterone</p>  <p>Progesterone</p> 
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Glicocorticóides

Doença de Addison's autoimunidade contra o cortex adrenal

Doença de Cushing's hipersecreção de glicocorticóide



Bibliografía

