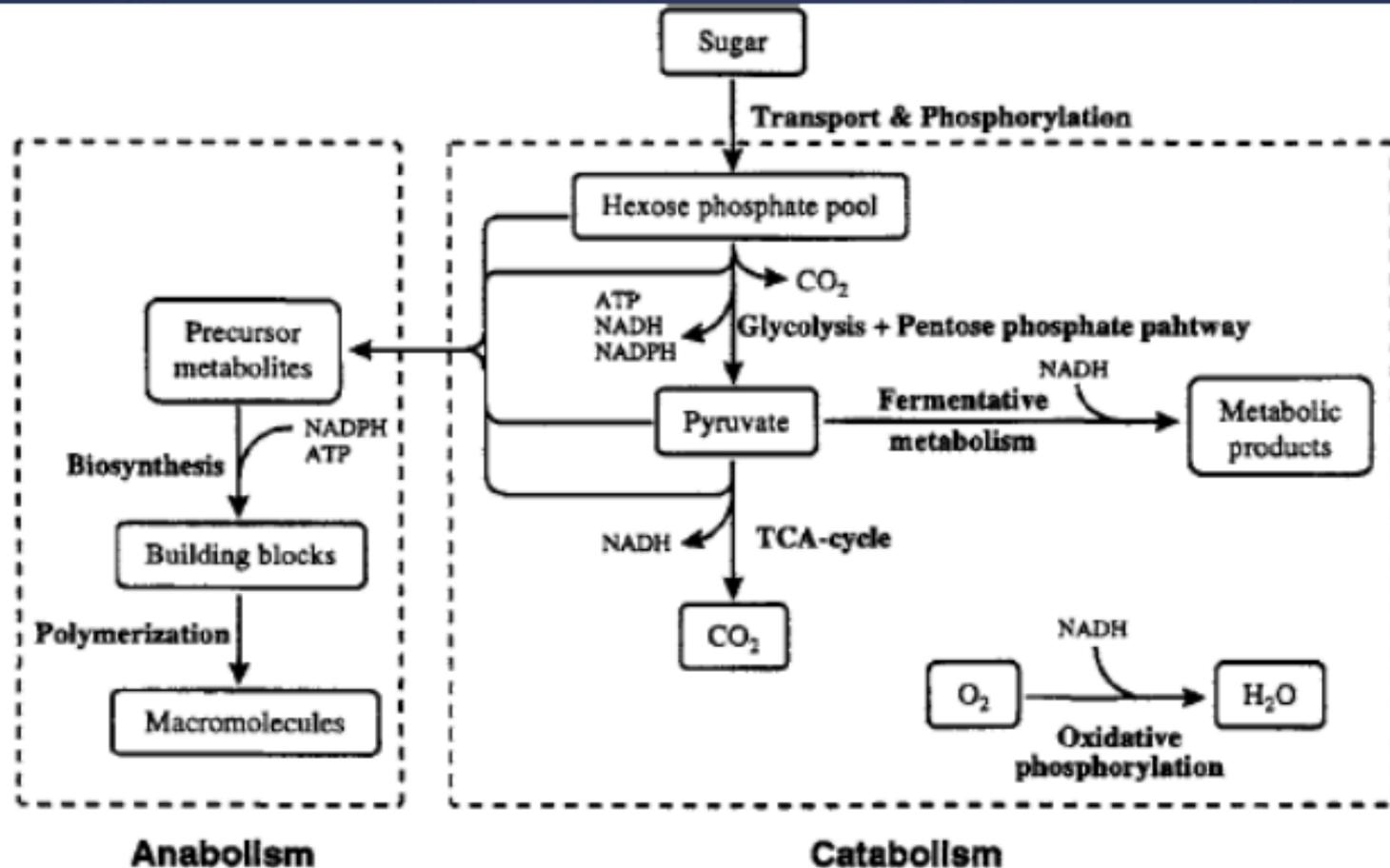


# Metabolismo III

## BIOSSÍNTESE

# Síntese de uma célula a partir de açúcares



# Biossíntese

\* Composição em macromoléculas de *E. coli*

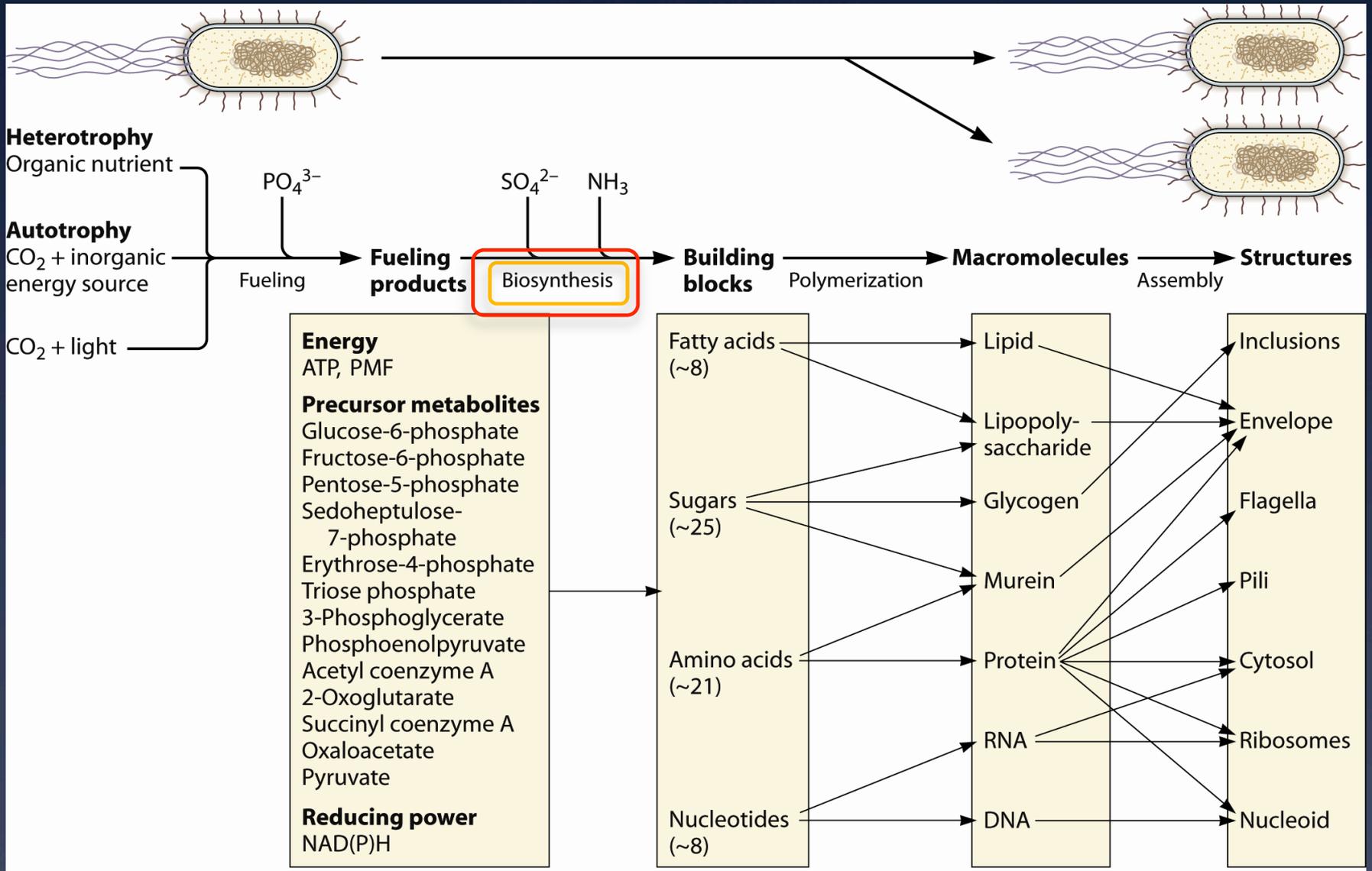
Macromolecule	Percentage of total dry weight	Different kinds of molecules
Protein	55.0	1050
RNA	20.5	
rRNA	16.7	3
tRNA	3.0	60
mRNA	0.8	400
DNA	3.1	1
Lipid	9.1	4
Lipopolysaccharide	3.4	1
Peptidoglycan	2.5	1
Glycogen	2.5	1
Soluble pool	3.9	

<sup>a</sup> The data are taken from Ingraham *et al.* (1983).

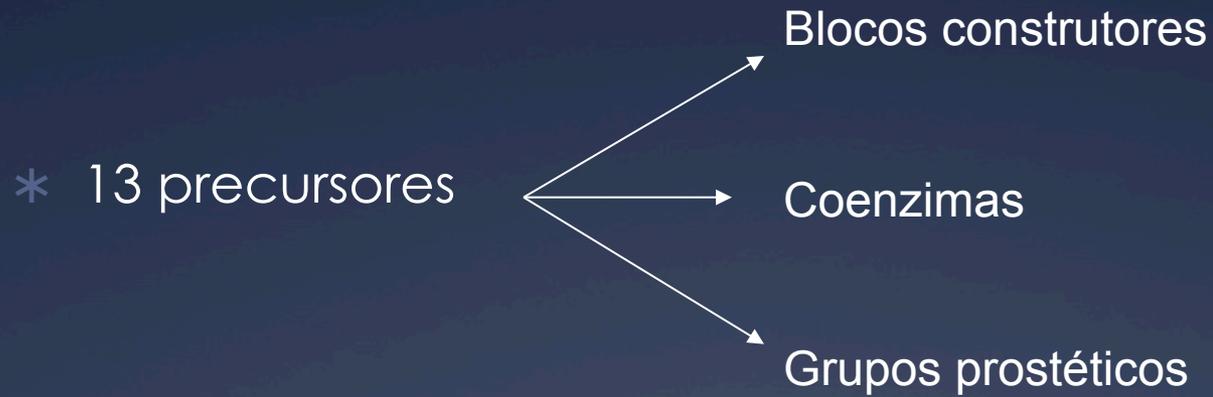
70 da célula = H<sub>2</sub>O . Demais componentes = Massa celular seca

# Biossíntese

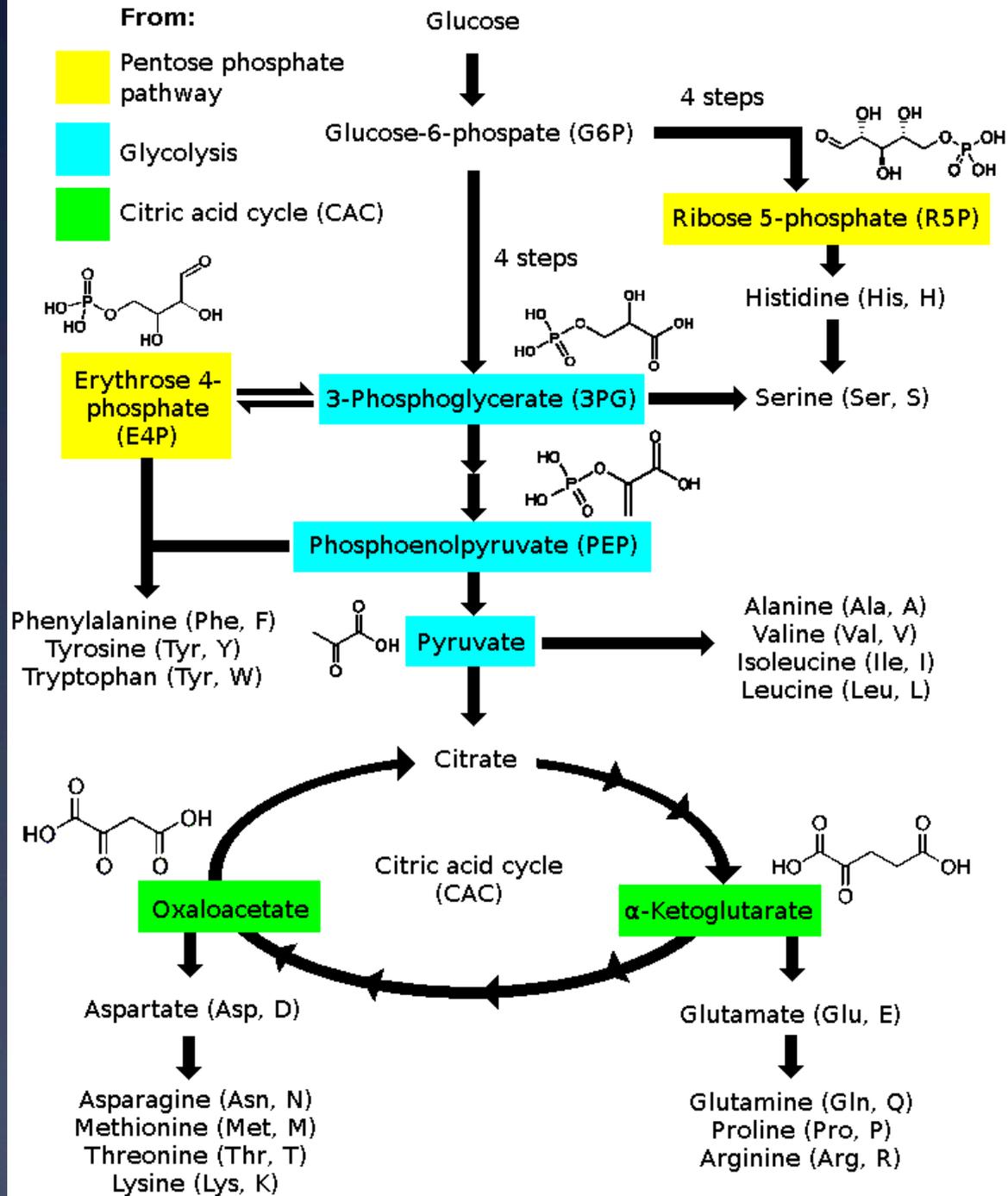
- \* Reações biossintéticas
  - \* Produzem
    - \* os blocos construtores usados na polimerização
    - \* Coenzimas
  - \* São reações sequenciais (vias)
    - \* controladas em bloco
    - \* Enzimas oriundas de um mRNA transcrito partir de um operon
  - \* Iniciam-se a partir de um dos 13 metabólitos precursores ou ramificação de via correlata



# Biossínthese



Número entre  
75-100

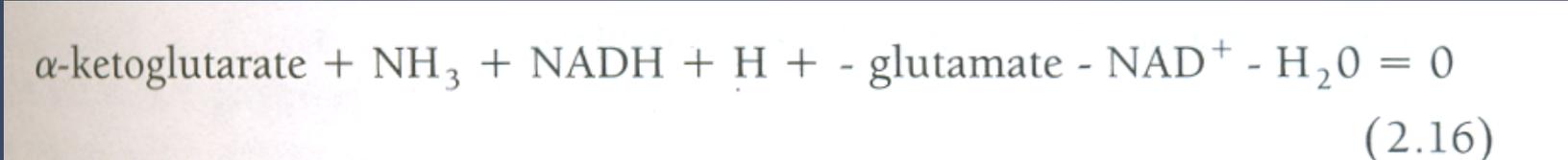
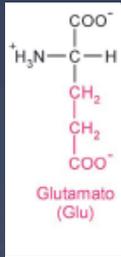
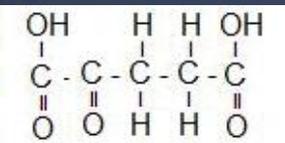


# Biossíntese de aminoácidos



Breakdown product	Amino acids
Pyruvate	Alanine (1), serine (1), cysteine (3), and glycine (2)
Acetyl-CoA	Threonine (1), lysine (10), leucine (8), tyrosine (7), phenylalanine (8), and tryptophan (12)
$\alpha$ -Ketoglutarate	Glutamate (1), glutamine (2), proline (3), arginine (4) and histidine (5)
Succinyl-CoA	Methionine (9), isoleucine (9), and valine (8)
Oxaloacetate	Aspartate (1) and asparagine (2)

<sup>a</sup> The figure in the parenthesis is the number of steps in the breakdown pathway in the higher eukaryotes. For most of the amino acids where this number is one the breakdown product is directly formed by deamination according to eq. (2.16).



# Biossíntese de aminoácidos

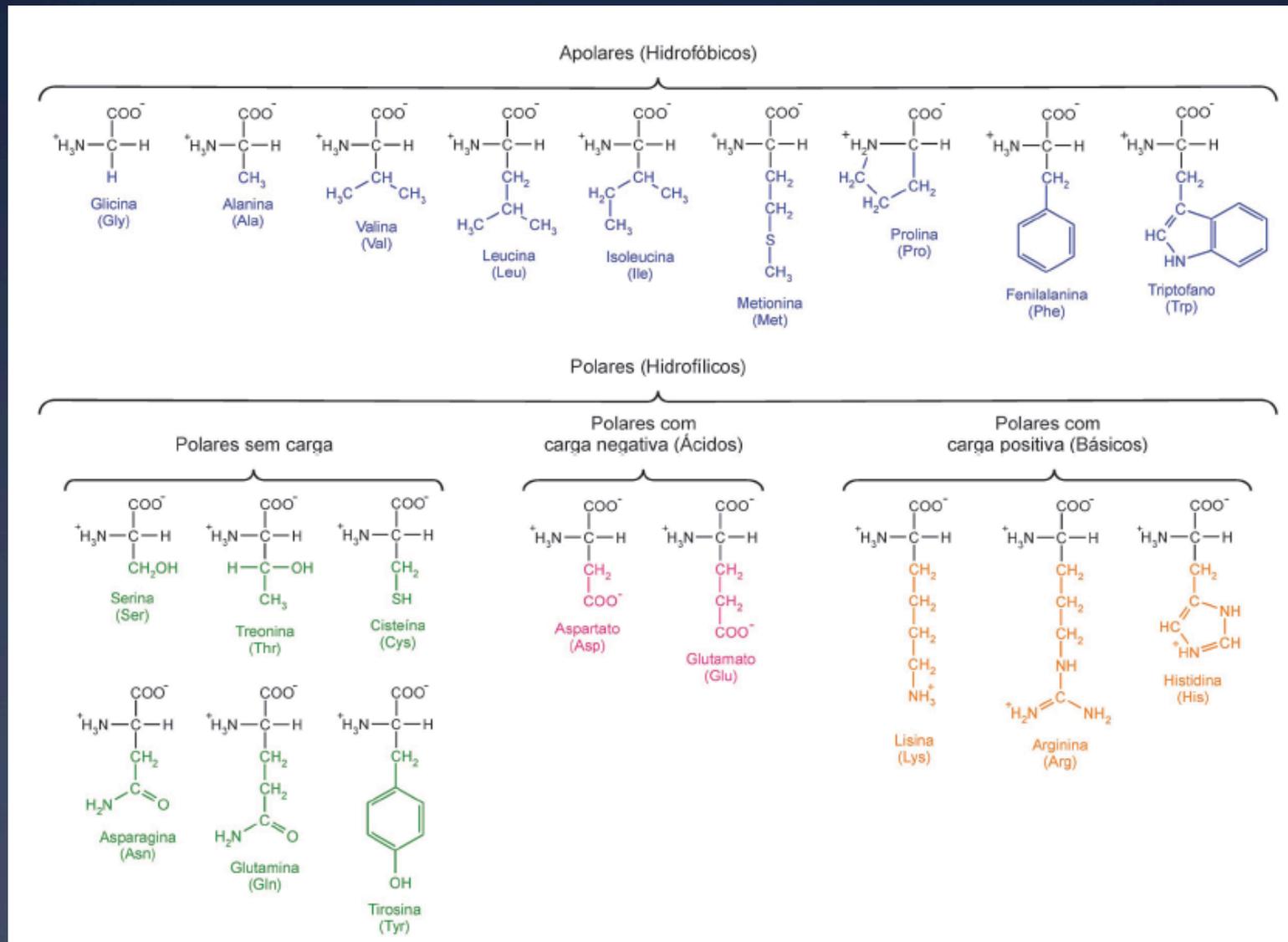
\* Aminoácidos :

\* Precursores de  
proteínas

\* Aminoácidos :

\* Precursores de  
metabólitos  
secundários  
ex. Penicilina

# Estrutura dos aminoácidos



# Biossíntese de aminoácidos

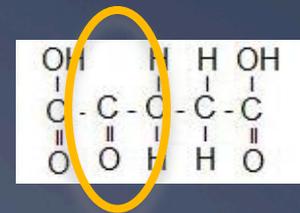
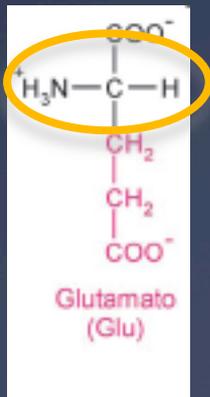
- \* Etapa inicial:

Assimilação de nitrogênio

- \* Fixação de uma molécula de amônia

- \* Incorporação a uma molécula orgânica

Isto ocorre pela biossíntese de L-glutamato a partir de  $\alpha$ -cetoglutarato (ou 2oxoglutarato)

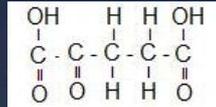


# Biossíntese de *L*-glutamato a partir de $\alpha$ -cetoglutarato

- \* **VIA GDH**      Glutamato desidrogenase
  
- \* **VIA GS-GOGAT** glutamina amida-2-oxoglutarato aminotransferase ( *ou glutamato sintase* )

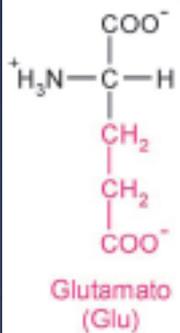
# Biossíntese de *L*-glutamato a partir de $\alpha$ -cetoglutarato

VIA GDH



L-glutamate + NADP<sup>+</sup> + H<sub>2</sub>O -  $\alpha$ -ketoglutarate

- NH<sub>3</sub> - NADPH - H<sup>+</sup> = 0



Enzima envolvida:

GDH

Glutamato desidrogenase ligada a NADP

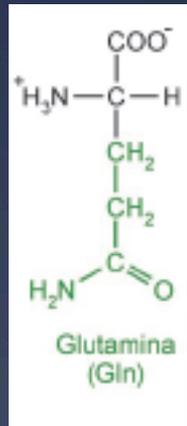
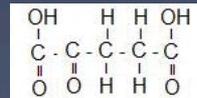
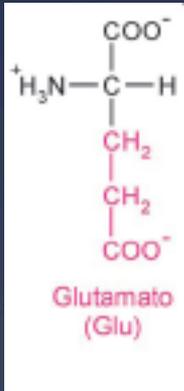
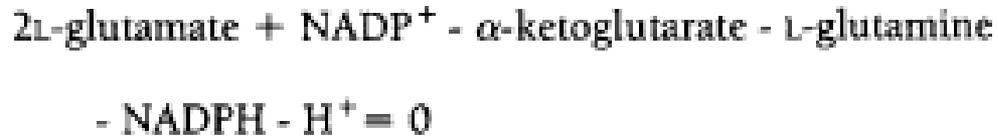
# Biossíntese de L-glutamato a partir de $\alpha$ -cetoglutarato

## VIA GS-GOGAT

2 etapas:

1) L-glutamina atua como um amino doador para o  $\alpha$ -cetoglutarato

São formados 2 moléculas de L- glutamato



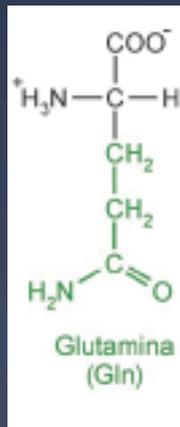
**GOGAT** = glutamina amida-2-oxoglutarato aminotransferase  
( ou glutamato sintase)

# Biossíntese de *L*-glutamina a partir de $\alpha$ -cetoglutarato

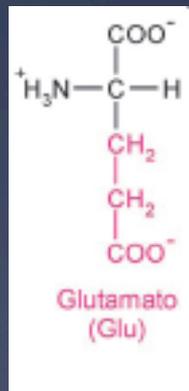
## VIA **GS-GOGAT**

2 etapas:

2) Regeneração da glutamina



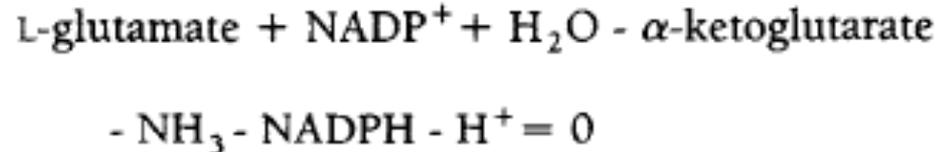
**GS** = Glutamina sintase



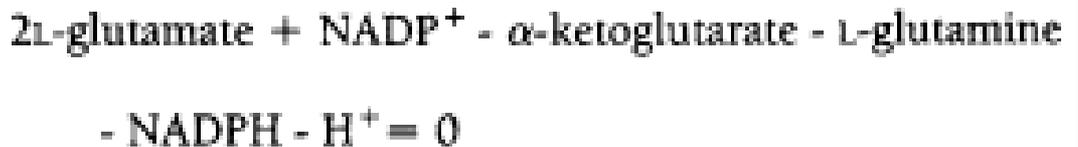
# Biossíntese de *L*-glutamato a partir de $\alpha$ -cetoglutarato

Soma das equações em cada caso

VIA GDH



VIA GS-GOGAT



Síntese de glutamato a partir de  $\alpha$ -cetoglutarato

Com GS-GOGAT há gasto de ATP

# Biossíntese de L-glutamato a partir de $\alpha$ -cetoglutarato

## \* **GS-GOGAT**

- \* Sistema de alta afinidade para assimilação de amônia
- \* Ativo em baixas concentrações de amônia

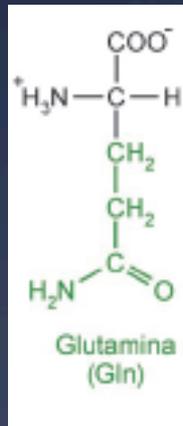
*E coli* é capaz de expressar ambas as vias GDH ou GS-GOGAT, dependendo das condições de cultivo

- \* GOGAT (glutamato sintase) é reprimida por amônia

- \* GS (glutamina sintase) é reprimida por glutamina
- \* Inibição por qualquer via relacionada a L

glutamina:

- \* AMP
- \* GTP
- \* L-glicina
- \* L-histidina

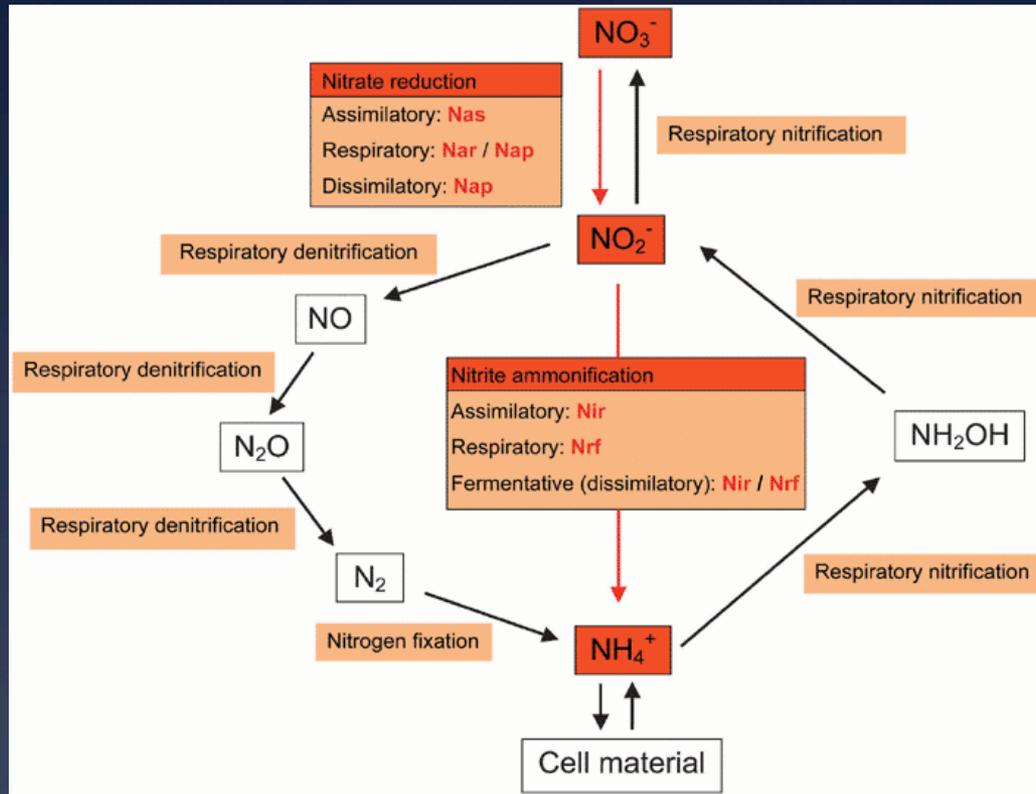


## \* L-glutamina

- \* Doador de nitrogênio (amônia) para vários compostos nitrogenados
- \* Importante ponto de ramificação para o metabolismo celular

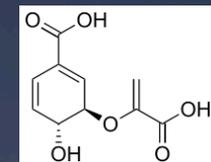
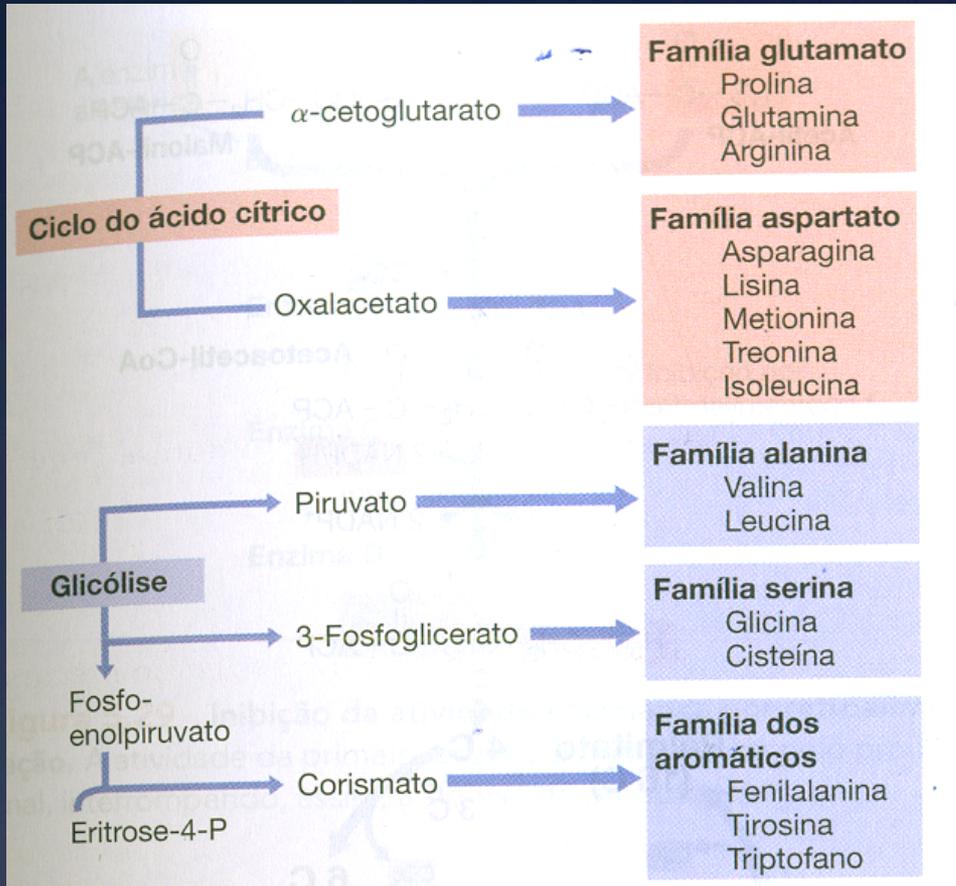


## Enzymology and bioenergetics of respiratory nitrite ammonification



The biological nitrogen cycle. Nitrate reduction and nitrite ammonification are categorized as assimilatory, respiratory or dissimilatory processes and the abbreviations of the corresponding enzymes are given. The reactions marked by the red arrows are the subject of this article. The designated assimilatory processes are carried out under both aerobic and anaerobic conditions, while the respiratory and dissimilatory processes of nitrate reduction, nitrite ammonification and denitrification are typical anaerobic processes. Nitrogen fixation and nitrification require the presence of oxygen. The 'anammox' process in which ammonia is oxidized anaerobically at the expense of nitrite to yield  $\text{N}_2$  and  $2 \text{H}_2\text{O}$  is left out for clarity. Nas, assimilatory nitrate reductase; Nar, respiratory nitrate reductase; Nap, periplasmic nitrate reductase; Nir, NADH-dependent nitrite reductase; Nrf, cytochrome c nitrite reductase

FEMS Microbiology Reviews, Volume: 26, Issue: 3, Pages: 285-309, First published: 09 January 2006, DOI: (10.1111/j.1574-6976.2002.tb00616.x) Simon, 2006.



ácido corísmico

**Figura 5.25 Famílias de aminoácidos.** A maioria dos aminoácidos é derivada do ciclo do ácido cítrico ou da glicólise. A síntese dos vários aminoácidos de uma família frequentemente requer muitas etapas distintas, enzimaticamente catalisadas, iniciadas a partir do aminoácido parental (apresentado em negrito).

# Biossíntese de aminoácidos

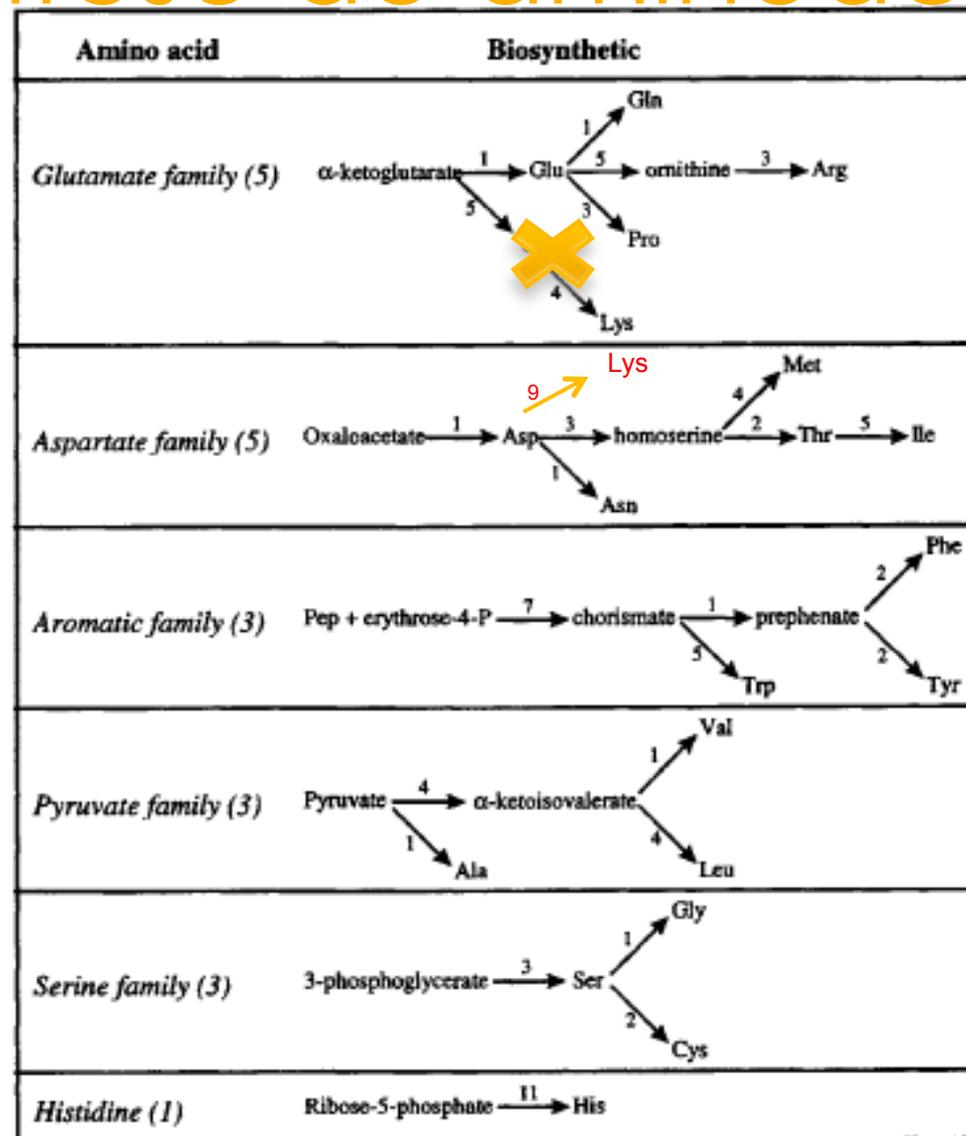
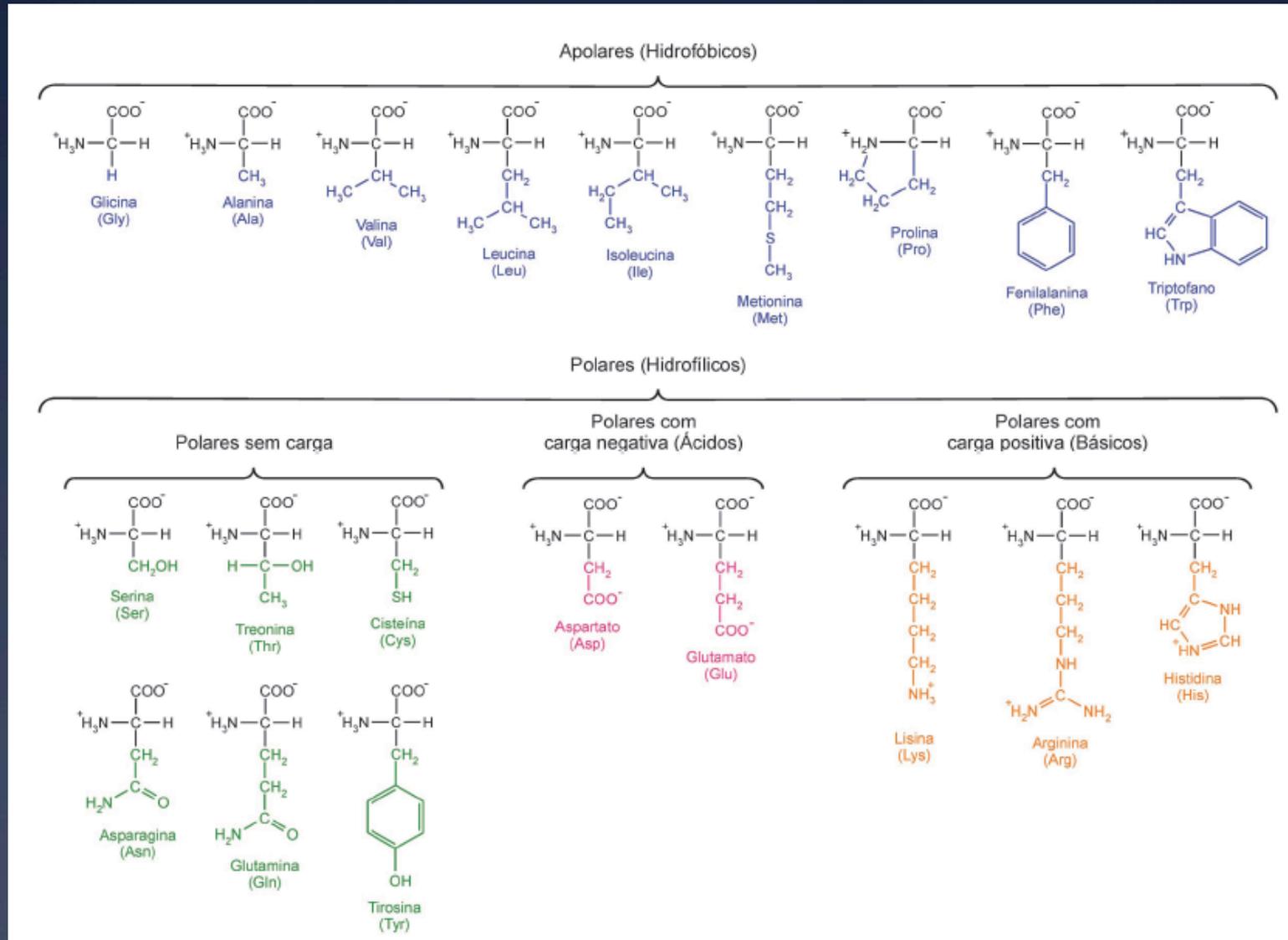
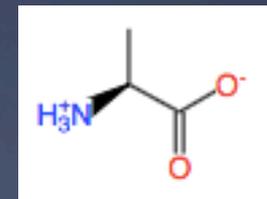
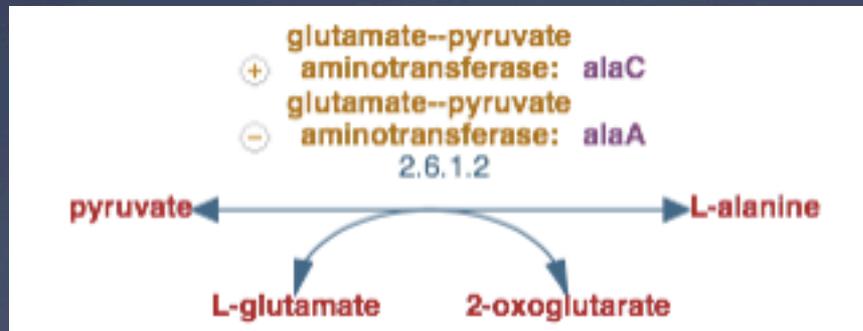
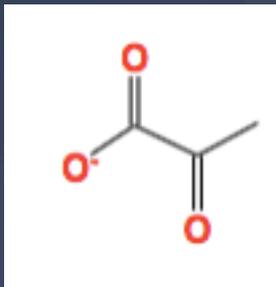
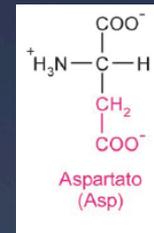
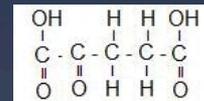
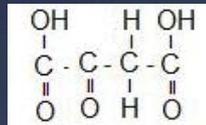
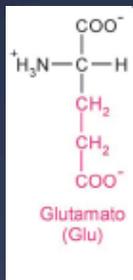
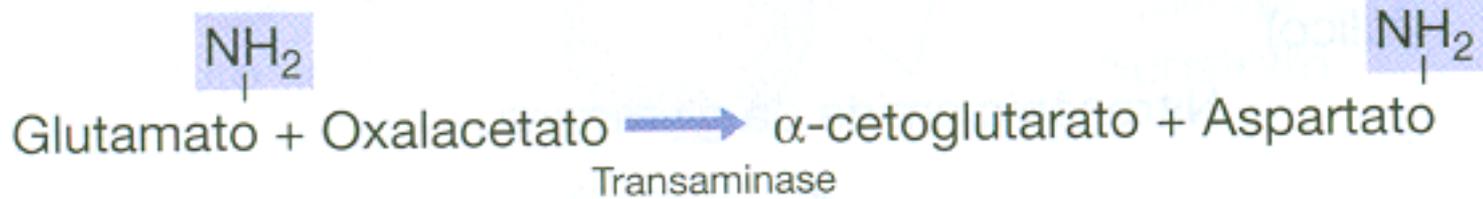


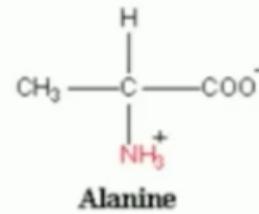
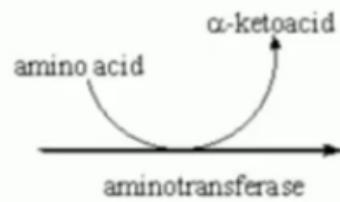
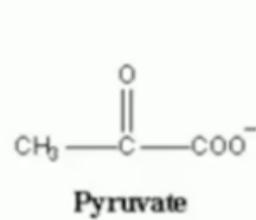
FIGURE 2.12 Overview of amino acid biosynthesis in eukaryotes. The amino acids are classified into five families according to the specific precursor metabolite or amino acid that serves as the starting point for their synthesis. L-Histidine, which has a complex biosynthetic pathway, does not group with any of the other amino acids. The numbers indicate the reaction steps in the pathway. Except for L-lysine, these numbers are the same for bacteria. In bacteria L-lysine is synthesized from aspartate via diaminopimelic acid (an important building block for bacteria cell wall) in a sequence of nine reactions.

# Estrutura dos aminoácidos



As reações de transaminase transferem um grupo amino para um ácido orgânico





*Pyruvate family (3)*



# Custos metabólicos para produzir aa em bactérias e fungos

Amino acid	Precursor metabolites <sup>a</sup>	ATP <sup>b</sup>	NADH	NADPH	1-C <sup>c</sup>	NH <sub>3</sub>	S <sup>d</sup>
L-Alanine	1 pyr	0	0	-1	0	-1	0
L-Arginine	1 $\alpha$ kg	-7	1	-4	0	-4	0
L-Asparagine	1 oaa	-3	0	-1	0	-2	0
L-Aspartate	1 oaa	0	0	-1	0	-1	0
L-Cysteine <sup>e</sup>	1 pga	-4	1	-5	0	-1	-1
L-Glutamate	1 $\alpha$ kg	0	0	-1	0	-1	0
L-Glutamine	1 $\alpha$ kg	-1	0	-1	0	-2	0
L-Glycine	1 pga	0	1	-1	1	-1	0
L-Histidine	1 penP	-6	3	-1	-1	-3	0
L-Isoleucine	1 oaa, 1 pyr	-2	0	-5	0	-1	0
L-Leucine	2 pyr, 1 acCoA	0	1	-2	0	-1	0
L-Lysine (fungi)	1 akg, 1 acCoA	-2	2	-4	0	-2	0
L-Lysine	1 pyr, 1 oaa	-3	0	-4	0	-2	0
L-Methionine	1 oaa	-7	0	-8	-1	-1	-1
L-Phenylalanine	2 pep, 1 eryP	-1	0	-2	0	-1	0
L-Proline	1 $\alpha$ kg	-1	0	-3	0	-1	0
L-Serine	1 pga	0	1	-1	0	-1	0
L-Threonine	1 oaa	-2	0	-3	0	-1	0
L-Tryptophan	1 pep, 1 eryP, 1 penP	-5	2	-3	0	-2	0
L-Tyrosine	2 pep, 1 eryP	-1	1	-2	0	-1	0
L-Valine	2 pyr	0	0	-2	0	-1	0

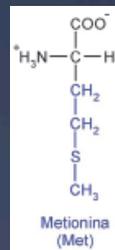
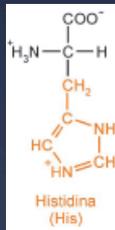
<sup>a</sup> acCoA, acetyl-CoA; eryP, erythrose-4-phosphate; fruP, fructose-6-phosphate; gluP, glucose-6-phosphate;  $\alpha$  kg,  $\alpha$ -ketoglutarate; glyP, glyceraldehyde-3-phosphate; oaa, oxaloacetate; penP, ribose-5-phosphate; pep, phosphoenolpyruvate; pga, 3-phosphoglycerate; pyr, pyruvate.

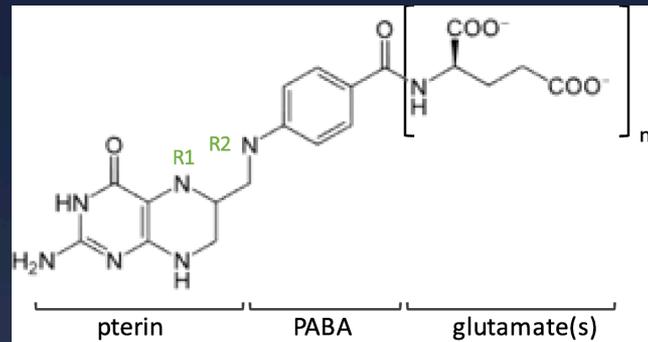
<sup>b</sup> For those reactions where ATP is hydrolyzed to AMP, it is assumed that two ATPs are used.

<sup>c</sup> 5,10-Methylene tetrahydrofolate is used as one-carbon donor which is converted to tetrahydrofolate. Other forms of tetrahydrofolate used in the biosynthesis of L-methionine and L-histidine are converted to this basis.

<sup>d</sup> Sulfate is used as S-source, which is reduced to H<sub>2</sub>S before assimilation.

<sup>e</sup> Direct sulphydrylation of L-serine is assumed.



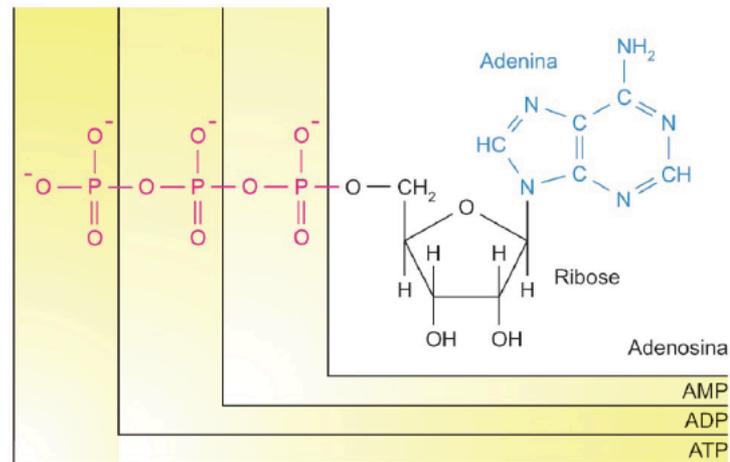


Tetrahydrofolate (THF)	R1	R2
5-methyl-THF	CH <sub>3</sub>	H
5-formyl-THF	CHO	H
10-formyl-THF	H	CHO
5,10-methenyl-THF	=CH-	
5,10-methylene-THF	-CH <sub>2</sub> -	

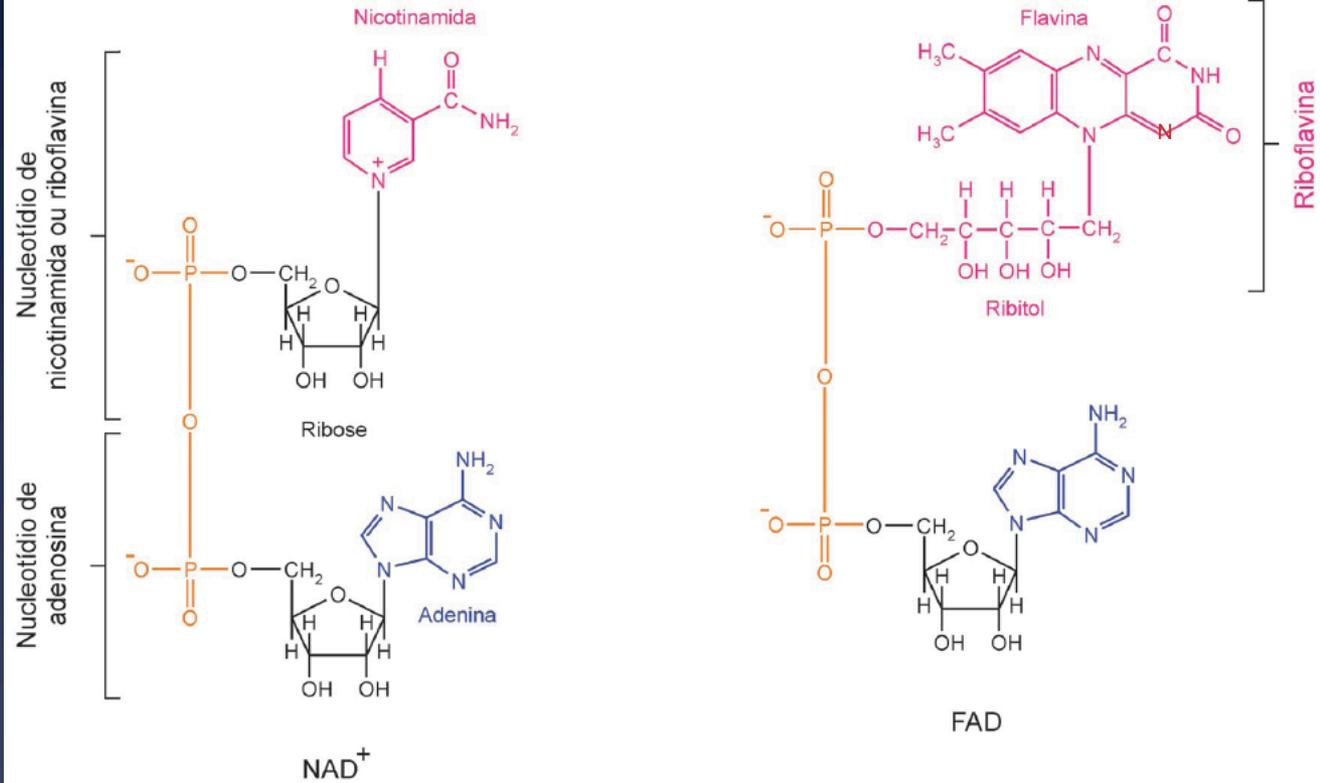
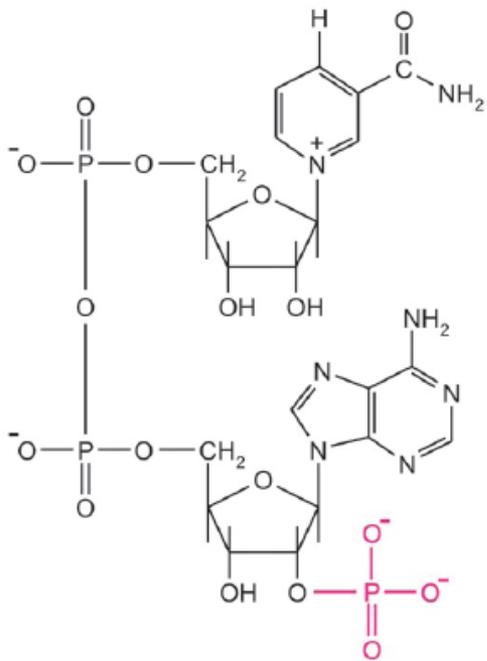
Structure of tetrahydrofolate (THF). THFs are composed of pterin, PABA, and glutamate. The pterin moiety is substituted at N5 (R1) and/or N10 (R2) nitrogen atoms with either a methyl (-CH<sub>3</sub>), formyl (-CH=O) methylene (=CH<sub>2</sub>), or methenyl (-CH<sub>4</sub>) group. THFs also vary in the length of their glutamate “tail,” which varies depending on function

# Biossíntese de ácidos nucleicos, ácidos graxos e outros blocos construtores

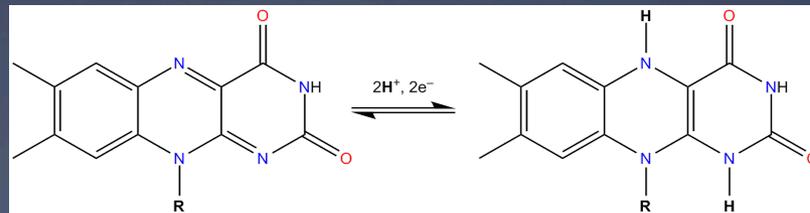
- \* Nucleotídios -  
precursores de RNA e  
DNA na forma de  
ribonucleotídios e  
desoxiribonucleotídios
- \* São constituintes de  
diversos cofatores:
  - \* NADH
  - \* NADPH
  - \* FAD
  - \* CoA
  - \* ATP tem diferentes  
funções no  
metabolismo



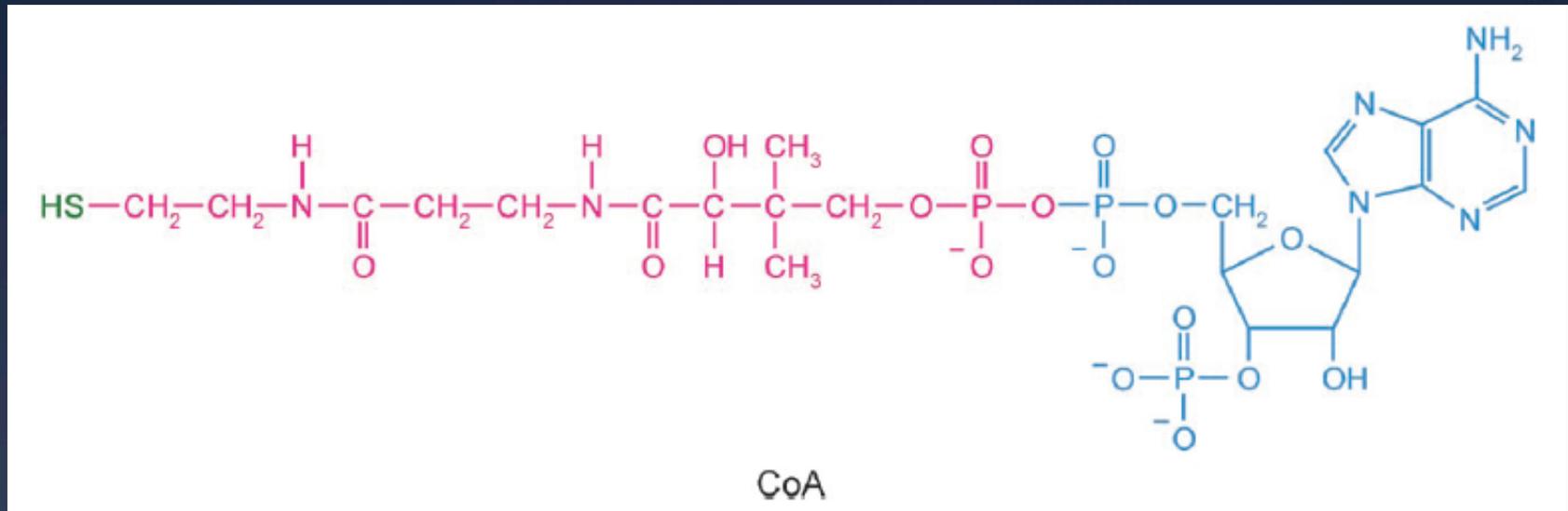
**Fig. 4.1** Estrutura da adenosina, adenosina monofosfato (AMP), adenosina difosfato (ADP) e adenosina trifosfato (ATP). Nos três nucleotídeos (AMP, ADP e ATP), o grupo fosfato está unido à ribose da adenosina por ligação éster fosfórico ( $\Delta G^{0'}$  de hidrólise =  $-15 \text{ kJ} \cdot \text{mol}^{-1}$ ); no ADP e no ATP, a ligação com o(s) outro(s) grupo(s) fosfato é do tipo anidrido fosfórico ( $\Delta G^{0'}$  de hidrólise =  $-31 \text{ kJ} \cdot \text{mol}^{-1}$ ).



NAD<sup>+</sup>



FAD a FADH<sub>2</sub>



A coenzima A se une a grupos acila por ligações tioéster com a sulfidril terminal (verde) do grupo fosfopanteteína (vermelho).

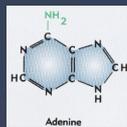
A fosfopanteteína está ligada ao grupo fosfato da 3' fosfoadenosina (azul) que compõe a Coenzima A.

# Biossintese de ácidos nucleicos, ácidos graxos e outros blocos construtores

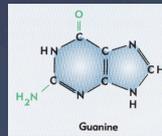
\* Precusores dos nucleotídios:

\* Ribose 5Pe 3 fosfoglicerato

\* Purinas (A, G)



Adenine



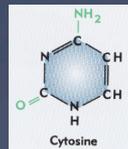
Guanine

\* Pirimidinas (T, C, U)

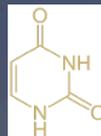
\* Ribose 5P e oxaloacetato



Thymine

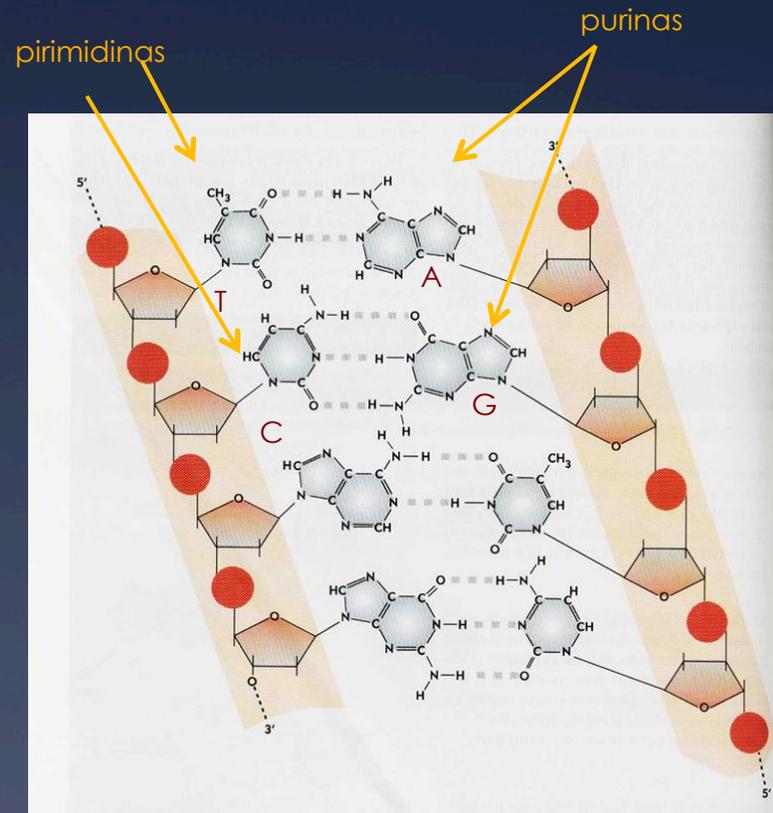
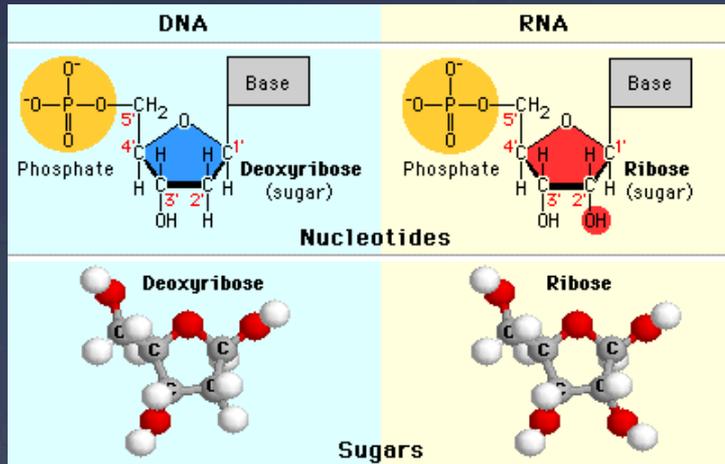


Cytosine



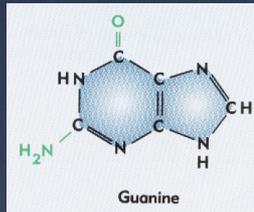
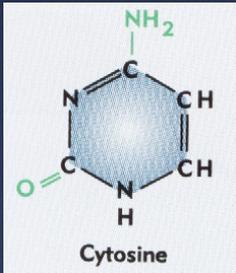
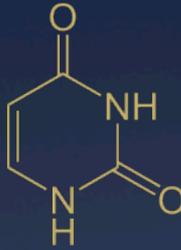
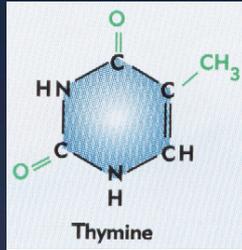
# Estrutura dos nucleotídeos

- \* Base nitrogenada heterocíclica (purina ou pirimidina)
- \* Um açúcar: ribose (no RNA) ou 2-desoxirribose (no DNA)
- \* Um grupo fosforil



DNA

# Estrutura dos nucleotídeos

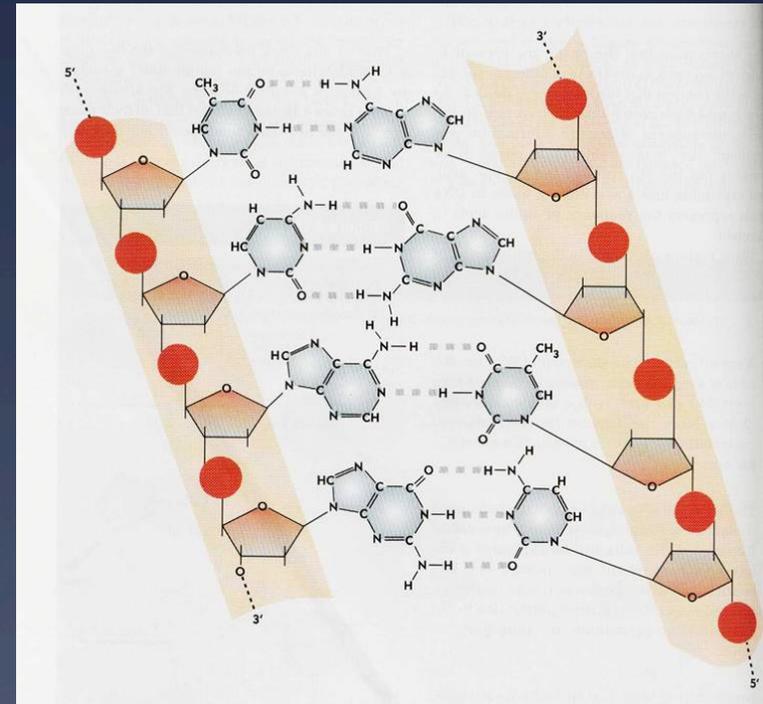
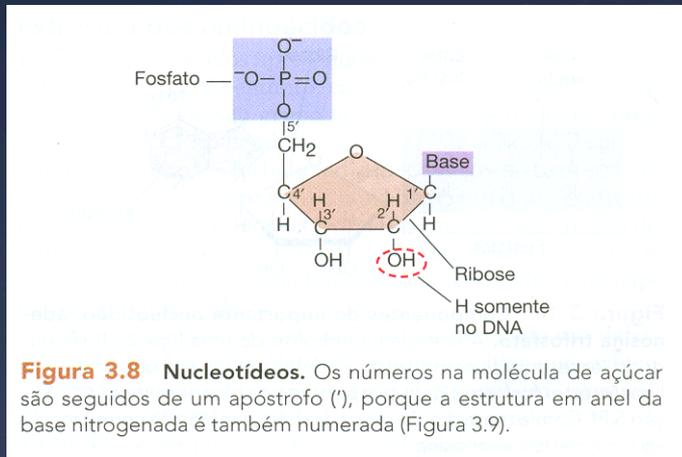


- \* AMP
- \* TMP (U no RNA)
- \* CMP
- \* GMP           geram
- \* dAMP
- \* dTMP
- \* dCMP
- \* dGMP

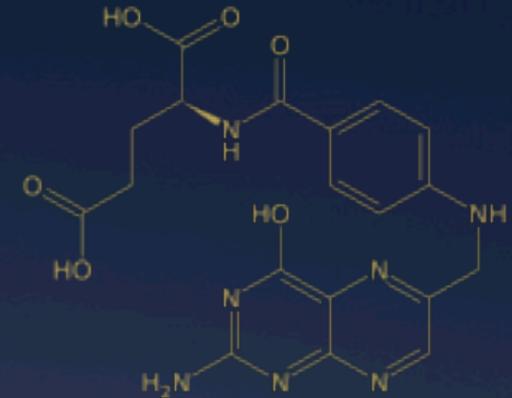
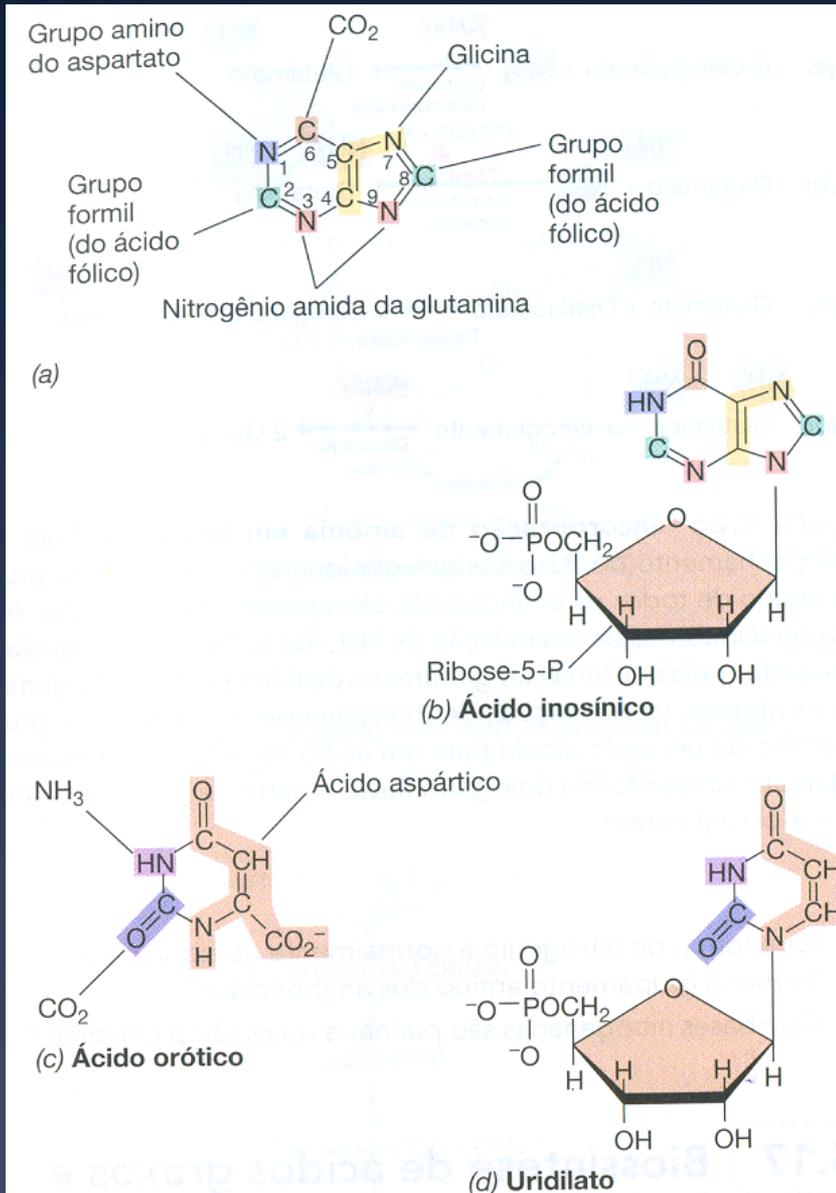
Bases nitrogenadas

dTMP resulta da metilação de dUMP

# Estrutura dos nucleotídeos

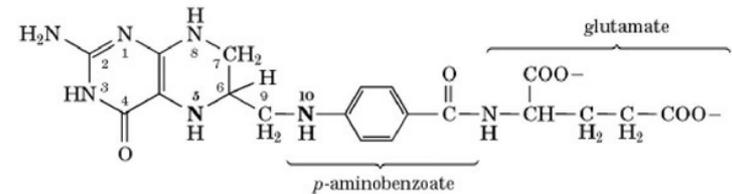


OH na posição 2' é substituída por H às custas de NADPH (ribose ou desoxirribose)



Ácido fólico (vitamina B9, pteroyl-L-glutamato)

2-amino-4-oxo-6-methylpteridine



**Figura 5.27** Biossíntese de purinas e pirimidinas. (a) Os precursores do esqueleto da purina. (b) Ácido inosínico, o precursor de todos os nucleotídeos purínicos. (c) O precursor do esqueleto de pirimidina, ácido orótico. (d) Uridilato, o precursor de todos os nucleotídeos pirimidínicos. O uridilato é formado a partir do orato, após uma descarboxilação e a adição de ribose-5-fosfato.

# Custos metabólicos para a biossíntese de nucleotídeos

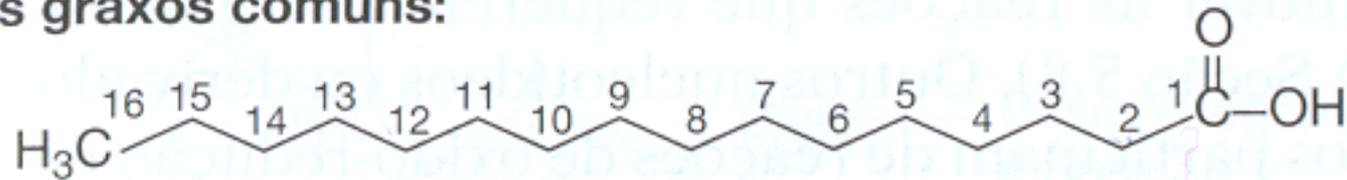
Nucleotide	Precursor metabolite <sup>a</sup>	ATP	NADH	NADPH	1-C	NH <sub>3</sub>
AMP	1 pga, 1 penP	-9	3	-1	-1	-5
GMP	1 pga, 1 penP	-11	3	0	-1	-5
UMP	1 oaa, 1 penP	-5	0	-1	0	-2
CMP	1 oaa, 1 penP	-7	0	-1	0	-3
dAMP	1 pga, 1 penP	-9	3	-2	-1	-5
dGMP	1 pga, 1 penP	-11	3	-1	-1	-5
dTMP <sup>b</sup>	1 oaa, 1 penP	-5	0	-3	-1	-2
dCMP	1 oaa, 1 penP	-7	0	-2	0	-3

<sup>a</sup> See Table 2.4 for nomenclature.

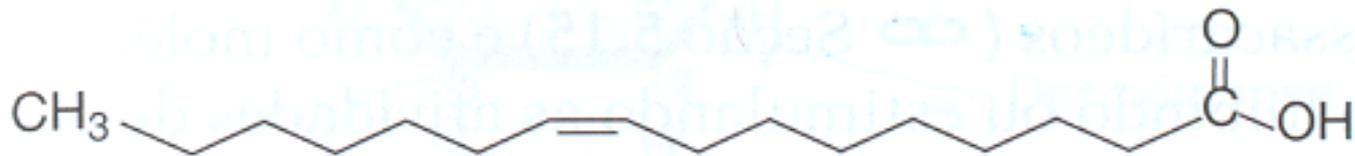
<sup>b</sup> The costs for dTMP biosynthesis are the same as for synthesis from dUMP. dTMP may also be synthesized from dCMP with higher costs, i.e., nine ATPs. For *E. coli*, Ingraham *et al.* (1983) state that 75% of the dTMP is synthesized from dCMP and 25% from dUMP.

# Biossíntese de ácidos graxos

Ácidos graxos comuns:

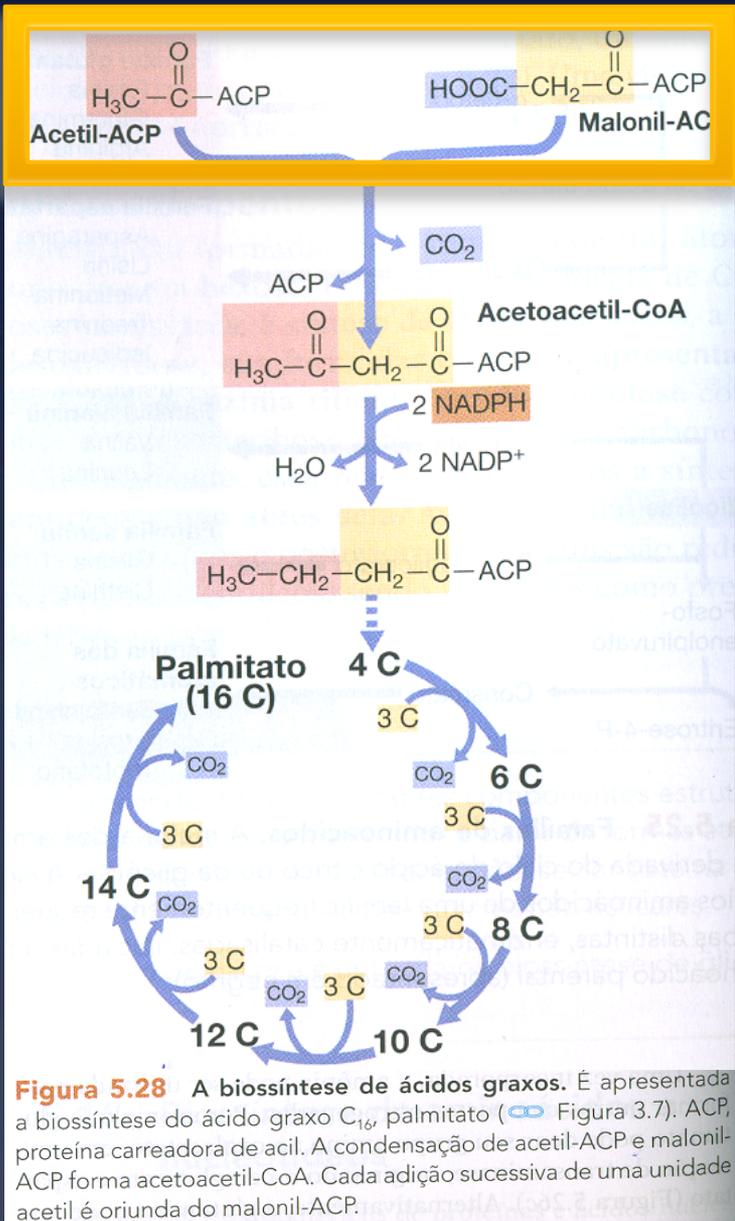


C<sub>16</sub> saturado (palmítico)

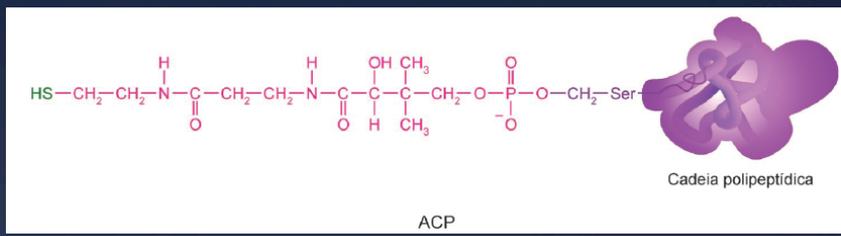


C<sub>16</sub> monoinsaturado (palmitoleico)

Os ácidos graxos diferem quanto ao comprimento, à posição e ao número de ligações duplas.

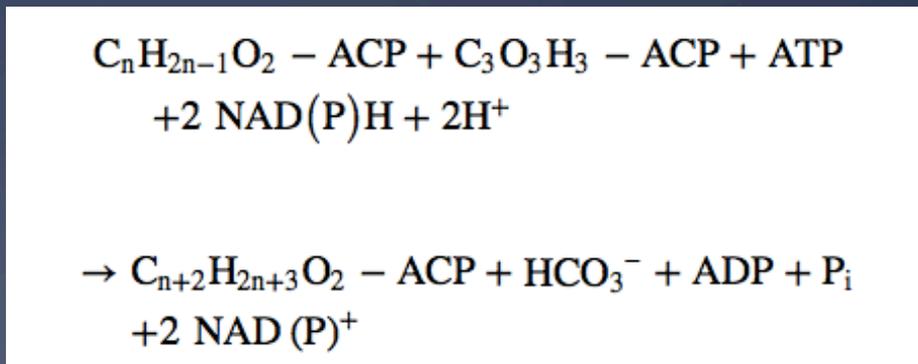


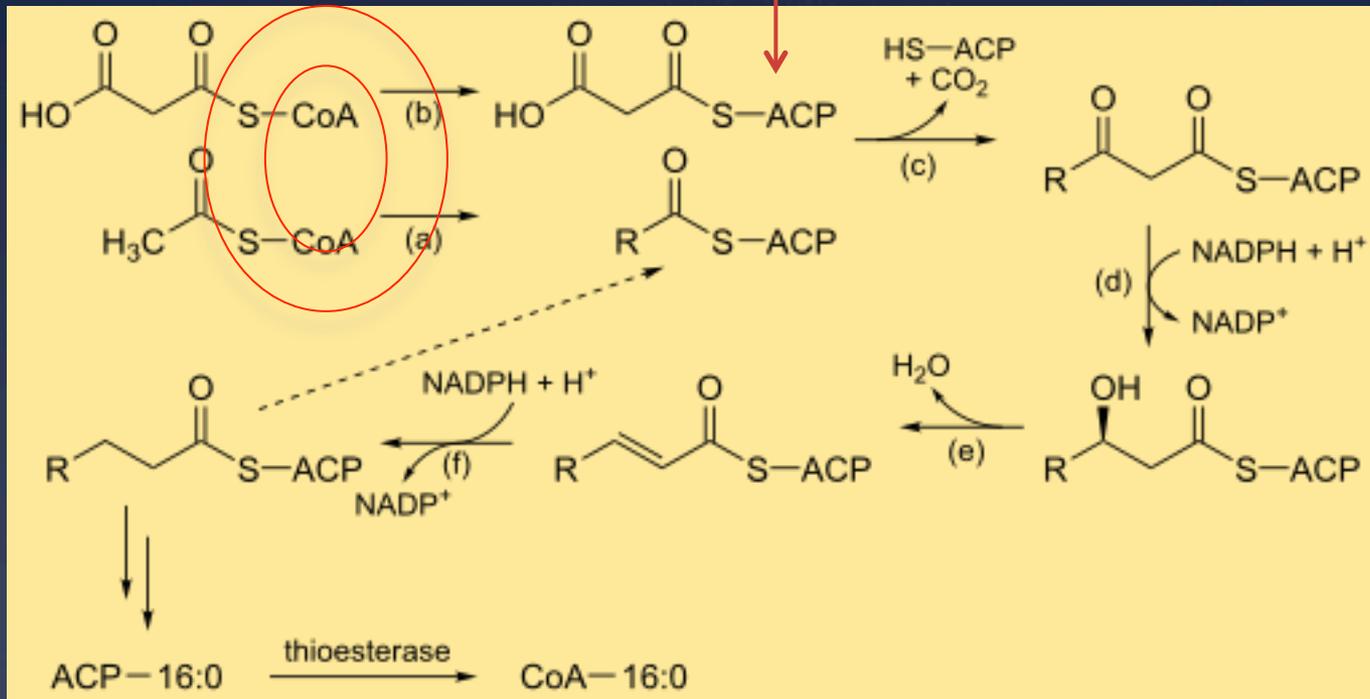
**Figura 5.28** A biosíntese de ácidos graxos. É apresentada a biosíntese do ácido graxo  $\text{C}_{16}$ , palmitato (Figura 3.7). ACP, proteína carreadora de acil. A condensação de acetil-ACP e malonil-ACP forma acetoacetyl-CoA. Cada adição sucessiva de uma unidade acetil é oriunda do malonil-ACP.



Acyl carrier protein (ACP) é o carreador de acil

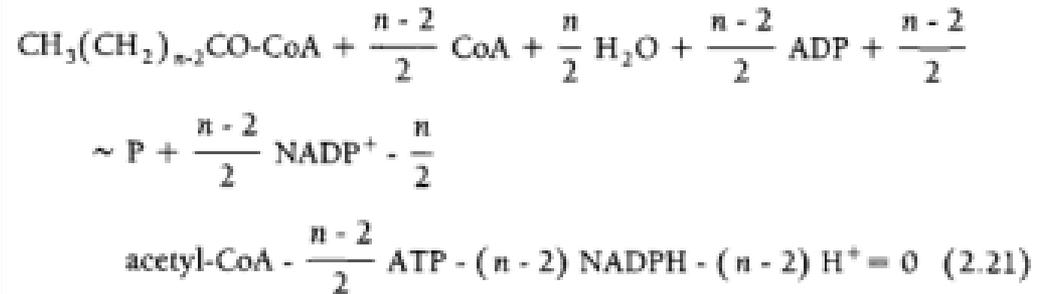
Malonil resulta da carboxilação de acetil



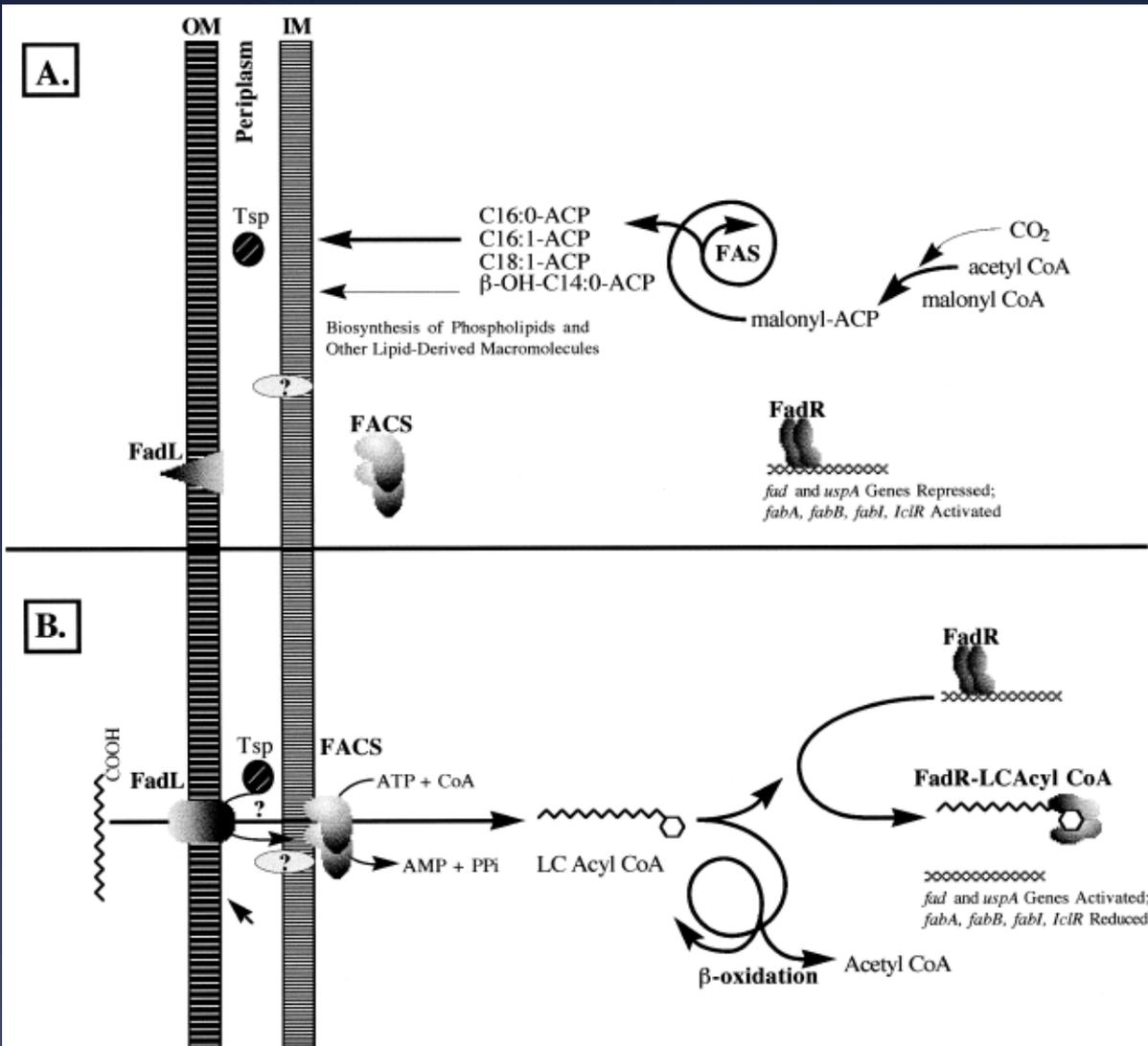


Em *E. coli* as reações ocorrem via Fatty acid synthase II – FAS II

# Biossíntese de ácidos graxos



# Biossíntese de ácidos graxos



A model of the interrelationship between fatty acid transport and fatty acid-dependent transcriptional regulation.

(A). In the absence of exogenous fatty acids, envelope lipid synthesis is dependent on the de novo pathway (FAS). FadR is active in DNA binding and the *fad* genes including *fadD* and *fadL* are synthesized at low levels while several *fab* genes and *iclR* are synthesized at high levels. Fatty acyl-CoA synthetase (FACS) is hypothesized to be cytoplasmic.

(B). When long chain fatty acids are supplied exogenously, they enter the cell via FadL and are activated to long-chain fatty acyl-CoA (LC Acyl-CoA) by FACS in an ATP-dependent reaction. The LC Acyl-CoA binds to FadR and changes the conformation of the protein so that it no longer binds DNA. This results in derepression of the *fad* genes and *uspA* and reduced expression of select *fab* genes and *iclR*. The increased free fatty acid (presumably dissolved in the inner membrane) and ATP facilitate the membrane association of the FACS. The role of Tsp is to potentiate fatty acid transport but the

mechanism is undefined. Fig 8 Di Russo et al, 1999

# Biossíntese de ácidos graxos

\* Outros precursores importantes para a síntese de lipídios:

→ EMP

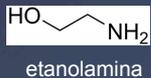
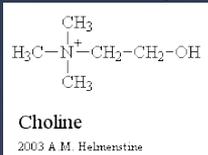
\* Glicerol 3P (esqueleto de fosfolipídios e triacil gliceróis)

\* Molécula alcoólica dos fosfolipídios

\* colina em fungos

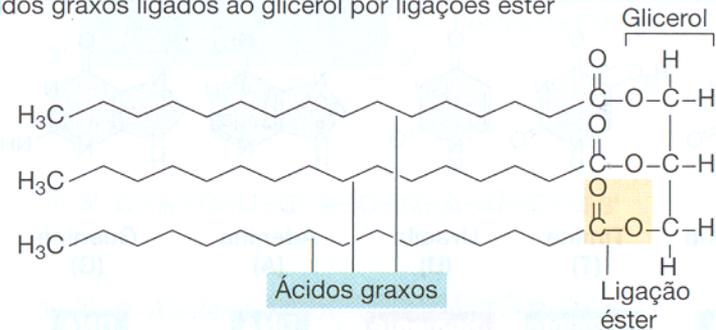
\* Fosfatidiletanolaminas, fosfatidilgliceróis e cardiolipinas em bactérias

\* Esteróis (fungos e leveduras)



## Lipídeos simples (triglicerídeos):

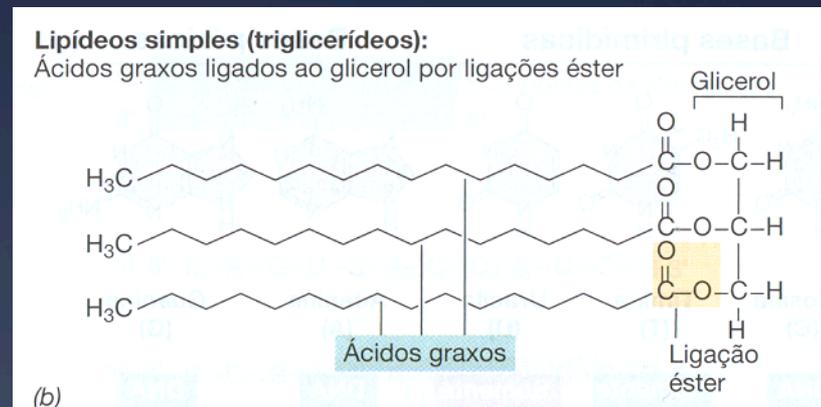
Ácidos graxos ligados ao glicerol por ligações éster



(b)

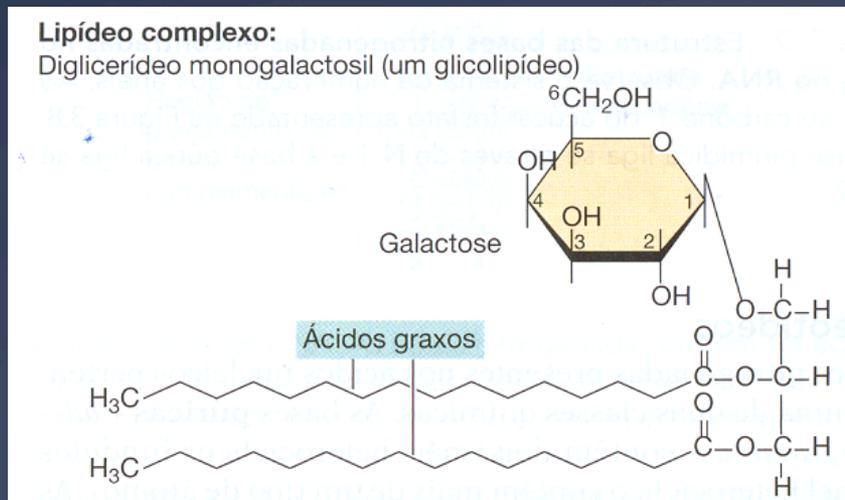
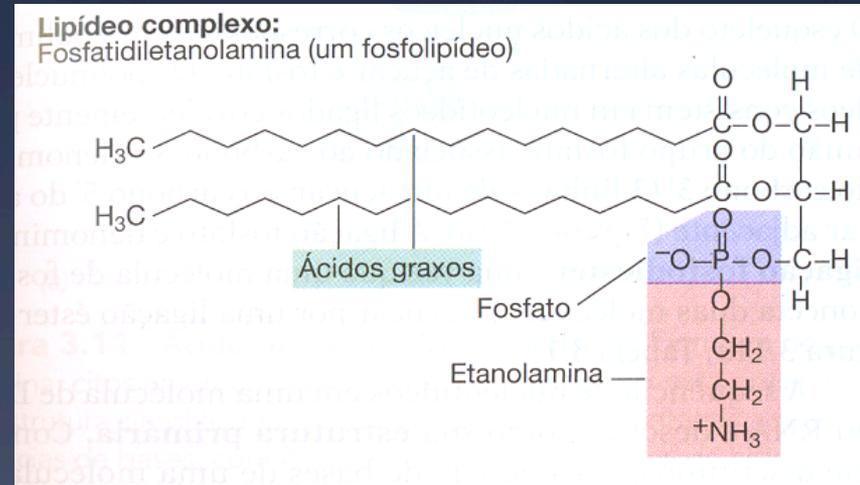
# Montagem final de lipídios

- \* Três carbonos do glicerol são esterificados com ácidos graxos

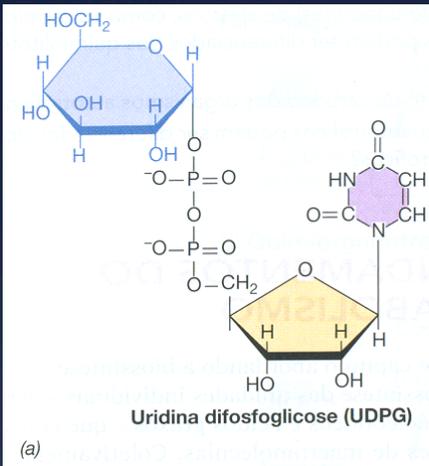


# Montagem final de lipídios

- \* Em lipídeos complexos o C do glicerol se liga a
  - \* fosfato,
  - \* etanolamina,
  - \* um açúcar
  - \* ou outra substância polar



# Biossíntese de carboidratos



Os polissacarídeos são sintetizados a partir de formas ativadas de glicose como UDPG

*N*-acetilglicosamina, ácido *N*-acetil murâmico ( no peptídioglicano)

LPS (membrana externa de Gram negativos)

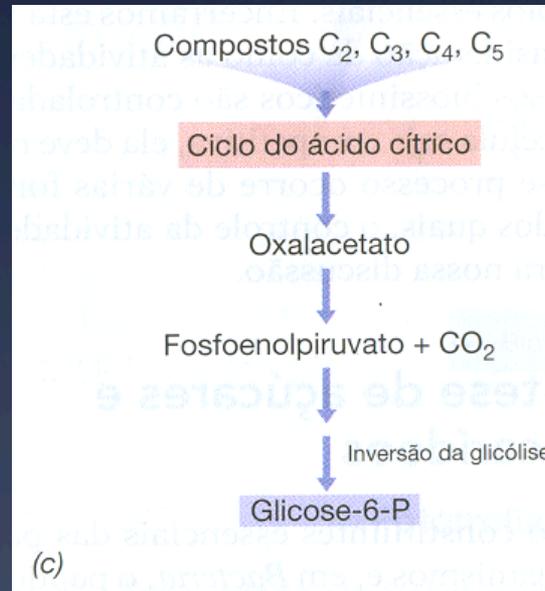
# Biossíntese de carboidratos



(b)

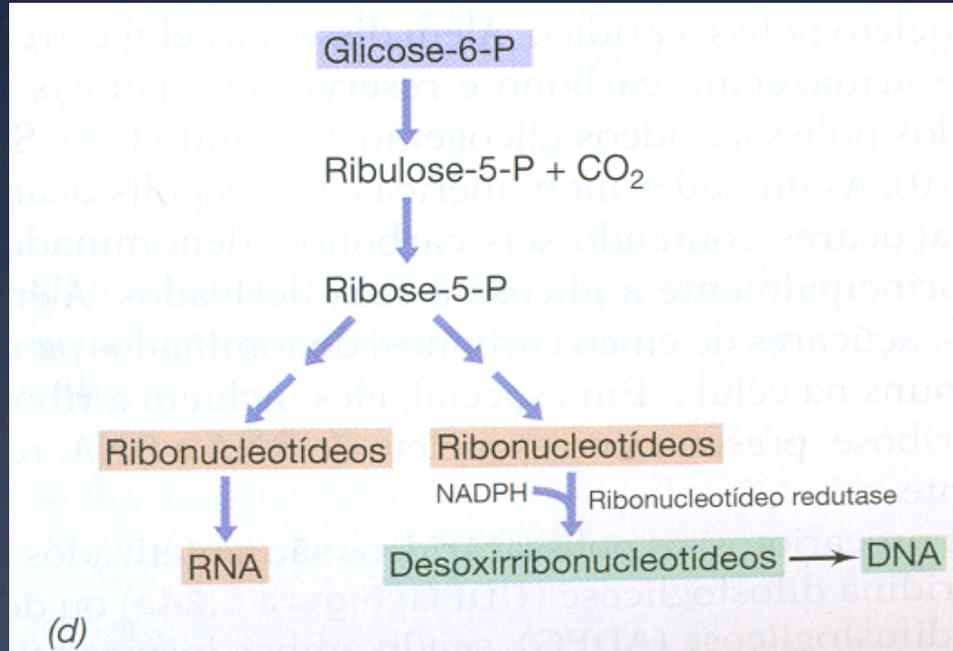
O Glicogênio é sintetizado a partir de ADPG (adenosina-difosfoglicose) pela adição sequencial de glicose

# Biossíntese de carboidratos



Gliconeogênese – quando há necessidade de glicose, sua síntese ocorre a partir de outros compostos

# Biossíntese de carboidratos

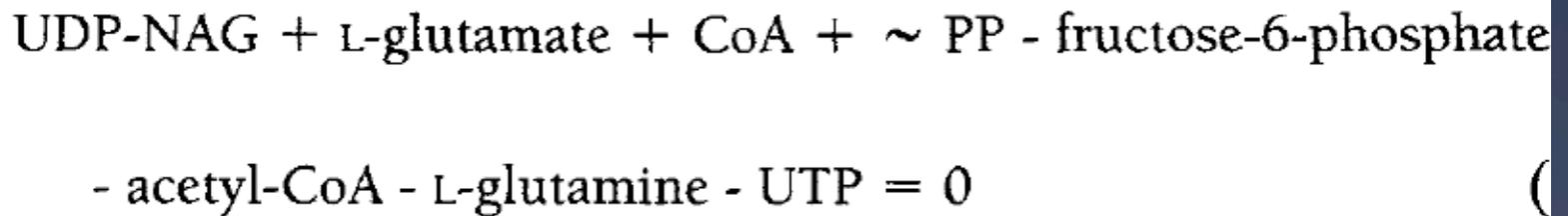


As pentoses são oriundas das hexoses, que são descarboxiladas.

# Biossíntese de carboidratos

Biossíntese do peptidoglicano requer 5 monômeros:

UDP-*N*-acetilglicosamina (UDP-NAG),  
ácido UDP-*N*-acetilmurâmico (UDP-NAM),  
alanina D e L,  
diaminopimelato e  
glutamato.



**TABLE 2.7 Metabolic Costs for Biosynthesis of Lipids and Carbohydrate Building Blocks**

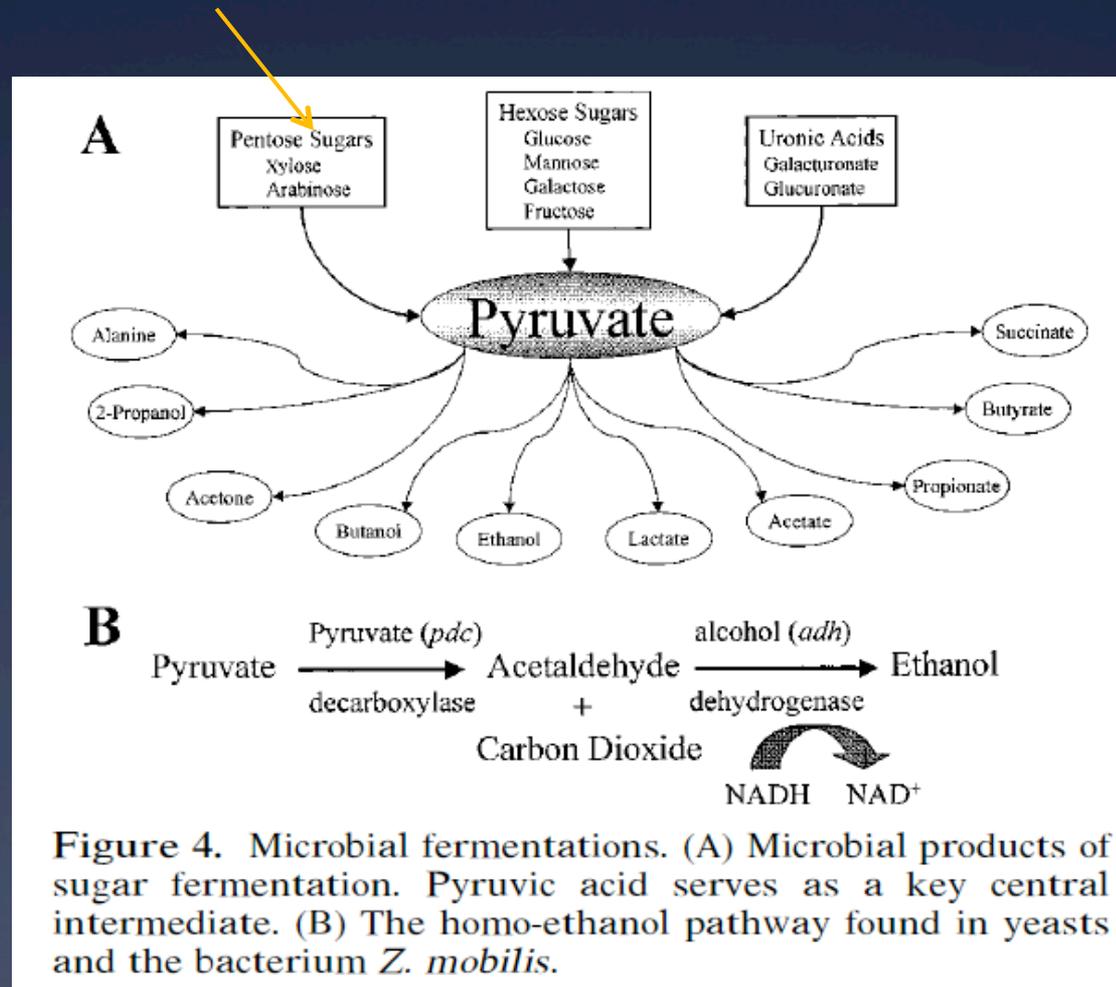
Building block	Precursor metabolite <sup>a</sup>	ATP	NADH	NADPH	1-C	NH <sub>3</sub>
Glycerol-3-phosphate	1 glyP	0	-1	0	0	0
Palmitoyl-CoA	8 acCoA	-7	0	-14	0	0
Palmitoleoyl-CoA <sup>b</sup>	8 acCoA	-7	0	-14	0	0
Stearoyl-CoA	9 acCoA	-8	0	-16	0	0
Oleoyl-CoA	9 acCoA	-8	1	-16	0	0
Linoleoyl-CoA	9 acCoA	-8	2	-16	0	0
Linolenoyl-CoA	9 acCoA	-8	3	-16	0	0
Ethanolamine <sup>c</sup>	1 pga	0	1	-1	0	-1
Choline	1 pga	0	1	-1	-3	-1
Inositol	1 gluP	0	1	0	0	0
Ergosterol	18 acCoA	-18	0	-13	0	0
UDP-Glucose	1 gluP	-1	0	0	0	0
UDP-Galactose	1 gluP	-1	0	0	0	0
UDP-NAG	1 fruP, 1 acCoA	-2	0	0	0	-1
UDP-NAM	1 fruP, 1 pep, 1 acCoA	-2	0	-1	0	-1
Diaminopimelate	1 oaa, 1 pyr	-2	0	-3	0	-2

<sup>a</sup> See Table 2.4 for nomenclature.

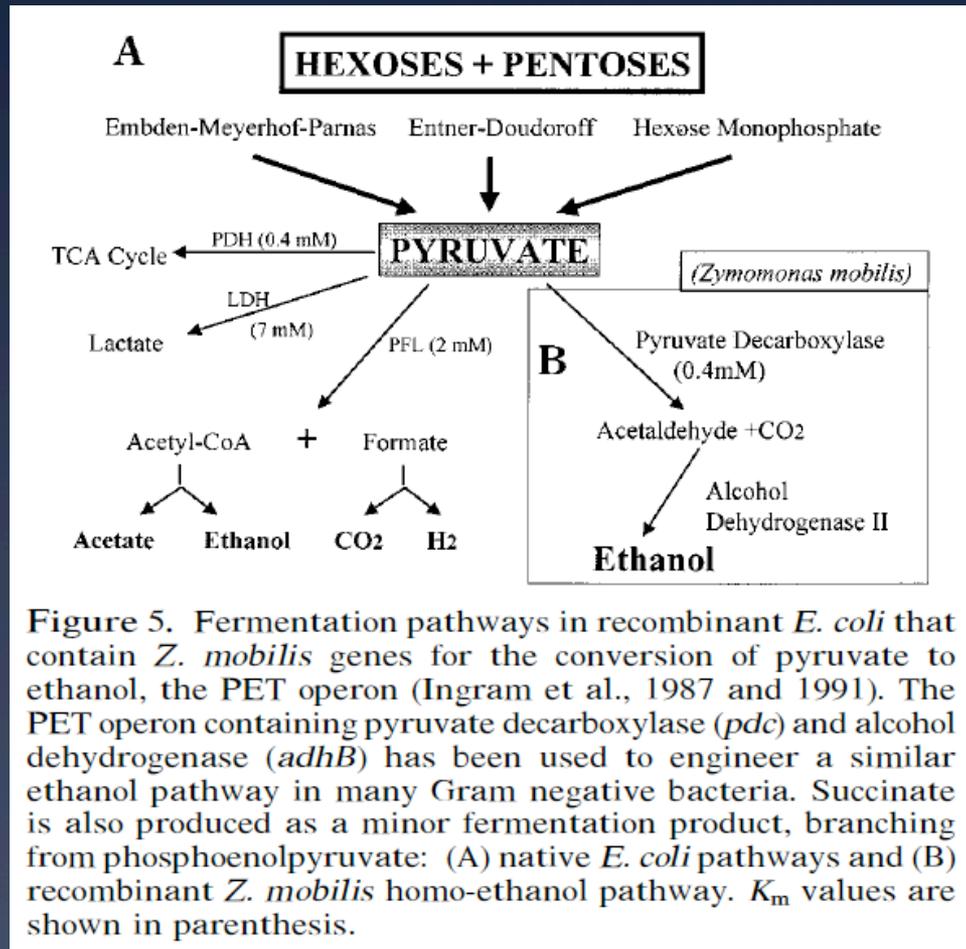
<sup>b</sup> The costs are for the biosynthesis of palmitoleoyl-CoA via the anaerobic pathway.

<sup>c</sup> Because the pathway from squalene to ergosterol is not known in detail, the metabolic cost for the biosynthesis of ergosterol is taken to be the same as that for squalene.

# Produtos biotecnológicos



# Produtos biotecnológicos

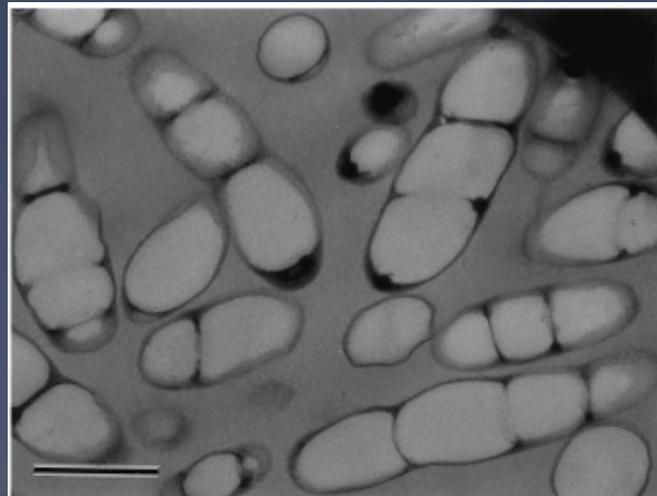
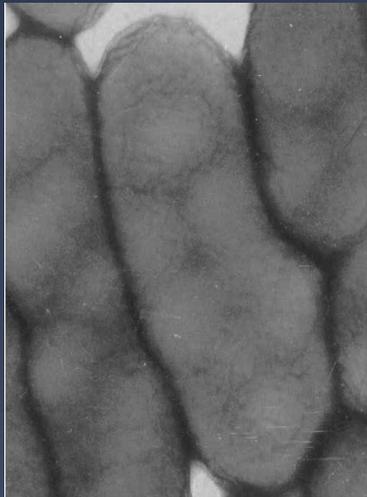
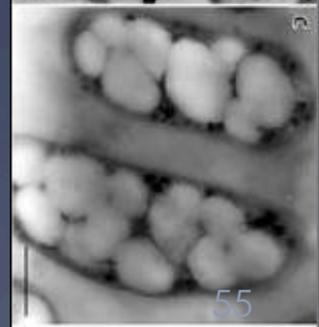
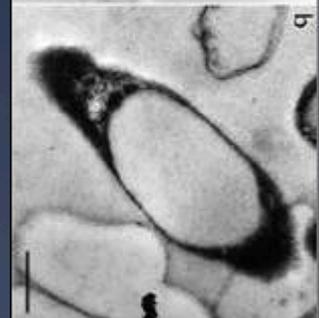
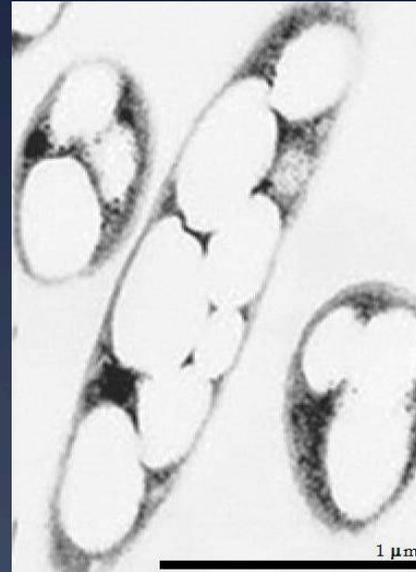


**Figure 5.** Fermentation pathways in recombinant *E. coli* that contain *Z. mobilis* genes for the conversion of pyruvate to ethanol, the PET operon (Ingram et al., 1987 and 1991). The PET operon containing pyruvate decarboxylase (*pdc*) and alcohol dehydrogenase (*adhB*) has been used to engineer a similar ethanol pathway in many Gram negative bacteria. Succinate is also produced as a minor fermentation product, branching from phosphoenolpyruvate: (A) native *E. coli* pathways and (B) recombinant *Z. mobilis* homo-ethanol pathway.  $K_m$  values are shown in parenthesis.

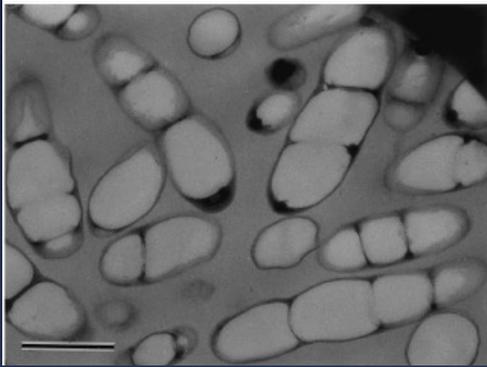
# Produtos biotecnológicos

“Polihidroxicanoatos”  
PHA

# PHA são acumulados por bactérias



# PHA são acumulados por bactérias



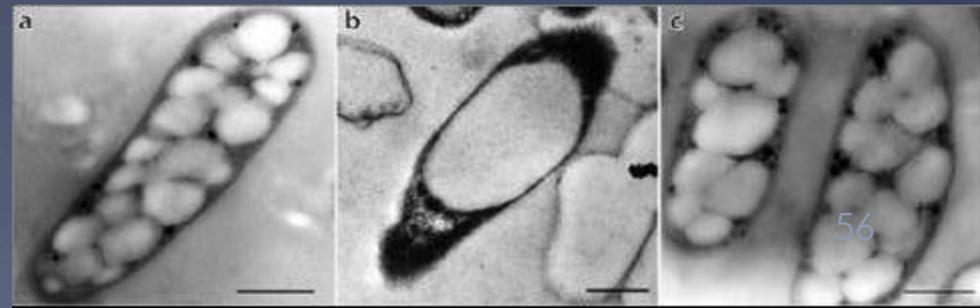
Condições para acúmulo mais expressivo

Meio de cultivo desbalanceado:

- excesso de fonte de C e
- carência de um nutriente essencial (N, P, O...)

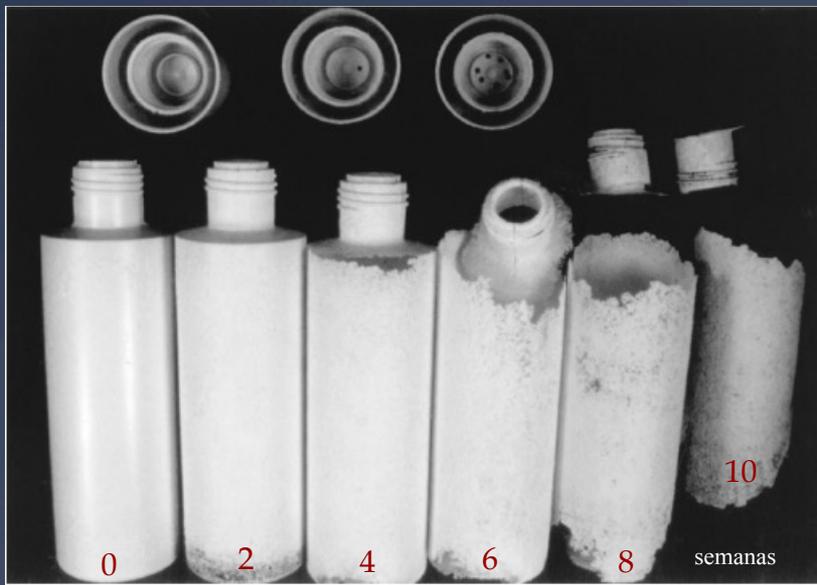
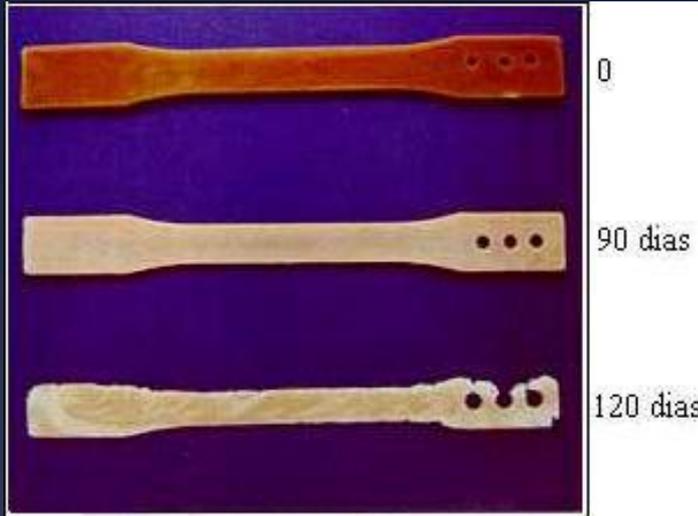
Função dos grânulos de PHA para a célula:

- Fonte de Carbono,
- Fonte de Energia e
- equivalentes redutores



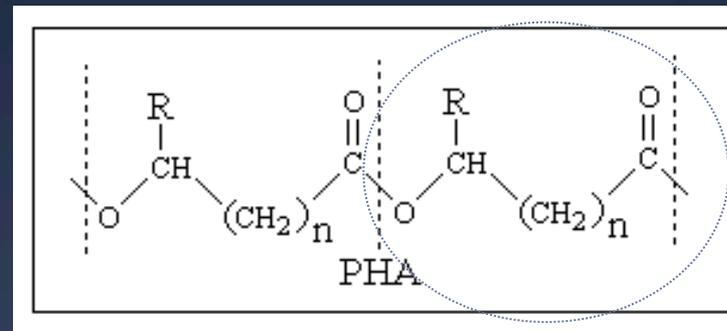
# PHA são materiais termoplásticos

Biodegradáveis e biocompatíveis



Madison & Huisman, 1999

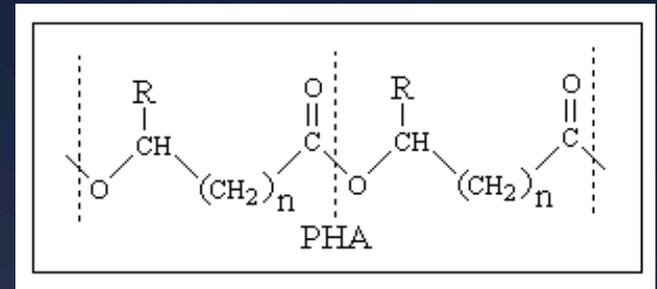
# Estrutura química dos PHA



100 - 30000

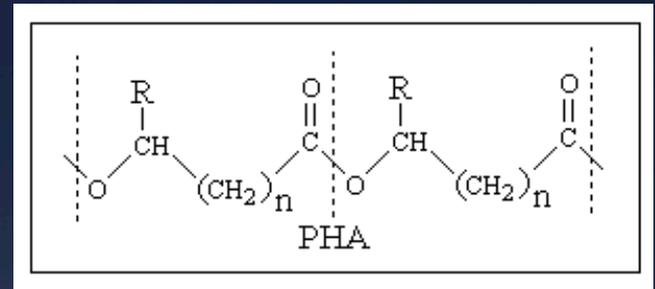
n = 1	R =	hydrogen	poly (-3-hydroxypropionate)
		methyl	poly (-3-hydroxybutyrate)
		ethyl	poly (-3-hydroxyvalerate)
		propyl	poly (-3-hydroxyhexanoate)
		pentyl	poly (-3-hydroxyoctanoate)
		nonyl	poly (-3-hydroxydodecanoate)
n = 2	R =	hydrogen	poly (-4-hydroxybutyrate)
n = 3	R =	hydrogen	poly (-5-hydroxyvalerate)

# Aplicações x propriedades x composição dos PHA



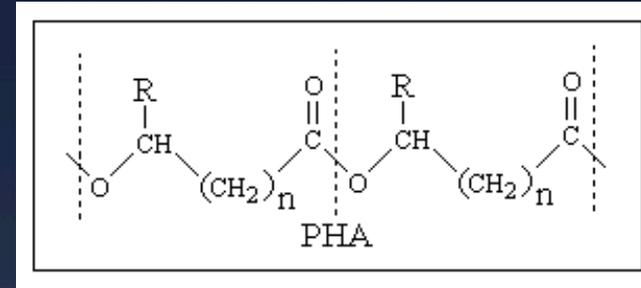
*Bucci, 2003*

# Aplicações x propriedades x composição dos PHA



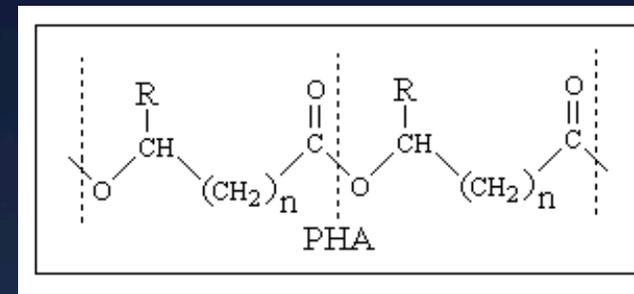
# Aplicações x propriedades x composição dos PHA

([www.tepha.com](http://www.tepha.com))



Bucci, 2003

## Propriedades dos PHA e polipropileno



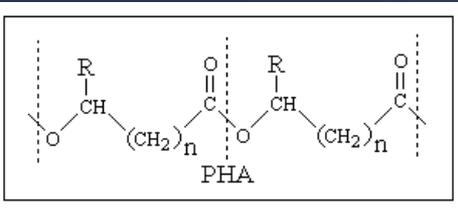
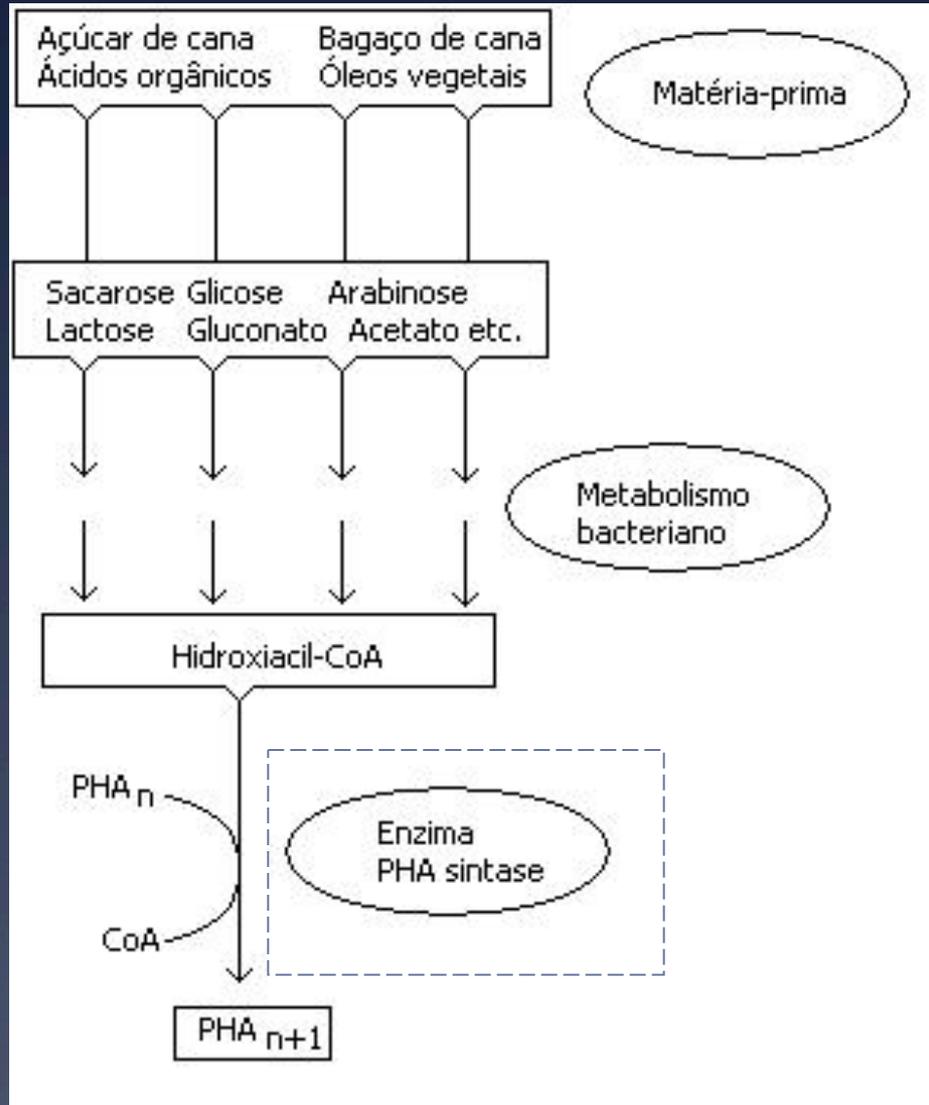
### Parâmetro

	<b>P(3HB)</b>	<b>P(3HB-3HV)</b>	<b>P(3HB-4HB)</b>	<b>P(3HO-3HH)</b>	<b>PP</b>
$T_m$ (°C)	177	145	150	61	176
$T_g$ (°C)	2	-1	-7	-36	-10
Cristalinidade (%)	70	56	45	30	60
Extensão até ruptura (%)	5	50	444	300	400

- P(3HB) poly(3-hydroxybutyrate),
- P(3HB-3HV) poly(3-hydroxybutyrate-co-3-hydroxyvalerate) containing 20% 3HV,
- P(3HB-4HB) poly(3-hydroxybutyrate-co-4-hydroxybutyrate) containing 16% 4HB,
- P(3HO-3HH) poly(3-hydroxyoctanoate-co-3-hydroxyhexanoate) containing 11% 3HH,
- PP polypropylene.
- T<sub>m</sub> melting temperature.
- T<sub>g</sub> glass transition temperature.

*Madison e Huisman 1999*

# Como as bactérias sintetizam PHA?



PHASCL

C<sub>4</sub>-C<sub>5</sub>

PHAMCL

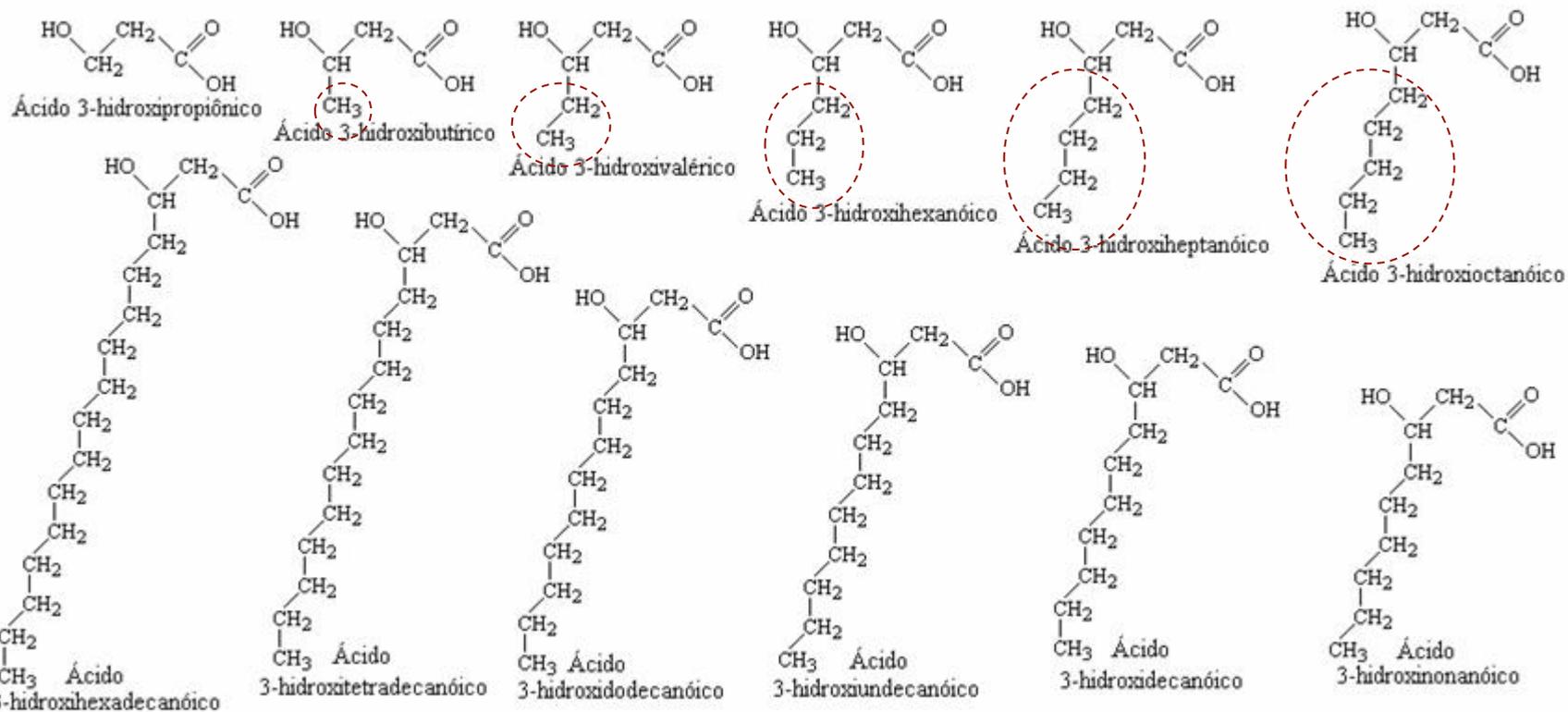
C<sub>6</sub>-C<sub>16</sub>

MCL - medium chain length

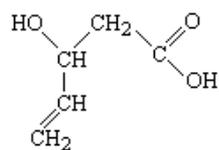
SCL - short chain length

Biodiversidade como fator chave

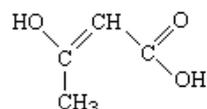
(I) 3-hidroxiácidos



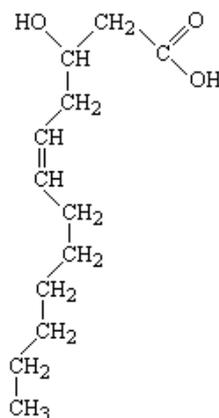
(I) 3-hidroxiácidos



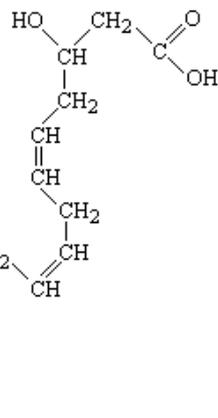
Ácido 3-hidroxi-4-pentenóico



Ácido 3-hidroxi-2-butenóico

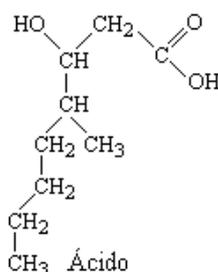


Ácido 3-hidroxi-5-cis-dodecenóico

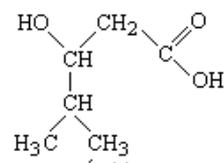


Ácido 3-hidroxi-5,8-cis-cis-tetradecenóico

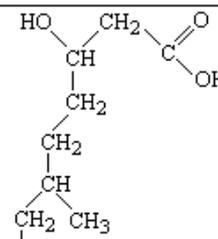
(II) 3-hidroxiácidos com grupos metila



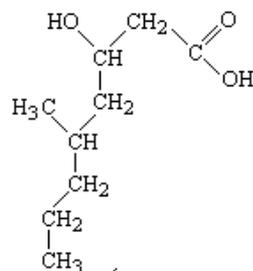
Ácido 3-hidroxi-4-metiloctanóico



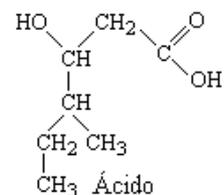
Ácido 3-hidroxi-4-metilvalérico



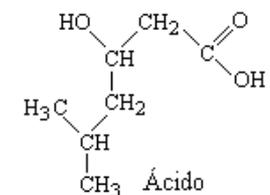
Ácido 3-hidroxi-6-metiloctanóico



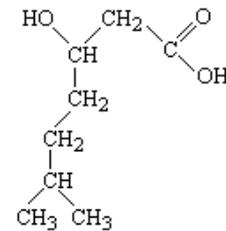
Ácido 3-hidroxi-5-metiloctanóico



Ácido 3-hidroxi-4-metilhexanóico



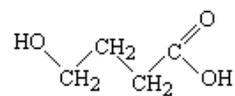
Ácido 3-hidroxi-5-metilhexanóico



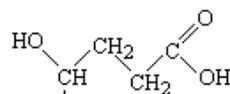
Ácido 3-hidroxi-6-metilheptanóico



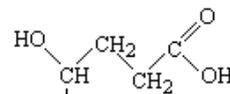
(iv) 4, 5 e 6-hidroxicarboxílicos



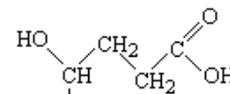
Ácido 4-hidroxi-butírico



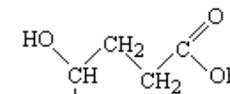
Ácido 4-hidroxi-valérico



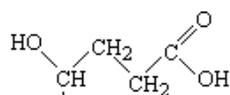
Ácido 4-hidroxi-hexanoico



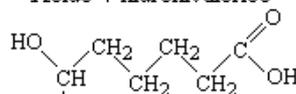
Ácido 4-hidroxi-heptanoico



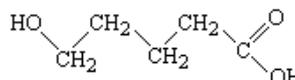
Ácido 4-hidroxi-octanoico



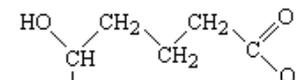
Ácido 4-hidroxi-decanoico



Ácido 6-hidroxi-dodecanoico

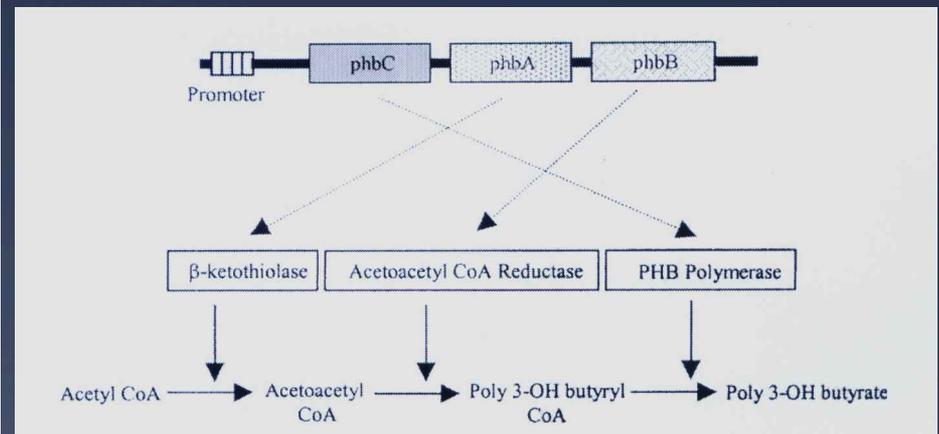
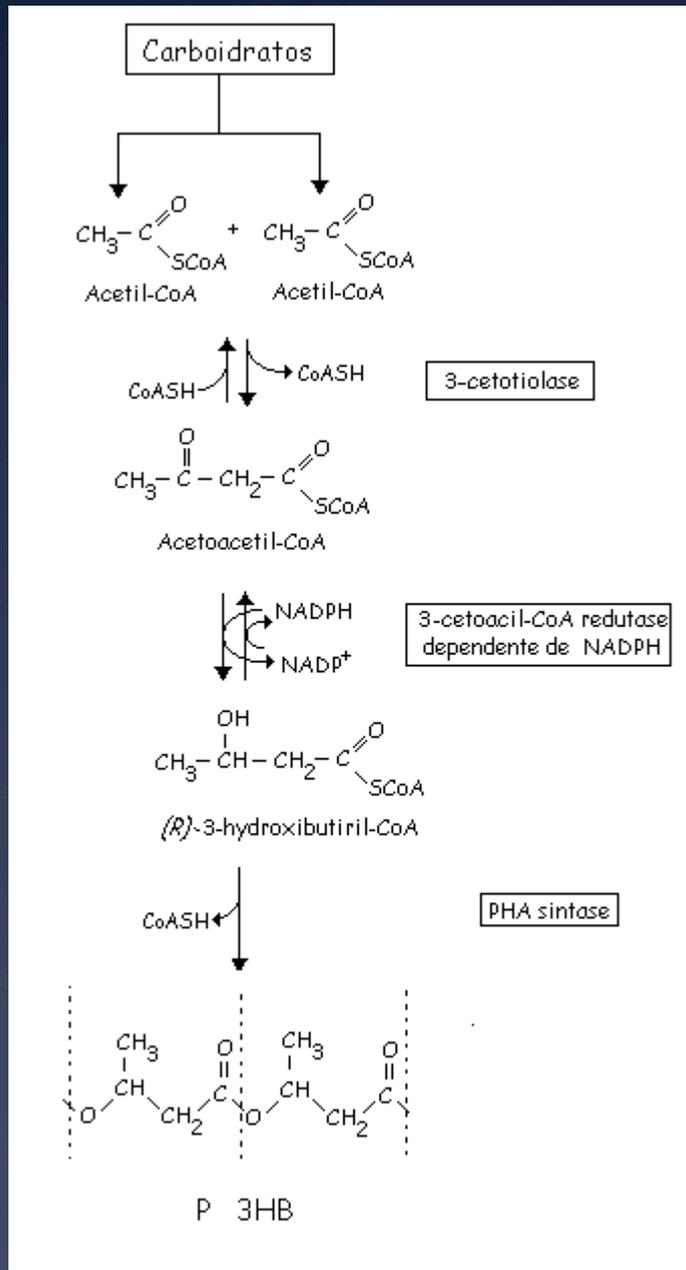


Ácido 5-hidroxi-valérico



Ácido 5-hidroxi-hexanoico

# Via de síntese de PHA

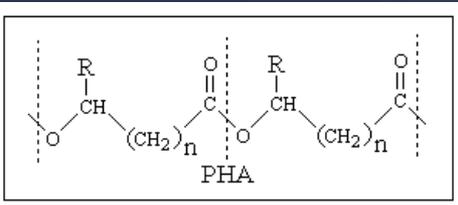
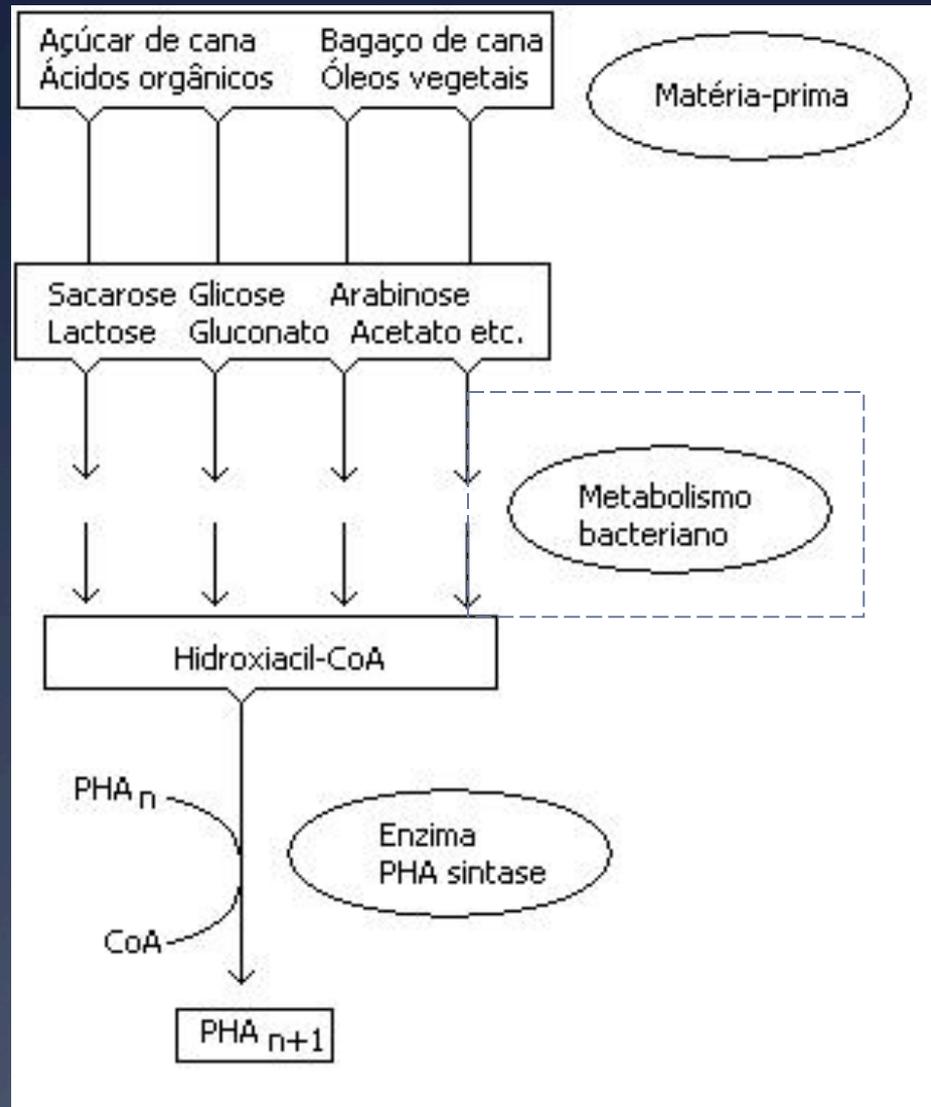


# Especificidade da enzima PHA sintase

Class	Subunits	Species	Substrate
I	 ~60–73 kDa	<i>Cupriavidus necator</i>	3HA <sub>SCL</sub> -CoA (~C3–C5) 4HA <sub>SCL</sub> -CoA, 5HA <sub>SCL</sub> -CoA, 3MA <sub>SCL</sub> -CoA
II	 ~60–65 kDa	<i>Pseudomonas aeruginosa</i>	3HA <sub>MCL</sub> -CoA (~≥C5)
III	 ~40 kDa ~40 kDa	<i>Allochromatium vinosum</i>	3HA <sub>MCL</sub> -CoA (3HA <sub>MCL</sub> -CoA [~C6–C8], 4HA-CoA, 5HA-CoA)
IV	 ~40 kDa ~22 kDa	<i>Bacillus megaterium</i>	3HA <sub>SCL</sub> -CoA

*Rehm, 2003*

# Fatores interferentes na composição do PHA



PHAscl

C<sub>4</sub>-C<sub>5</sub>

PHAmcl

C<sub>6</sub>-C<sub>16</sub>

Biodiversidade como fator chave

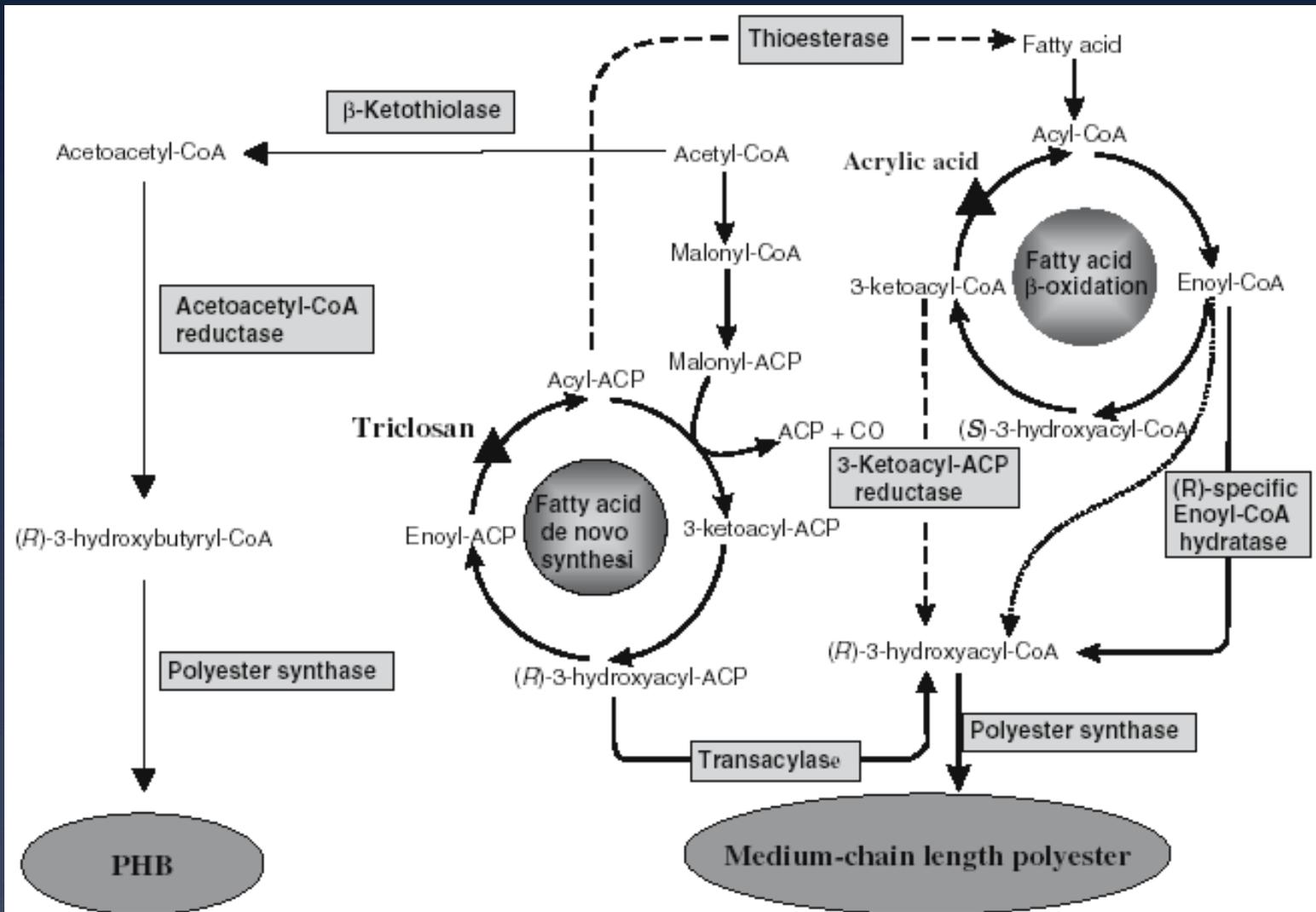
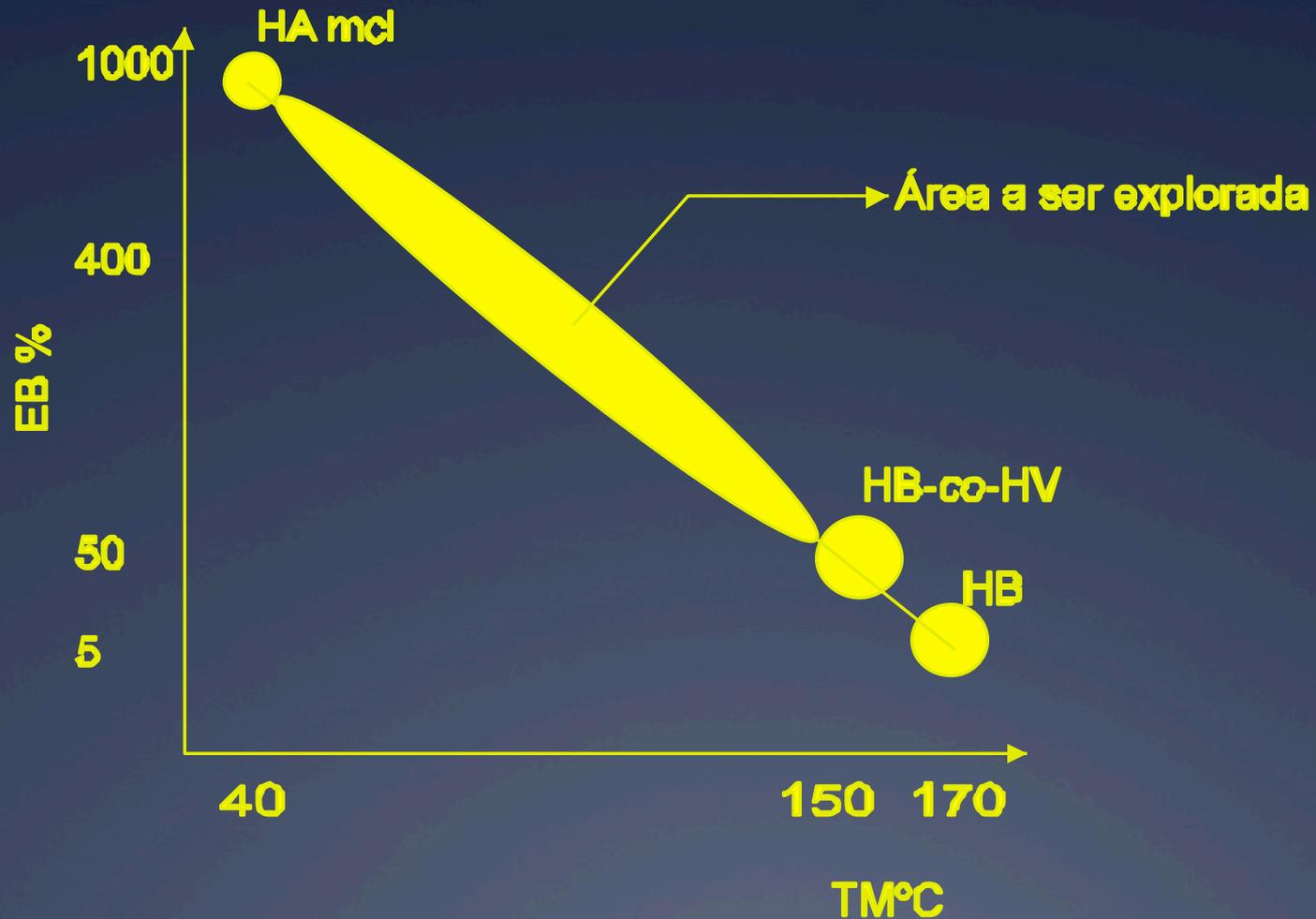


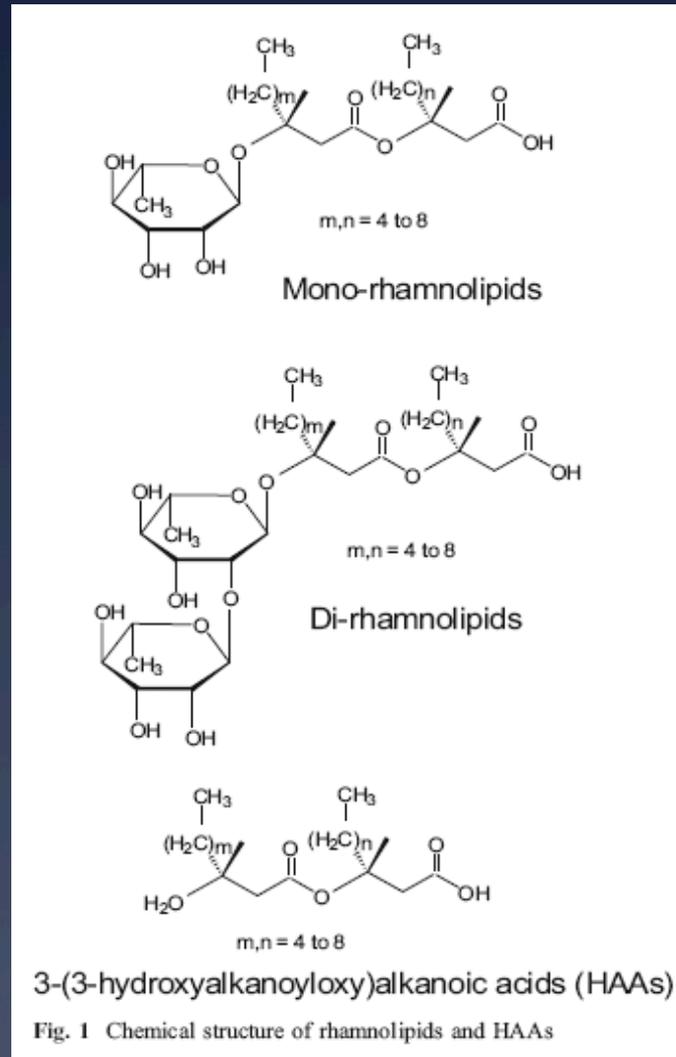
Fig. 1. Metabolic routes towards biopolyester synthesis. Dashed lines represent engineered biosynthesis routes. Triangles depict targets for inhibitors enabling biopolyester synthesis. Enzymes indicated on shaded boxes on solid lines are biopolyester biosynthesis enzymes.

# Perspectivas para a produção de PHA no Brasil

## Propriedades

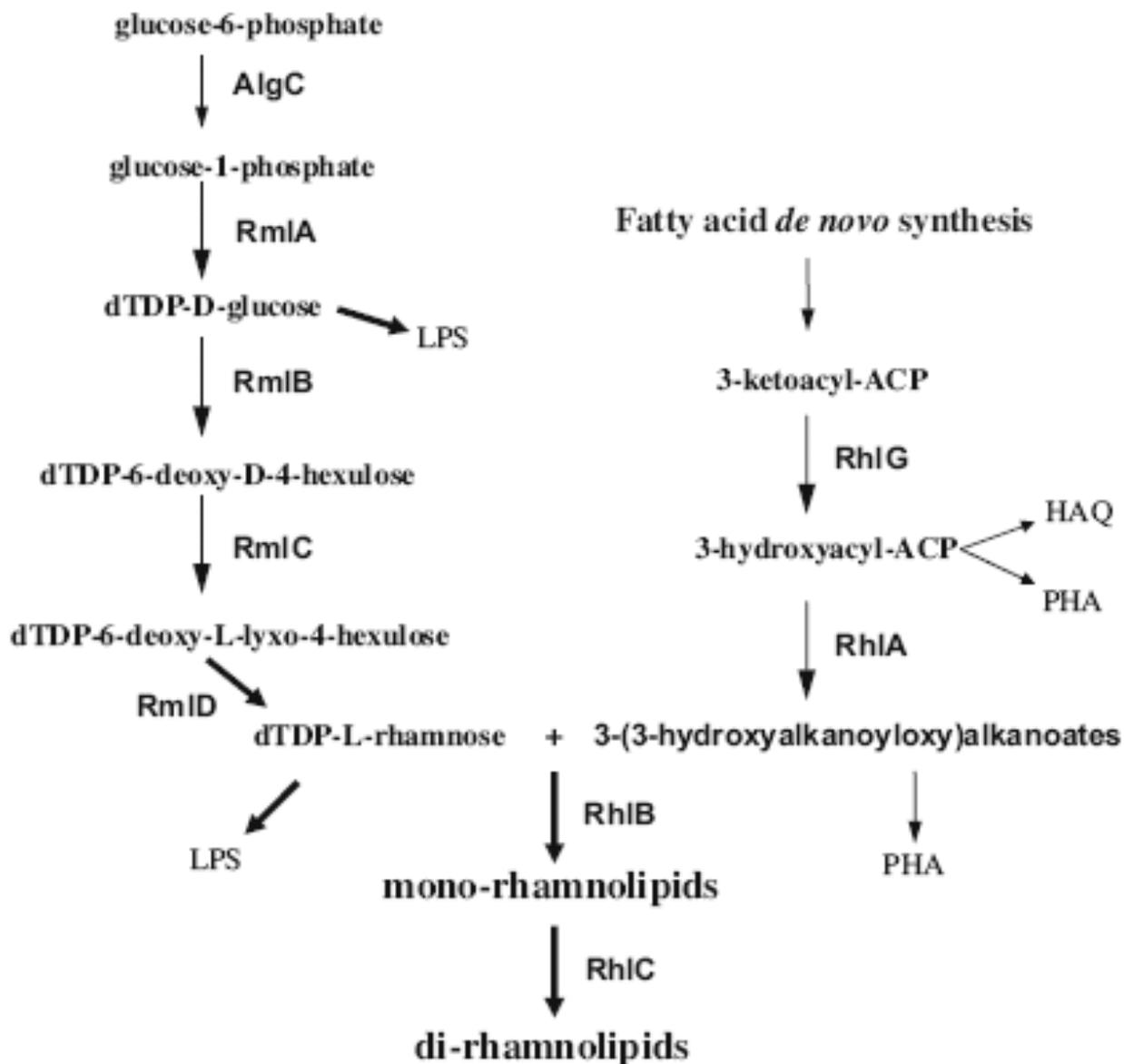


# Produtos biotecnológicos



- Surfactantes:
- 1 ou 2 moléculas de rhamnose ligadas a 3HAAs
- Aplicação
- MEOR – microbial enhanced oil recovery
- Eliminação de fitopatógenos
- tratamento de fermentos
- Cosméticos ( hidratantes, shampoos, etc
- Fonte de rhamnose, etc

## Rhamnolipids Biosynthetic Pathway



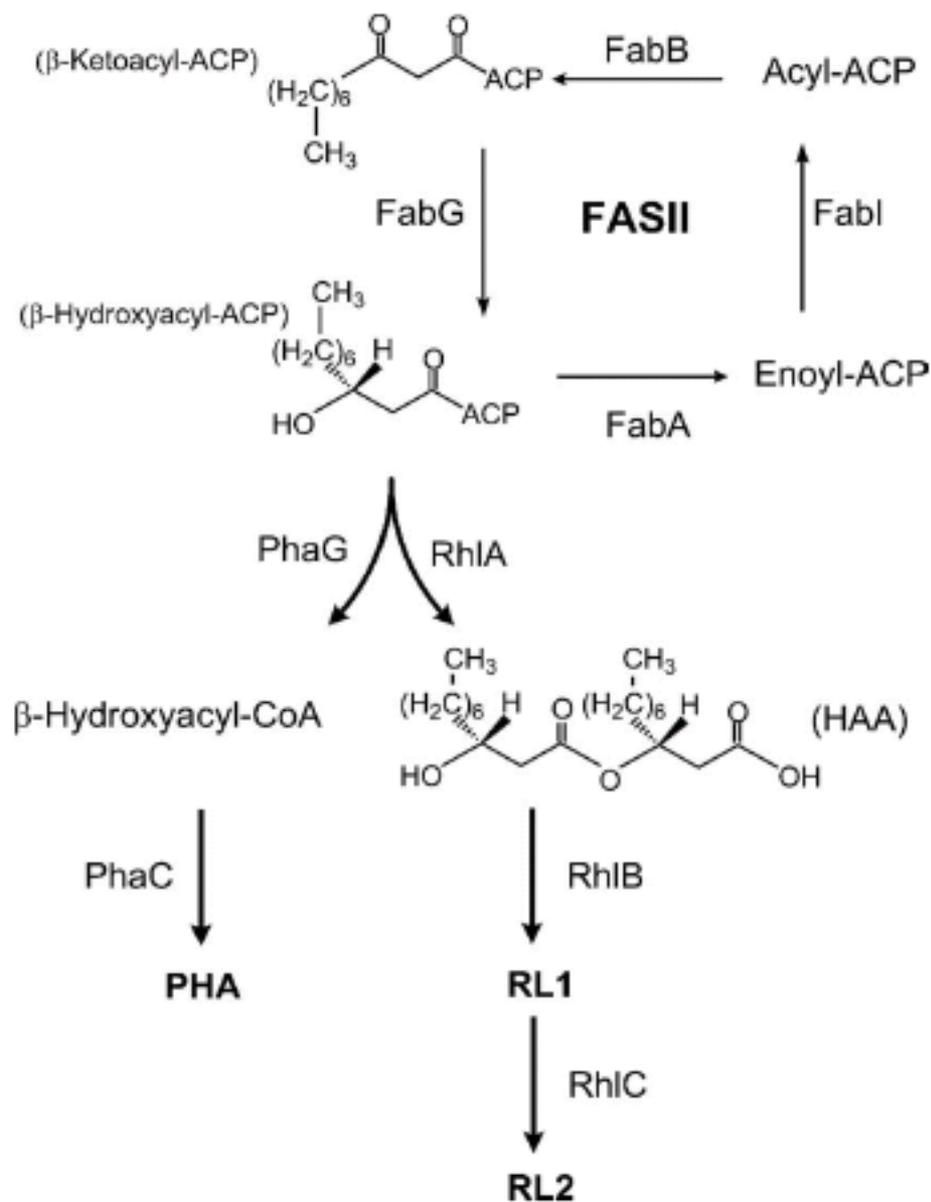


FIG. 7. Proposed rhamnolipid biosynthetic pathway. RhIA is responsible for diverting the  $\beta$ -hydroxydecanoyl-ACP intermediate from the FASII cycle and directly competes with FabA and FabI for this intermediate. RhIA is the only protein required to convert two molecules of  $\beta$ -hydroxyacyl-ACP to HAA. Thus, the amount of HAA

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