# Introduction to Metabolism

Bulk elements
Trace elements
1 H
2 He
3 Li
4 Be
5 B
6 C
7 N
8 O
9 F
10 Ne
11 Na
12 Mg
13 Al
14 Si
15 P
16 S
17 Cl
18 Ar
19 K
20 Ca
21 Sc
22 Ti
23 V
24 Cr
25 Mn
26 Fe
27 Co
28 Ni
29 Cu
30 Zn
31 Ga
32 Ge
33 As
34 Se
35 Br
36 Kr
37 Rb
38 Sr
39 Y
40 Zr
41 Nb
42 Mo
43 Tc
44 Ru
45 Rh
46 Pd
47 Ag
48 Cd
49 In
50 Sn
51 Sb
52 Te
53 I
54 Xe
55 Cs
56 Ba
72 Hf
73 Ta
74 W
75 Re
76 Os
77 Ir
78 Pt
79 Au
80 Hg
81 Tl
82 Pb
83 Bi
84 Po
85 At
86 Rn
87 Fr
88 Ra
Lanthanides
Actinides

## TABLE 2–5 Four Types of Noncovalent ("Weak") Interactions among Biomolecules in Aqueous Solvent

| | |
|---|---|
| Hydrogen bonds | |
| Between neutral groups | |
| Between peptide bonds | |
| Ionic interactions | |
| Attraction | |
| Repulsion | |
| Hydrophobic interactions | |
| van der Waals interactions | Any two atoms in close proximity |

## Strengths of Bonds Found in Biochemistry

| Bond Type | Strength (kcal/mol) | Strength (kJ/mol) |
|---|---|---|
| Covalent (C—H) | 105 | 413 |
| Covalent (O—H) | 110 | 460 |
| Ionic interactions | 1–20 | 4–80 |
| Ion–dipole | 5 | 20 |
| Hydrogen bonds | 5 | 20 |
| Van der Waals interactions | 1 | 4 |

Metal ion coordination
Hydrophobic interactions
Electrostatic attraction
N
$M^{2+}$
$O^-$
C
O
H
O
$NH_3^+$
$COO^-$
C
Leu
Val
Ile
$CH_2$
S
S
$CH_2$
Side chain hydrogen bonding
Helical structure
Sheet structure
Disulfide bond

R1
H R2
H3N—CH—C—OH + H—N—CH—COO−
O
H2O
H2O
R1
H R2
H3N—CH—C—N—CH—COO−
O

Nonpolar, aliphatic R groups
Glycine
Alanine
Proline
Valine
Leucine
Isoleucine
Methionine

Aromatic R groups
Phenylalanine
Tyrosine
Tryptophan

Positively charged R groups
Lysine
Arginine
Histidine

Polar, uncharged R groups
Serine
Threonine
Cysteine
Asparagine
Glutamine

Negatively charged R groups
Aspartate
Glutamate

# Insulin structure

O
R
1.24 Å
1.53 Å
1.46 Å
C
Cα
N
1.32 Å
Cα
H
Amino terminus
N–Cα
Cα–C
C–N

Antiparallel β sheets
Parallel β sheets
Collagen triple helix
Right-twisted β sheets
Left-handed α helix
Right-handed α helix
+180
120
60
0
−60
−120
−180
ψ (degrees)
−180
0
+180
ϕ (degrees)
(a)

Figure 2

LEVELS OF PROTEIN STRUCTURE
Primary Structure
Secondary Structure
β-Sheet
α-Helix
Tertiary Structure
Quaternary Structure
Particle Sciences

"distal His"
"proximal His"
Fe

Heme group
Myoglobin
β subunit of hemoglobin

His HC3
α2
β1
β2
α1
His HC3
T state
α2
β1
His HC3
β2
α1
R state

**(c) Enzyme complementary to transition state**

| | | | | |
|---|---|---|---|---|
| **Nucleotide:** | Deoxyadenylate (deoxyadenosine 5′-monophosphate) | Deoxyguanylate (deoxyguanosine 5′-monophosphate) | Deoxythymidylate (deoxythymidine 5′-monophosphate) | Deoxycytidylate (deoxycytidine 5′-monophosphate) |
| **Symbols:** | A, dA, dAMP | G, dG, dGMP | T, dT, dTMP | C, dC, dCMP |
| **Nucleoside:** | Deoxyadenosine | Deoxyguanosine | Deoxythymidine | Deoxycytidine |

**(a) Deoxyribonucleotides**

| | | | | |
|---|---|---|---|---|
| **Nucleotide:** | Adenylate (adenosine 5′-monophosphate) | Guanylate (guanosine 5′-monophosphate) | Uridylate (uridine 5′-monophosphate) | Cytidylate (cytidine 5′-monophosphate) |
| **Symbols:** | A, AMP | G, GMP | U, UMP | C, CMP |
| **Nucleoside:** | Adenosine | Guanosine | Uridine | Cytidine |

**(b) Ribonucleotides**

5′
3′
C
G
A
T
Adenine
Guanine
3′
5′
2.8 Å
3.0 Å
11.1 Å
Thymine
2.9 Å
3.0 Å
2.9 Å
10.8 Å
Cytosine

Side view

~ 2° twist in center of base pair

T-A

A-T

Major groove ~2.2 nm

C-G

C-G

T-A

Pitch, 3.46 nm

"Stacked" base pairs are in van der Waals contact

G-C

A base pair can be recognized by groups facing the grooves. This is a GC pair

G-C

Minor groove ~1.2 nm

T-A

T-A

C-G

G-C

0 1.0 nm

**Coenzyme A**

**Nicotinamide adenine dinucleotide ($NAD^+$)**

**Flavin adenine dinucleotide (FAD)**

DNA
replication
DNA
Transcription
Reverse
transcription
RNA
RNA
replication
Translation
Protein

Two
chromatids
(10 coils each)
One coil
(30 rosettes)
One rosette
(6 loops)
Nuclear
scaffold
One loop
(~75,000 bp)
30 nm Fiber
"Beads-on-
a-string"
form of
chromatin
DNA

3′
5′
Leading strand
Direction of movement of replication fork
3′
5′
3′
5′
Okazaki fragments
5′
3′
3′
5′
Lagging strand

Dimeric replicative DNA polymerase
β subunit "sliding clamp"
SSB
Leading strand template
DNA gyrase
Okazaki fragment
Primer
Primer
Primer
Helicase/primase
Lagging strand template

Core (αεθ)
β clamp
β clamp (open)
τ
δ
γ
δ′
τ
DnaB helicase

(a)

Binding
σ
5′
3′
3′
5′
−35
−10
+1
Closed complex

Open complex

Initiation

Negative supercoils
Positive supercoils
5′
RNA
3′
Direction of transcription
(c)

transcription initiation
promoter clearance
σ
Elongation form

transcription
and 5′ capping
DNA
5′
Exon
Intron
5′ Cap
Pol II
completion of
primary transcript
Primary
transcript
Noncoding
end sequence
5′
3′
cleavage,
polyadenylation,
and splicing
Mature
mRNA
5′
–AAA(A)n 3′

The translation process incorporates 20 different amino acids in the precise sequence dictated by the three-base codons built from and alphabet of four bases. The process in the ribosome builds the polypeptide chains tha will become proteins.

Large subunit
Initiator tRNA
Small subunit
2 Large and small ribosomal subunits join to form a functional ribosome.
Amino acid
tRNA
Anticodon
mRNA
Codons
3 Anticodon of incoming tRNA pairs with next mRNA codon beside initiator tRNA.
Amino acid
Initiator tRNA
Anticodon
mRNA
mRNA binding site
Start codon
Small subunit
1 Initiator tRNA attaches to a start codon.
4 Amino acid on initiator tRNA forms a peptide bond with the amino acid beside it.
New peptide bond
mRNA movement
5 Initiator tRNA leaves the ribosome; ribosome shifts by one codon; tRNA binds to newly exposed codon; steps 3 – 5 repeat.
Stop codon
6 Protein synthesis stops when the ribosome reaches the stop codon on mRNA.
Key:
= Adenine
= Guanine
= Cytosine
= Uracil
mRNA
Growing protein
Complete protein
Summary of movement of ribosome along mRNA

mRNA
Ribosome
Protein
Hydroxylation
Attaches a hydroxyl group (-OH) to a side chain of a protein
OH
R
Phosphorylation
Adds a phosphate to serine, threonine or tyrosine
P
Methylation
Adds a methyl group, usually at lysine or arginine residues
Me
Glycosylation
Attaches a sugar, usually to an "N" or "O" in an amino acid side chain
Lipidation
Attaches a lipid, such as a fatty acid, to a protein chain
Ubiquitination
Adds ubiquitin to lysine residue of a target protein for degradation
Ub
Acetylation
Adds an acetyl group to an N-terminus of a protein or at lysine residues
Ac
SUMOylation
Adds a small protein SUMO (small ubiquitin-like modifier) to a target protein
Su
Disulfide Bond
Covalently links the "S" atoms of two different cysteine residues
S—S
ROCKLAND
antibodies & assays

α-D-Ribofuranose

α-D-Glucopyranose

α-D-Mannopyranose

α-D-Galactopyranose

Dihydroxyacetone

D-Erythrulose

D-Ribulose

D-Fructose

$\alpha$-D-Fructofuranose

$\beta$-D-Fructofuranose

Glucose 1-phosphate

Glucose 6-phosphate

Glucose 1,6-bisphosphate

β-D-Glucose

β-D-Glucosamine

**2-deoxyribose**

D-Sorbitol

D-glucuronic acid

D-Gluconate

D-Glucono-δ-lactone

Maltose
α-D-glucopyranosyl-(1→4)-D-glucopyranose

Lactose (α form)
β-D-galactopyranosyl-(1→4)-α-D-glucopyranose
Gal(β1→4α)Glc

Sucrose
α-D-glucopyranosyl β-D-fructofuranoside
Glc(α1↔2β)Fru

LIPIDS
Fatty acids
Steroids
Lipid vitamins
Terpenes
Isoprenoids
Eicosanoids
Triacylglycerols
Waxes
Sphingolipids
Glycerophospholipids
Ceramides
Plasmalogens
Phosphatidates
Sphingomyelins
Cerebrosides
Gangliosides
Phosphatidyl-ethanolamines
Phosphatidyl-serines
Phosphatidyl-cholines
Phosphatidyl-inositols
Other phospholipids
Other glycosphingolipids
Phospholipids
Glycosphingolipids

t,t-linoleic acid (linolelaidic acid)

c,c-linoleic acid

## Waxes

## Eicosanoids

Prostaglandin $E_1$
($PGE_1$)

Thromboxane $A_2$

Leukotriene $A_4$

## Sterols

Taurocholic acid
(a bile acid)

Testosterone
(a steroid hormone)

| | | |
|---|---|---|
| Phosphatidic acid | — | —H |
| Phosphatidylethanolamine | Ethanolamine | $-CH_2-CH_2-\overset{+}{N}H_3$ |
| Phosphatidylcholine | Choline | $-CH_2-CH_2-\overset{+}{N}(CH_3)_3$ |
| Phosphatidylserine | Serine | $-CH_2-CH(COO^-)-\overset{+}{N}H_3$ |
| Phosphatidylglycerol | Glycerol | $-CH_2-CH(OH)-CH_2-O$ |
| Phosphatidylinositol 4,5-bisphosphate | *myo*-Inositol 4,5-bisphosphate | |

Sphingolipid (general structure)

| Name of sphingolipid | Name of X | Formula of X |
|---|---|---|
| Ceramide | — | —H |
| Sphingomyelin | Phosphocholine | |
| Neutral glycolipids<br>Glucosylcerebroside | Glucose | |
| Lactosylceramide (a globoside) | Di-, tri-, or tetrasaccharide | |
| Ganglioside GM2 | Complex oligosaccharide | |

EXTERIOR
Oligosaccharide chains of glycoproteins
Lipid-anchored protein
Peripheral membrane protein
Oligosaccharide chains of glycosphingolipids
Peripheral membrane protein
CYTOSOL
Integral membrane protein
Integral membrane proteins

Passive
Active
Nonmediated
Transporter mediated
A
B
C
D
ATP
ADP
+
$P_i$
A
B
C
D

Extracellular matrix
and cell wall
polysaccharides
Glycogen,
starch, sucrose
synthesis of
structural
polymers
storage
Glucose
oxidation via
pentose phosphate
pathway
oxidation via
glycolysis
Ribose 5-phosphate
Pyruvate

# BIOENERGETICS AND METABOLISM

Cell macromolecules
Proteins
Polysaccharides
Lipids
Nucleic acids
Energy-containing nutrients
Carbohydrates
Fats
Proteins
Anabolism
ADP + HPO$_4^{2-}$
NAD$^+$
NADP$^+$
FAD
ATP
NADH
NADPH
FADH$_2$
Chemical energy
Catabolism
Precursor molecules
Amino acids
Sugars
Fatty acids
Nitrogenous bases
Energy-depleted end products
$CO_2$
$H_2O$
$NH_3$

## VITAMIN A

**RETINOL**
*active form in mammalian tissues*

Important for eyesight. Also strengthens immune system and keeps skin and linings of parts of the body healthy.

## VITAMIN B1

**THIAMIN**
*can also occur in pyrophosphate ester form*

Used to keep nerves & muscle tissue healthy. Also important for processing of carbohydrates and some proteins.

## VITAMIN B2

**RIBOFLAVIN**
*excess turns urine bright yellow*

Important for body growth, red blood cell production, and keeping the eyes healthy. Also helps processing of carbohydrates.

## VITAMIN B3

**NICOTINIC ACID** **NICOTINEAMIDE**
*niacin is collective name for these compounds*

Helps with digestion and digestive system health. Also helps with the processing of carbohydrates.

## VITAMIN B5

**PANTOTHENIC ACID**
*also occurs in pyrophosphate ester form*

Important for manufacturing red blood cells and maintaining a healthy digestive system. Also helps process carbohydrates.

## VITAMIN B6

**PYRIDOXAL PHOSPHATE**
*active form in mammalian tissues*

Helps make some brain chemicals; needed for normal brain function. Also helps make red blood cells and immune system cells.

## VITAMIN B7

**BIOTIN**
*produced by intestinal bacteria*

Needed for metabolism of various compounds. Often recommended for strengthening hair, but evidence is variable.

## VITAMIN B12

**COBALAMIN**
*usually contains CN as the R group*

Important for the nervous system, for making red blood cells, and helps in the production of DNA and RNA.

## VITAMIN C

**ASCORBIC ACID**
*deficiency can cause scurvy*

Important for a healthy immune system; helps produce collagen, used to make skin and other tissues. Also helps wound healing.

## VITAMIN D

**CHOLECALCIFEROL**
*natural form; different form used in supplements*

Important for bone health and maintaining the immune system function. May also have a preventative role in cancers.

## VITAMIN E

**ALPHA-TOCOPHEROL**
*group includes tocopherols & tocotrienols*

An antioxidant that helps prevent damage to cells and may have a preventative role in cancer. Also helps make red blood cells.

## VITAMIN B9

**FOLIC ACID**
*found as tetrahydrofolate in food*

Important for brain function & mental health. Aids production of DNA & RNA. Important when tissues are growing quickly.

## VITAMIN K

**MENADIONE**
*all K vitamins are menadione or derivatives*

Helps blood clot properly, & plays a key role in bone health. Newborns receive vitamin K injections to prevent bleeding.

## Key

**Vitamins can be divided broadly into two classes.**

**WATER-SOLUBLE VITAMINS**
These vitamins are not stored in the body. As such, generally, they are required more frequently than the fat-soluble vitamins.

**FAT-SOLUBLE VITAMINS**
These vitamins are stored in the liver and fatty tissues until required. As such, they can be harmful if too much is taken in.

Glucose
glycolysis
(10 successive
reactions)
hypoxic or
anaerobic
conditions
2 Pyruvate
hypoxic or
anaerobic
conditions
2 Ethanol + $2CO_2$
aerobic
conditions
$2CO_2$
2 Lactate
Fermentation to
ethanol in yeast
2 Acetyl-CoA
Fermentation to lactate
in vigorously contracting
muscle, in erythrocytes,
in some other cells, and
in some microorganisms
citric
acid
cycle
$4CO_2 + 4H_2O$
Animal, plant, and
many microbial
cells under aerobic
conditions

(a) Preparatory phase
Phosphorylation of glucose and its conversion to glyceraldehyde 3-phosphate
first priming reaction
second priming reaction
cleavage of 6-carbon sugar phosphate to two 3-carbon sugar phosphates
Glucose
ATP
ADP
1
hexokinase
Glucose 6-phosphate
2
phosphohexose isomerase
Fructose 6-phosphate
ATP
ADP
3
phospho-fructokinase-1
Fructose 1,6-bisphosphate
4
aldolase
Glyceraldehyde 3-phosphate
+
Dihydroxyacetone phosphate
5
triose phosphate isomerase

**(b) Payoff phase**

Oxidative conversion of glyceraldehyde 3-phosphate to pyruvate and the coupled formation of ATP and NADH

oxidation and phosphorylation

first ATP-forming reaction (substrate-level phosphorylation)

second ATP-forming reaction (substrate-level phosphorylation)

(2) Glyceraldehyde 3-phosphate

$2P_i$

$2NAD^+$

$2\ NADH + 2H^+$

6 glyceraldehyde 3-phosphate dehydrogenase

(2) 1,3-Bisphosphoglycerate

2ADP

2 ATP

7 phosphoglycerate kinase

(2) 3-Phosphoglycerate

8 phosphoglycerate mutase

(2) 2-Phosphoglycerate

$2H_2O$

9 enolase

(2) Phosphoenolpyruvate

2ADP

2 ATP

10 pyruvate kinase

(2) Pyruvate

Trehalose
trehalase
Lactose
lactase
D-Galactose
Dietary glycogen; starch
Endogenous glycogen
H2O
α-amylase
D-Glucose
Sucrose
sucrase
P1
phosphorylase
UDP-galactose
UDP-glucose
Glucose 1-phosphate
ATP
hexokinase
phosphoglucomutase
Glucose 6-phosphate
D-Mannose
D-Fructose
ATP
hexokinase
ATP
hexokinase
Mannose 6-phosphate
ATP
fructokinase
Fructose 6-phosphate
phosphomannose isomerase
Fructose 1-phosphate
fructose 1-phosphate aldolase
Fructose 1,6-bisphosphate
Glyceraldehyde + Dihydroxyacetone phosphate
ATP
triose kinase
triose phosphate isomerase
Glyceraldehyde 3-phosphate

Nonreducing end
Glycogen (starch)
n glucose units
glycogen (starch)
phosphorylase
Glucose
1-phosphate
Glycogen (starch)
(n−1) glucose units

(a)
(C16) R—CH2—CH2—CH2—C—S-CoA
Palmitoyl-CoA
acyl-CoA dehydrogenase
FAD
FADH2
R—CH2—C=C—C—S-CoA
trans-Δ2-Enoyl-CoA
enoyl-CoA hydratase
H2O
R—CH2—C—CH2—C—S-CoA
L-β-Hydroxy-acyl-CoA
β-hydroxyacyl-CoA dehydrogenase
NAD+
NADH + H+
R—CH2—C—CH2—C—S-CoA
β-Ketoacyl-CoA
acyl-CoA acetyltransferase (thiolase)
CoA-SH
(C14) R—CH2—C—S-CoA + CH3—C—S-CoA
Acyl-CoA (myristoyl-CoA)
Acetyl-CoA

Leucine
Lysine
Phenylalanine
Tryptophan
Tyrosine
Acetoacetyl-CoA
Acetyl-CoA
Isoleucine
Leucine
Threonine
Tryptophan

Stage 1
Acetyl-CoA
production
Amino
acids
Fatty
acids
Glucose
Glycolysis
Pyruvate
pyruvate
dehydrogenase
complex
$CO_2$
Acetyl-CoA
Stage 2
Acetyl-CoA
oxidation
Citrate
Oxaloacetate
Citric
acid cycle
$CO_2$
$CO_2$
NADH,
$FADH_2$
(reduced $e^-$ carriers)
Stage 3
Electron transfer
and oxidative
phosphorylation
$2H^+ + \frac{1}{2}O_2$
Respiratory
(electron-transfer)
chain
$H_2O$
ADP + $P_i$
ATP

Citric acid cycle
Acetyl-CoA
CH3—C(=O)—S-CoA
citrate synthase
H2O
CoA-SH
1
Claisen condensation: methyl group of acetyl-CoA converted to methylene in citrate.
Citrate
Oxaloacetate
8
Dehydrogenation: oxidation of —OH completes oxidation sequence; generates carbonyl positioned to facilitate Claisen condensation in next step.
malate dehydrogenase
7
Malate
Hydration: addition of water across double bond introduces —OH group for next oxidation step.
fumarase
H2O
Fumarate
6
Dehydrogenation: introduction of double bond initiates methylene oxidation sequence.
FADH2
succinate dehydrogenase
Succinate
succinyl-CoA synthetase
CoA-SH
GTP (ATP)
GDP (ADP) + Pi
5
Substrate-level phosphorylation: energy of thioester conserved in phosphoanhydride bond of GTP or ATP.
Succinyl-CoA
(3) NADH
α-ketoglutarate dehydrogenase complex
CoA-SH
CO2
4
Oxidative decarboxylation: pyruvate-dehydrogenase-like mechanism; dependent on carbonyl on adjacent carbon.
α-Ketoglutarate
CO2
isocitrate dehydrogenase
3
Oxidative decarboxylation: —OH group oxidized to carbonyl, which in turn facilitates decarboxylation by stabilizing carbanion formed on adjacent carbon.
Isocitrate
aconitase
H2O
2b
(Rehydration)
cis-Aconitate
aconitase
H2O
2a
Dehydration/rehydration: —OH group of citrate repositioned in isocitrate to set up decarboxylation in next step.

Leucine
Lysine
Phenylalanine
Tryptophan
Tyrosine
Ketone bodies
Glutamate
Arginine
Glutamine
Histidine
Proline
Isocitrate
α-Ketoglutarate
Acetoacetyl-CoA
Citric acid cycle
Citrate
Succinyl-CoA
Isoleucine
Methionine
Threonine
Valine
Acetyl-CoA
Succinate
Oxaloacetate
Fumarate
Phenylalanine
Tyrosine
Malate
$CO_2$
Pyruvate
Glucose
Isoleucine
Leucine
Threonine
Tryptophan
Alanine
Cysteine
Glycine
Serine
Threonine
Tryptophan
Asparagine
Aspartate
Glucogenic
Ketogenic

Amino acids
Alanine (from muscle)
α-Ketoglutarate
α-Keto acid
Glutamine (from extrahepatic tissues)
Glutamate
Glutamine
glutaminase
Glutamate
Oxaloacetate
glutamate dehydrogenase
aspartate aminotransferase
α-Keto-glutarate
Aspartate
$NH_4^+$
$HCO_3^-$
2 ATP
2ADP + $P_i$
carbamoyl phosphate synthetase I
Carbamoyl phosphate
$P_i$
Mitochondrial matrix
Ornithine
Citrulline
Cytosol
Citrulline
ATP
$PP_i$
Urea cycle
Ornithine
Urea
$H_2O$
Citrullyl-AMP intermediate
Aspartate
AMP
Arginine
Fumarate
Argininosuccinate

4H+
4H+
2H+
Cyt c
Intermembrane space
I
II
III
IV
Q
Succinate
Fumarate
NADH + H+
NAD+
Matrix
½ O2 + 2H+
H2O
ADP + Pi
ATP
Fo
F1
H+
Chemical potential ΔpH (inside alkaline)
ATP synthesis driven by proton-motive force
Electrical potential Δψ (inside negative)

Photosynthetic cells
$CO_2$
$H_2O$
$O_2$
Carbo hydrate
Heterotrophic cells

$H_2O$
$O_2$
Light reactions
$NADP^+$
$ADP + P_i$
NADPH
ATP
Carbon-assimilation reactions
Carbohydrate
$CO_2$

Stroma (N side)
Light
Light
$NADP^+ + H^+$
NADPH
$2H^+$
Cyt $b_6f$ complex
Fd
PSII
PQ
$PQH_2$
PSI
$Mn_4Ca$
$H_2O$
$\frac{1}{2}O_2 + 2H^+$
$4H^+$
Plastocyanin
Lumen (P side)
Thylakoid membrane
$CF_o$
ATP
$CF_1$
$ADP + P_i$

Photosystem I
Photosystem II
P700*
A0
A1
Fe-S
Fd
Fd:NADP+ oxidoreductase
NADP+
NADPH
Light
P700
Plastocyanin
Cyt b6f complex
Proton gradient
P680*
Pheo
PQA
PQB
Light
P680
O2 evolving complex
H2O
1/2 O2
e−
E'° (volts)
−1.0
0
1.0
PQA = plastoquinone
PQB = second quinone
A0 = electron acceptor chlorophyll
A1 = phylloquinone

**nilation in**
cules fixed,
eraldehyde
six NADPH

Fatty acid
Glyoxysome
β oxidation
Acetyl-CoA
CH3—C—S-CoA
Citrate
Oxaloacetate
Glyoxylate cycle
Isocitrate
Succinate
⁻OOC—CH2—CH2—COO⁻
Malate
Glyoxylate
Acetyl-CoA
CH3—C—S-CoA
Mitochondrion
Succinyl-CoA
α-Ketoglutarate
Succinate
Isocitrate
Citric acid cycle
Fumarate
Citrate
Malate
Oxaloacetate
Oxaloacetate
⁻OOC—C—CH2—COO⁻
Cytosol
CO2
Phosphoenolpyruvate
gluconeogenesis
Fructose 6-phosphate
Sucrose
Glucose 6-phosphate

Glycolysis
Gluconeogenesis
Glucose
ATP
hexokinase
ADP
Glucose 6-phosphate
$P_i$
glucose 6-phosphatase
$H_2O$
Fructose 6-phosphate
ATP
phospho-fructokinase-1
ADP
Fructose 1,6-bisphosphate
$P_i$
fructose 1,6-bisphosphatase-1
$H_2O$
Dihydroxyacetone phosphate
Dihydroxyacetone phosphate
(2) Glyceraldehyde 3-phosphate
$2P_i$
$2NAD^+$
$2NADH + 2H^+$
(2) 1,3-Bisphosphoglycerate
2ADP
2ATP
(2) 3-Phosphoglycerate
(2) 2-Phosphoglycerate
(2) Phosphoenol-pyruvate
2ADP
pyruvate kinase
2ATP
2GDP
PEP carboxykinase
2GTP
(2) Oxaloacetate
2ADP
pyruvate carboxylase
2ATP
(2) Pyruvate

Blood glucose
Glycogen
Glycoproteins
Disaccharides
Other monosaccharides
Starch
Sucrose
Glucose 6-phosphate
Energy
Animals
Plants
Phosphoenol-pyruvate
Citric acid cycle
Pyruvate
Glucogenic amino acids
Glycerol
3-Phospho-glycerate
Lactate
Triacyl-glycerols
$CO_2$ fixation

**FIGURE 15–32 Glycogen synthesis.** A glycogen chain is elongated by glycogen synthase. The enzyme transfers the glucose residue of UDP-glucose to the nonreducing end of a glycogen branch (see Fig. 7-13) to make a new ($\alpha$1→4) linkage.

Nonoxidative phase
Oxidative phase
NADPH
Glucose 6-phosphate
NADP+
2 GSH
glutathione reductase
NADPH
GSSG
transketolase, transaldolase
6-Phosphogluconate
Fatty acids, sterols, etc.
NADP+
reductive biosynthesis
CO2
NADPH
Precursors
Ribulose 5-phosphate
Ribose 5-phosphate
Nucleotides, coenzymes, DNA, RNA

2 Acetyl-CoA
thiolase
CoA-SH
Acetoacetyl-CoA
HMG-CoA synthase
Acetyl-CoA + H2O
CoA-SH
β-Hydroxy-β-methylglutaryl-CoA (HMG-CoA)
HMG-CoA lyase
Acetyl-CoA
Acetoacetate
acetoacetate decarboxylase
CO2
NADH + H+
NAD+
D-β-hydroxybutyrate dehydrogenase
Acetone
D-β-Hydroxybutyrate

**FIGURE 21–6 Sequence of events during synthesis of a fatty acid.** The mammalian FAS I complex is shown schematically, with catalytic domains colored as in Figure 21–3. Each domain of the larger polypeptide represents one of the six enzymatic activities of the complex, arranged in a large, tight S shape. The acyl carrier protein (ACP) is not resolved in the crystal structure shown in Figure 21–3, but is attached to the KS domain. The phosphopantetheine arm of ACP ends in an —SH. After the first panel, the enzyme shown in color is the one that will act in the next step. As in Figure 21–4, the initial acetyl group is shaded yellow, C-1 and C-2 of malonate are shaded light red, and the carbon released as $CO_2$ is shaded green. Steps ❶ to ❻ are described in the text.

Glucose
Pyruvate
pyruvate carboxylase
Acetyl-CoA
Fatty acids, sterols
PEP carboxykinase
Phosphoenolpyruvate (PEP)
Oxaloacetate
Citrate
PEP carboxylase
Glutamine
Proline
Arginine
Citric acid cycle
Serine
Glycine
Cysteine
Phenylalanine
Tyrosine
Tryptophan
Aspartate
Asparagine
Pyrimidines
Malate
α-Ketoglutarate
Glutamate
malic enzyme
Pyruvate
Succinyl-CoA
Purines
Porphyrins, heme

Glucose
Glucose 6-phosphate
4 steps
Ribose 5-phosphate
Histidine
4 steps
Erythrose 4-phosphate
3-Phosphoglycerate
Serine
Glycine
Cysteine
Phosphoenolpyruvate
Tryptophan
Phenylalanine
Tyrosine
Pyruvate
Alanine
Valine
Leucine
Isoleucine
Citrate
Oxaloacetate
α-Ketoglutarate
Aspartate
Glutamate
Asparagine
Methionine
Threonine
Lysine
Glutamine
Proline
Arginine

$CO_2$
Aspartate
Glycine
Formate
Formate
Amide N
of glutamine

**URE 22–35 De novo synthesis of purine nucleotides: construction of the ine ring of inosinate (IMP).** Each addition to the purine ring is shaded to ch Figure 22–34. After step ❸, R symbolizes the 5-phospho-D-ribosyl up on which the purine ring is built. Formation of 5-phosphoribosylamine p ❸) is the first committed step in purine synthesis. Note that the prod- of step ❾, AICAR, is the remnant of ATP released during histidine biosyn- sis (see Fig. 22–22, step ❸). Abbreviations are given for most intermedi- s to simplify the naming of the enzymes. Step ⑥ is the alternative path

Aspartate
Carbamoyl phosphate
aspartate trans-carbamoylase
$P_i$
N-Carbamoylaspartate
dihydroorotase
$H_2O$
L-Dihydroorotate
$NAD^+$
dihydroorotate dehydrogenase
$NADH + H^+$
Orotate
PRPP
orotate phosphoribosyl-transferase
$PP_i$
Orotidylate
orotidylate decarboxylase
$CO_2$
Uridylate (UMP)
2 ATP
kinases
2ADP
Uridine 5'-triphosphate (UTP)
Gln
Glu
cytidylate synthetase
ATP
$ADP + P_i$
Cytidine 5'-triphosphate (CTP)

High blood glucose
↑Insulin
GLUT2
↑Insulin-sensitive protein kinase
↑PKB
Synthesis of hexokinase II, PFK-1, pyruvate kinase
↑PP1
↓GSK-3
↑[Glucose]inside
↓Phosphorylase kinase
↑Glycogen synthase
↓Glycogen phosphorylase
↓Glycogen breakdown
↑Glycogen synthesis
↑Glycolysis

↑Glycogen breakdown
↓Glycogen synthesis
↓Glycolysis
↑Glycogen phosphorylase
↓Glycogen synthase
↓PFK-1
↓F26BP
↑Phosphorylase kinase
↑FBPase-2
↓PFK-2
↓Pyruvate kinase L
↑PKA
↑cAMP
↑Glucagon
Low blood glucose