Module 4

Amino acids and Methylation

Muscles and their meridian relationship.

Meridian	Muscles
Bladder	Tibialis ant, Tibialis post, Peroneus long/ brevis, Peroneus tertius
Kidney	Psoas, Iliacus, Upper trap
Gall bladder	Popliteus
Liver	PMS, Rhomoids
Large Intestine	TFL, Hamstrings, QL
Lung	Deltoid, Serratus ant, Coracobrachialis
CV	Supraspinatus, Diaphragm
GV	Teres major
Triple warmer	Teres minor, Infraspinatus
Circulation / sex	Glut max, Glut med/min, Piriformis, Adductors, Sartorius, Gracilis
Stomach	PMC, Neck flexors, Biceps, Brachialis, Pronator teres, Pronator quadratus
Spleen	Lat dorsi, Mid trap, Lower trap, Triceps
Small intestine	Quads, Abdominals
Heart	Subscapularis

Nutrition / Muscle relationship.

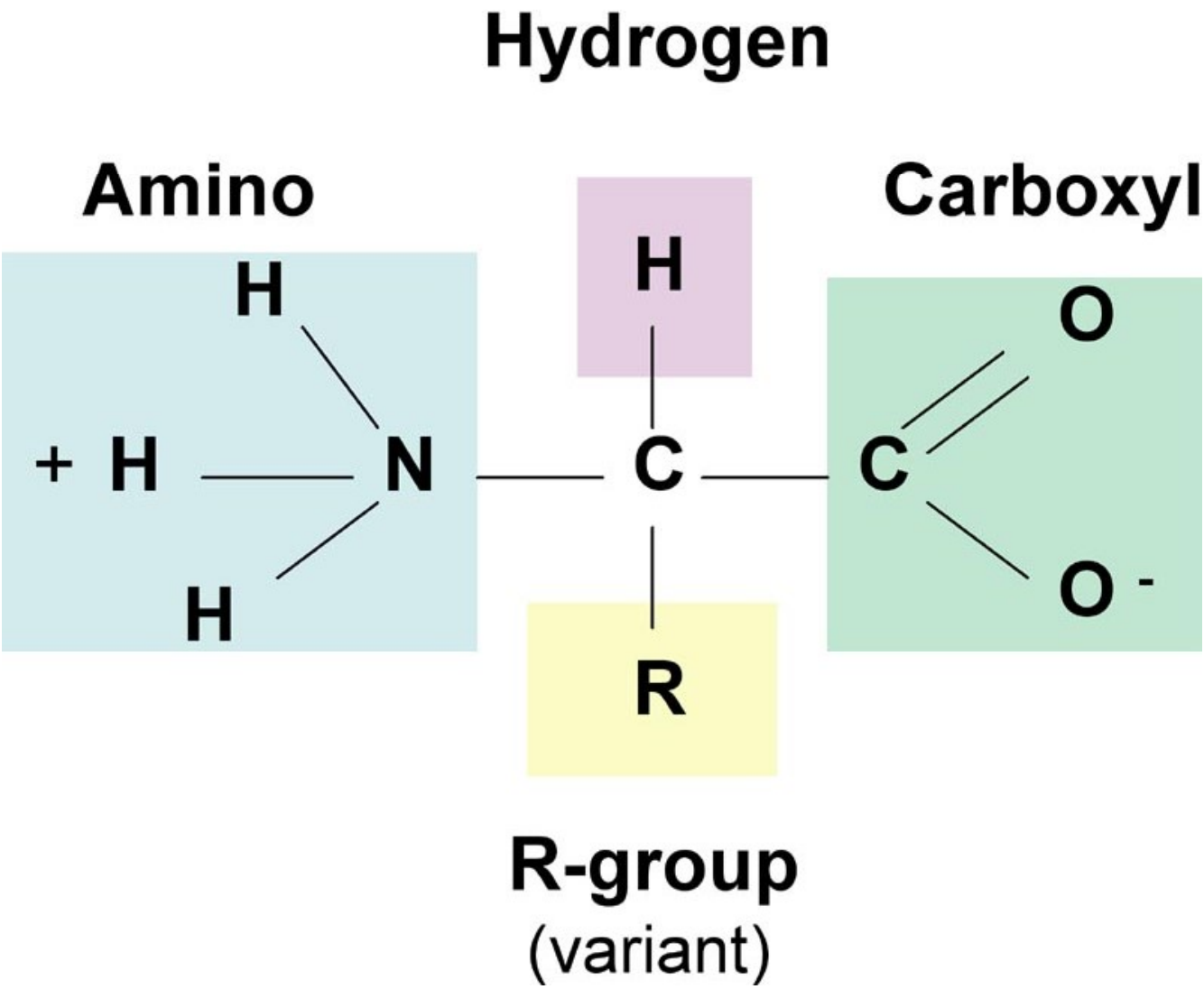
Vitamin A - Latissimus dorsi, Pectoralis major clavicular, Pectoralis minor, Piriformis, Popliteus, Psoas, Quadratus lumborum, Rhomboids,Sacrospinalis, Tibialis anterior.
B. Complex - Pectoralis major clavicular, Pectoralis minor, Peroneals, Quadriceps, Subscapularis, Upper trapezius, Supinator.
Vitamin B1
Vitamin B2 - Neck extensors
Vitamin B3 - Gracilis, Neck flexors, Pectoralis minor
Vitamin B5 - Sartorius
Vitamin B6 - Opponens digiti minimi
Folic acid
Vitamin B12
Biotin
Vitamin C - Coracobrachialis, Deltoid, Diaphragm, Quadratus lumborum, Sacrospinalis, Sartorius, Serratus anterior, Middle trapezius, Lower trapezius
Vitamin D - Quadriceps, Tensor fascia lata, ICV
Vitamin E - Abdominals, Adductors, Gluteus maximus, Gluteus medius, Hamstrings, Quadratus lumborum, Sacrospinalis, Subscapularis
Vitamin K
Co-enzyme Q10
SAMe

Muscle / Meridian / Nutrition relationship.

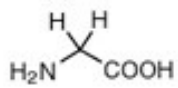
Muscle	Meridian	Nutrition
Abdominals	SI	Vit E
Adductors	Cx	Vit E
Biceps	St	HCl, Chlorophyll
Brachio Radialis	St	HCl
Coracobrachialis	Lung	Vit C
Deltoid	Lung	Vit C, RNA
Diaphragm	CV	Vit C
Gastrocnemius	Cx	Adrenal
Gluteus max	Cx	Vit E
Gluteus med	Cx	Vit E
Gracilis	Cx	Vit B3, Adrenal
Hamstrings	LI	Vit E, HCl, Ca
ICV		Chlorophyll, Ca, Vit D, HCl
Infraspinatus	TW	Thymus
Latissimus dorsi	Sp	Vit A, EFAs, Zn
Neck extensors	St	Vit B2, B3, B6, Iodine
Neck flexors	St	Vit B3, B6
Opponens digiti min	St	Vit B6
Pectoralis major clav	St	Vit B, B12, HCl
Pectoralis major sternal	Liv	Vit A, Bile salts
Pectoralis minor		RNA, Vit A, B, B3, Zn
Peroneals	Bl	Vit B, Ca
Piriformis	Cx	Vit A
Popliteus	Gb	Vit A
Psoas / Iliacus	Kid	Vit A, E
Quadratus lumborum	LI	Vit A, C, E
Rhomboids	Liv	Vit A
Sacrospinalis	Bl	Vit A, C, E, P, Ca
Sartorius	Cx	Vit B5, B6, C, Adrenal, Zn, Ginseng
Serratus anterior	Lung	Vit C
Soleus	Cx	Vit C
SCMastoid	St	Vit B3, B6, Iodine
Subclavius		Mg
Subscapularis	Ht	Vit B, C, E
Supinator	St	Vit B, G, HCl
Supraspinatus	CV	RNA
Tensorfacialata	LI	Vit D, Probiotics, Iron
Teres major	GV	Alkaline minerals, K, P
Teres minor	TW	Iodine
Tibilais anterior	Cx /Bl	Adrenal
Tibialis posterior	Bl	Vit A
Trapezius upper	Kid	Vit A, B, EFAs, Ca
Trapezii mid & lower	Sp	Vit C, Ca
Triceps	Sp	Vit A, HCl

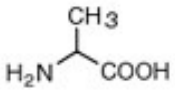
AMINO ACIDS

Amino Acid Structure

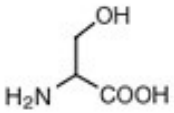


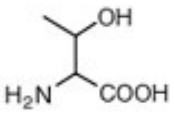
Small

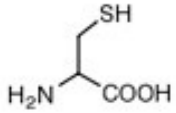

Glycine (Gly, G)
MW: 57.05


Alanine (Ala, A)
MW: 71.09

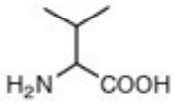
Nucleophilic

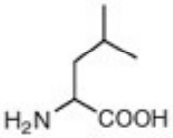

Serine (Ser, S)
MW: 87.08, pK_a ~ 16

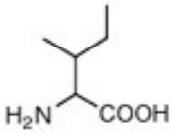

Threonine (Thr, T)
MW: 101.11, pK_a ~ 16

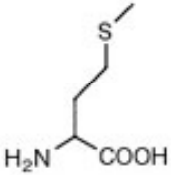

Cysteine (Cys, C)
MW: 103.15, pK_a = 8.35

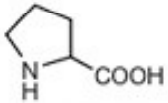
Hydrophobic


Valine (Val, V)
MW: 99.14

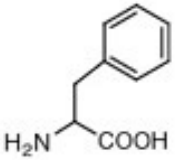

Leucine (Leu, L)
MW: 113.16

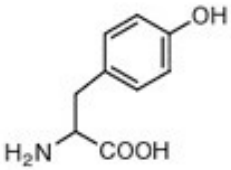

Isoleucine (Ile, I)
MW: 113.16

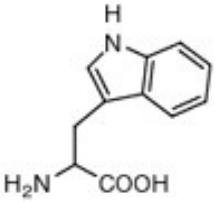

Methionine (Met, M)
MW: 131.19


Proline (Pro, P)
MW: 97.12

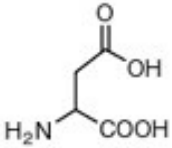
Aromatic

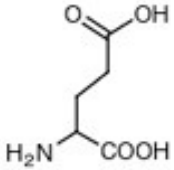

Phenylalanine (Phe, F)
MW: 147.18


Tyrosine (Tyr, Y)
MW: 163.18

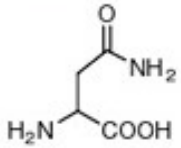

Tryptophan (Trp, W)
MW: 186.21

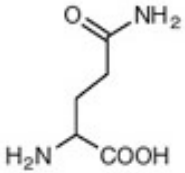
Acidic


Aspartic Acid (Asp, D)
MW: 115.09, pK_a = 3.9

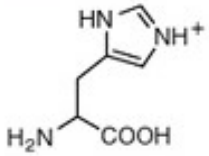

Glutamic Acid (Glu, E)
MW: 129.12, pK_a = 4.07

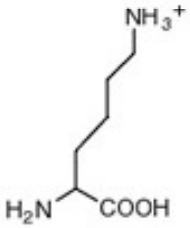
Amide

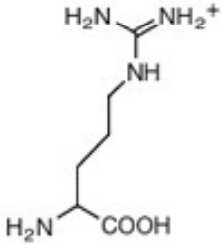

Asparagine (Asn, N)
MW: 114.11


Glutamine (Gln, Q)
MW: 128.14

Basic


Histidine (His, H)
MW: 137.14, pK_a = 6.04


Lysine (Lys, K)
MW: 128.17, pK_a = 10.79


Arginine (Arg, R)
MW: 156.19, pK_a = 12.48

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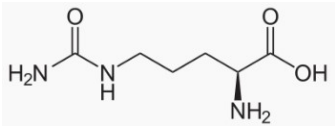
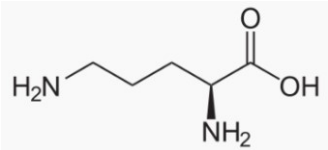
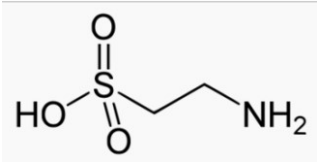
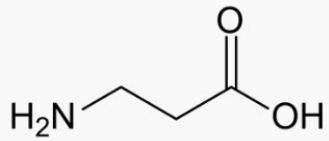

Citrulline


Ornithine


Taurine

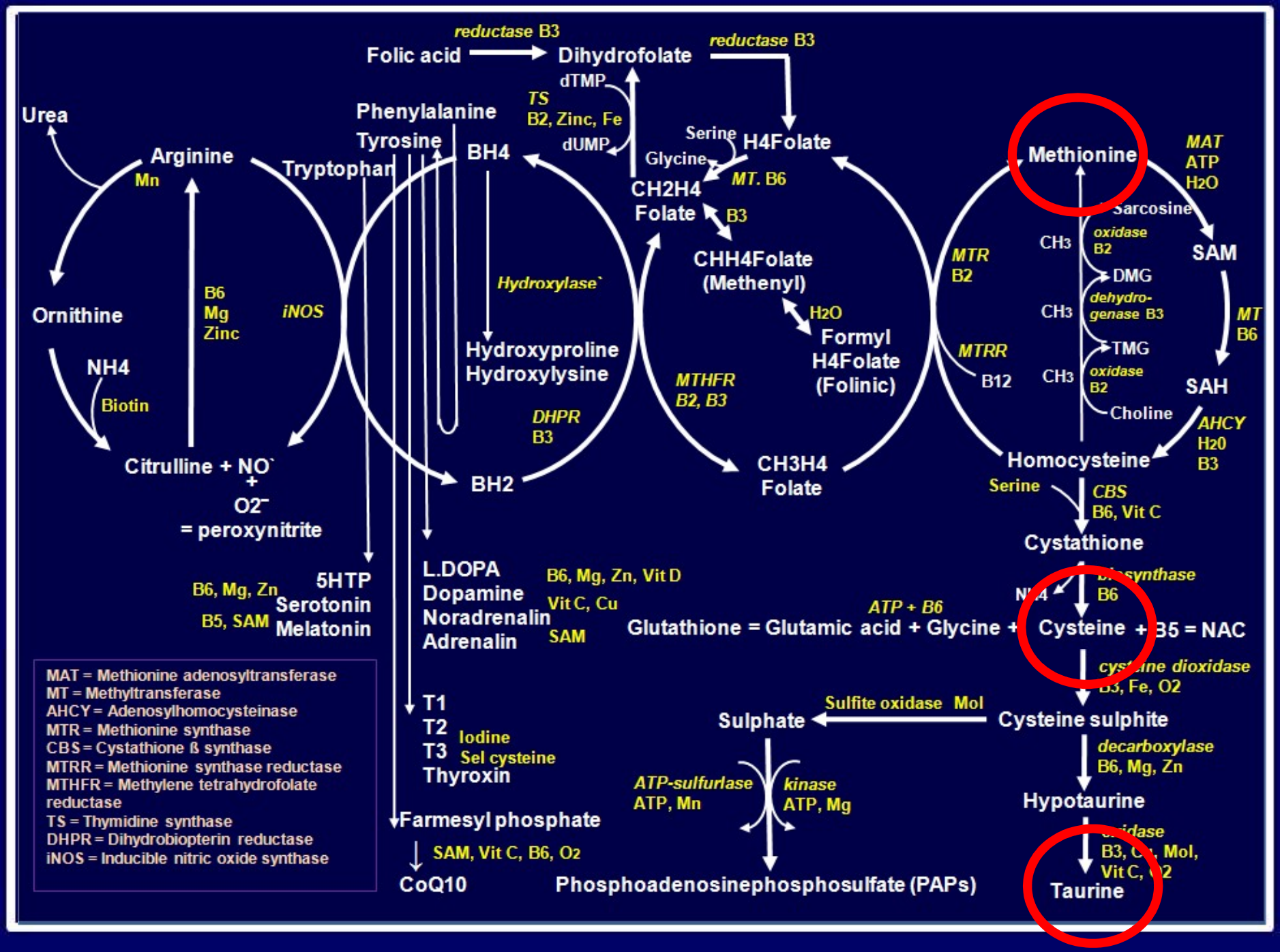

B-Alanine

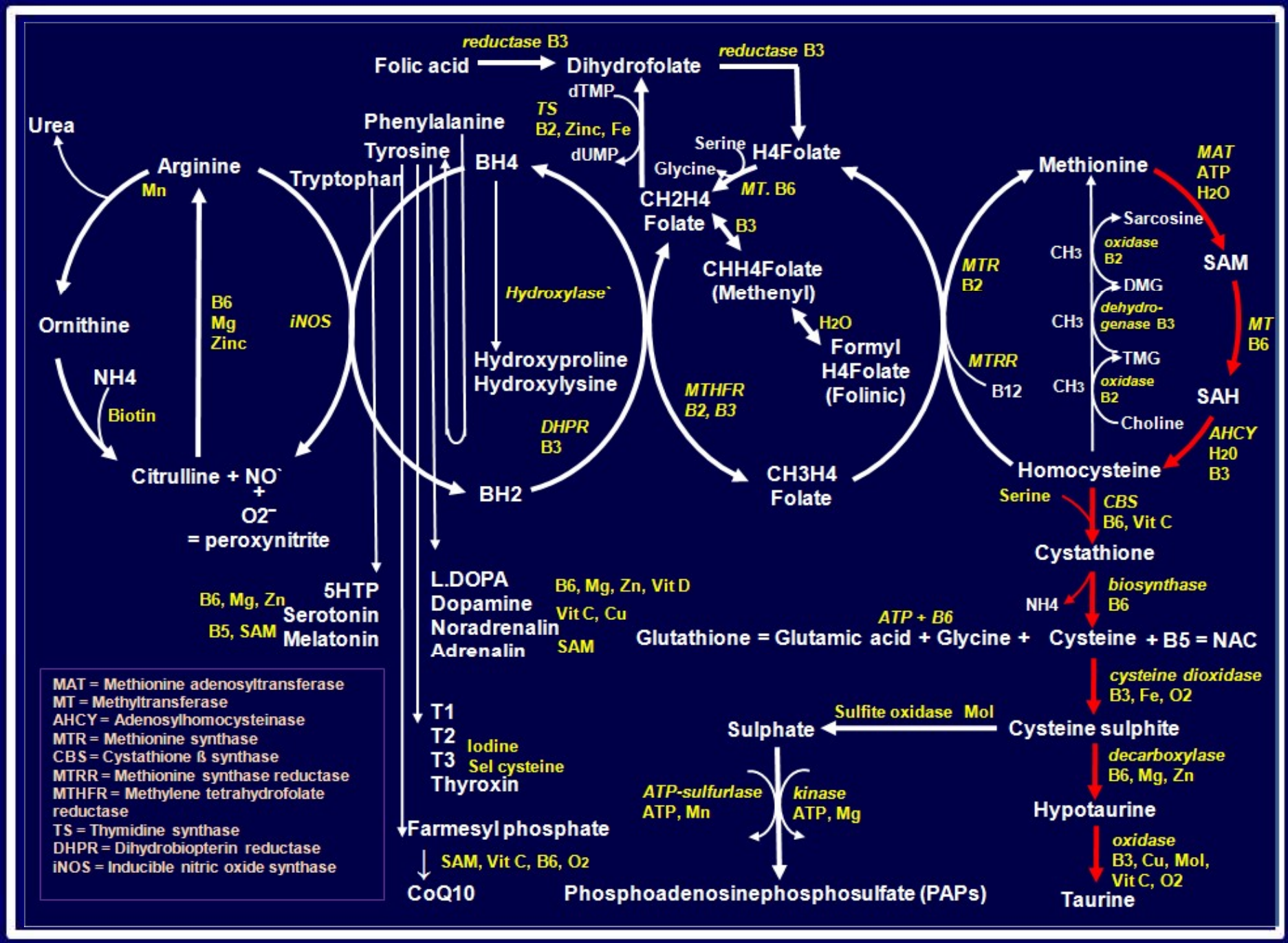
Sulphur containing Amino Acids

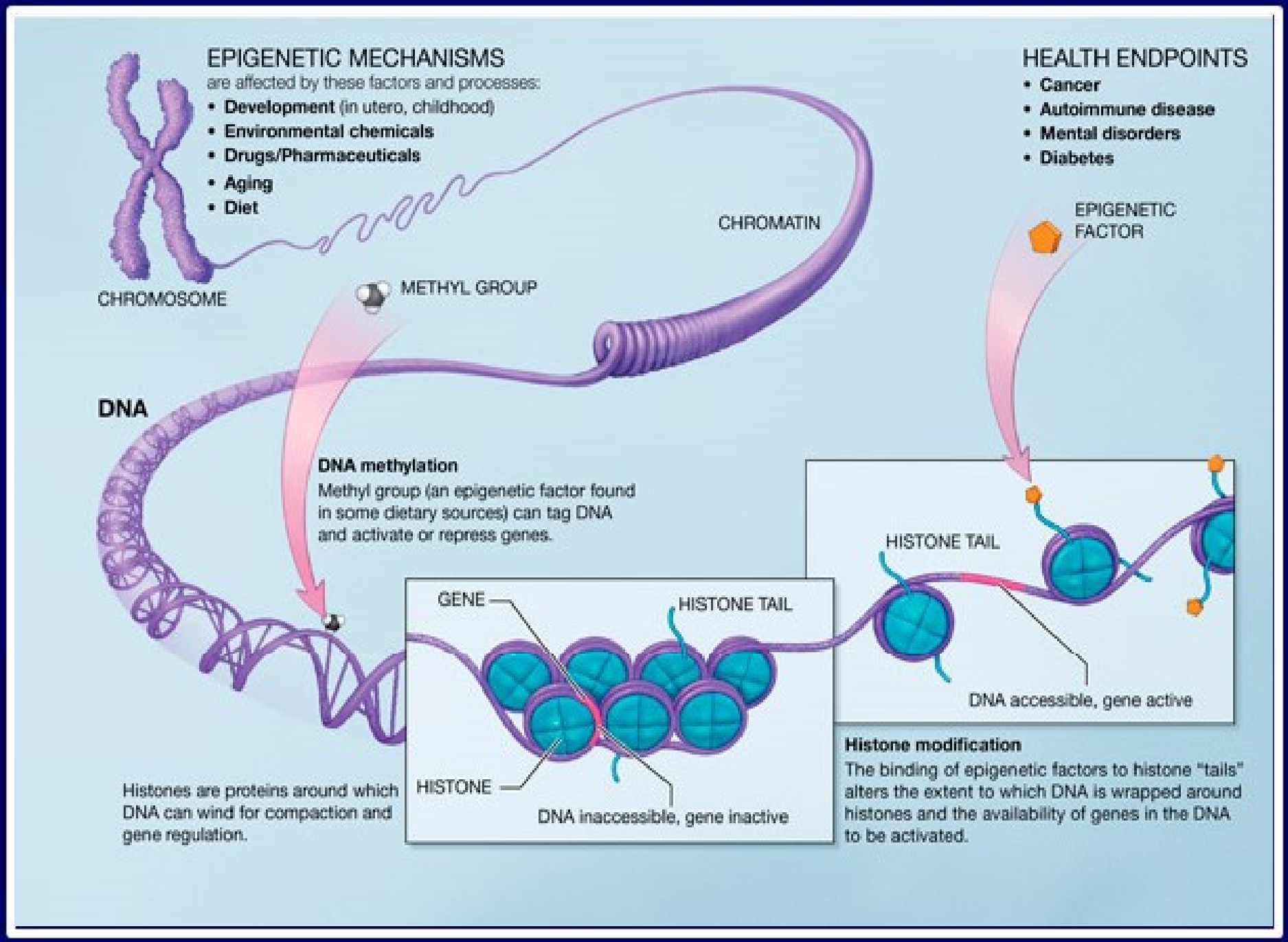
- Methionine
- Cysteine
- Taurine

Sulphur containing Amino Acids

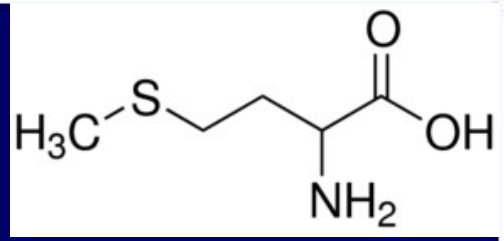
- Chemically different from other amino acids since they contain a sulphur molecule
- Sulphur combines with hydrogen molecules to become powerful anti-oxidants to fight free radicals
- Methionine, cysteine, taurine


reductase B3
Folic acid
Dihydrofolate
reductase B3
dTMP
TS
B2, Zinc, Fe
dUMP
Urea
Arginine
Mn
Phenylalanine
Tyrosine
Tryptophan
BH4
Serine
H4Folate
Glycine
MT. B6
CH2H4
Folate
B3
CHH4Folate
(Methenyl)
H2O
Formyl
H4Folate
(Folinic)
Methionine
MAT
ATP
H2O
Sarcosine
oxidase
B2
CH3
DMG
dehydro-
genase B3
CH3
TMG
oxidase
B2
CH3
Choline
SAM
MT
B6
SAH
AHCY
H20
B3
MTR
B2
MTRR
B12
Ornithine
B6
Mg
Zinc
iNOS
Hydroxylase`
Hydroxyproline
Hydroxylysine
NH4
Biotin
DHPR
B3
MTHFR
B2, B3
Citrulline + NO`
+
O2⁻
= peroxynitrite
BH2
CH3H4
Folate
Homocysteine
Serine
CBS
B6, Vit C
Cystathione
synthase
B6
NH4
B6, Mg, Zn
5HTP
Serotonin
B5, SAM
Melatonin
L.DOPA
Dopamine
Noradrenalin
Adrenalin
B6, Mg, Zn, Vit D
Vit C, Cu
SAM
ATP + B6
Glutathione = Glutamic acid + Glycine +
Cysteine + B5 = NAC
cysteine dioxidase
B3, Fe, O2
MAT = Methionine adenosyltransferase
MT = Methyltransferase
AHCY = Adenosylhomocysteinase
MTR = Methionine synthase
CBS = Cystathione ß synthase
MTRR = Methionine synthase reductase
MTHFR = Methylene tetrahydrofolate reductase
TS = Thymidine synthase
DHPR = Dihydrobiopterin reductase
iNOS = Inducible nitric oxide synthase
T1
T2
T3
Iodine
Sel cysteine
Thyroxin
Sulfite oxidase Mol
Sulphate
Cysteine sulphite
decarboxylase
B6, Mg, Zn
Hypotaurine
ATP-sulfurlase
ATP, Mn
kinase
ATP, Mg
Farmesyl phosphate
SAM, Vit C, B6, O2
CoQ10
Phosphoadenosinephosphosulfate (PAPs)
B3, Mol,
Vit C,
Taurine


Folic acid
reductase B3
Dihydrofolate
reductase B3
dTMP
TS
B2, Zinc, Fe
dUMP
Urea
Arginine
Mn
Phenylalanine
Tyrosine
Tryptophan
BH4
Serine
Glycine
H4Folate
MT. B6
CH2H4
Folate
B3
CHH4Folate
(Methenyl)
H2O
Formyl
H4Folate
(Folinic)
Methionine
MAT
ATP
H2O
Sarcosine
oxidase
B2
DMG
dehydro-
genase B3
TMG
oxidase
B2
Choline
CH3
CH3
CH3
SAM
MT
B6
SAH
AHCY
H20
B3
MTR
B2
MTRR
B12
Ornithine
B6
Mg
Zinc
iNOS
NH4
Biotin
Hydroxylase`
Hydroxyproline
Hydroxylysine
DHPR
B3
MTHFR
B2, B3
Citrulline + NO`
+
O2⁻
= peroxynitrite
BH2
CH3H4
Folate
Homocysteine
Serine
CBS
B6, Vit C
Cystathione
biosynthase
B6
NH4
B6, Mg, Zn
5HTP
Serotonin
B5, SAM
Melatonin
L.DOPA
Dopamine
Noradrenalin
Adrenalin
B6, Mg, Zn, Vit D
Vit C, Cu
SAM
ATP + B6
Glutathione = Glutamic acid + Glycine + Cysteine + B5 = NAC
cysteine dioxidase
B3, Fe, O2
Sulfite oxidase Mol
Sulphate
Cysteine sulphite
decarboxylase
B6, Mg, Zn
Hypotaurine
oxidase
B3, Cu, Mol,
Vit C, O2
Taurine
T1
T2
T3
Iodine
Sel cysteine
Thyroxin
Farmesyl phosphate
SAM, Vit C, B6, O2
CoQ10
ATP-sulfurlase
ATP, Mn
kinase
ATP, Mg
Phosphoadenosinephosphosulfate (PAPs)
MAT = Methionine adenosyltransferase
MT = Methyltransferase
AHCY = Adenosylhomocysteinase
MTR = Methionine synthase
CBS = Cystathione ß synthase
MTRR = Methionine synthase reductase
MTHFR = Methylene tetrahydrofolate reductase
TS = Thymidine synthase
DHPR = Dihydrobiopterin reductase
iNOS = Inducible nitric oxide synthase


EPIGENETIC MECHANISMS
are affected by these factors and processes:
• Development (in utero, childhood)
• Environmental chemicals
• Drugs/Pharmaceuticals
• Aging
• Diet
HEALTH ENDPOINTS
• Cancer
• Autoimmune disease
• Mental disorders
• Diabetes
CHROMOSOME
CHROMATIN
METHYL GROUP
EPIGENETIC FACTOR
DNA
DNA methylation
Methyl group (an epigenetic factor found in some dietary sources) can tag DNA and activate or repress genes.
GENE
HISTONE TAIL
HISTONE
DNA inaccessible, gene inactive
HISTONE TAIL
DNA accessible, gene active
Histones are proteins around which DNA can wind for compaction and gene regulation.
Histone modification
The binding of epigenetic factors to histone "tails" alters the extent to which DNA is wrapped around histones and the availability of genes in the DNA to be activated.

Methionine - Methylation



- Gene regulation
- Represses or activates genes
- DNA is coiled around proteins called histones
- Each histone has a loose end or tail to which chemicals can attach
- Alters how tightly the DNA is wound around the histone

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Leon Chaitow "Thorsons Guide to Amino acids" page 49

Methionine - Methylation

- So long as the DNA remains tightly coiled the gene does not activate, to activate the DNA must be partially unwound
- Adding a methyl group switches the gene off and removing a methyl group switches it back on

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Methionine - Methylation

- Maintaining the integrity of our DNA over our lifetime is critical to prevent aging, cancer and degenerative diseases
- Methyl groups decide which genes are expressed
- Methyl groups depleted in toxic environment

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Some Methylation functions

Phosphatidylethanolamine to phosphatidylcholine

Noradrenalin to adrenalin

Metabolism Dopamine, Noradrenalin and Serotonin

Metabolism of Estrogens and Testosterone

DNA methyltransferase

Methyl Caps DNA /RNA

Synthesis of Creatine, Carnitine

Histone methyltransferases

Synthesis of myelin

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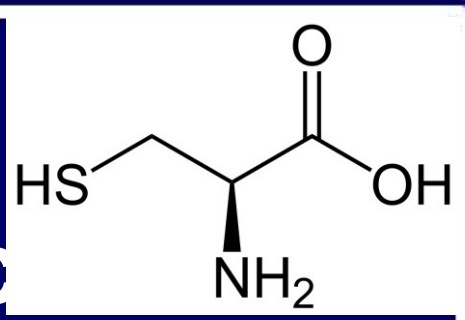
Cysteine – the Detoxifier



- Contains a sulphur molec
  and so becomes a powerful antioxidant
- Cysteine is highly reactive, rapidly converted to the more stable cystine
- Converts to NAC

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Leon Chaitow "Thorsons Guide to Amino acids" page 77

Cysteine – the Detoxifier

- Thiol groups at end of each cysteine molecule to prevent oxidation and eliminate toxic chemicals and heavy metals
- Produces NAC and glutathione, powerful detoxifying agents in body

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Cysteine – the Detoxifier

- Active part in fatty acid synthase. Uses the thiol groups to fasten carbon atoms, two at a time, onto the lengthening chains that make up each fatty acid

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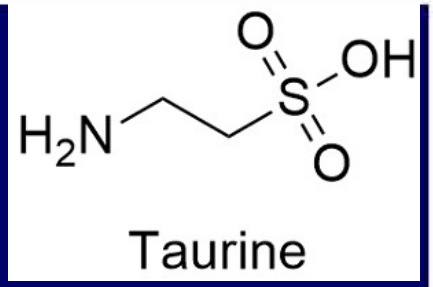
Cysteine – the Detoxifier

- Horny layers of the skin, hair and nails are high in cysteine

Selenocysteine is an alpha amino acid found in proteins from every domain of life. A selenium atom replaces the sulfur of its structural analog, cysteine.
It is thus referred to as the 21st amino acid.

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 18

Taurine – Good for the Heart



- By-product of sulphurous amino acids cysteine and methionine
- Not contain a carboxyl group and not used in protein strings
- An amino sulphonic acid
- Critical in preterm and new-borns – normal growth and development

Amino acids Biochemistry and Nutrition by Guoyao Wu Pub CRC Press page 361

Leon Chaitow "Thorsons Guide to Amino acids" page 68

Taurine

- Increases levels of prolactin
- Concentrated in CNS, heart, and retina
- Facilitates the passage of sodium, potassium, calcium and magnesium ions in and out of cell and electrically stabilises the cell membrane

Amino acids Biochemistry and Nutrition by Guoyao Wu Pub CRC Press page 361

Leon Chaitow "Thorsons Guide to Amino acids" page 68

Taurine

Brain and CNS

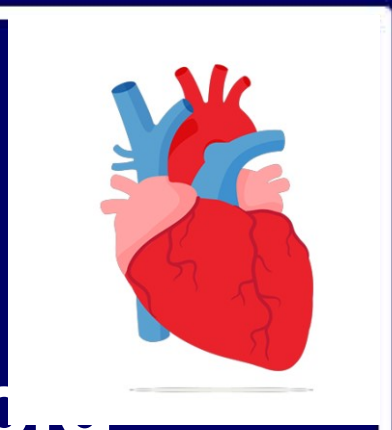
- Most plentiful amino acid in developing brain and second in the adult brain. Mostly in olfactory bulb, hippocampus and pineal
- Inhibitory neurotransmitter, anti-anxiety and protects against glutamate excitotoxicity

Leon Chaitow "Thorsons Guide to Amino acids" page 68

Amino acids Biochemistry and Nutrition by Guoyao Wu Pub CRC Press page 361

Taurine

Heart



- Most abundant free amino acid
- Metabolism of calcium for the transmission of nerve impulses
- Depleted in arrhythmia or abnormal heartbeats
- Promotes pumping, increases force of heart muscle contraction

Leon Chaitow "Thorsons Guide to Amino acids" page 68

Amino acids Biochemistry and Nutrition by Guoyao Wu Pub CRC Press page 361

Taurine

Hypertension

- Antagonist to blood pressure increasing effect of angiotensin
- With low levels of taurine, renin is activated and angiotensin is formed and blood pressure rises
- Taurine breaks the renin-angiotensin feedback loop

Leon Chaitow "Thorsons Guide to Amino acids" page 68

Amino acids Biochemistry and Nutrition by Guoyao Wu Pub CRC Press page 361

Taurine

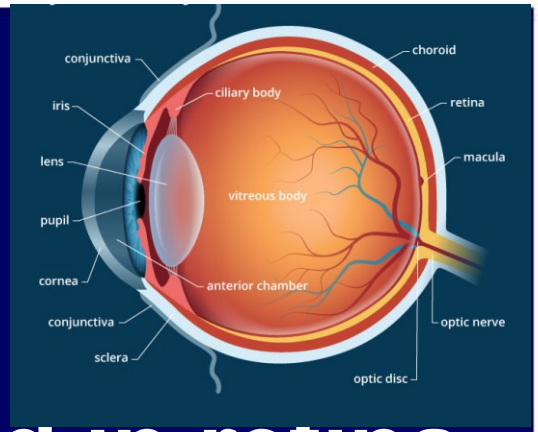
Gall Bladder function

- Stimulates taurocholic acid, bile salt which breaks down fats in SI
- Increases the cholesterol excretion in bile
- Improves fat metabolism in the liver and lowers atherosclerotic plaque in the arteries

Leon Chaitow "Thorsons Guide to Amino acids" page

Amino acids Biochemistry and Nutrition by Guoyao Wu Pub CRC Press page 361

Taurine



Eye

- Most abundant amino acid in retina
- Low levels in retinitis pigmentosa
- Protects the eye from toxins

Antioxidant

- Particularly effective against hypochlorite (swimming baths)

Leon Chaitow "Thorsons Guide to Amino acids" 68

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Taurine

- Can be used in prevention of epileptic seizures
- Acts as an antioxidant and protects against toxicity, such as lead and cadmium

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"Taurine Plays Major Roles in the Body

Current research describes taurine as a primary nutrient. It controls muscle metabolism and much more. It also stabilizes cell membranes, and has antioxidant and anti-inflammatory actions. Therefore, it plays many biological roles, including conjugation of bile acids, helps maintain fluid homeostasis, stabilizes cell membrane, and manages calcium signaling. It's essential for cardiovascular function, the development and function of skeletal muscles, the retina, and the central nervous system. Few other nutrients do so much!.

Taurine is a potent antioxidant. Yet, researchers found that it is neither a classical free radical scavenger nor a regulator of antioxidant defenses. It serves as a regulator of mitochondrial protein synthesis for protecting mitochondria from superoxide generation. (Jong, Azuma, & Schaffer, 2012). In additon, taurine's antioxidant effects can protect against age-related lipid peroxidation. (Yildirim & Kilic, 2011).

Benefits and consequences of its deficit

Taurine deficiency may be more common than expected. Low taurine levels in the body are associated with retinal degeneration, growth retardation, and cardiovascular disease. When low, it decreases ATP generation up to 25%. It also reduces respiratory function and contributes to the severity of cardiomyopathy. (Schaffer, Jong, Shetewy, Ramila, & Ito, 2017).

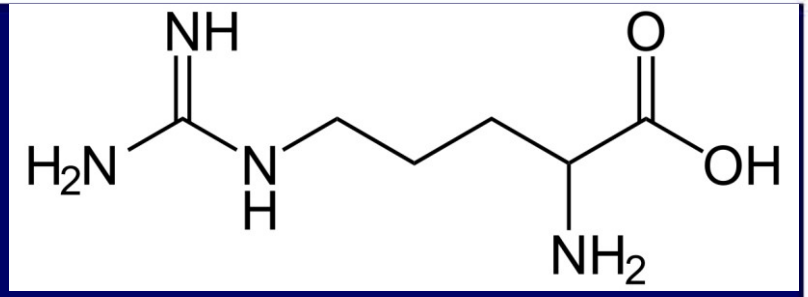
Because this amino acid mainly occurs in animal foods, vegetarians are at risk for a deficiency. A study in 1988, found that strict vegetarians had a significantly lower plasma and urinary levels of taurine. (Laidlaw, Shultz, Cecchino, & Kopple, 1988) A 2004 study also suggests that it is an important supplement for a low-fat vegan diet. (McCarty, 2017).
Since methionine and cysteine are precursors of taurine, diets low in these amino acids can also result in a deficiency. In addition, not enough vitamins A, B12, pyridoxal-5-phosphate, and zinc is associated with low taurine. Candida albicans overgrowth causes overproduction of beta-alanine that competes with taurine resorption. Consequently, this results in excessive excretion of the amino acid in the urine.

***The symptoms of the deficiency*: Persistent fatigue, brain fog, depression, impaired vision, unexplained weight gain, reduced post-exercise recovery, low thyroid gland function.**

Taurine plays a role in eye health by exerting a protective effect on the retina. Therefore, infusions of taurine reduce the damaging effects of diabetes on the retina. Additionally, this amino acid is useful for age-related degenerative vision changes.

***Some benefits of Taurine*: Prevents cataracts (Choudhary & Bodakhe, 2016), reduces oxidative stress caused by diabetes (Patel & Lau-Cam, 2017), limits complications of diabetes (Ito, Schaffer, & Azuma, 2012), reverses cardiovascular risk factors, reduces atrial fibrillation, treats fatty liver, alleviates seizures, reverses tinnitus, fights obesity, lowers inflammation, lowers cholesterol, improves kidney function, decreases blood pressure (Liang et al., 2017), lowers homocysteine, helps muscles work harder and longer, enhances bone remodeling (Choi, 2009), prevents age-related vision loss, protective effects in brain injury (Wang et al., 2016), improves memory, delays muscle atrophy during aging (De Luca, Pierno, & Camerino, 2015).**

Arginine – Urea amino acid



- Can be essential for children, releases growth hormone
- Functions in urea cycle to excrete excess nitrogen in urine from the breakdown of proteins
- Elimination of ammonia which is produced during deamination,

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Arginine – Urea amino acid

- Eliminates ammonia from parasites and metabolism of other amino acids and DNA bases
- Created from ammonia and carbon dioxide >citrulline > arginine > ornithine

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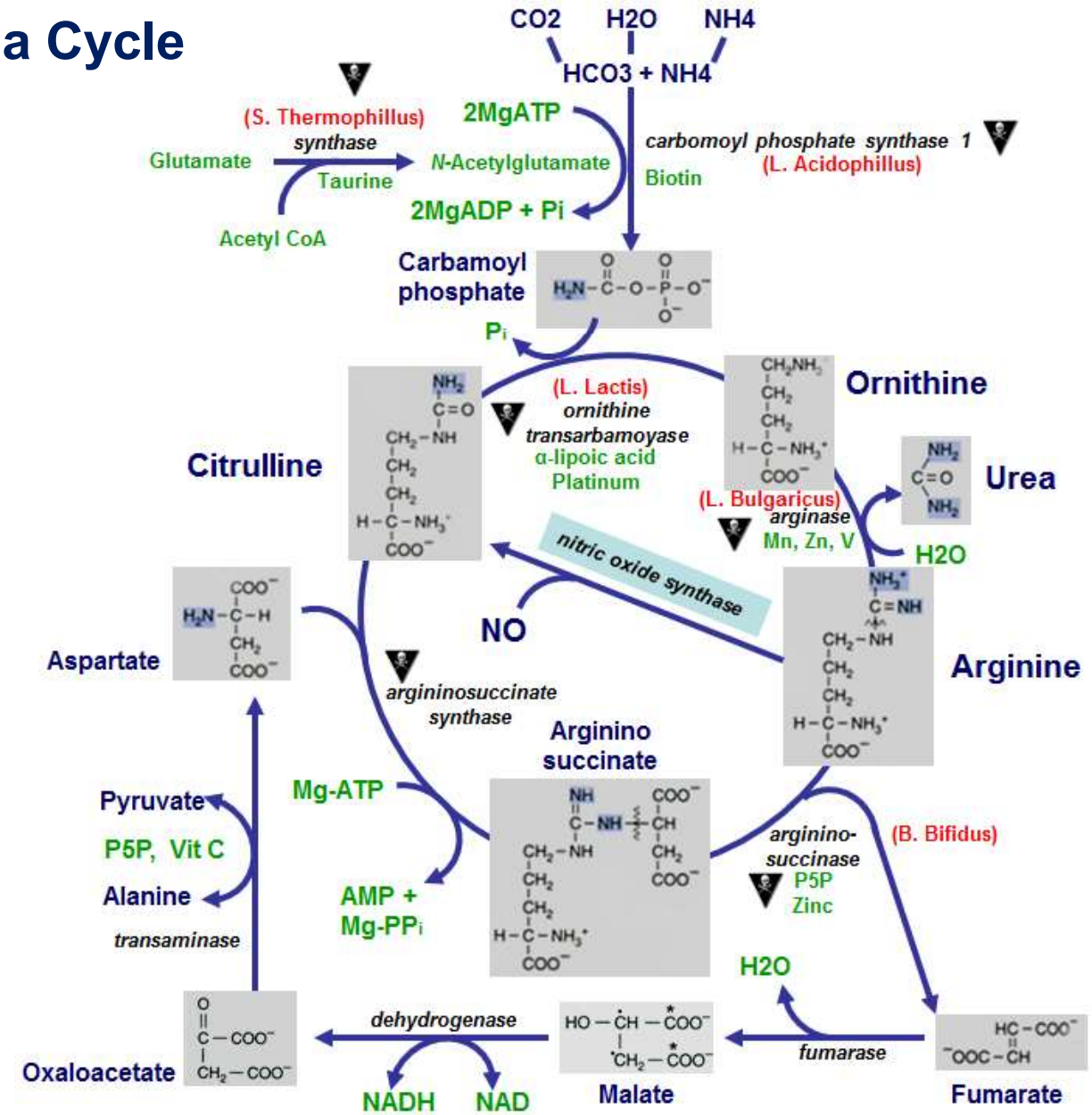
The Urea Cycle



The Urea Cycle

1. L-ornithine
2. carbamoyl phosphate
3. L-citrulline
4. argininosuccinate
5. fumarate
6. L-arginine
7. urea

L-Asp L-aspartate

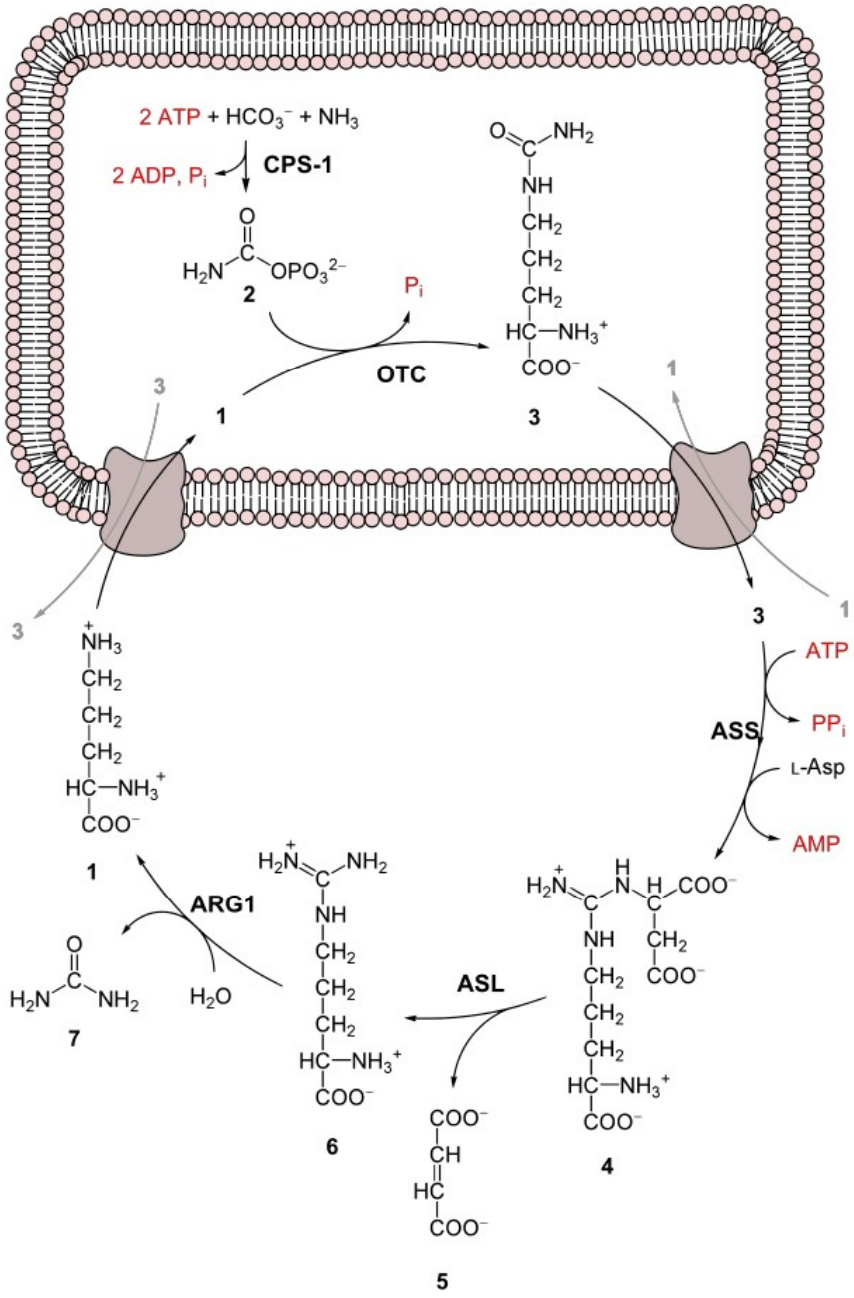
CPS-1 carbamoyl phosphate synthetase I

OTC ornithine transcarbamylase

ASS argininosuccinate synthetase

ASL argininosuccinate lyase

ARG1 Arginase 1



Yikrazuul - Own work by uploader; Mitochondrium angepasst aus Hoffis Bild

Arginine – Nitric Oxide

- Precursor to nitric oxide, helps to dilate and relax the blood vessels
- CV prevention. Helps with high BP, clogged arteries, angina, heart failure, coronary heart disease, erectile dysfunction
- Nitric oxide kills gram negative bacteria, viruses and fungi

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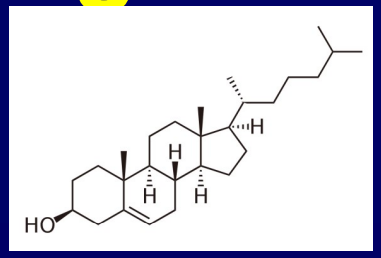
Arginine – the Cholesterol Fighter



Cholesterol Regulation

- Lowers blood cholesterol and inhibits fat absorption
- The higher the Arginine to Lysine ratio, the lower the cholesterol

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Arginine – "Lean and Mean"

- Helps to reduce body fat and increase lean muscle mass. It forms the building blocks of creatine, needed for making energy in the muscles.
- Lack of sperm and sterility

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Arginine

- Is glycogenic.
- Linked to manganese and aids utilization.
- Activates thymus gland.
- Schizophenics must avoid supplementation with arginine.

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Lower arginine levels seen in depressed patients

By Tim Cutcliffe

26-Feb-2018 - Last updated on 26-Feb-2018

Source: *Journal of Affective Disorders*
Volume 229, Pages 145–151. DOI: 10.1016/j.jad.2017.12.030
"Global arginine bioavailability ratio is decreased in patients with major depressive disorder"
Authors: Toni Ali-Sisto *et al*

Major depressive disorder (MDD) appears to be linked with lower levels of arginine bioavailability, a new report suggests.

Arginine is an amino acid that the body uses to produce nitric oxide. Decreased arginine bioavailability (for which global arginine bioavailability ratio (GABR) is a key biomarker), may result in impaired nitric oxide production. This may in turn increase oxidative stress and inflammation of the central nervous system (CNS), which is thought to be involved in MDD, explained the research team led by the University of Eastern Finland, Kuopio.

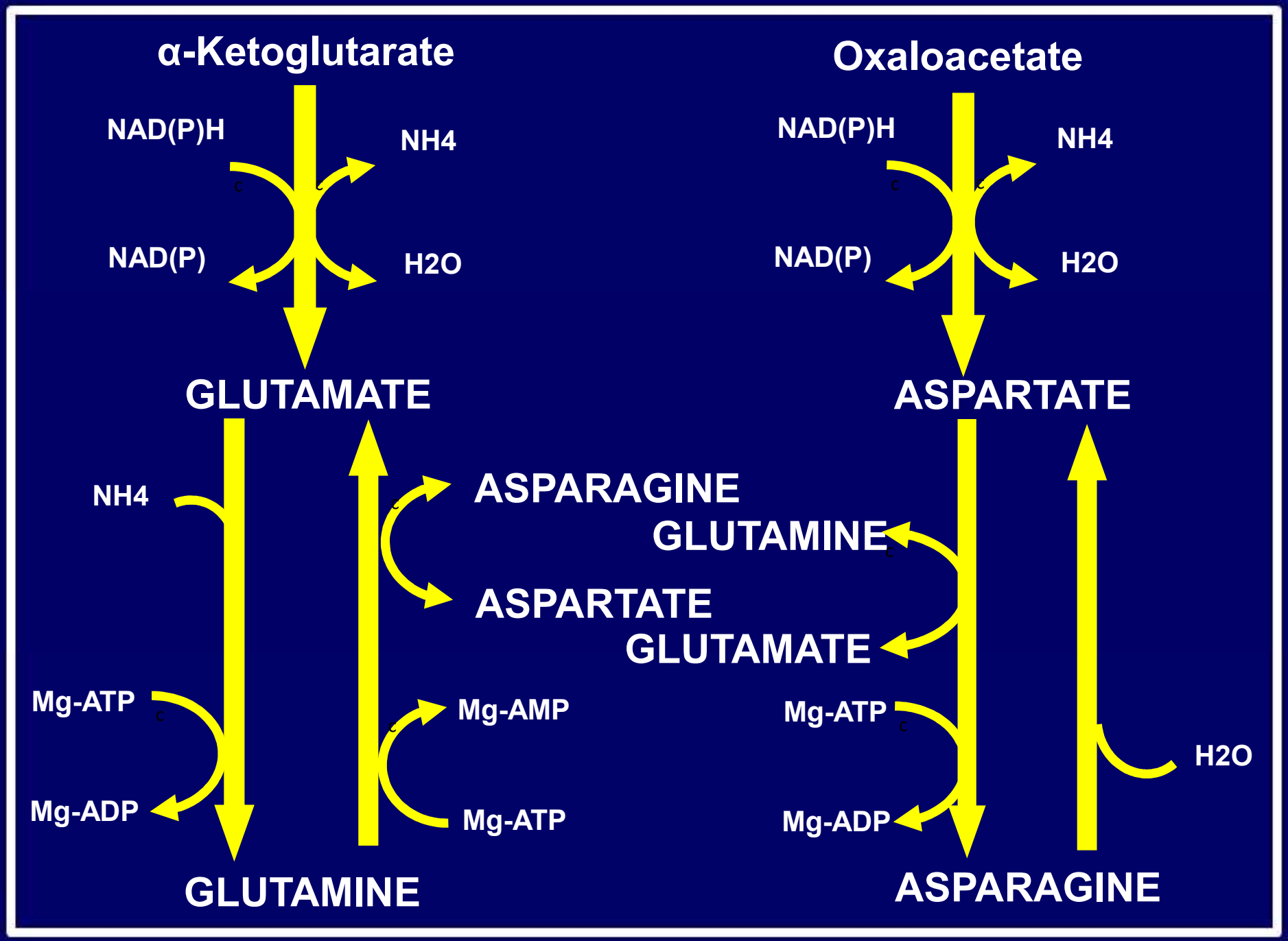
The scientists found that baseline levels of both serum arginine and GABR were lower in MDD patients than in non-depressed controls.

This relationship remained valid after adjusting for confounding variables including smoking, physical exercise, gender and age. The association was seen both in patients taking anti-depressants and those not on medication.

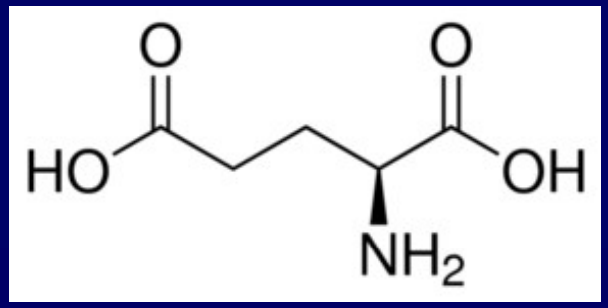
Contrary to the researchers' hypothesis, at follow-up, individuals who had achieved remission had only marginally higher levels of arginine bioavailability than those who remained depressed.

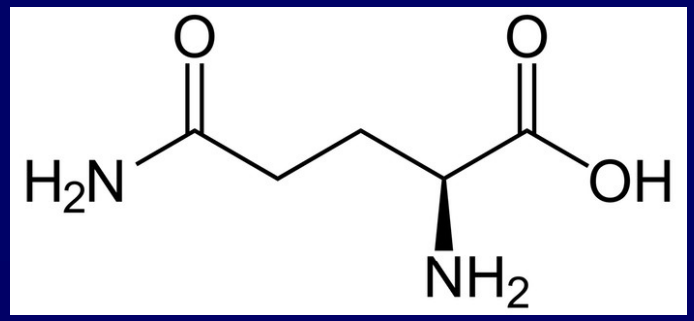
Glutamate Amino Acids

- Glutamic Acid
- Glutamine
- Proline
- Aspartic Acid
- Asparagine


α-Ketoglutarate
NAD(P)H
NH4
NAD(P)
H2O
GLUTAMATE
Oxaloacetate
NAD(P)H
NH4
NAD(P)
H2O
ASPARTATE
NH4
ASPARAGINE
GLUTAMINE
ASPARTATE
GLUTAMATE
Mg-ATP
Mg-ADP
Mg-AMP
Mg-ATP
Mg-ATP
Mg-ADP
H2O
GLUTAMINE
ASPARAGINE

Glutamic Acid & Glutamine – Brain





- GA made from alpha-ketoglutarate
- Glutamic Acid is an excitatory neurotransmitter
- High concentration in the brain, in cranial nerves and hippocampus
- Mental performance, alertness, attentiveness.

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Glutamic Acid + unpasterised butter

- Role transferring calcium to the bone and decalcifying the arteries
- GA is imported into the walls of the arteries where it binds to calcium and removes it from the blood vessels
- K2 (unpasteurised butter) integrates calcium into the bone

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Glutamic Acid & Glutamine – Brain

Glutamine

- Primary source of brain fuel
- Made from Glutamic Acid
- Mediator of GA and GABA activity, maintains balance in CNS
- Each molecule contains 2 nitrogen atoms, good for transporting nitrogen

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Glutamic Acid & Glutamine – Brain

Glutamine

- Role in DNA by contributing nitrogen in making of purines and pyrimidines.
- Denotes nitrogen to form niacin.
- Participates in metabolism of arginine.

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Glutamic Acid & Glutamine – Brain

Glutamine

- Helps clear ammonia from tissues, specially the brain.
- Role in metabolism of sugar and fats.
- Used to treat intestinal permeability.

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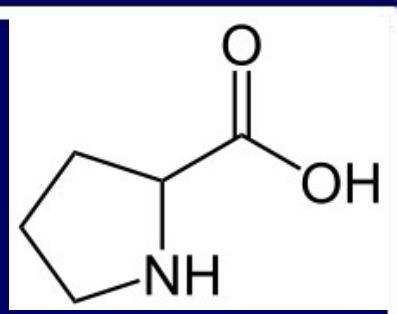
Proline – Collagen synthesis



- Proline and hydroxyproline are constituents of collagen.
- Healing wounds and cartilage, maintaining joints, tendons, ligaments.
- Maintaining strength of heart muscle.

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Proline – Collagen synthesis

- Made from the breakdown of glutamic acid
- Improves skin texture by making collagen and reducing the loss through the aging process

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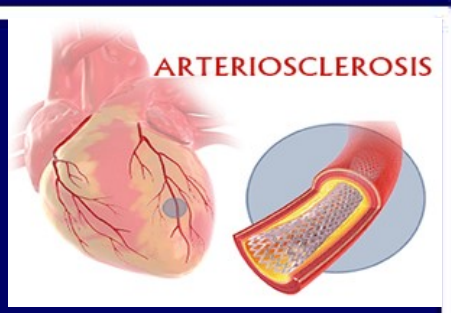
Proline



- Prevention of Arterioscelerosis
- Proline enables the walls of arteries to release fat build up into the bloodstream
- So decreasing the pressure built up by fatty blockages

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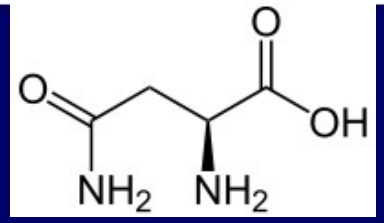
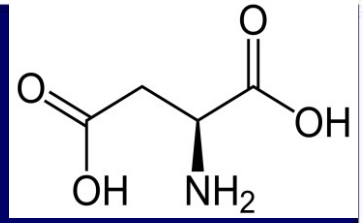
Aspartic acid & Asparagine - Energy





- 2 similar structures involved in generation and transport of energy
- Aspartic acid made from glutamate
- Asparagine made from Aspartic acid and ATP
- Asparagine combines with ammonia to form aspartic acid , reversible reaction

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Aspartic acid & Asparagine - Energy

- Asparagine maintains the balance between too much or too little stimulation in CNS

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Aspartic acid - Energy

- Krebs cycle, helps to activate the process by transporting energy into the mitochondria*
- In urea cycle – forms carbamyl phosphate, the key enzyme which starts the urea cycle**

*Amino acids Biochemistry and Nutrition by Guoyao Wu Pub CRC Press page 107

**Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page

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Aspartic acid - Energy

- Helps to move magnesium and potassium across the intestinal lining, which helps improve energy production in muscles
- Deficiency may lead to Chronic Fatigue Syndrome

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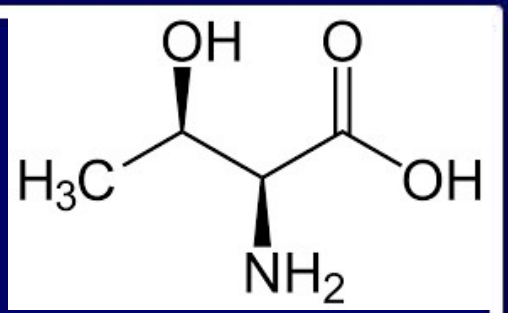
Threonine Amino Acids

- Threonine
- Glycine
- Serine
- Alanine

Threonine – the Immunity Booster



- Promotes the growth of the thymus, vital for immune defence
- Rats supplemented with threonine showed significant increase in thymus weight and increased immunoglobulin (IgA, IgE, IgG, IgM) response

Role of Nutrition in Health and Disease by W.E. Cornatzer, Pub Thomas. Page 73

Leon Chaitow "Thorsons Guide to Amino acids"

Threonine – the Immunity Booster

- Identified as protecting against mental instability and irritability
- Helps with digestion and improves intestinal absorption
- Helps to metabolise fats and controls fat build up in the liver

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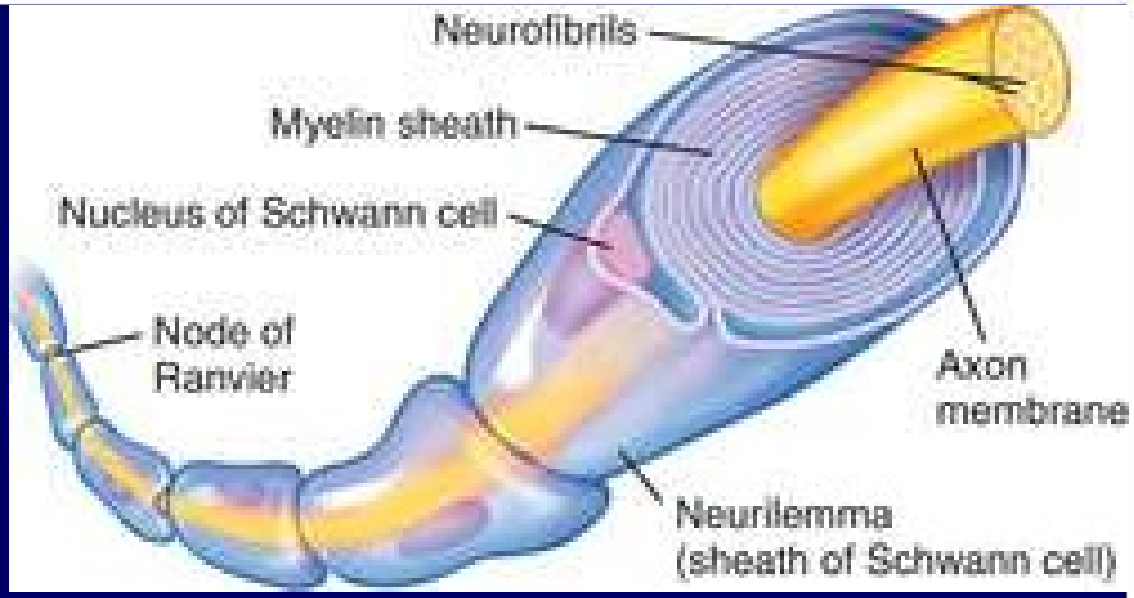
Threonine



- **Useful in treating CNS, studies shown to help MS as it helps build myelin.**

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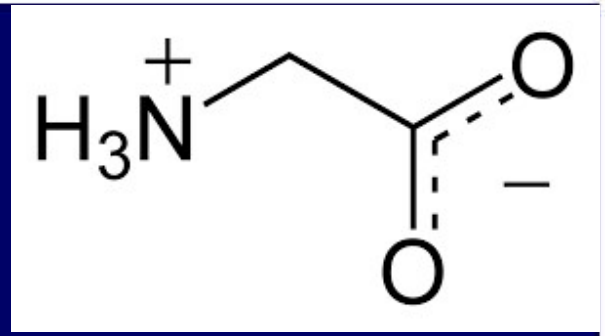
Glycine – collagen helper



- Derived from serine and threonine, also dimethylglycine
- Collagen contains glycine, proline and lysine
- Helps with storing energy, builds up glycogen levels
- Major inhibitory neurotransmitter

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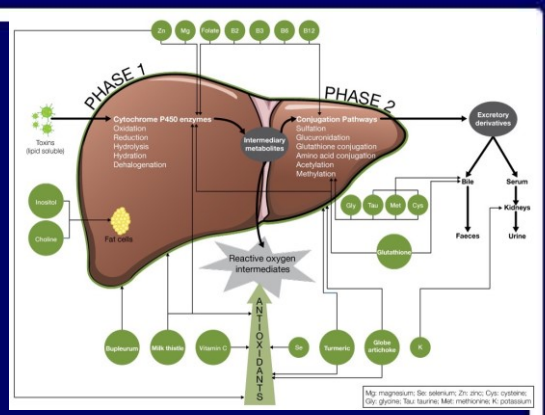
Glycine – detoxification



Detoxification

- Stimulates the production of glutathione
- Detoxifies benzoic acid
- Reduces levels of uric acid

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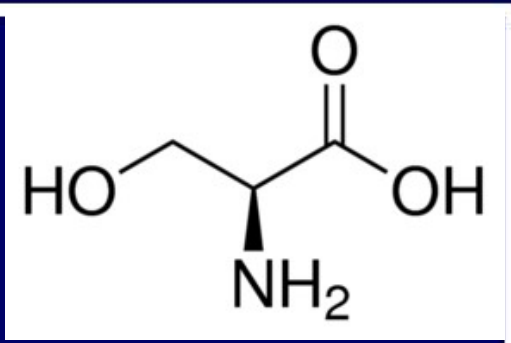
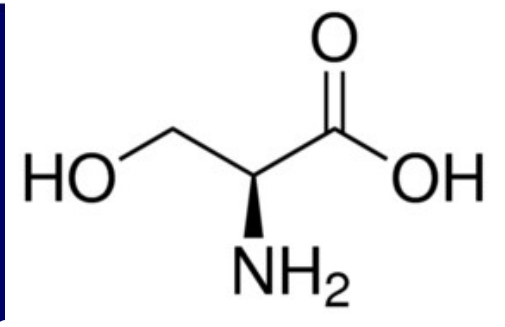
Serine - Memory



- Derived from threonine and glycine
- Phosphatidylserine – abundant in nerve cells and active throughout the brain, particularly the hippocampus
- Memory problems, learning problems, dementia, Alzheimer's

Serine - Memory



Role in Homocysteine and cysteine metabolism.

Catabolism of pyruvate

Formation of methylene tetrahydrofolate

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 269, 285, 537

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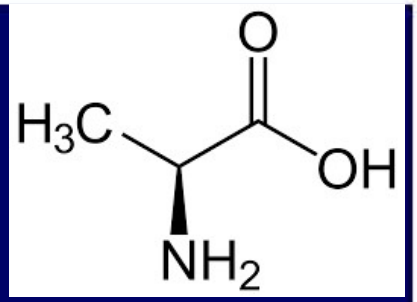
Alanine – the hypoglycaemia helper



- Good for glycemic control
- It can be converted quickly by the liver to usable glucose
- Regulation of blood sugar levels in hypoglycaemia and diabetes
- Triggers the release of the hormone glucagon, which releases glucose from the cell.

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Alanine – the hypoglycaemia helper

- Largely concentrated in the muscle
- One of most important amino acids released by muscles as a form of circulating energy
- Transports nitrogen from muscles to the liver and guards against the accumulation of toxins in aerobic exercise

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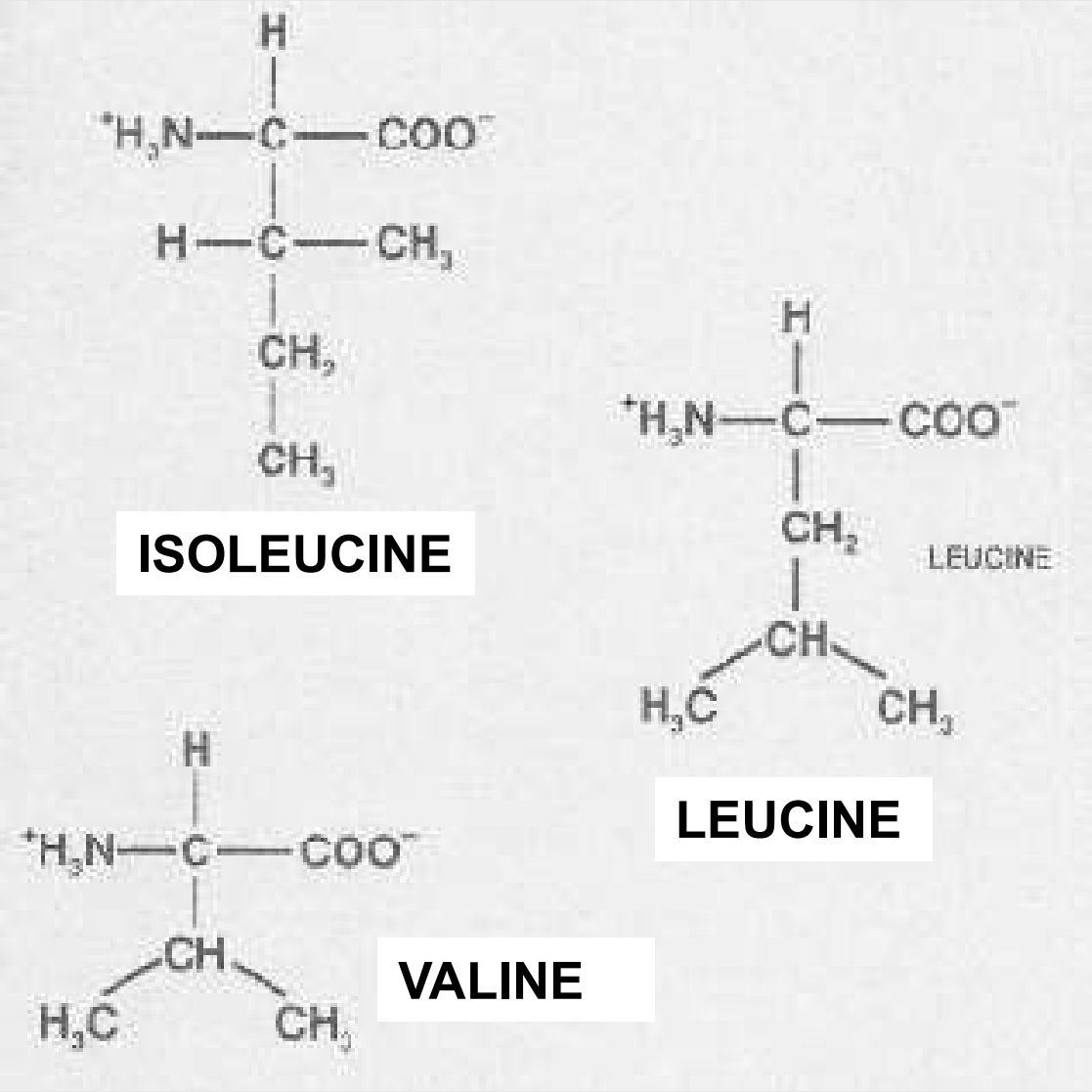
Branch Chain Amino Acid - Muscle



Branch Chain Amino Acid - Muscle

- Leucine, isoleucine, valine
- Protect muscle during stress or high energy states
- Act as a fuel for muscle building
- Repair muscle and prevent the breakdown of muscle
- Enhance energy and increase endurance

Sowers S. "A Primer On Branched Chain Amino Acids“ (PDF). Huntington College of Health Sciences. Retrieved 22 March 2011.

Branch Chain Amino Acid - Muscle

- When deficient, a “wearing out” syndrome, leading to decreased muscle mass and bone density
- Constituents of neuropeptides capable of producing a calming and pain relieving effect
- Enkephalins contain high amounts of leucine

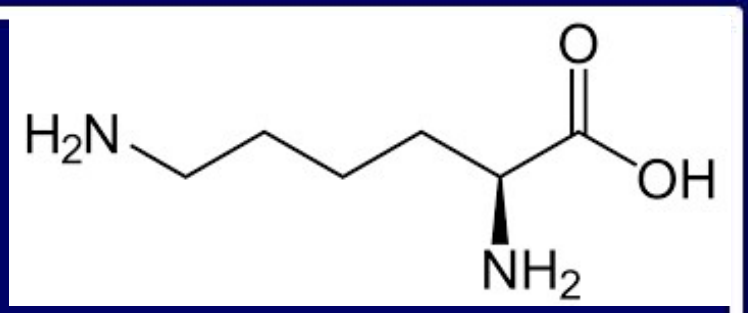
Monirujjaman M (2014). "Metabolic and Physiological Roles of Branched-Chain Amino Acids". *Advances in Molecular Biology*. 2014: 1–6

Branch Chain Amino Acid - Muscle

- Leucine stimulates insulin release. In muscles insulin stimulates protein synthesis and inhibits protein breakdown
- Valine deficiency causes neurological defects in brain
- Low Isoleucine - muscle tremors
- Decreased in liver disease

Monirujjaman M (2014). "Metabolic and Physiological Roles of Branched-Chain Amino Acids". *Advances in Molecular Biology*. 2014: 1–6

Lysine – Immunity, Herpes killer



- Proper growth & development in children
- Well known for fighting cold sores
- Broader immune-enhancing capabilities
- Increase growth of thymus
- Stimulate thymus factors, T & B cells

Lysine. The Biology Project, Department of Biochemistry and Molecular Biophysics, University of Arizona.

Lysine – Immunity, Herpes killer

- Lysine & Arginine share a common transport system – antagonistic
- Lysine is sacrificed in stressful situations, psychological and mental stress
- Antiviral effect by blocking the activity of arginine which promotes HSV replication

Lysine. The Biology Project, Department of Biochemistry and Molecular Biophysics, University of Arizona.

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Lysine v Arginine in HSV prevention

- Increase lysine foods and reduce foods high in arginine
- Foods high in arginine are: beer, peanuts, almonds, walnuts, wheat, soybeans, sunflower seeds, chocolate

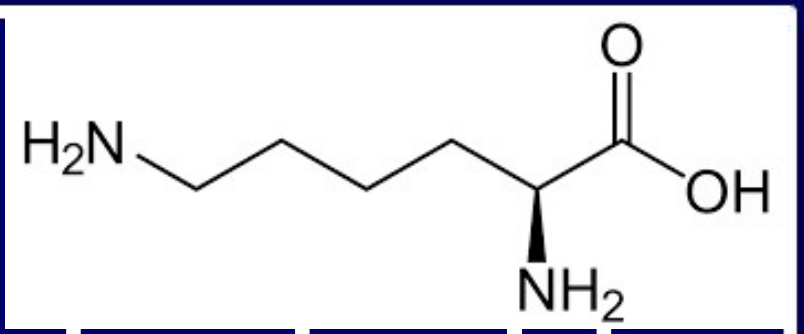
Leon Chaitow "Thorsons Guide to Amino acids" 46
Gaby AR (2006). "Natural remedies for Herpes simplex". *Altern Med Rev*. 11 (2): 93–101.

Lysine – Collagen builder

- Role in formation of collagen, made from Proline, Glycine, Lysine*
- Helpful in osteoporosis
- Studies suggest that lysine along with arginine make bone building cells more active and enhances collagen production

Leon Chaitow "Thorsons Guide to Amino acids" 46
*Shoulders MD, Raines RT (2009). "Collagen structure and stability". *Annual Review of Biochemistry*. 78: 929–58.

Lysine



- Lysine helps body absorb calcium and decreases the amount lost in urine

Produces Carnitine, responsible for converting fatty acids into energy and lowers cholesterol*

Leon Chaitow "Thorsons Guide to Amino acids" 46

*Vaz FM, Wanders RJ (February 2002). "Carnitine biosynthesis in mammals". *The Biochemical Journal*. 361 (Pt 3): 417–29.

Histidine – the Arthritis Fighter

- Low levels found in Rheumatoid Arthritis and arthritic synovial fluid
- Has been shown to have anti-inflammatory properties
- Regulation of growth and repair mechanisms so can lead to slow regeneration of tissue

Histidine

- Deficiency can lead to slow development in children
- Conversion to histamine, regulates the immune defence, response to allergic reactions*
- Methionine counteracts the formation of histamine from histidine

*Amino acids Biochemistry and Nutrition by Guoyao Wu Pub CRC Press page 178

Leon Chaitow "Thorsons Guide to Amino acids"

Histidine – the Arthritis Fighter

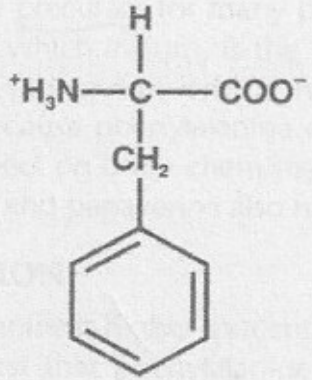
- Histamine – neurotransmitter, arousal*
- Can improve sexual functioning
- Stimulates the secretion of pepsin and hydrochloric acid
- Helpful in hypertension due to its vasodilatory effects

Leon Chaitow "Thorsons Guide to Amino acids" 41

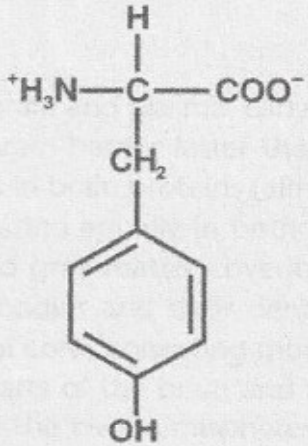
*Neurotransmitters and Drugs by Z. Kruk and C. Pycock. Pg 133

Aromatic Amino Acids

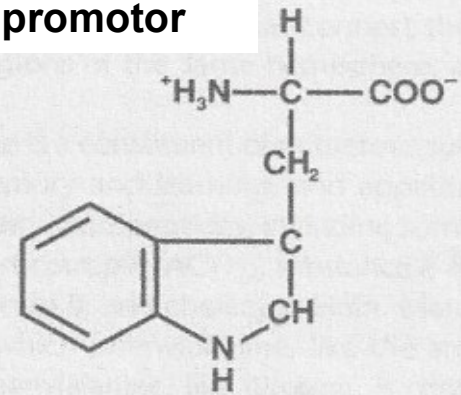
Phenylalanine
the pain reliever



Tyrosine
the addiction fighter



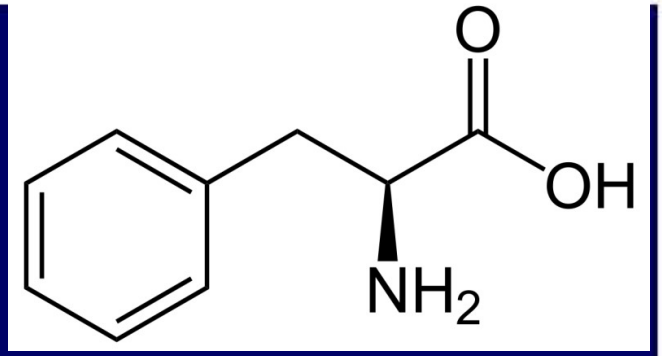
Tryptophan
the sleep promotor



Aromatic Amino Acids

- Aromatic ring in their structure
- Similar in structure and function to amphetamines
- Natural stimulants
- Phenylalanine
- Tyrosine
- Tryptophan

Phenylalanine – the Pain Reliever



- Constituent of numerous substances in the brain that affect mood, pain, memory, learning and appetite
- Blocks enzyme enkephalinase which breaks down endorphins and enkephalins

Leon Chaitow "Thorsons Guide to Amino acids" page 52
Role of Nutrition in Health and Disease by W.E. Cornatzer, Pub Thomas. Page

Phenylalanine – the Pain Reliever

- Studies have shown that beneficial in cases of osteoarthritis, RA, low back pain, joint pains, menstrual cramps, migraines
- Shown to curb cravings
- Decreased by drinking caffeine

Leon Chaitow "Thorsons Guide to Amino acids" page 52
Role of Nutrition in Health and Disease by W.E. Cornatzer, Pub Thomas. Page

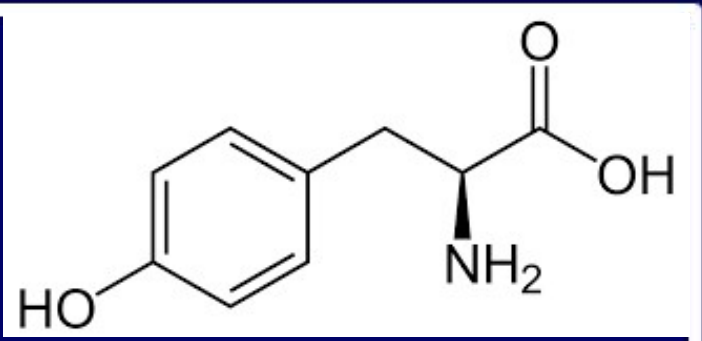
Phenylalanine – the Pain Reliever

- Precursor of tyrosine which produces dopamine, adrenaline and noradrenaline – promote alertness
- Useful for depression as raises noradrenaline
- Converted to phenylethylamine triggers the releases of endorphins

Leon Chaitow "Thorsons Guide to Amino acids" page 52

Role of Nutrition in Health and Disease by W.E. Cornatzer, Pub Thomas. Page

Tyrosine



- Precursor of thyroid hormones
- Precursor of melanin
- Precursor of neurotransmitters dopamine, noradrenaline and adrenaline*
- Reducing symptoms of carvings in addiction

Leon Chaitow "Thorsons Guide to Amino acids" page 73

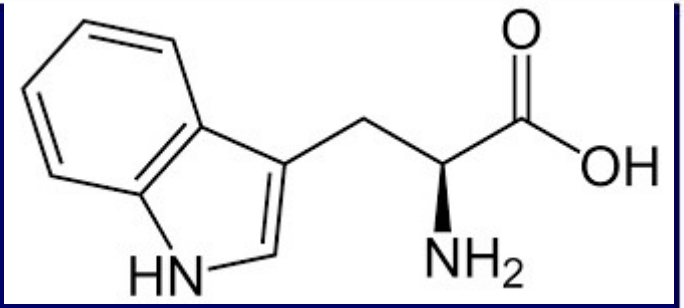
*Amino acids Biochemistry and Nutrition by Guoyao Wu Pub CRC Press page 179

Tyrosine

- Research at the University of Texas on using tyrosine to reduce cocaine and alcohol cravings
- As precursor to dopamine it supplies a reward, anti craving effect
- Fights stress because it is a precursor to adrenaline

Leon Chaitow "Thorsons Guide to Amino acids" page 73
*Amino acids Biochemistry and Nutrition by Guoyao Wu Pub CRC Press page 179

Tryptophan – the Feel Good Factor



- Converted into **serotonin** so lifts depression and restores emotional equilibrium
- Single most studied nutrient in psychiatric community
- Converts to **melatonin** promotes sleep

Leon Chaitow "Thorsons Guide to Amino acids" page 57
Role of Nutrition in Health and Disease by W.E. Cornatzer, Pub Thomas. Page 65

Tryptophan – the Feel Good Factor

- Serotonin helps to dampen the craving for carbohydrates that increase body fat
- Tryptophan inhibits insulin release, raises blood sugar and decreases appetite
- More of a calming than stimulatory effect, modified anti-amphetamine

Leon Chaitow "Thorsons Guide to Amino acids" page 57

Role of Nutrition in Health and Disease by W.E. Cornatzer, Pub Thomas. Page 65

5-Hydroxytryptophan (5-HTP),
also known as oxitriptan, is a naturally occurring amino acid and chemical precursor as well as a metabolic intermediate in the biosynthesis of the neurotransmitter serotonin.*

Leon Chaitow "Thorsons Guide to Amino acids" page 57

*Swiss Pharmaceutical Society (2000). *Index Nominum 2000: International Drug Directory (Book with CD-ROM)*. Boca Raton: Medpharm Scientific Publishers. ISBN 3-88763-075-0

TRYPTOPHAN

O_2

Inhibited by Co, DDT, Mn, Ni, Zn)

H4 Biopterin

tryptophan hydroxylase

(stimulated by Vit D, Cu, Fe, S)

D4 Biopterin

11p 384nm

NADH

Vit C

5-Hydroxytryptophan

Inhibited by high levels of CO2, Mg, Ca

CO_2

7p 380nm

5-hydroxytryptophane decarboxylase

P-5-P

Zn, Glutathione, Light

SEROTONIN

Summary of Amino Acid function

Sulphur Group	
Methionine	Methylation Detoxification
Cysteine	Detoxifier
Taurine	Heart, Brain, GB, eye, anxiety

Summary of Amino Acid function

Urea Amino acid	
Arginine	Urea cycle
	Nitric Oxide
	Cholesterol fighter
	"Lean and Mean"

Summary of Amino Acid function

Glutamate Group	
Glutamic Acid &	
Glutamine	Brain
Aspartic Acid &	
Asparagine	Energy
Proline	Collagen

Summary of Amino Acid function

Threonine Group

Threonine	Immunity Booster
Glycine	Collagen
Serine	Memory
Alanine	Hypoglycaemia

Summary of Amino Acid function

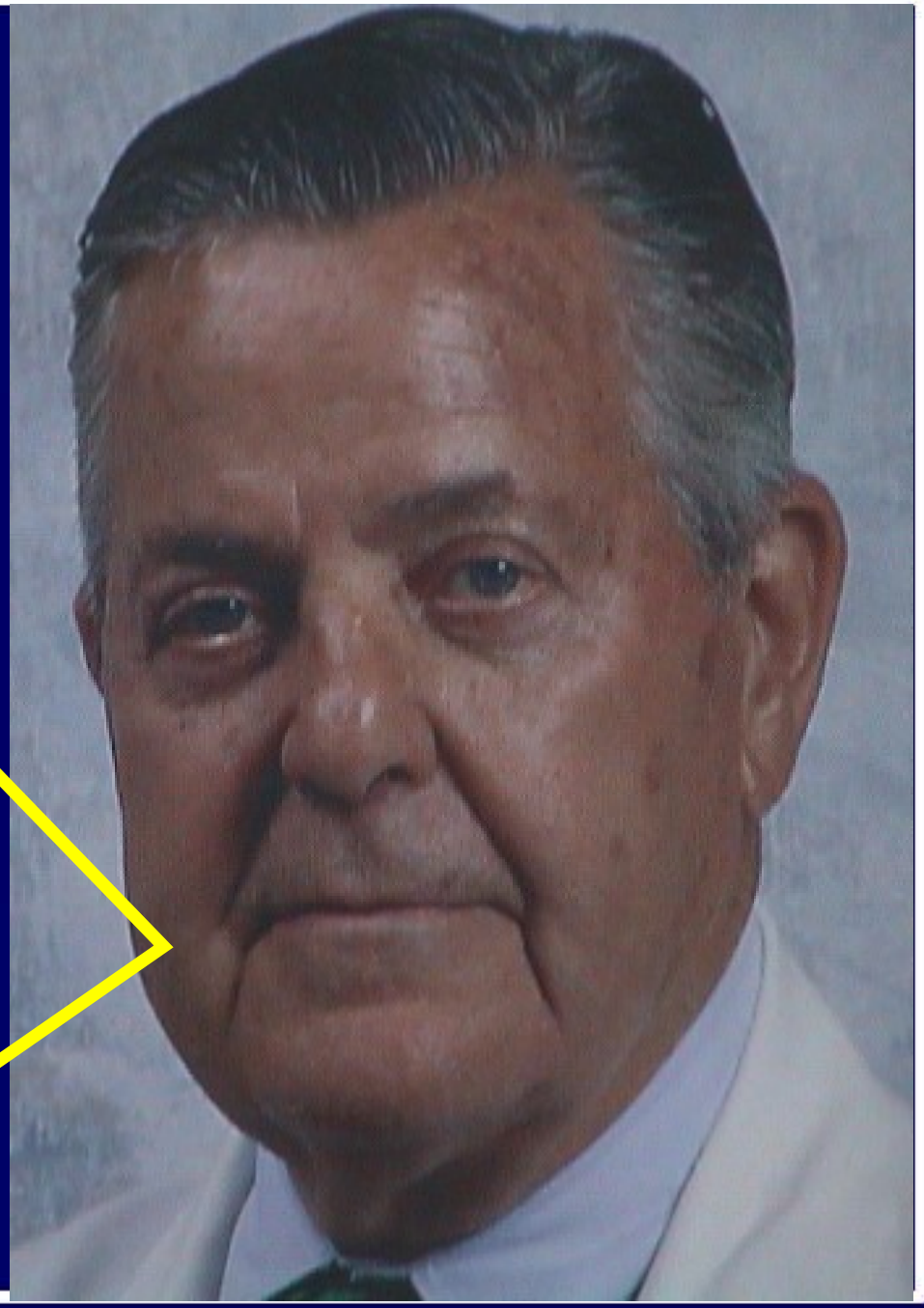
Branch Chain Amino Acids

Leucine, Isoleucine, Valine Muscle

Lysine	HSV, Immunity Collagen
Histidine	Arthritis fighter Histamine

Dr Goodheart says use branched chain amino acids 1 hour before aerobic exercise. 3mg per Kg body weight.

Cortisol peaks at 7am to 9am and 7pm to 9pm whilst exercising. Do not exercise at these times without branched chain amino acid support.



Summary of Amino Acid function

Aromatic Amino Acids

Phenylalanine	Pain reliever
Tyrosine	Thyroid
Tryptophan	Feel good factor

Essential Amino Acid

Histidine
Isoleucine
Leucine
Lysine
Methionine
Phenylalanine
Threonine
Tryptophan
Valine

Non-Essential Amino Acid

Alanine
Arginine
Asparagine
Aspartic Acid
Cysteine
Glutamic Acid
Glutamine
Glycine
Proline
Serine
Tyrosine
Taurine

Table 26-2 Essential and Nonessential Amino Acids in Humans.

Essential	Nonessential
Arginine[a]	Alanine
Histidine	Asparagine
Isoleucine	Aspartate
Leucine	Cysteine
Lysine	Glutamate
Methionine	Glutamine
Phenylalanine	Glycine
Threonine	Proline
Tryptophan	Serine
Valine	Tyrosine

[a]Although mammals synthesize arginine, they cleave most of it to form urea (Sections 26-2D and 26-2E).

Non-proteinogenic Amino Acids

N. Acetylcysteine (NAC)

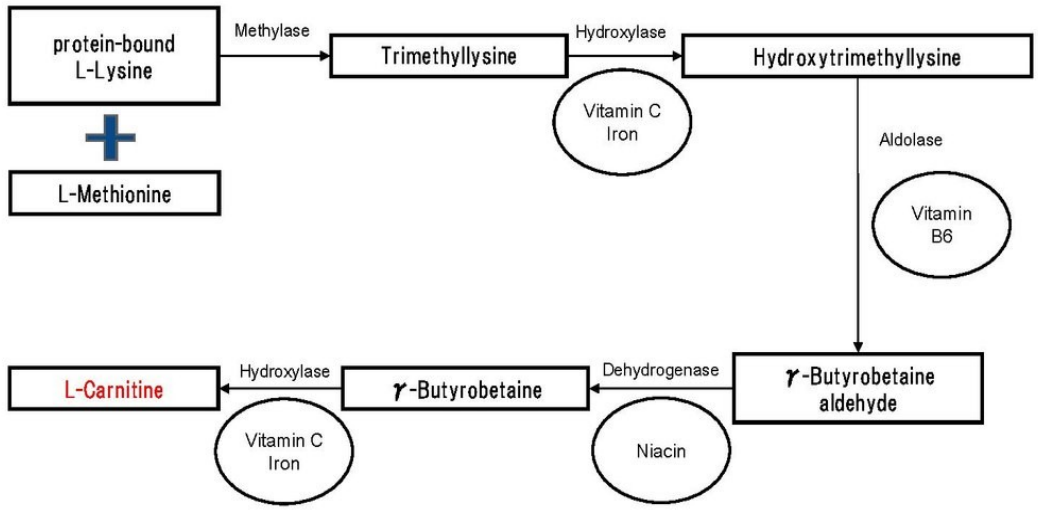
may activate detoxification via -

1. Glutathione
2. Acetylation
3. Sulfation
4. Cysteine

"Acetylcysteine" The American Society of Health-System Pharmacists. Archived from the original on 23 September 2015. Retrieved 22 August 2015.

Carnitine

Used in the Carnitine Shuffle.



Leon Chaitow "Thorsons Guide to Amino acids" page 72
"*Acetyl-L-carnitine. Monograph"(PDF). *Alternative Medicine Review*. 15 (1): 76–83. April 2010.

N. Acetylcarnitine

an acetylated form of L-carnitine. It is naturally produced by the body, although it is often taken as a dietary supplement. Acetylcarnitine is broken down in the blood
by plasma esterases to carnitine which is used by the body to transport fatty acids into
the mitochondria for breakdown.*

"*Acetyl-L-carnitine. Monograph"(PDF). *Alternative Medicine Review*. 15 (1): 76–83. April 2010.

Ornithine is a non-proteinogenic amino acid that plays a role in the urea cycle. Ornithine is abnormally accumulated in the body in ornithine transcarbamylase deficiency. Ornithine transcarbamylase deficiency is the most common urea cycle disorder in humans. It is an inherited disorder which causes toxic levels of ammonia to build up in the blood.*

**"Ornithing transcarbamylase deficiency". United States National Library of Medicine. 22 May 2018.*

Leon Chaitow "Thorsons Guide to Amino acids" page 83

The Urea Cycle

1. L-ornithine
2. carbamoyl phosphate
3. L-citrulline
4. argininosuccinate
5. fumarate
6. L-arginine
7. urea

L-Asp L-aspartate

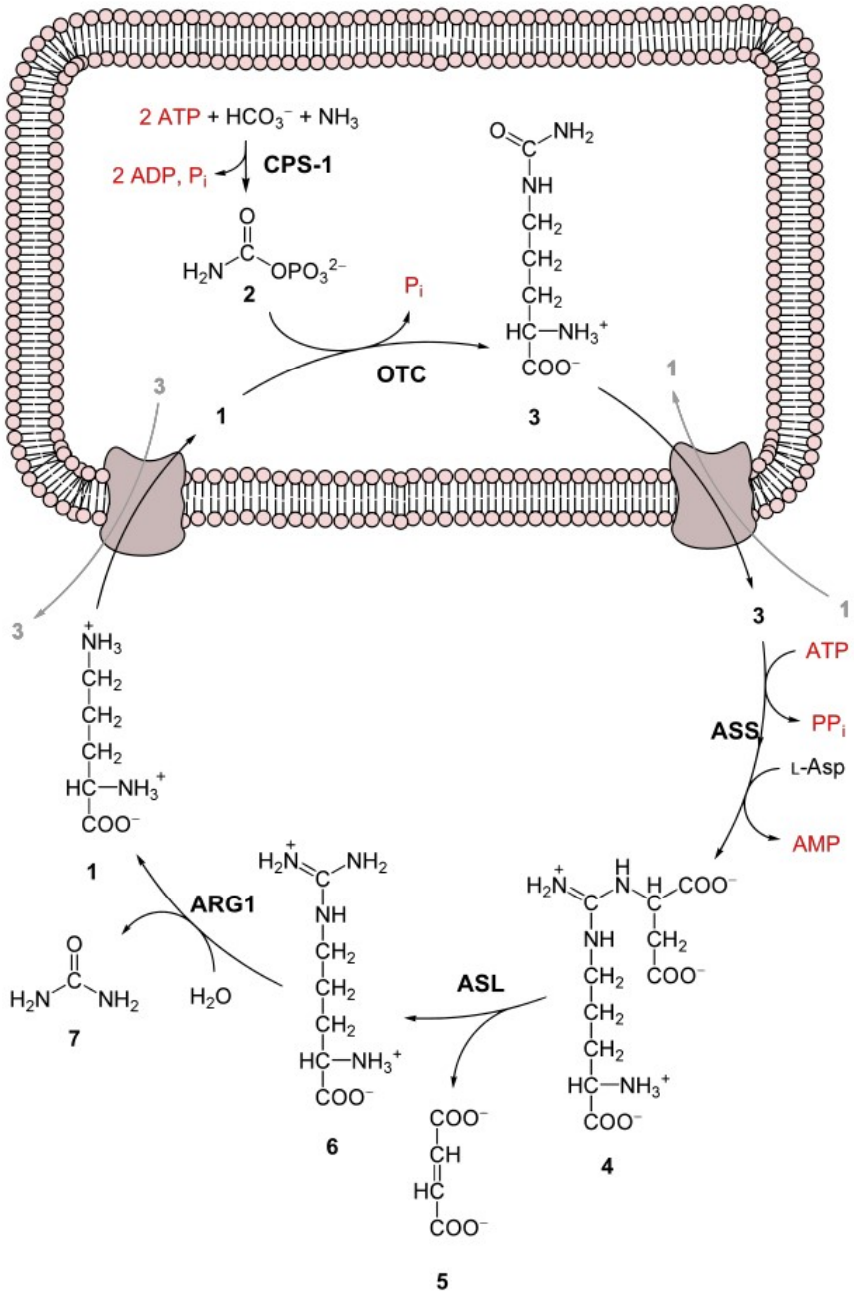
CPS-1 carbamoyl phosphate synthetase I

OTC ornithine transcarbamylase

ASS argininosuccinate synthetase

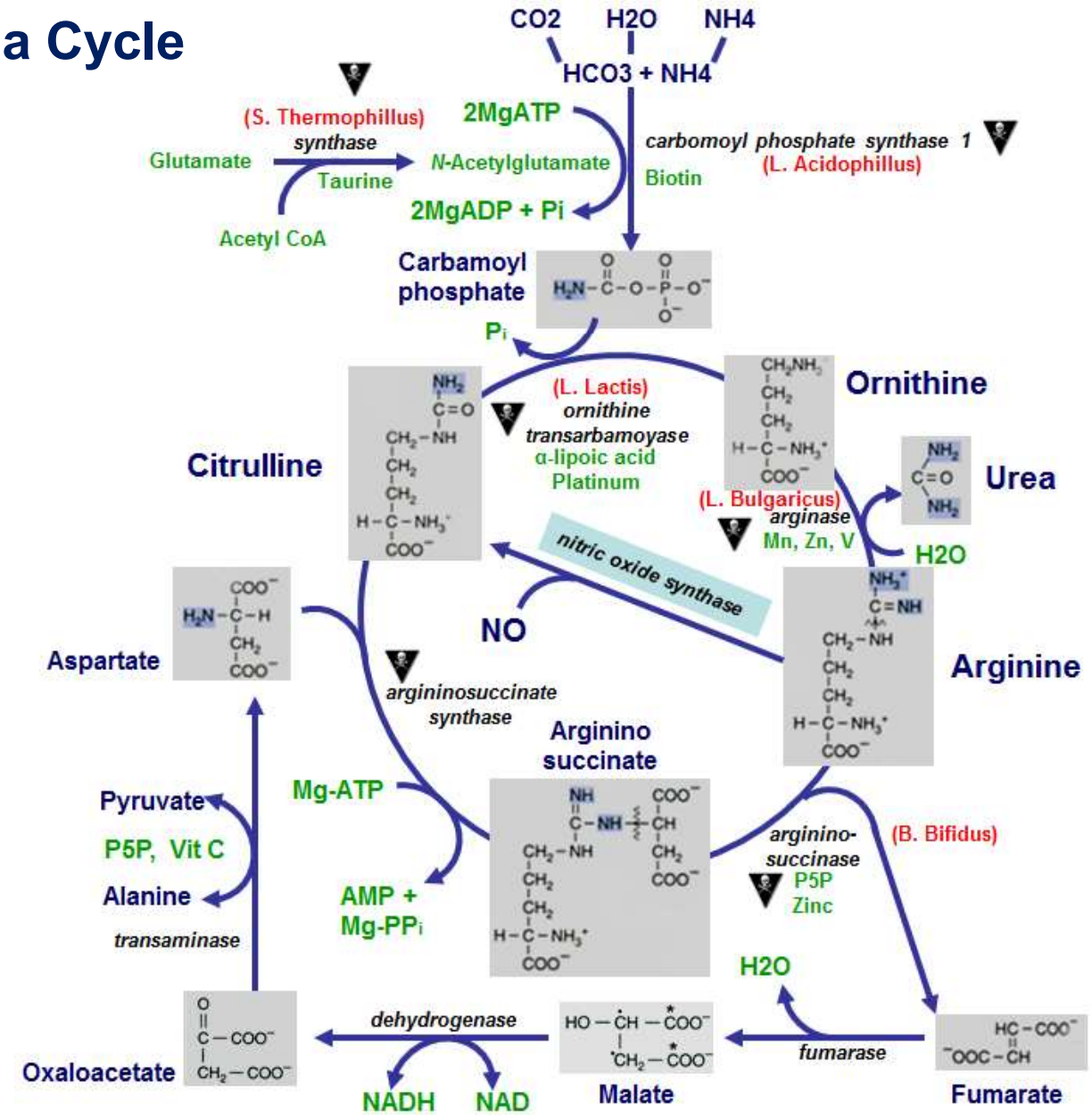
ASL argininosuccinate lyase

ARG1 Arginase 1



Yikrazuul - Own work by uploader; Mitochondrium angepasst aus Hoffis Bild

The Urea Cycle



Citrulline is a key intermediate in the urea cycle, the pathway by which mammals
excrete ammonia by converting it into urea. It is also produced as a by product of the enzymatic production of nitric oxide from arginine, catalyzed by nitric oxide synthase*

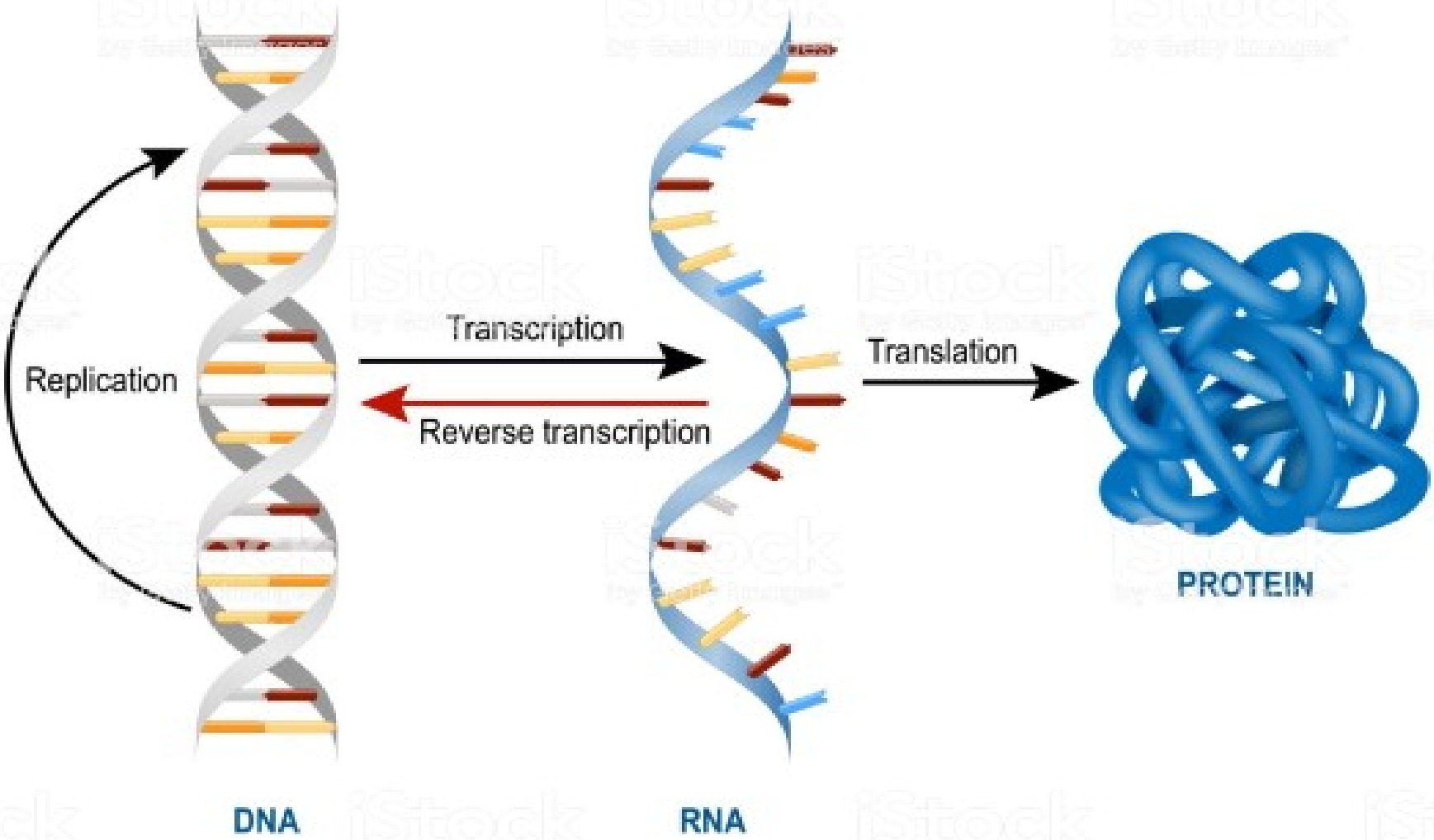
"*Nos2 - Nitric Oxide Synthase". *Uniprot.org*. Uniprot Consortium. Retrieved 10 February 2015.

S-Adenosyl Methionine (SAMe) is a common cosubstrate involved in methyl group transfers, transsulfuration. Most SAM-e is produced and consumed in the liver.* More than 40 methyl transfers from SAM-e are known, to various substrates.

*Cantoni, GL (1952). "The Nature of the Active Methyl Donor Formed Enzymatically from L-Methionine and Adenosinetriphosphate". *J Am Chem Soc*. 74 (11): 2942–3.

Phenotype
v
Genotype

Transcription and Translation



When examining **health issues** there are two aspects to consider

1. Phenotype- how genes express themselves to repair, regenerate and maintain health and wellness.
2. Genotype- What you were conceived with from your parents genome. Your constitution.

My Family Tree

Name.....

My Grandfather
Illnesses
Current age Died aged

My Grandmother
Illnesses
Current age Died aged

My Grandfather
Illnesses
Current age Died aged

My Grandmother
Illnesses
Current age Died aged

My Uncle
Illnesses
Current age

My Uncle
Illnesses
Current age

My Father
Illnesses
Current age Died aged

My Mother
Illnesses
Current age Died aged

My Aunt
Illnesses
Current age

My Aunt
Illnesses
Current age

My Brother / Sister
Illnesses
Current age

Me
Illnesses
Current age

My Brother / Sister
Illnesses
Current age

The function of the nucleus, that contains the genes is to store the blueprints for tissue repair.

Genes encode for protein synthesis.

Enzymes are proteins but not all proteins are enzymes. There are 6953 known enzymes to date.

Basically the DNA, is a giant ocean. It has six billion bases (that is, six billion letters) that define the genetic code for all of the genes and producing, basically, what you are. The gene part of it—the part that actually winds up encoding for RNAs and later encode for proteins—is really only a few percent, probably on the order of about one-and-a-half percent of the genome encodes genes that make proteins, and a little bit more encodes RNAs that don't make proteins.

Michael Snyder, PhD Functional Medicine Update Oct 2013

It's still a very small fraction of the giant ocean of DNA that's in our genome. One of the things that has become clear over the last 10 years or so as people started looking at this DNA that was not coding proteins, people have come to realize that it does have a lot of other things. It has, first of all, a lot of regulatory RNAs, so genes that encode regulatory RNAs. But perhaps most surprising is it has a lot of the control elements— the regulatory sequences, or switches that control the expression of our genes.

Michael Snyder, PhD Functional Medicine Update Oct 2013

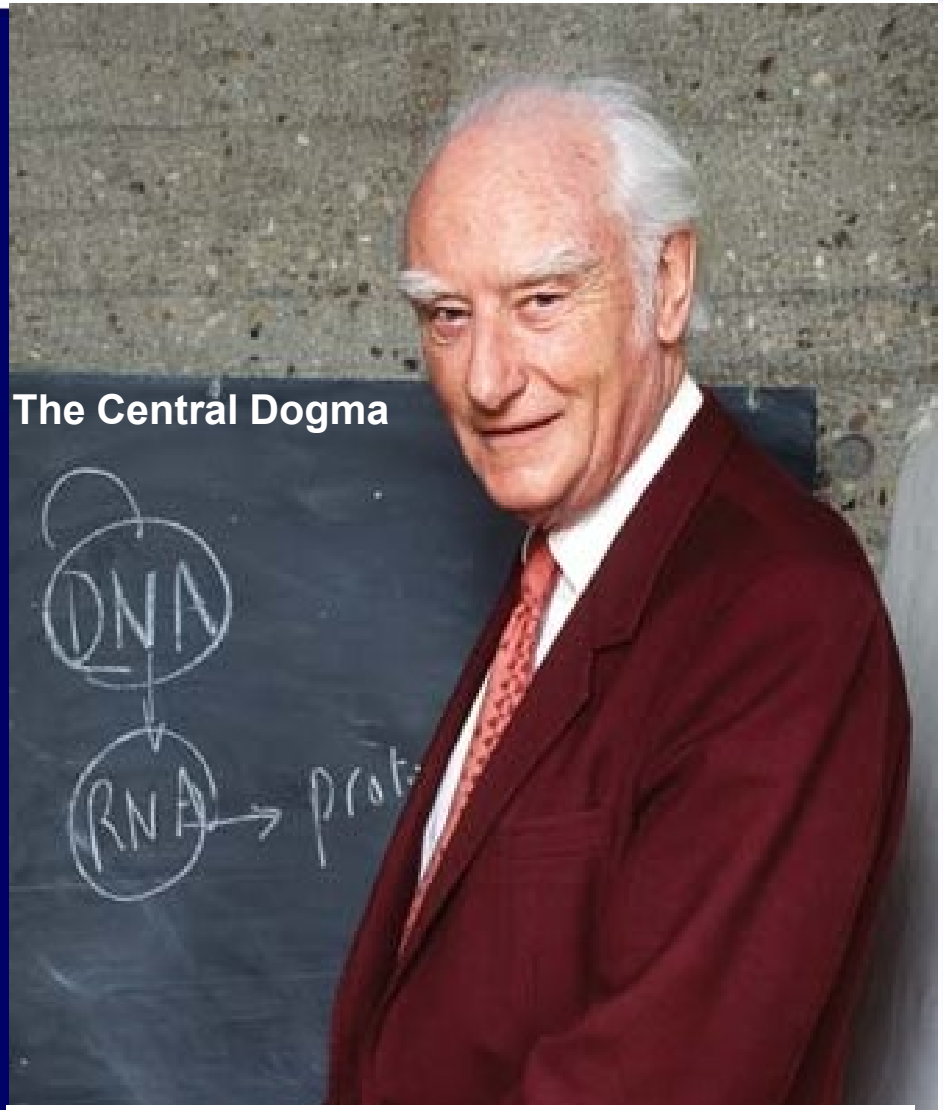
The amount of information that controls the gene is probably more than the gene itself. So the switches that decide when genes are turned on or turned off or how much of a gene is expressed in each tissue are really just getting mapped out now, although there is a long ways to go.

Michael Snyder, PhD Functional Medicine Update Oct 2013

These switches are important because a lot of the things that make people different…it's not the genes themselves, but it's the control sequences for the genes and it's something we really need to understand in order to be able to understand why people are different from one another, and actually why we're even different from our most closely related species. The difference between chimpanzees and humans, in fact, is mostly due to gene regulation more than to the genes themselves.

Michael Snyder, PhD Functional Medicine Update Oct 2013

Francis Crick was the first person to propose the Central Dogma. It is the foundation pillar of molecular genetics.



Crick, F.H.C. (1958). "On Protein Synthesis". In F.K. Sanders. *Symposia of the Society for Experimental Biology, Number XII: The Biological Replication of Macromolecules*. Cambridge University Press. pp. 138–163.

The character of an organism was thus thought to be pre-programmed in its DNA.

Hence the concept of "Genetic Determinism". (fate is pre-programmed from the moment of conception!)
We would be thus victims of our heredity.

Biology of Belief by Bruce Lipton

The Human Genome project 1987-2001

Thought that for every protein in the human body you need a gene.

There are over 100,000 proteins in the human body and so it was thought there must be over 100,000 genes (+ regulatory DNA genes 20-40,000).

Biology of Belief by Bruce Lipton

The results showed that humans only have 25,000 genes, little more than fruit flies. Expectations were that as an organism evolves there would be greater numbers of genes.

Biology of Belief by Bruce Lipton

The nucleus was thought to be the brain of the cell.
But over 100 years ago experiments were performed which showed that genes did not control life. De-nucleating cells were shown to continue living quite satisfactorily for many months until either injured, starved or toxified. (environmental change)

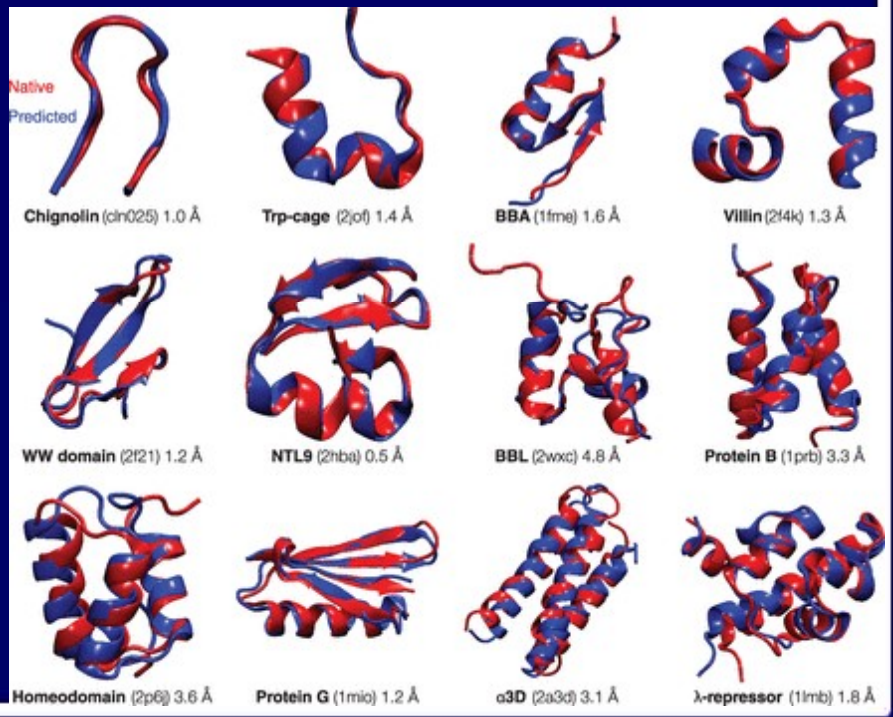
Biology of Belief by Bruce Lipton

What is it that controls life if it is not the nucleus (DNA)?

Stem cells have the same DNA but can mature into different kinds of cells depending upon the environment that they are in.

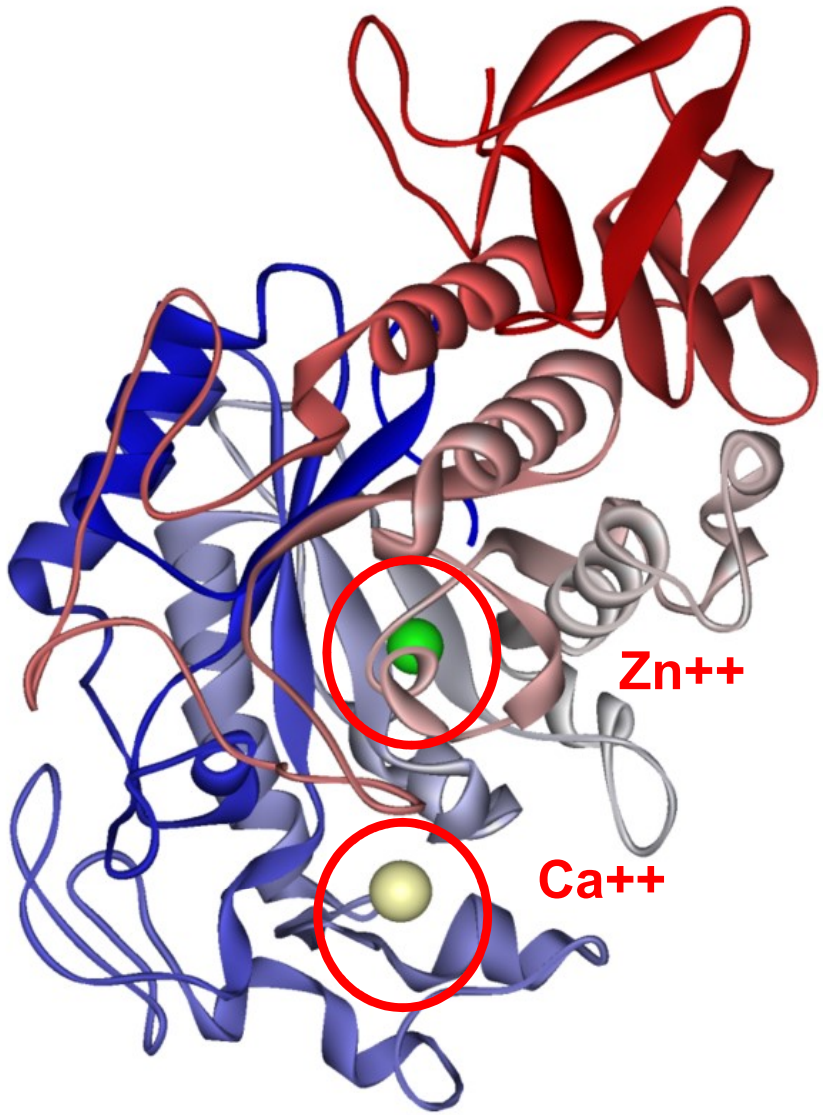
Biology of Belief by Bruce Lipton

Proteins are linear molecules but when synthesised the protein folds up into complex shapes which is due to a balancing of the positive and negative charges on the amino acids of the protein.



Biology of Belief by Bruce Lipton

Amylase (Calcium dependent)



Ramasubbu N, Paloth V, Luo Y, Brayer GD, Levine MJ (May 1996). "Structure of human salivary alpha-amylase at 1.6 A resolution: implications for its role in the oral cavity". *Acta Crystallographica D*. 52 (Pt 3): 435–46. doi10.1107/S0907444995014119 PMID 15299664.

Proteins are made of amino acids

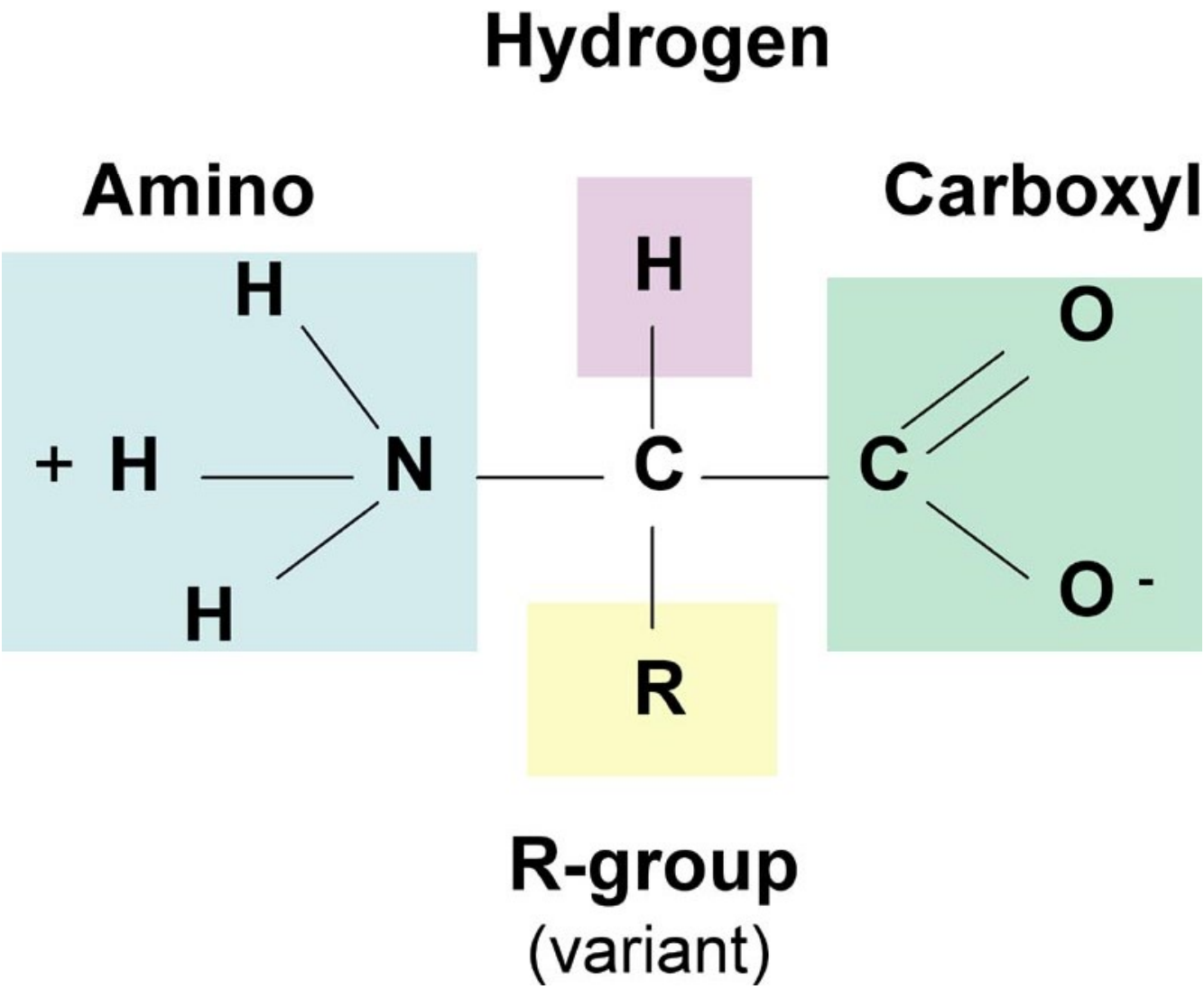
1. Build tissues
2. Transport molecules
3. Form antibodies
4. Form enzymes
5. Build chemical messengers i.e. hormones and neurotransmitters

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 17

Amino acids are biologically important organic compounds composed of amine (-NH_2) and carboxylic acid (-COOH) functional groups, along with a side-chain specific to each amino acid. The key elements of an amino acid are carbon, hysrogen, oxygen and nitrogen.

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 18

Amino Acid Structure



Small

Glycine (Gly, G)
MW: 57.05

Alanine (Ala, A)
MW: 71.09

Nucleophilic

Serine (Ser, S)
MW: 87.08, pK_a ~ 16

Threonine (Thr, T)
MW: 101.11, pK_a ~ 16

Cysteine (Cys, C)
MW: 103.15, pK_a = 8.35

Hydrophobic

Valine (Val, V)
MW: 99.14

Leucine (Leu, L)
MW: 113.16

Isoleucine (Ile, I)
MW: 113.16

Methionine (Met, M)
MW: 131.19

Proline (Pro, P)
MW: 97.12

Aromatic

Phenylalanine (Phe, F)
MW: 147.18

Tyrosine (Tyr, Y)
MW: 163.18

Tryptophan (Trp, W)
MW: 186.21

Acidic

Aspartic Acid (Asp, D)
MW: 115.09, pK_a = 3.9

Glutamic Acid (Glu, E)
MW: 129.12, pK_a = 4.07

Amide

Asparagine (Asn, N)
MW: 114.11

Glutamine (Gln, Q)
MW: 128.14

Basic

Histidine (His, H)
MW: 137.14, pK_a = 6.04

Lysine (Lys, K)
MW: 128.17, pK_a = 10.79

Arginine (Arg, R)
MW: 156.19, pK_a = 12.48

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 18

Citrulline

Ornithine

Taurine

B-Alanine

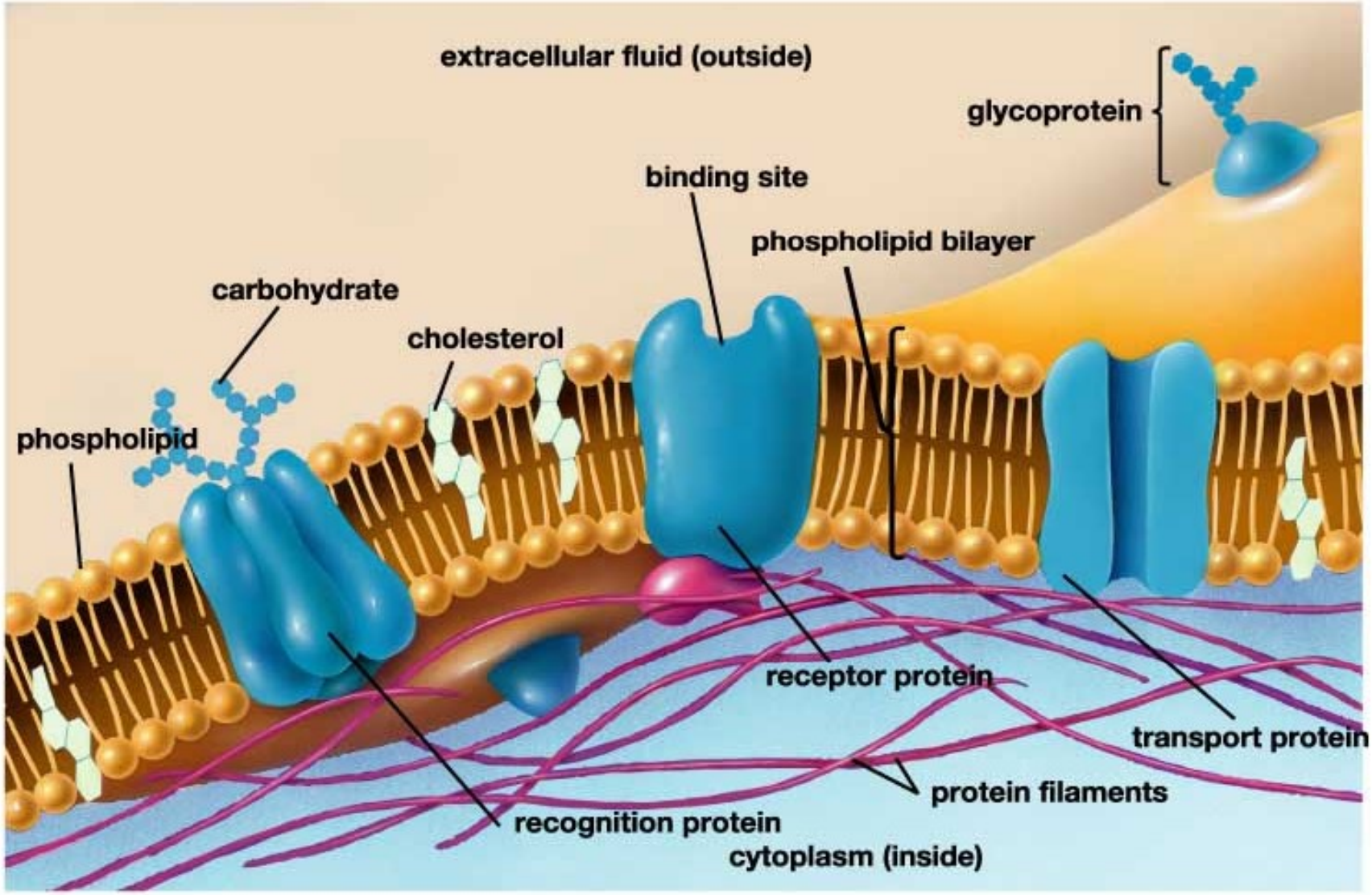
Selenocysteine is an alpha amino acid found in proteins from every domain of life. A selenium atom replaces the sulfur of its structural analog, cysteine.
It is thus referred to as the 21st amino acid.

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 18

Essential			Nonessential		
Histidine	N 90%,	Hydrophobic	Alanine	N	Hydrophobic
Isoleucine	N	Hydrophobic	Arginine	+ve	Hydrophilic
Leucine	N	Hydrophobic	Asparagine	N	Hydrophilic
Lysine	+ve	Hydrophilic	Aspartic acid	–ve	Hydrophilic
Methionine	N	Hydrophobic	Cysteine	N	Hydrophobic
Phenylalanine	N	Hydrophobic	Glutamic acid	–ve	Hydrophilic
Threonine	N	Hydrophilic	Glutamine	N	Hydrophilic
Tryptophan	N	Hydrophobic	Glycine	N	Hydrophobic
Valine	N	Hydrophobic	Ornithine		
			Proline	N	Hydrophobic
			Selenocysteine		
			Serine	N	Hydrophilic
			Tyrosine	N	Hydrophilic

Left brain weakness give hydrophilic
Right brain weakness give hydrophobic

Being a Family Doctor by George Goodheart and Walther H. Schmitt published by Lance West DC


extracellular fluid (outside)
glycoprotein
binding site
phospholipid bilayer
carbohydrate
cholesterol
phospholipid
receptor protein
transport protein
protein filaments
recognition protein
cytoplasm (inside)

When a protein changes shape it performs movement i.e. as it changes from Conformation A to Conformation B. This movement is harnessed by the cell to carry out functions such as digestion, respiration, muscle contraction etc.

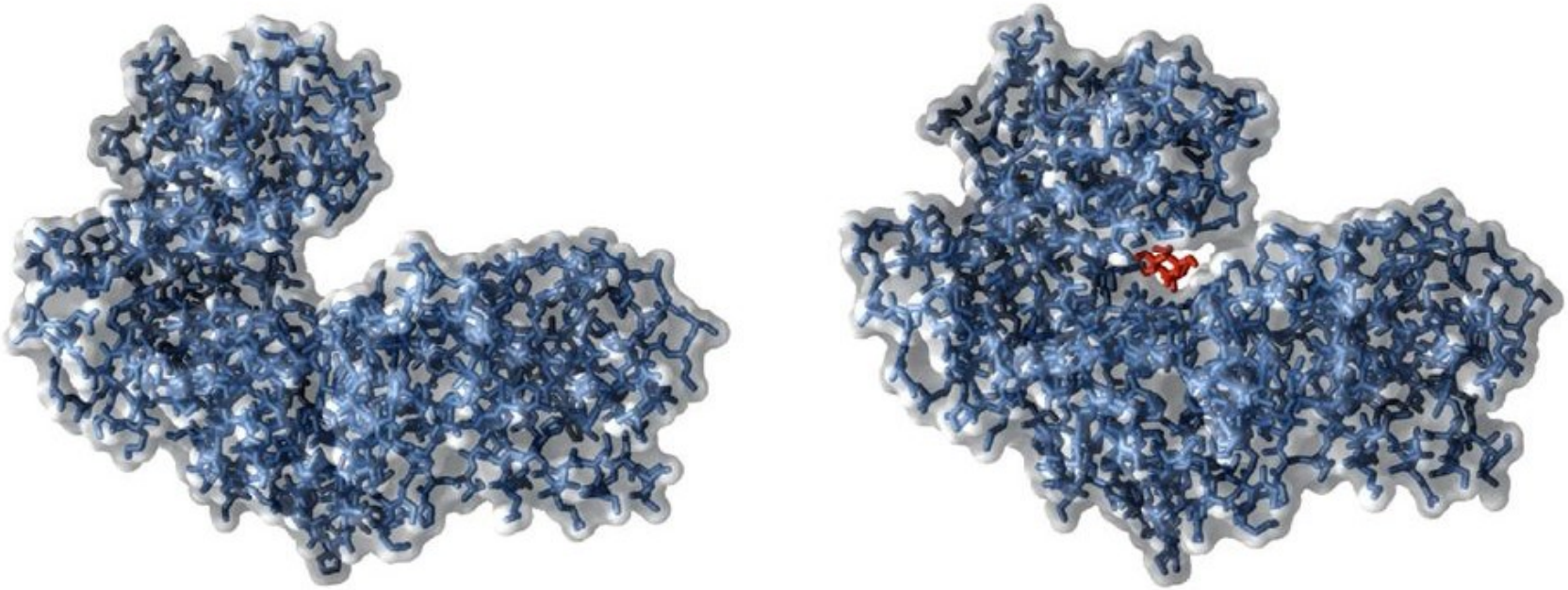
Compare a human cadaver to a living human. Life is movement.

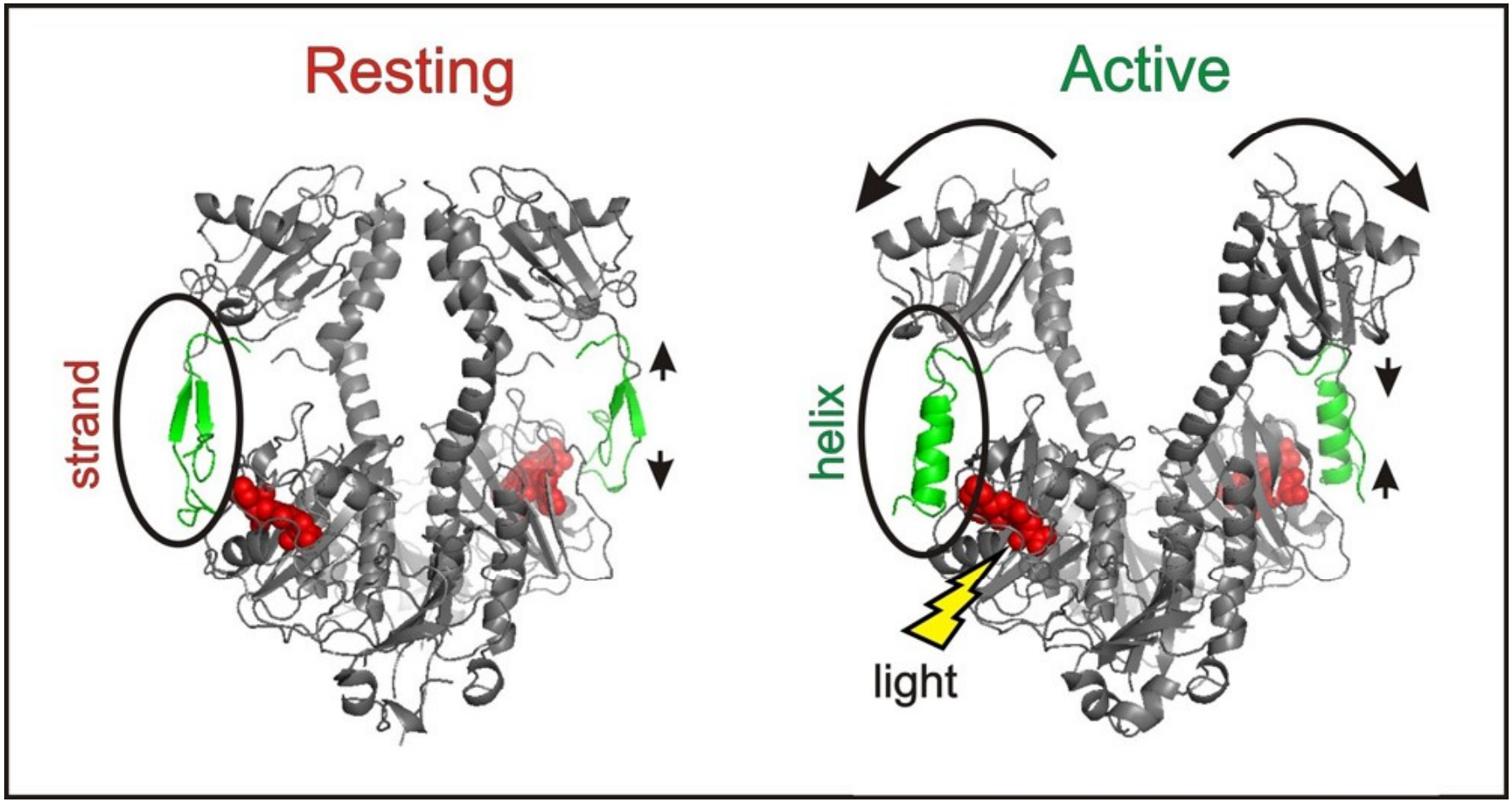
Biology of Belief by Bruce Lipton

Conformation A Conformation B

Example

Hexokinase undergoes a conformational change on binding glucose (induced fit)




Resting
strand
Active
helix
light

What makes a protein change shape is called a signal. A signal may be a particle (drugs, hormones, growth factors etc) or an energy (such as light (e.g. acetates), sound, EM waves (e.g biomarker vials), thoughts). Normal shape of a protein is when all the positive and negative charges are balanced.

Biology of Belief by Bruce Lipton

These proteins have little clefts on their surfaces that can plug into signals.

So the protein can be like a **baseball glove** and the signal is like the baseball.

So the signal has to have the precise shape to fit into the glove and the right charge so it can attach.

Biology of Belief by Bruce Lipton

This changes the charge and thus the protein conformation. So the movement can be used to drive work which creates functions e.g. a digestive enzyme and a food particle. The movement crushes the food particle. If a number of fragments are inserted into the glove then synthesise will occur.

Biology of Belief by Bruce Lipton

Genes provide the blueprint of the protein but the life of the protein is determined by the signal.

Thus two parts to life – the physical part (protein) and the signal part that controls the movement.

Behaviour is thus dependant on the proteins and the signals.

Biology of Belief by Bruce Lipton

Disease is a defect in the behaviour of the proteins and the signals.

< 5% is due to defects in the protein from birth defects (but more as we age)

95+% is due to defects in the signal.

Biology of Belief by Bruce Lipton

Only 3 ways that a signal can cause a dysfunction in the protein mechanism

1. Trauma by affecting the nervous system
2. Interference of the signals by toxicity
3. We send the wrong signal at an inappropriate time by inappropriate behaviours. From the mind.

Biology of Belief by Bruce Lipton

Mechanics

Toxicity

Toxic metals
Chemicals
    Environment
    Foods
Radiation

Biology of Belief by Bruce Lipton

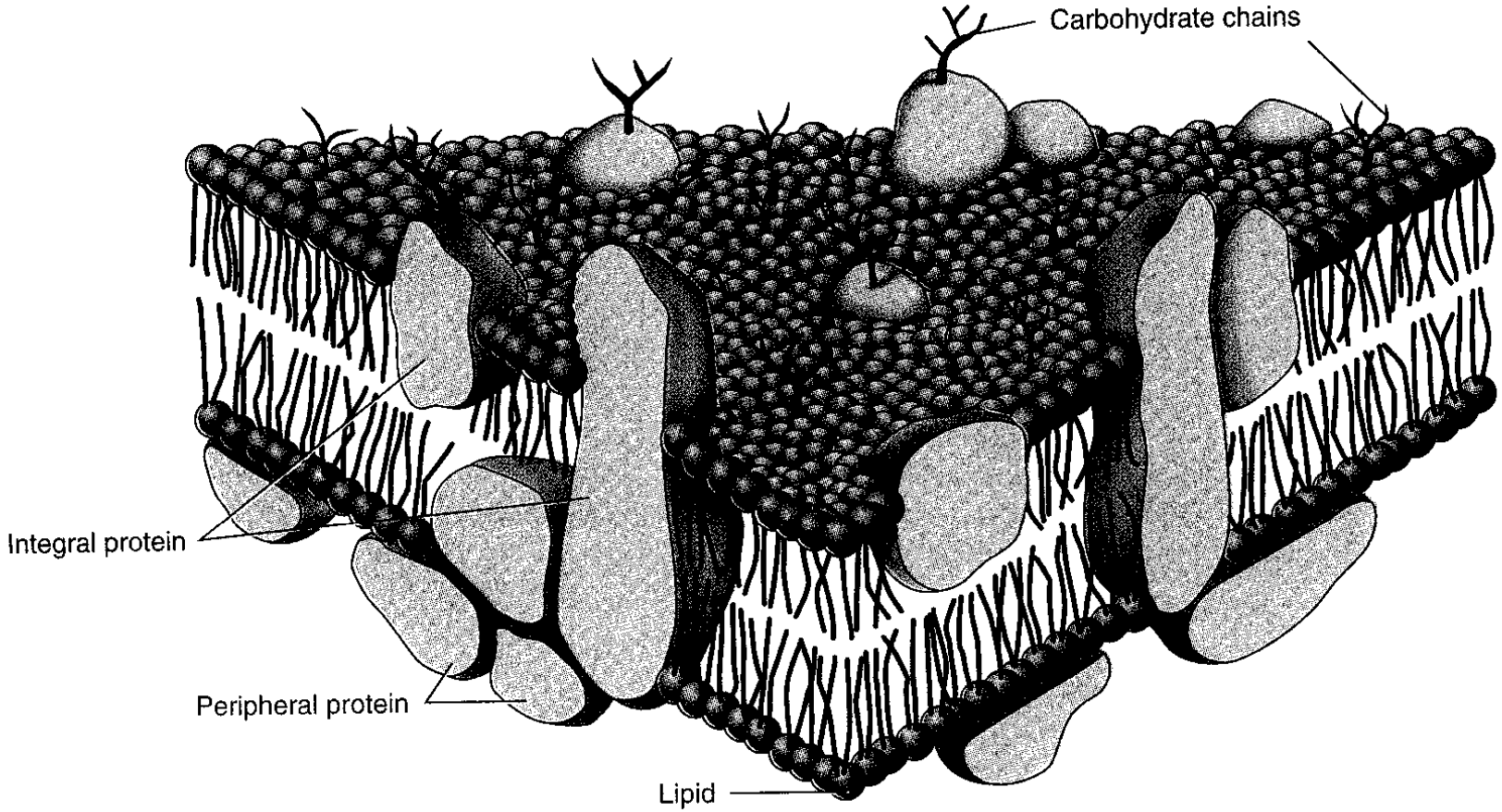
Wrong signal from the mind e.g. Anorexia nervosa

Biology of Belief by Bruce Lipton

The proteins are on the inside of the cell. The signals come from the environment.
The cell membrane or skin contains protein receptor sites many of which pass through the cell membrane.

Biology of Belief by Bruce Lipton

Cell Membranes



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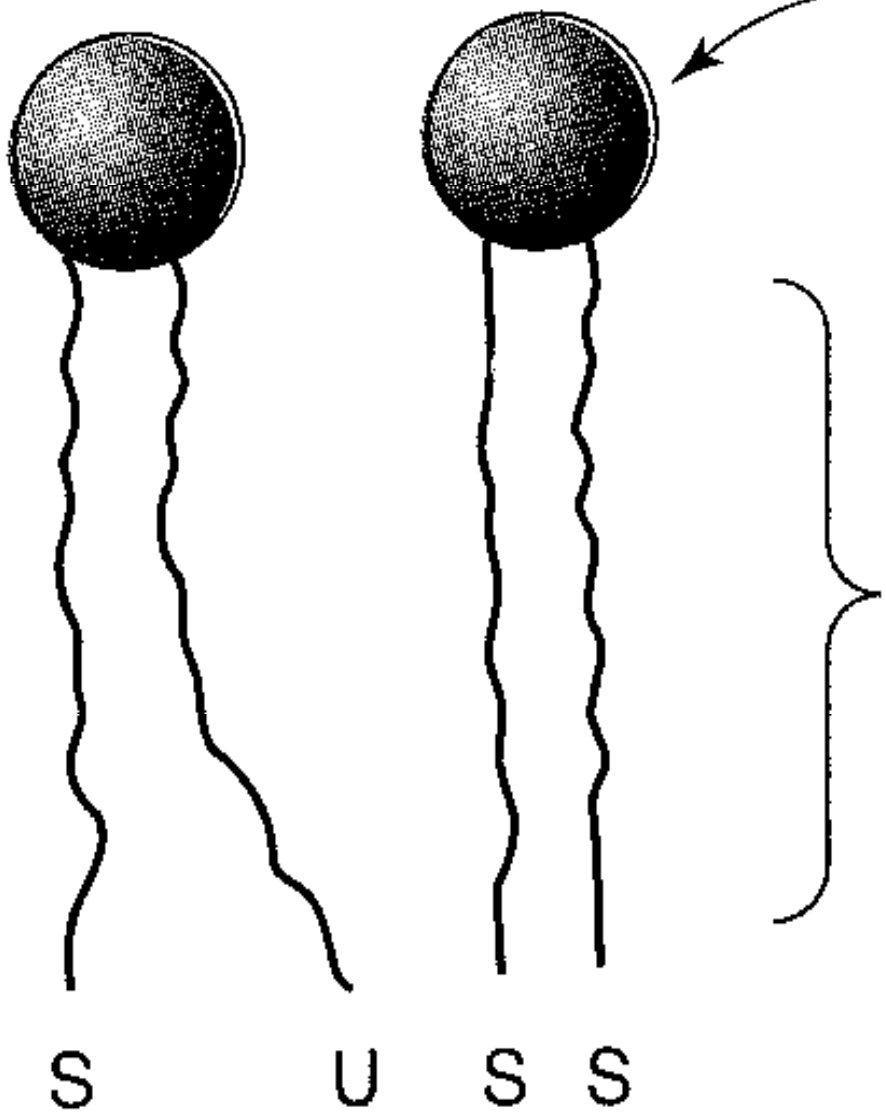
A Phospholipid



Polar head group

(hydrophilic)

Apolar, hydrocarbon tails

(hydrophobic)

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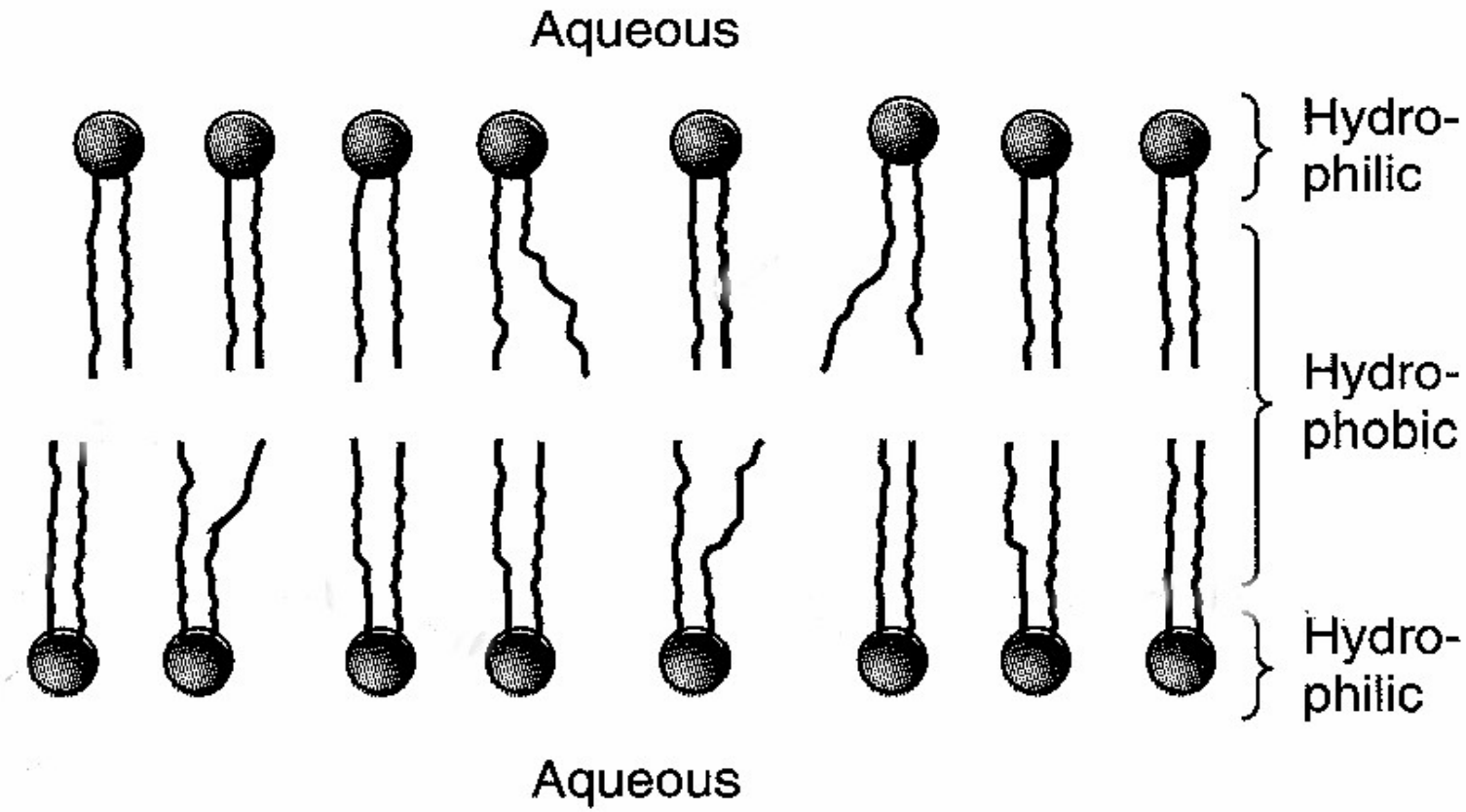
The unsaturated fatty acid tails are kinked and lead to more spacing between the polar heads and hence more movement.



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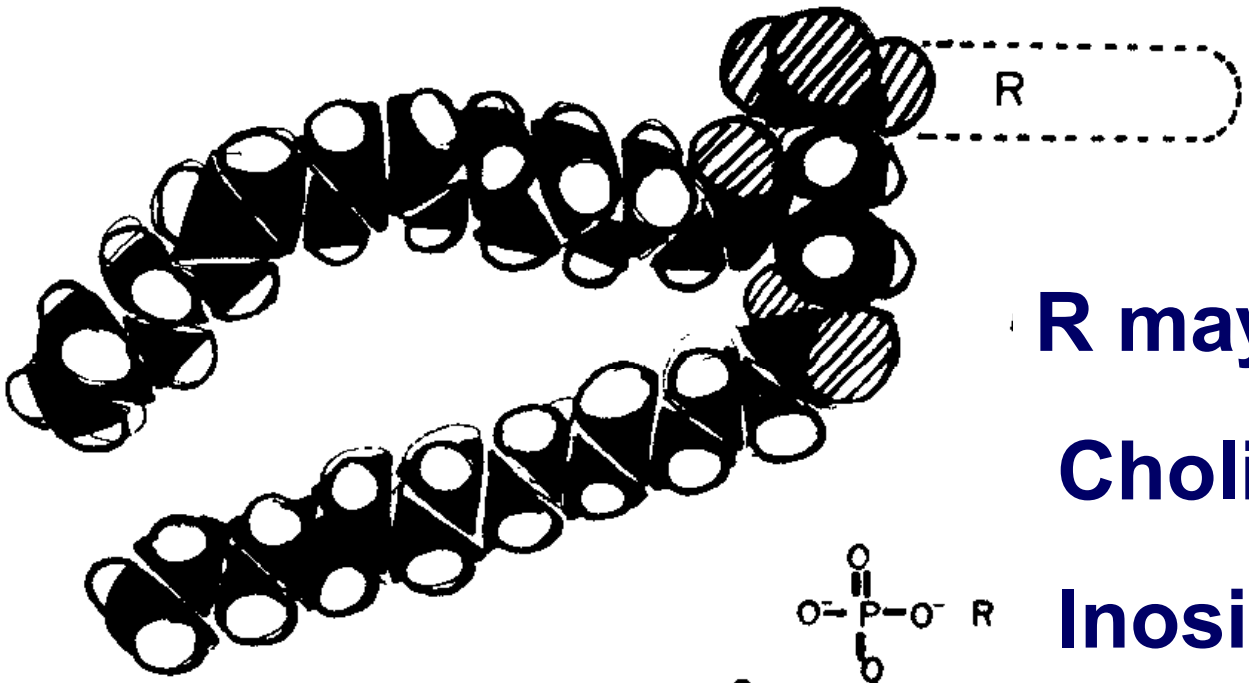

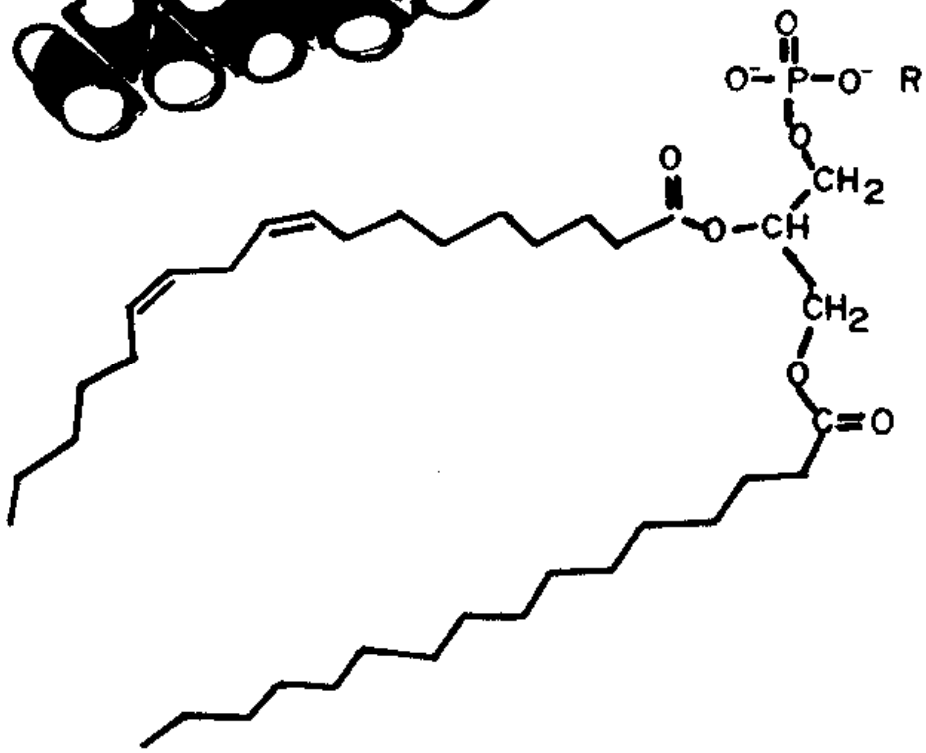

R maybe

Choline

Inositol

Ethanolamine

Serine

Threonine

The integral cell membrane proteins act as a conduit to allow nutrients to get into the cell from outside and waste products to be eliminated.

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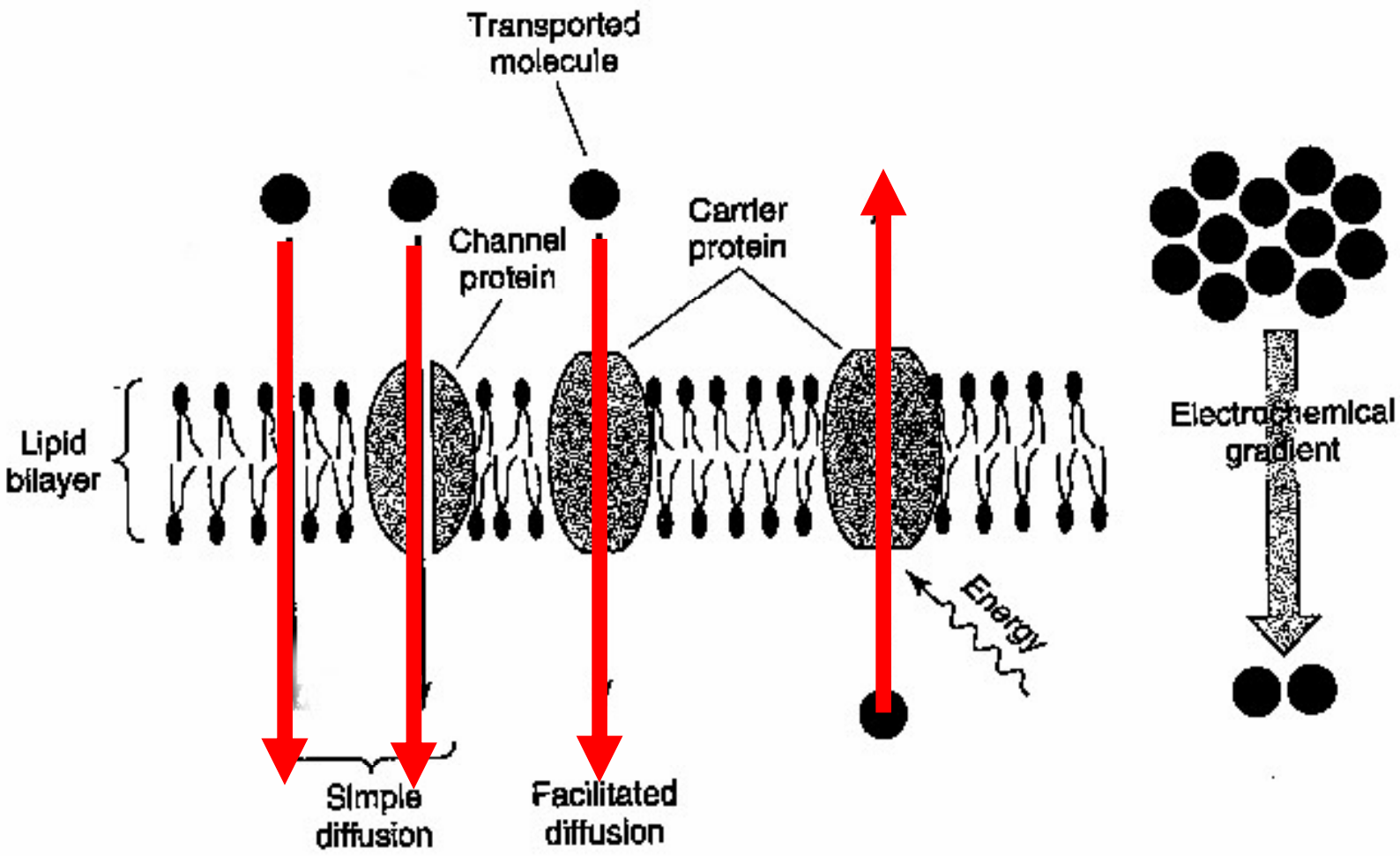

Passive transport Active transport

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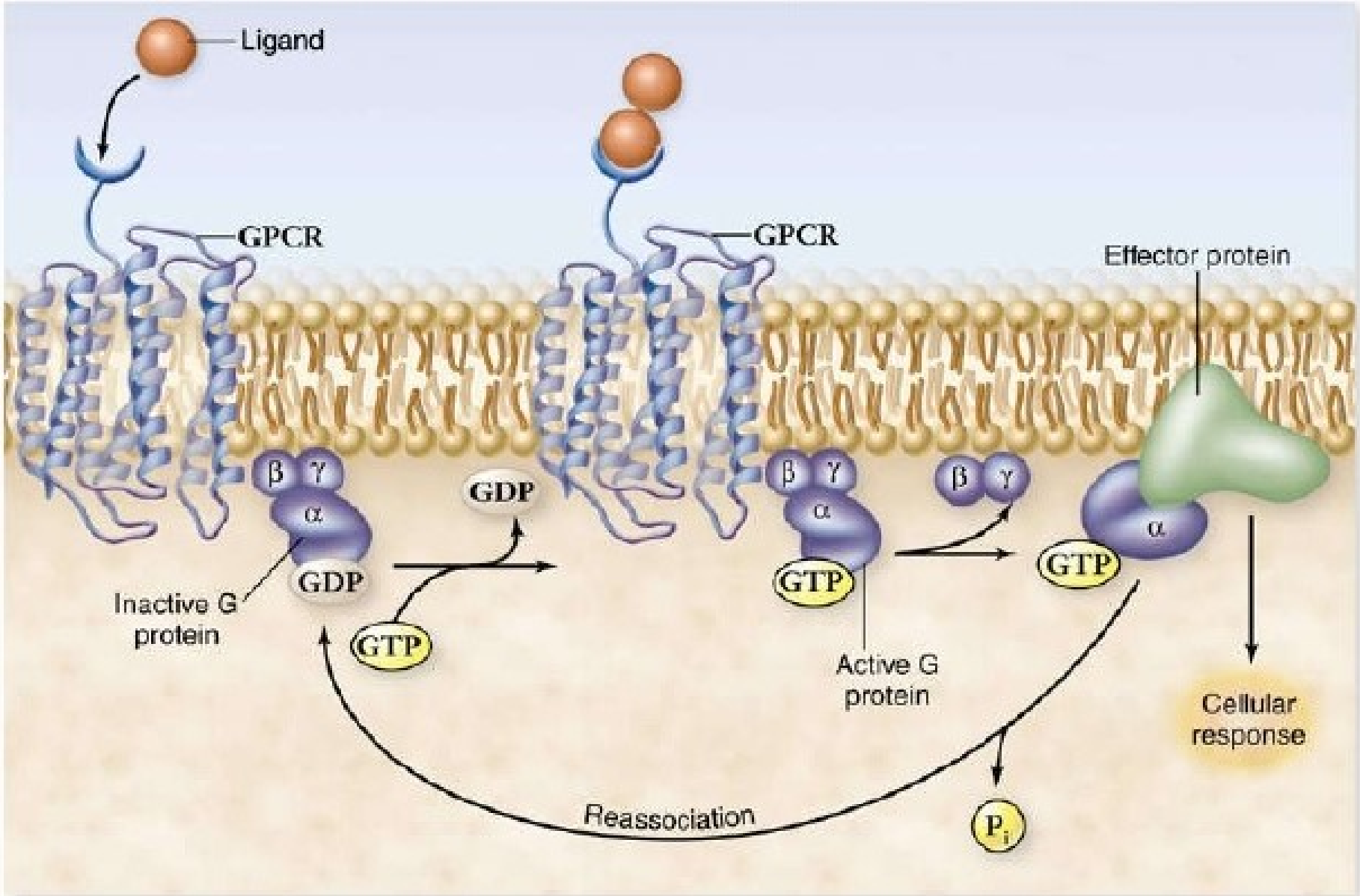
There are two classes of proteins built into the membrane

1. Receptor proteins
2. Effector proteins



Signal Receptor Effector

Signal → Receptor → Effector

There are thousands of protein receptors built into the cell membranes.

All functions carried out by the human (50 trillion cells) is carried out by each individual cell.

Biology of Belief by Bruce Lipton

The cell membrane reads the environment because it has receptors.

The human body also has a skin with receptors – big ones such as eyes, ears, nose, taste and small ones such as touch, temperature pain etc. to read the environment and send signals to the brain.

Biology of Belief by Bruce Lipton

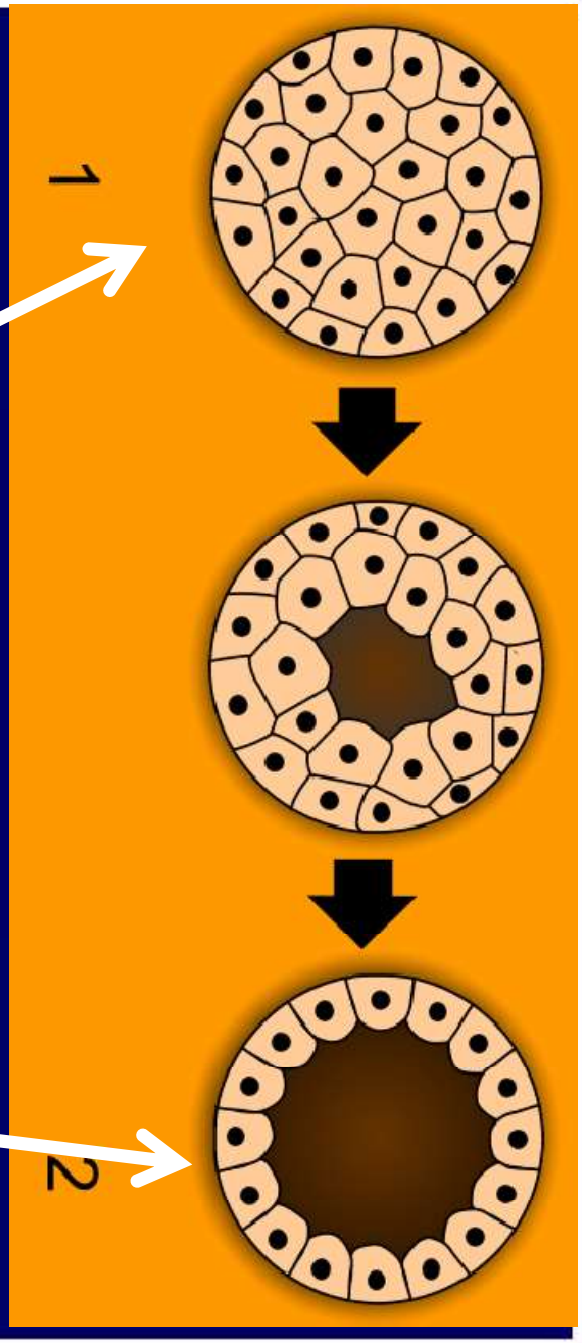
So the skin is really part of our brain.

Embryological connection-
Sperm and Egg
Zygote
Blastula → Gastrula
3 Dermal layers Ectoderm
Mesoderm
Endoderm

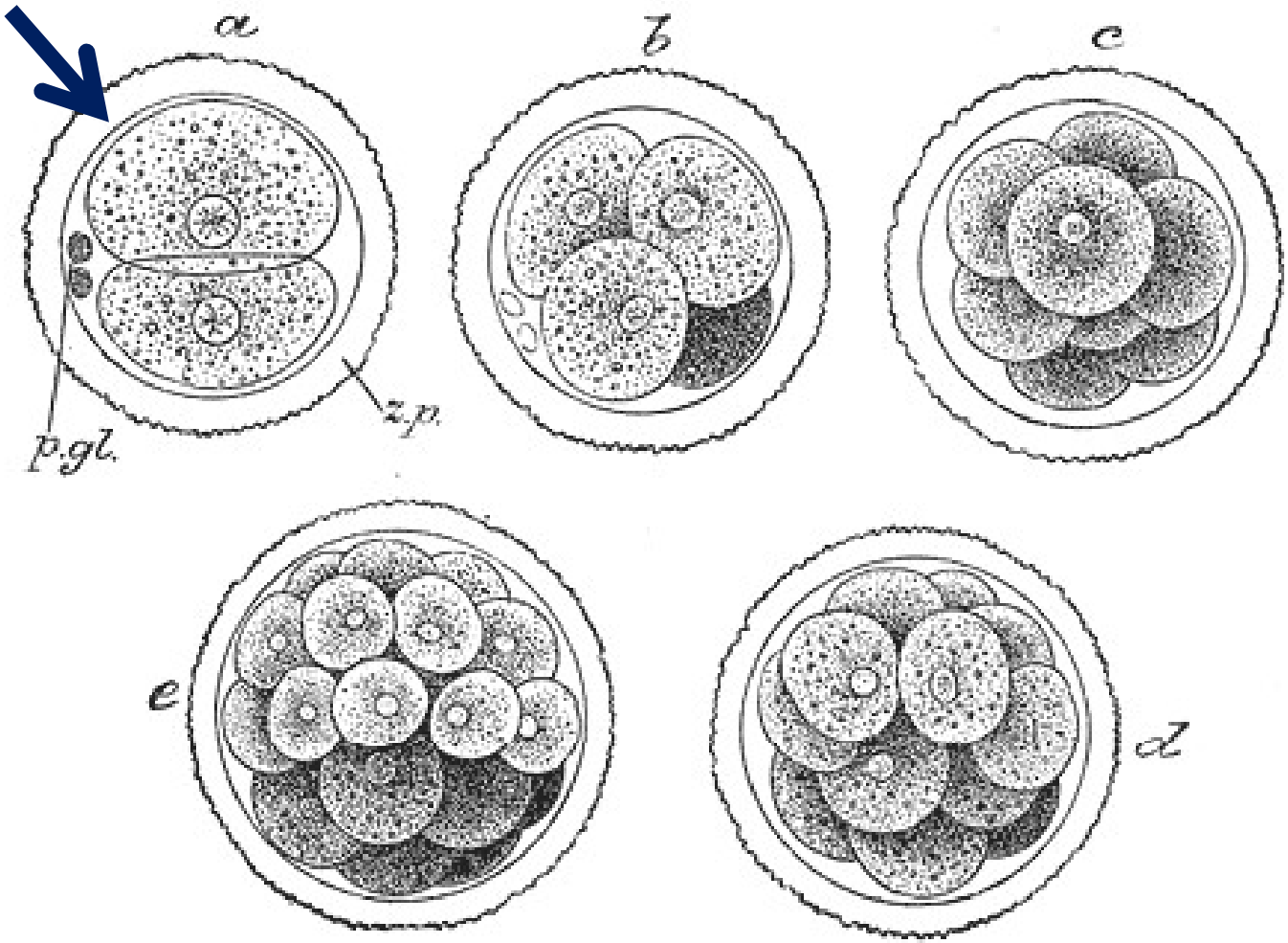
Biology of Belief by Bruce Lipton

Week 1

Fertilization
Oocyte activation
Zygote
Cleavage
Blastomere
Morula
Blastocoele
Blastocyst
Blastula
Inner cell mass
Trophoblast



The <u>zona pellucida</u> is a glycoprotein layer surrounding the plasma membrane of mammalian oocytes



First stages of division of mammalian embryo. Semidiagrammatic. (From a drawing by Allen Thomson.) z.p. Zona striata. p.gl. Polar bodies. a. Two-cell stage. b. Four-cell stage. c. Eight-cell stage. d, e. Morula stage.

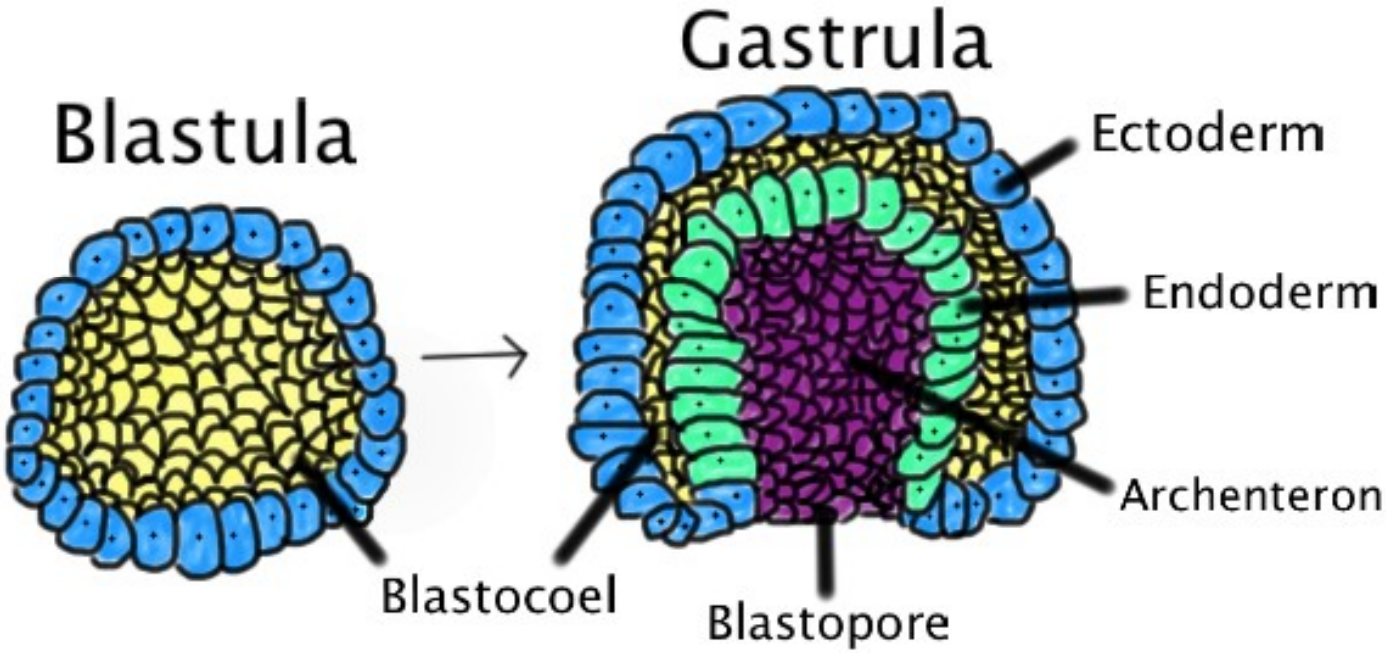
A morula is distinct from a blastocyst in that a morula (3–4 days post fertilization) is a 16-cell mass in a spherical shape whereas a blastocyst (4–5 days post fertilization) has a cavity inside the zona pellucida along with an inner cell mass.

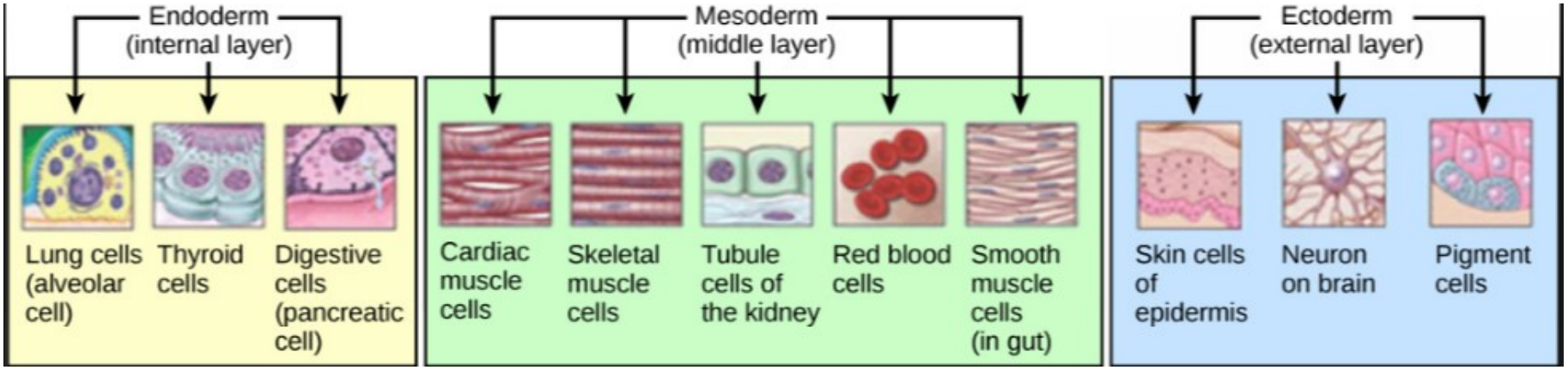
Boklage, Charles E. (2009). How New Humans Are Made: Cells and Embryos, Twins and Chimeras, Left and Right, Mind/Self/Soul, Sex, and Schizophrenia. World Scientific. p. 217.

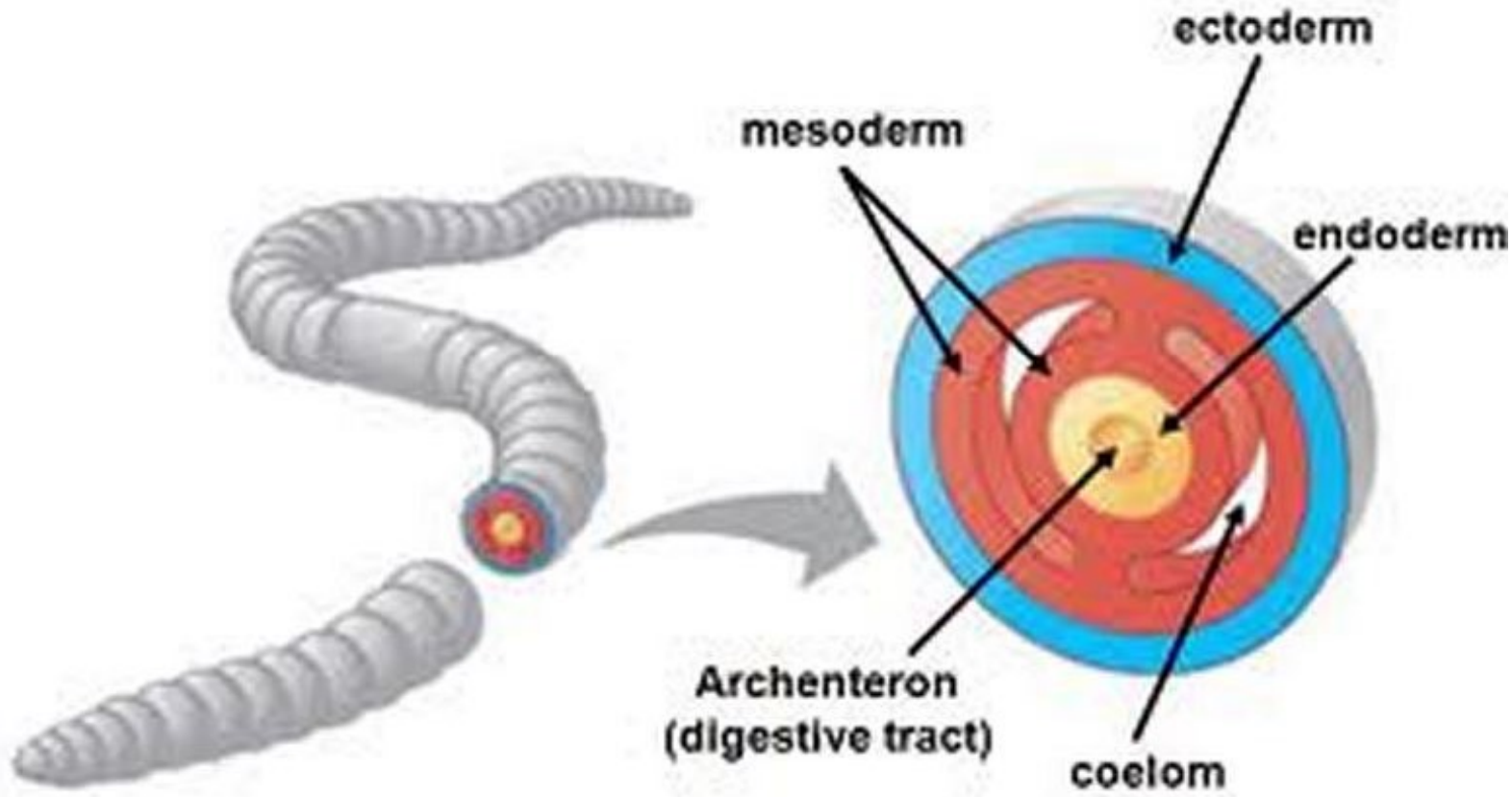
A morula, if untouched and allowed to remain implanted, will eventually develop into a blastocyst.

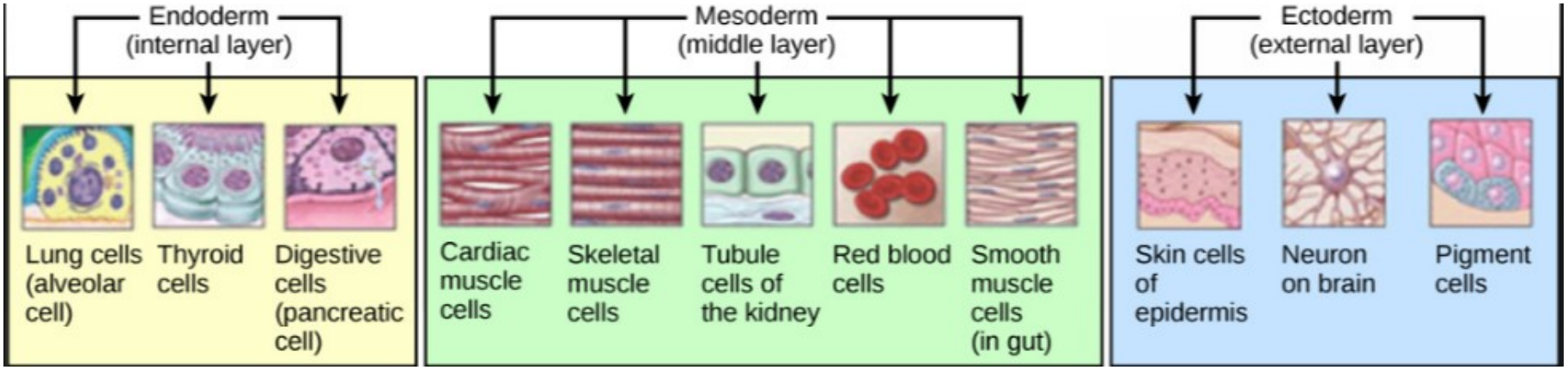
"The Morula and Blastocyst". the Endowment for Human Development. Retrieved 11 April 2015.

The Ectoderm provides for the Skin and the CNS






ectoderm
mesoderm
endoderm
Archenteron
(digestive tract)
coelom


Endoderm
(internal layer)
Lung cells (alveolar cell)
Thyroid cells
Digestive cells (pancreatic cell)
Mesoderm
(middle layer)
Cardiac muscle cells
Skeletal muscle cells
Tubule cells of the kidney
Red blood cells
Smooth muscle cells (in gut)
Ectoderm
(external layer)
Skin cells of epidermis
Neuron on brain
Pigment cells

The receptor and effector proteins represent switches. Some switches will be on and some off at any moment in time.

The receptors are awareness of the environment.

The effector send a physical signal into the cell to engage physiological mechanisms that are appropriate. i.e. PERCEPTION

Biology of Belief by Bruce Lipton

Perception controls behaviour. Life is not controlled by DNA. DNA is the blueprint to make the proteins which are controlled and mediated by the signals. What does a cell do if the signal is knocking but the cell does not have the protein? This is when the gene is activated to stimulate the product of the protein.

Biology of Belief by Bruce Lipton

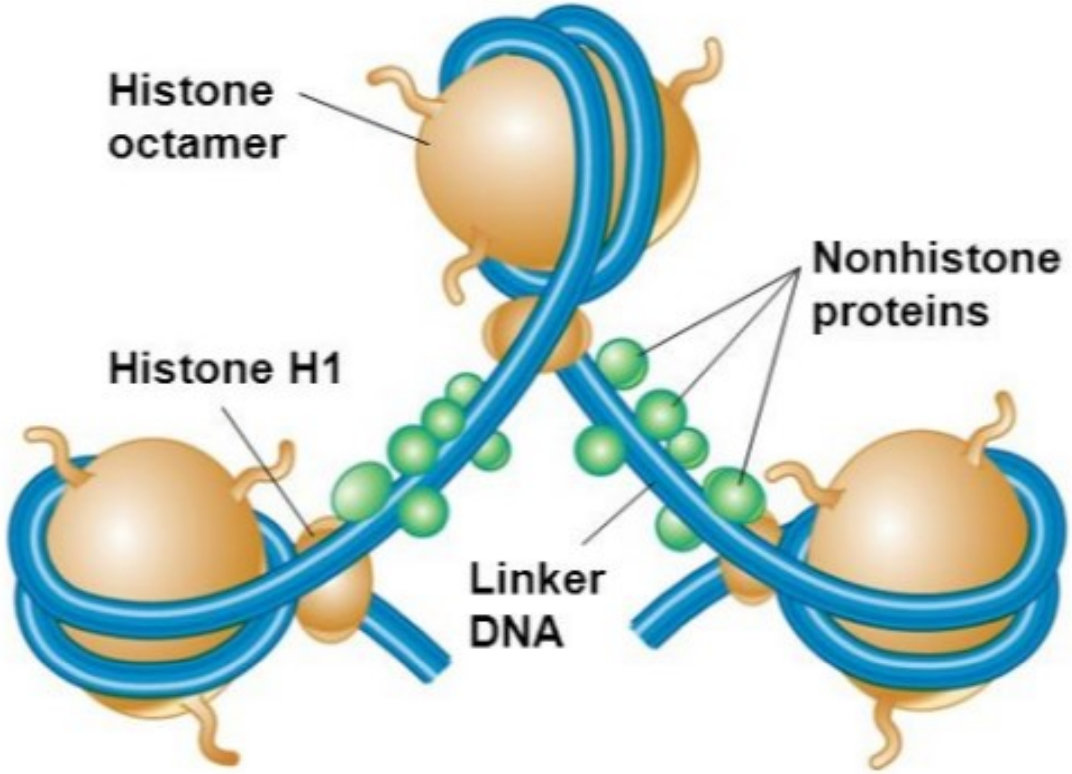
Genes do not turn on or off on their own but respond to the signals (perception).
If the gene is damaged or destroyed it no longer is the blueprint and so the protein is not manufactured and dysfunction occurs (telomeres and telomerase).

Biology of Belief by Bruce Lipton

50% of chromosomes is DNA but 50% is protein which surrounds the DNA like a sleeve. This protein is called non histone protein of which there are over 1000 and are involved with gene expression. The DNA of the gene is not exposed but covered by the protein. So to read the gene the protein sleeve has to be withdrawn.

Biology of Belief by Bruce Lipton

Non-histone proteins play role in chromosomes organization and compaction



Nucleosomes showing linker histones and nonhistone proteins

If there is no intracellular protein for the effector to effect then the signal sends its message direct to the gene. The signal effect specifically allow the exact protein sleeve to be uncovered as the protein sleeve convolution changes allowing the gene to be exposed and make a RNA copy.

Biology of Belief by Bruce Lipton

The RNA is a copy of the DNA and travels to the ribosome via the cytoplasm.

Genes control nothing. Genes are responsive to the signals of the environment. This is the definition of epigenetics.

A single gene maybe able to thus provide for over 2000 different proteins.

Biology of Belief by Bruce Lipton

Genetic Potential is ENDLESS!

30,000 Genes in the Human Genome.

https://www.genome.gov/11006943

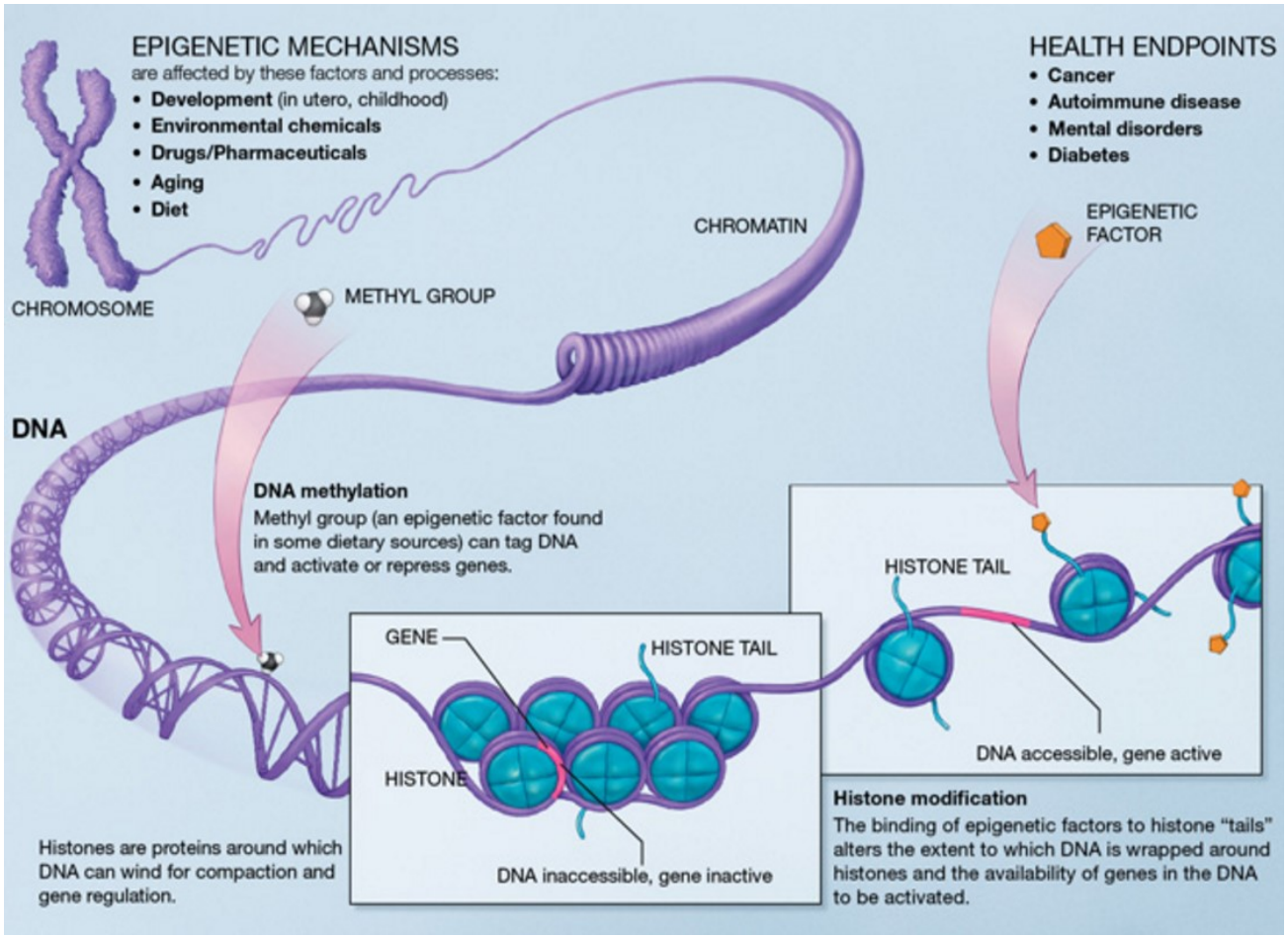
N^X or $30{,}000^2$ = A big number

"environmental information can modify the readout of each gene so as to create more than 30,000 variations from each blueprint."

- Bruce Lipton, PhD

$30{,}000^{30{,}000}$ = INFINITY!

Histones - (De)Methylation and (De)Acetylation Inherent or Acquired



DNA loosens when it is about to divide and when it is under stress. It tightens when repairing.

Histones are highly alkaline proteins found in eukaryotic cell nuclei that package and order the DNA into structural units called **nucleosomes** (a basic unit of DNA packaging consisting of a segment of DNA wound in sequence around eight histone protein cores).

Youngson RM (2006). *Collins Dictionary of Human Biology*. Glasgow: HarperCollins.

They are the chief protein components of chromatin* (a complex of macromolecules found in cells, consisting of DNA, protein, and RNA.) acting as spools around which DNA winds, and playing a role in gene regulation.

**Cox M, Nelson DR, Lehninger AL (2005). Lehninger Principles of Biochemistry. San Francisco: W.H. Freeman.*

Without histones, the unwound DNA in chromosomes would be very long (a length to width ratio of more than 10 million to 1 in human DNA). Each human cell has about 1.8 metres of DNA, (~6 ft) but wound on the histones it has about 90 micrometres (0.09 mm) of chromatin.

Redon C, Pilch D, Rogakou E, Sedelnikova O, Newrock K, Bonner W (Apr 2002). "Histone H2A variants H2AX and H2AZ". *Current Opinion in Genetics & Development*. 12 (2): 162–9.

They share the feature of long 'tails' on one end of the amino acid structure - this being the location of post-translational modification. *

*Strahl BD, Allis CD (Jan 2000). "The language of covalent histone modifications". Nature. 403 (6765): 41–5

The highly basic nature of histones, aside from facilitating DNA-histone interactions, contributes to their water solubility. Histones are subject to post translational modification by enzymes primarily on their N-terminal tails, but also in their globular domains.*

*Jenuwein T, Allis CD (Aug 2001). "Translating the histone code" (PDF). *Science*. 293 (5532): 1074–80.

Such modifications include

1. Methylation
2. Acetylation

This affects their function of gene regulation.

*Jenuwein T, Allis CD (Aug 2001). "Translating the histone code" (PDF). *Science*. 293 (5532): 1074–80.

In general, genes that are active have less bound histone, while inactive genes are highly associated with histones during interphase.

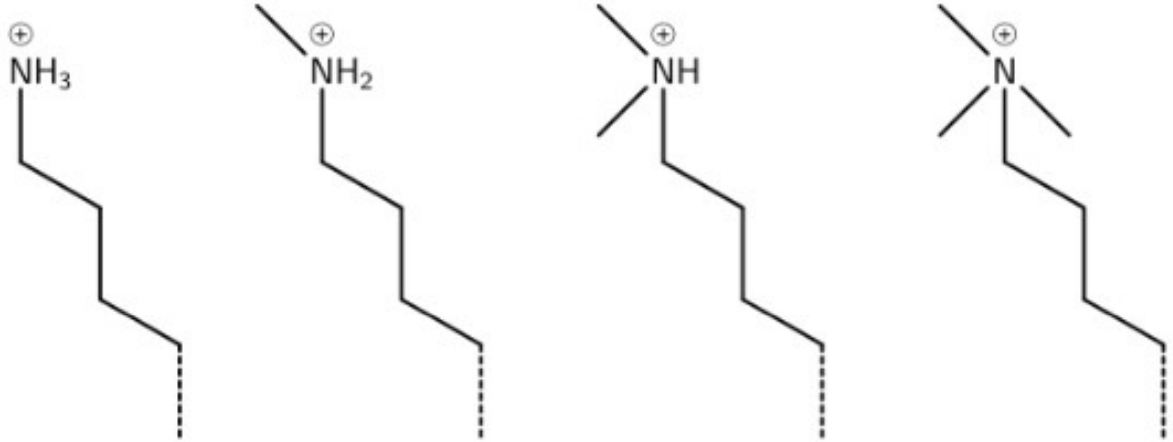
All histones have a highly positively charged N-terminus with many lysine and arginine residues.*

*Christophorou MA, Castelo-Branco G, Halley-Stott RP, Oliveira CS, Loos R, Radzisheuskaya A, Mowen KA, Bertone P, Silva JC, Zernicka-Goetz M, Nielsen ML, Gurdon JB, Kouzarides T (Mar 2014). "Citrullination regulates pluripotency and histone H1 binding to chromatin". *Nature*. 507 (7490): 104–8.

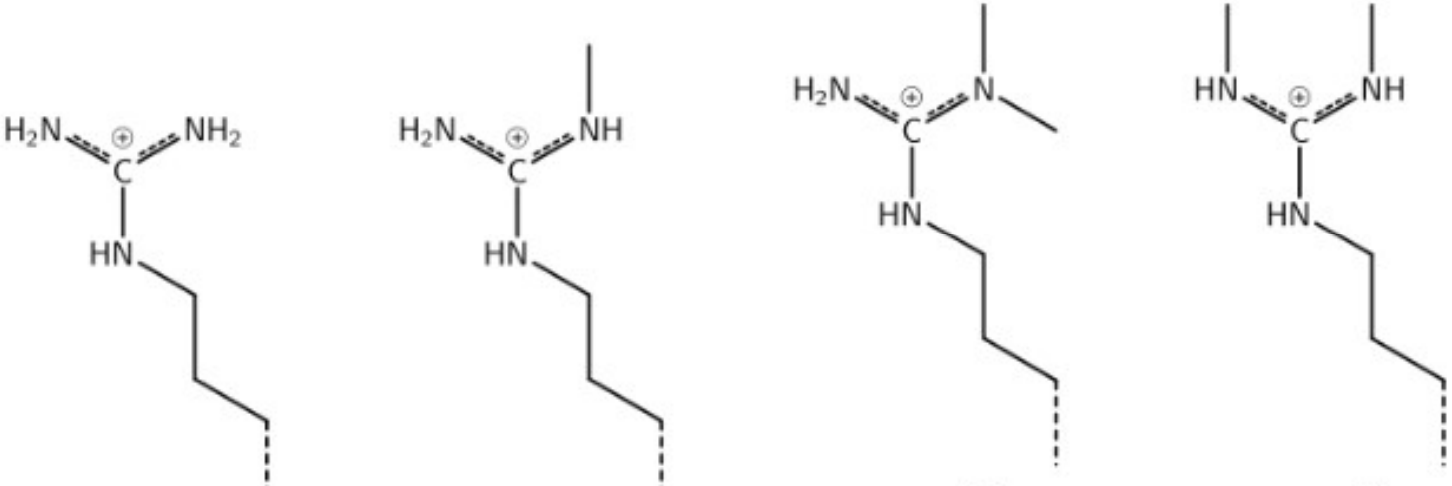
1. Methylation

The addition of one, two or three methyl groups to lysine or one or two methyl groups to arginine has little effect on the chemistry of the histone; methylation leaves the charge of the arginine or lysine intact and adds a minimal number of atoms so steric interactions are mostly unaffected.*

*Rana, Ajay K.; Ankri, Serge (2016-01-01). "Reviving the RNA World: An Insight into the Appearance of RNA Methyltransferases" *Front Genet*. 7: 99.



Lysine **Methyllysine** **Dimethyllysine** **Trimethyllysine**



Arginine **Methylarginine** **Asymmetric dimethylarginine** **Symmetric dimethylarginine**

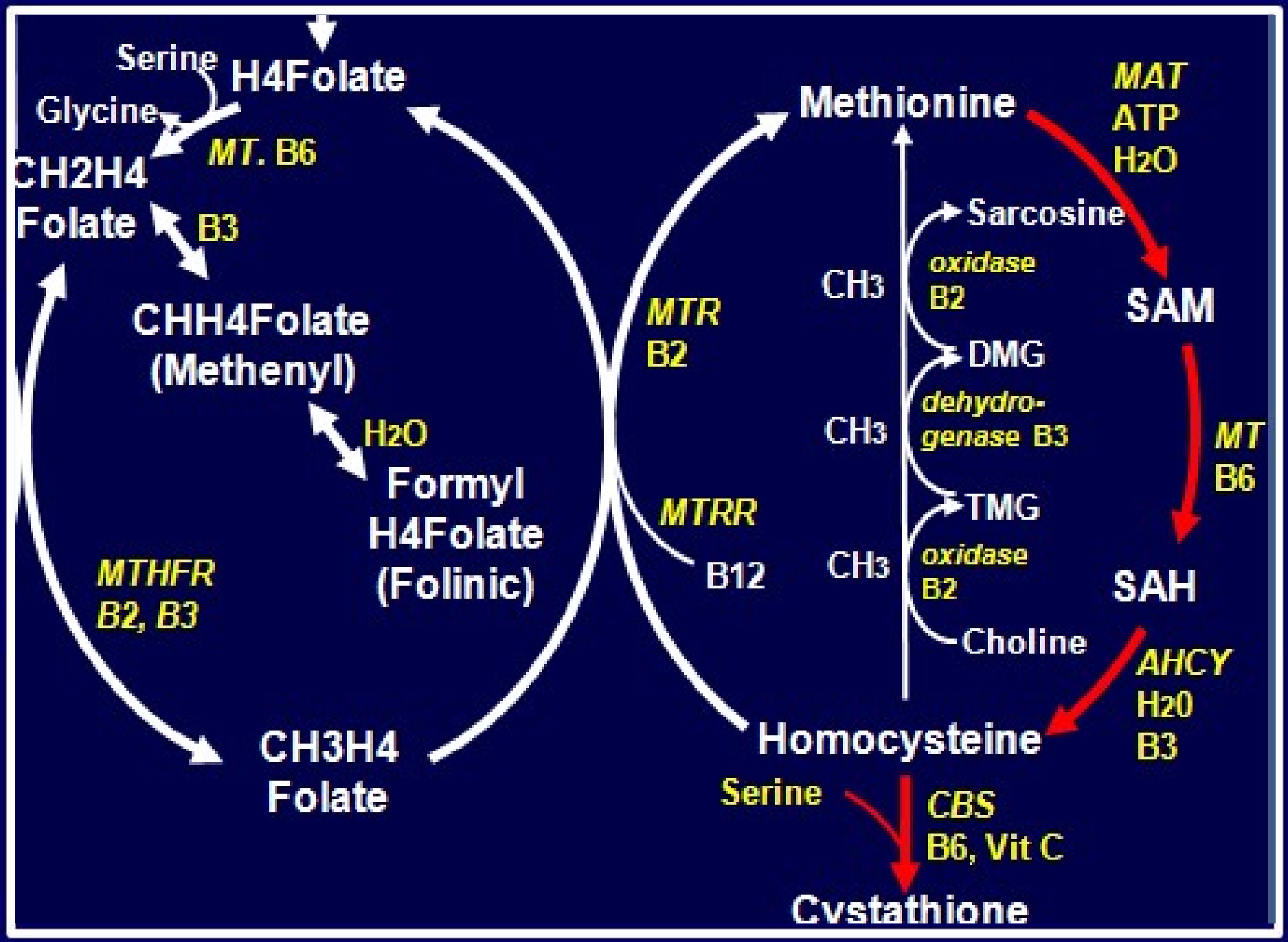
However, some special proteins can recognise arginine and lysine methylation with exquisite sensitivity and differentiate mono, di and tri-methyl lysine, to the extent that, for some they appear to have different meanings.*

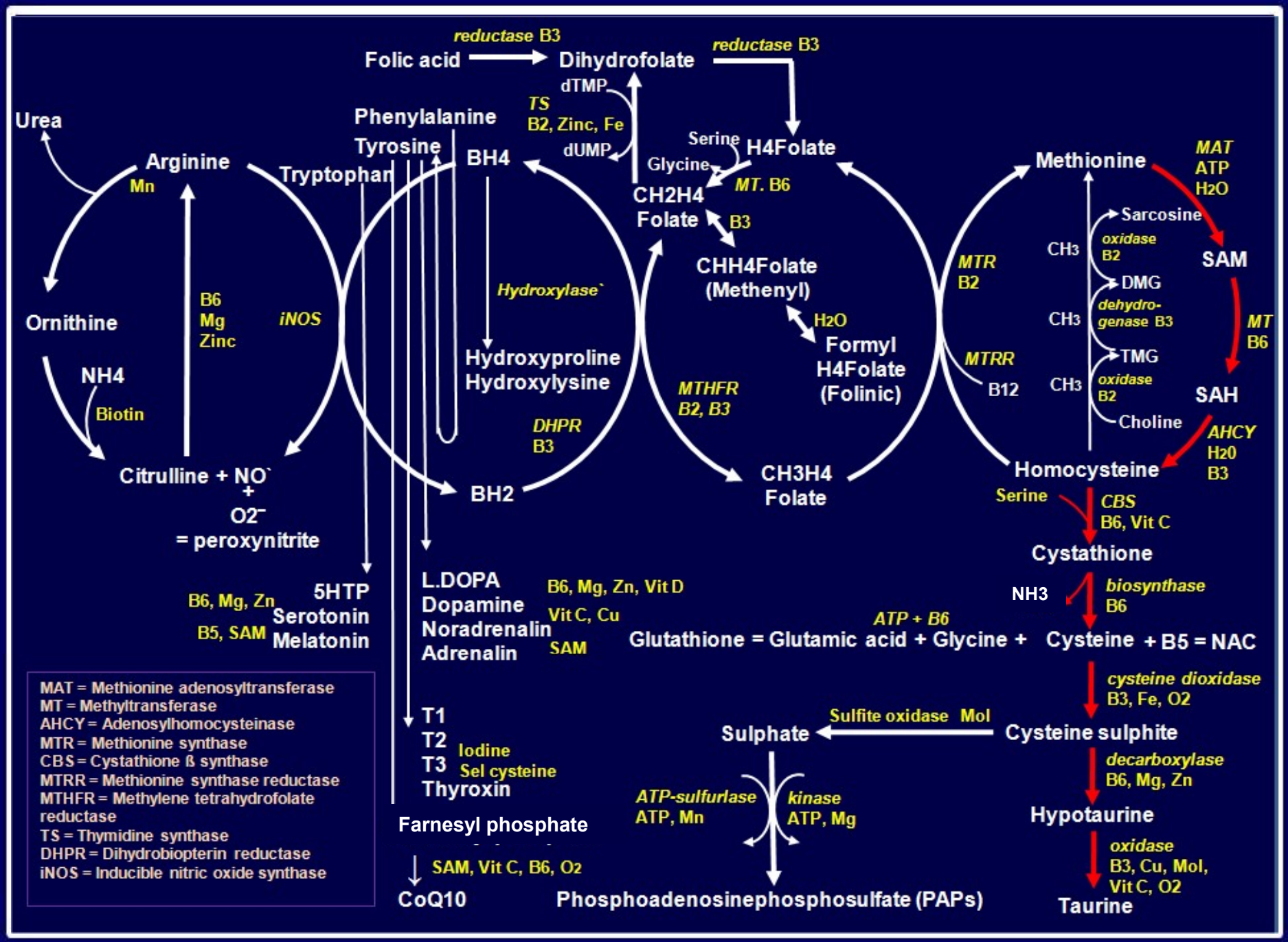
*Rana, Ajay K.; Ankri, Serge (2016-01-01). "Reviving the RNA World: An Insight into the Appearance of RNA Methyltransferases" *Front Genet*. 7: 99.

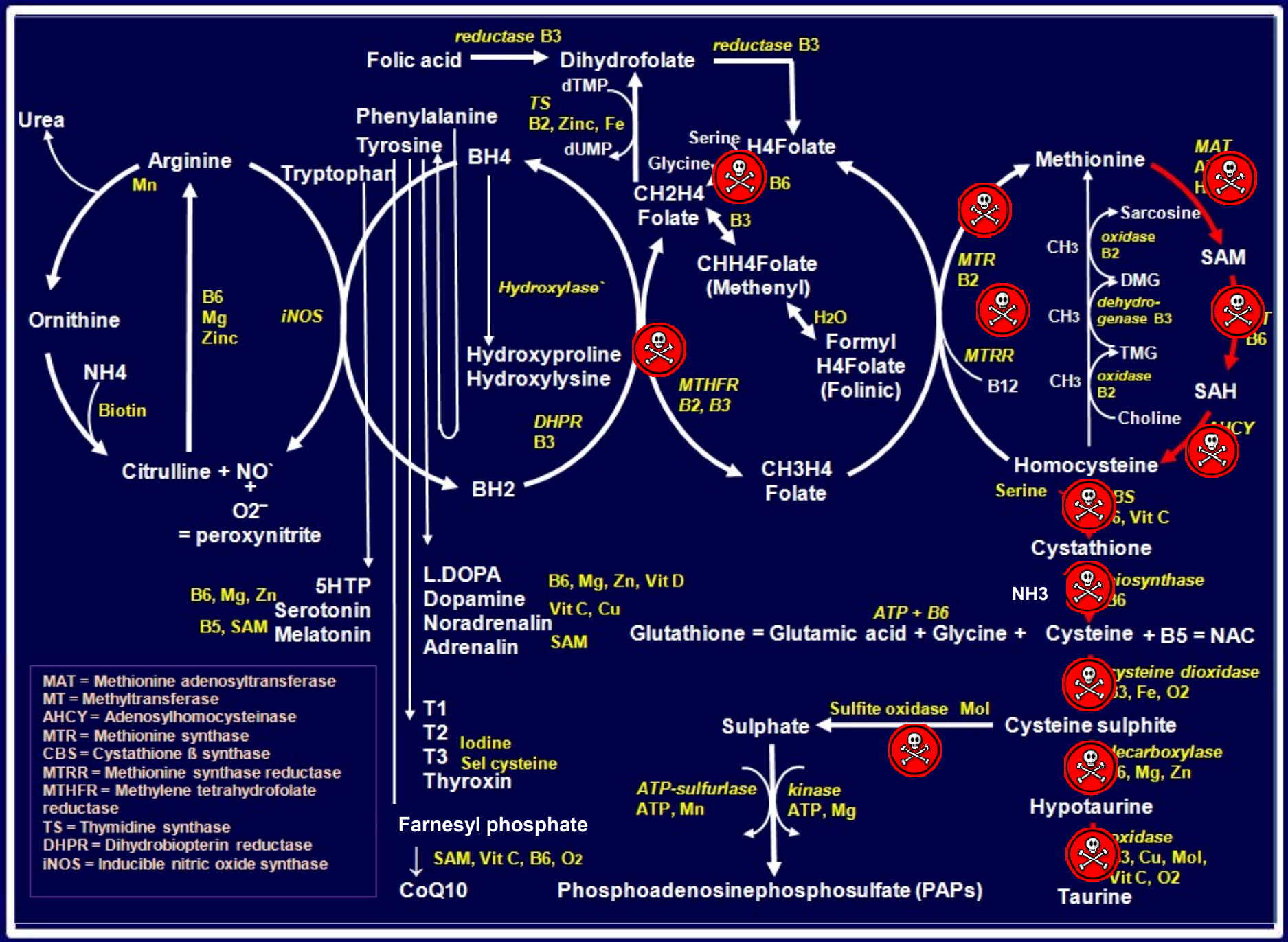
Because of this, lysine methylation tends to be a very informative mark and dominates the known histone modification functions.

Histones that are methylated on certain residues can act epigenetically to repress or activate gene expression.*

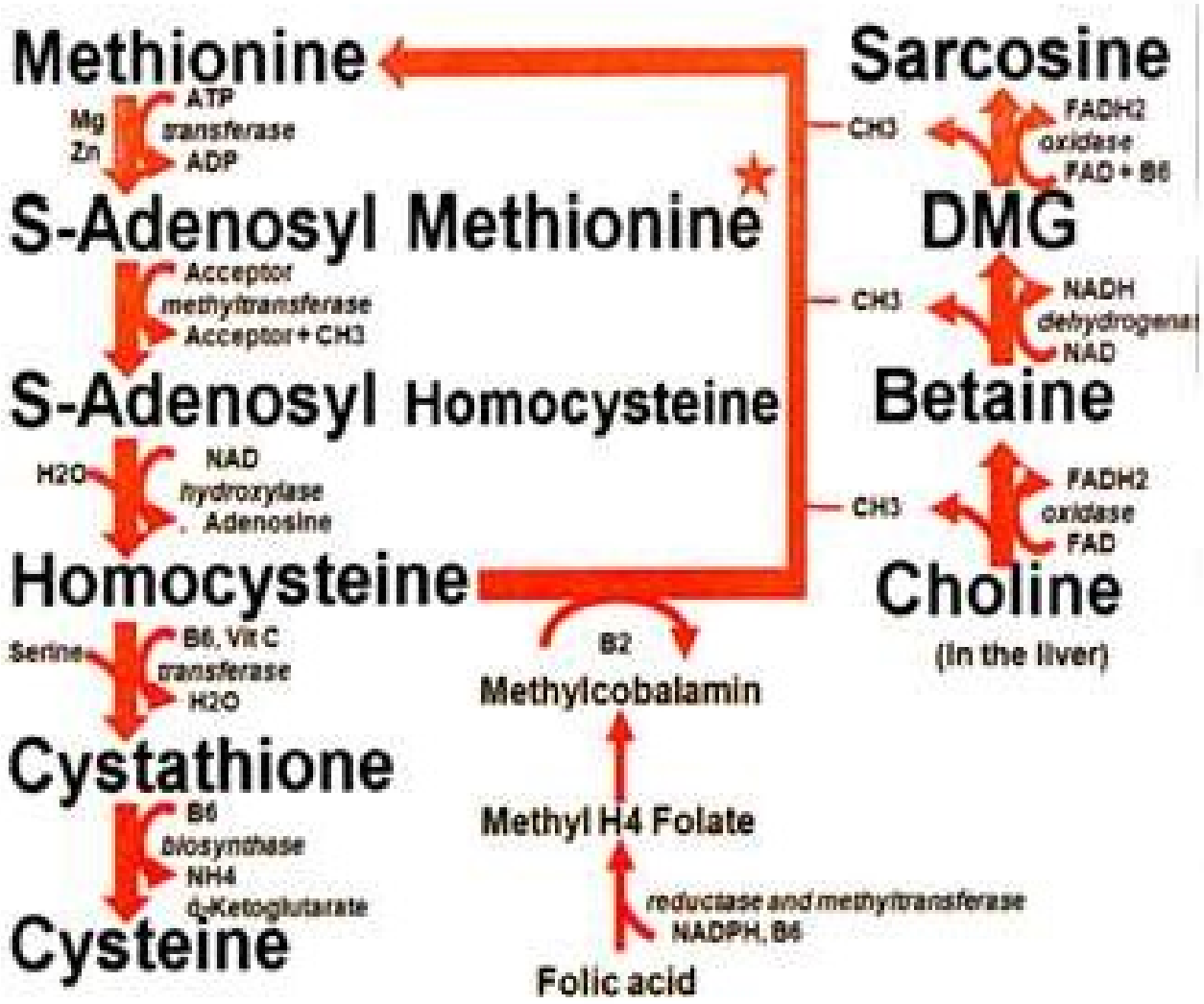
*Rana, Ajay K.; Ankri, Serge (2016-01-01). "Reviving the RNA World: An Insight into the Appearance of RNA Methyltransferases" *Front Genet*. 7: 99.


Serine
H4Folate
Glycine
MT. B6
CH2H4
Folate
B3
CHH4Folate
(Methenyl)
H2O
Formyl
H4Folate
(Folinic)
MTHFR
B2, B3
CH3H4
Folate
MTR
B2
MTRR
B12
Methionine
MAT
ATP
H2O
Sarcosine
oxidase
B2
CH3
SAM
DMG
dehydro-
genase B3
CH3
MT
B6
TMG
oxidase
B2
CH3
SAH
Choline
AHCY
H20
B3
Homocysteine
Serine
CBS
B6, Vit C
Cystathione


reductase B3
Folic acid
Dihydrofolate
reductase B3
dTMP
TS
B2, Zinc, Fe
dUMP
Urea
Arginine
Mn
Phenylalanine
Tyrosine
Tryptophan
BH4
Serine
Glycine
H4Folate
MT. B6
CH2H4
Folate
B3
CHH4Folate
(Methenyl)
H2O
Formyl
H4Folate
(Folinic)
Methionine
MAT
ATP
H2O
Sarcosine
oxidase
B2
DMG
dehydro-
genase B3
TMG
oxidase
B2
Choline
CH3
CH3
CH3
SAM
MT
B6
SAH
AHCY
H20
B3
MTR
B2
MTRR
B12
Ornithine
B6
Mg
Zinc
iNOS
NH4
Biotin
Hydroxylase`
Hydroxyproline
Hydroxylysine
DHPR
B3
MTHFR
B2, B3
Citrulline + NO`
+
O2⁻
= peroxynitrite
BH2
CH3H4
Folate
Homocysteine
Serine
CBS
B6, Vit C
Cystathione
NH3
biosynthase
B6
B6, Mg, Zn
5HTP
Serotonin
B5, SAM
Melatonin
L.DOPA
Dopamine
Noradrenalin
Adrenalin
B6, Mg, Zn, Vit D
Vit C, Cu
SAM
ATP + B6
Glutathione = Glutamic acid + Glycine +
Cysteine + B5 = NAC
cysteine dioxidase
B3, Fe, O2
MAT = Methionine adenosyltransferase
MT = Methyltransferase
AHCY = Adenosylhomocysteinase
MTR = Methionine synthase
CBS = Cystathione ß synthase
MTRR = Methionine synthase reductase
MTHFR = Methylene tetrahydrofolate reductase
TS = Thymidine synthase
DHPR = Dihydrobiopterin reductase
iNOS = Inducible nitric oxide synthase
T1
T2
T3
Thyroxin
Iodine
Sel cysteine
Sulfite oxidase Mol
Sulphate
Cysteine sulphite
decarboxylase
B6, Mg, Zn
Farnesyl phosphate
ATP-sulfurlase
ATP, Mn
kinase
ATP, Mg
Hypotaurine
oxidase
B3, Cu, Mol,
Vit C, O2
SAM, Vit C, B6, O2
CoQ10
Phosphoadenosinephosphosulfate (PAPs)
Taurine


reductase B3
Folic acid
Dihydrofolate
reductase B3
dTMP
TS
B2, Zinc, Fe
dUMP
Urea
Arginine
Mn
Phenylalanine
Tyrosine
Tryptophan
BH4
Serine
H4Folate
Glycine
B6
CH2H4
Folate
B3
CHH4Folate
(Methenyl)
H2O
Formyl
H4Folate
(Folinic)
Methionine
MAT
Sarcosine
oxidase
B2
CH3
SAM
MTR
B2
DMG
dehydro-
genase B3
CH3
B6
MTRR
TMG
CH3
oxidase
B2
B12
SAH
Choline
Ornithine
B6
Mg
Zinc
iNOS
Hydroxylase`
Hydroxyproline
Hydroxylysine
MTHFR
B2, B3
DHPR
B3
NH4
Biotin
Citrulline + NO`
+
O2⁻
= peroxynitrite
BH2
CH3H4
Folate
Homocysteine
Serine
Cystathione
NH3
ATP + B6
Glutathione = Glutamic acid + Glycine + Cysteine + B5 = NAC
B6, Mg, Zn
B5, SAM
5HTP
Serotonin
Melatonin
L.DOPA
Dopamine
Noradrenalin
Adrenalin
B6, Mg, Zn, Vit D
Vit C, Cu
SAM
T1
T2
T3
Iodine
Sel cysteine
Thyroxin
Sulfite oxidase Mol
Sulphate
Cysteine sulphite
Hypotaurine
Taurine
ATP-sulfurlase
ATP, Mn
kinase
ATP, Mg
Farnesyl phosphate
SAM, Vit C, B6, O2
CoQ10
Phosphoadenosinephosphosulfate (PAPs)
MAT = Methionine adenosyltransferase
MT = Methyltransferase
AHCY = Adenosylhomocysteinase
MTR = Methionine synthase
CBS = Cystathione ß synthase
MTRR = Methionine synthase reductase
MTHFR = Methylene tetrahydrofolate reductase
TS = Thymidine synthase
DHPR = Dihydrobiopterin reductase
iNOS = Inducible nitric oxide synthase

SAM


Methionine
ATP
Mg
Zn
transferase
ADP
S-Adenosyl Methionine
Acceptor
methyltransferase
Acceptor + CH3
S-Adenosyl Homocysteine
H2O
NAD
hydroxylase
Adenosine
Homocysteine
Serine
B6, Vit C
transferase
H2O
Cystathione
B6
biosynthase
NH4
α-Ketoglutarate
Cysteine
Sarcosine
CH3
FADH2
oxidase
FAD + B6
DMG
CH3
NADH
dehydrogenase
NAD
Betaine
CH3
FADH2
oxidase
FAD
Choline
(In the liver)
B2
Methylcobalamin
Methyl H4 Folate
reductase and methyltransferase
NADPH, B6
Folic acid

Main methylators are

S. Adenosylmethionine (SAMe)

Methylcobalamin

5MTHF

Choline, Betaine (TMG), DMG

Cofactors Zn

Also check for

H4Biopterin

Folinic acid

P-5-P

BRENDA (The Comprehensive Enzyme Information System)

Functional Test for Methylation Defects

Caffeine challenge test
Sellotape challenge test*

*Chris Astill-Smith ICAK-USA San Diego 2019

Demethylation

Cytochrome p450 enzymes

Alpha-ketoglutarate-dependent non-heme enzymes are active for demethylation of DNA.

Flavin adenine dinucleotide (FAD)-dependent amine oxidase

Vitamin C

Iron

Hydroxycobalamin

BRENDA (The Comprehensive Enzyme Information System)

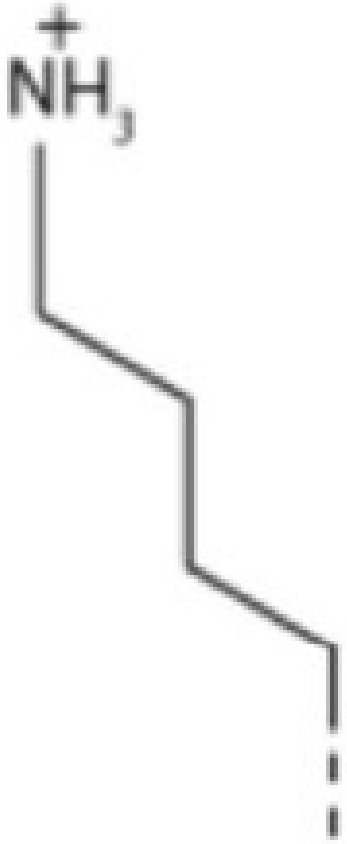
2. Acetylation

Addition of an acetyl group to lysine neutralises its positive charge. This reduces electrostatic attraction between the histone and the negatively charged DNA backbone, loosening the chromatin structure. *

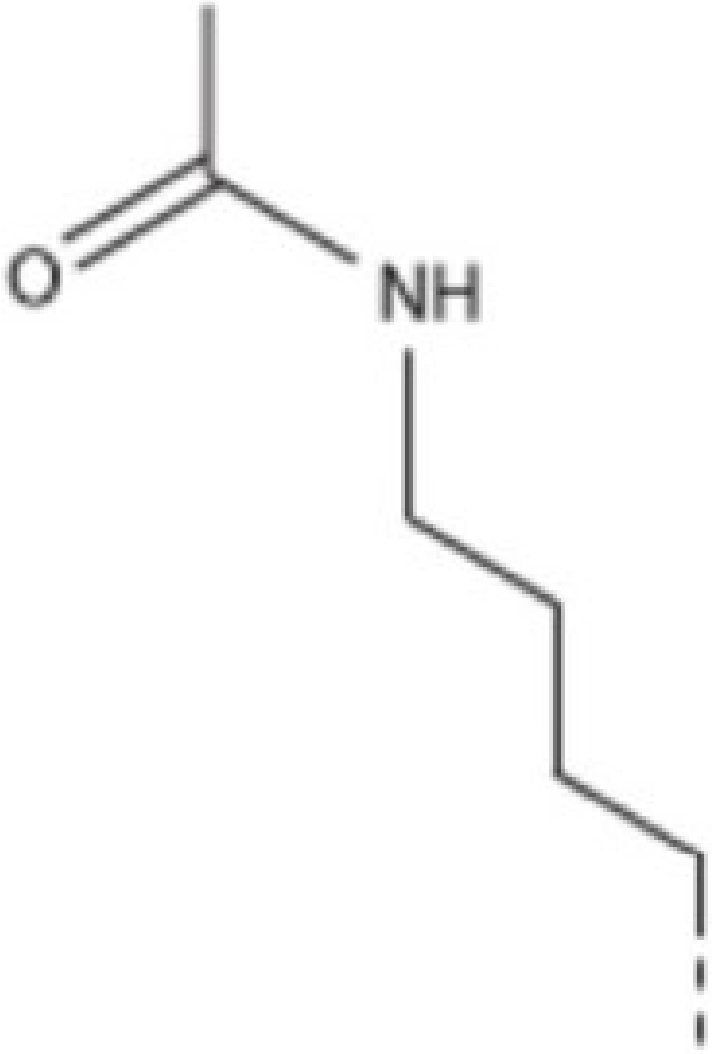
*Sadoul K, Boyault C, Pabion M, Khochbin S (2008). "Regulation of protein turnover by acetyltransferases and deacetylases". *Biochimie*. 90 (2): 306–12.

Highly **acetylated histones** form more accessible chromatin and tend to be associated with active transcription. Lysine acetylation appears to be less precise in meaning than methylation, in that histone acetyltransferases tend to act on more than one lysine.*

*Sadoul K, Boyault C, Pabion M, Khochbin S (2008). "Regulation of protein turnover by acetyltransferases and deacetylases". *Biochimie*. 90 (2): 306–12.



Lysine



Acetyllysine

DNA is wrapped around histones, and, by transferring an acetyl group to the histones, genes can be turned on and off. In general, histone acetylation increases gene expression.

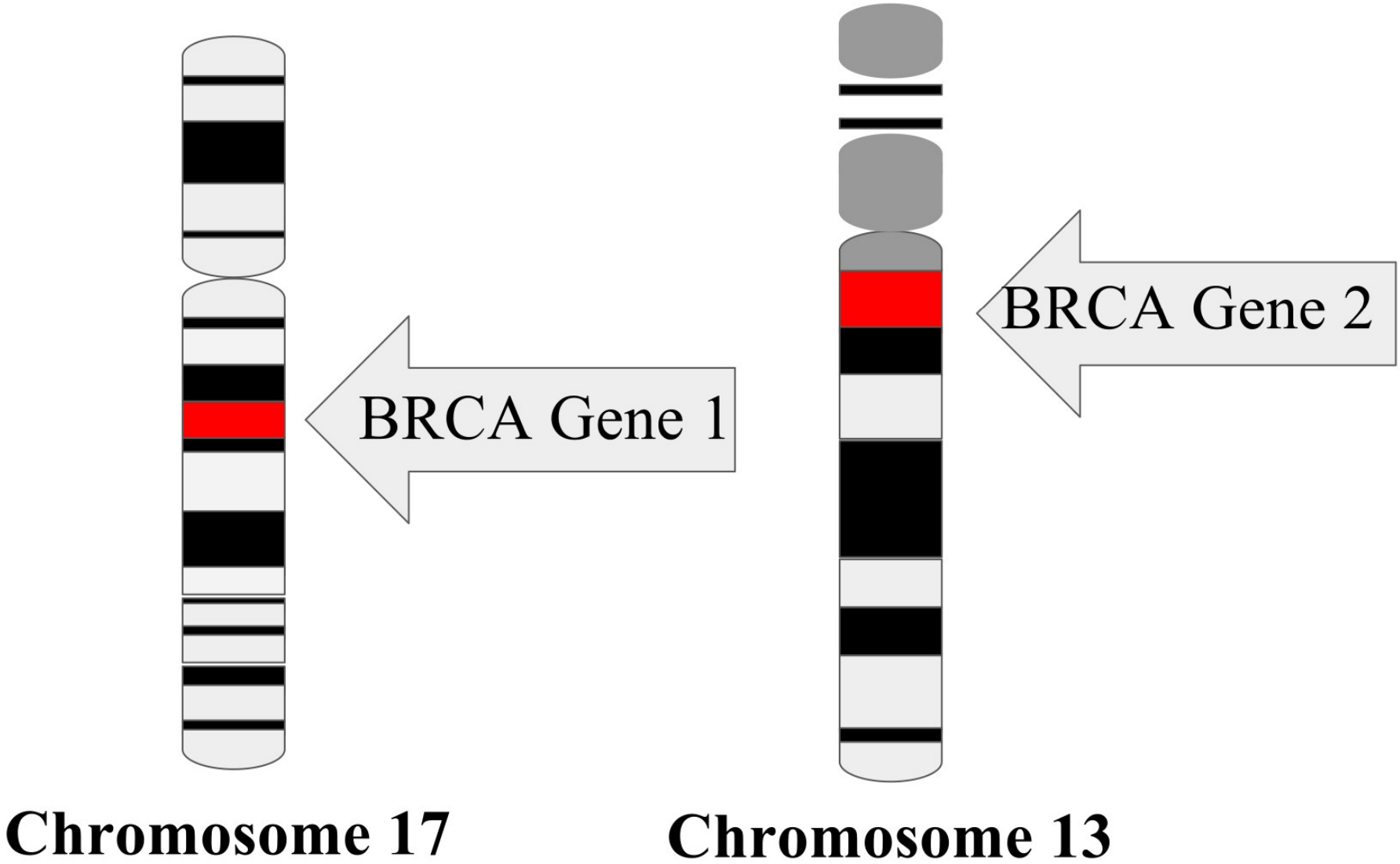
*Sadoul K, Boyault C, Pabion M, Khochbin S (2008). "Regulation of protein turnover by acetyltransferases and deacetylases". *Biochimie*. 90 (2): 306–12.

Histone **deacetylases** are a class of enzymes that remove acetyl group from an N-
acetyl lysine amino acid on
a histone, allowing the histones to wrap the DNA more tightly.
CoA. Resveratol, Butyric acid
ATP
Co-enzyme NAD+
Cofactors Zn and Na
Inhibited by Curcumin, peroxynitrite, aspirin

BRENDA (The Comprehensive Enzyme Information System)

Examples A ***BRCA* mutation*** is a mutation in either of the ***BRCA1*** and ***BRCA2*** genes, which are tumour suppressor genes. Hundreds of different types of mutations in these genes have been identified, some of which have been determined to be harmful, while others have no proven impact.

*Hamel PJ (2007-05-29). "BRCA1 and BRCA2: No Longer the Only Troublesome Genes Out There". HealthCentral. Retrieved 2010-07-02.



Both genes produce proteins that help repair damaged DNA, keeping the genetic material of the cell stable. A damaged BRCA gene in either location can lead to increased risk of cancer, particularly breast or ovarian in women.

Harmful mutations in these genes may produce a hereditary breast-ovarian cancer syndrome in affected persons. Only 5-10% of breast cancer cases in women are attributed to *BRCA1* and *BRCA2* mutations (with *BRCA1* mutations being slightly more common than *BRCA2* mutations).*

*Morris, Joi L.; Gordon, Ora K. (2010). *Positive Results: Making the Best Decisions When You're at High Risk for Breast or Ovarian Cancer*. Amherst, N.Y.: Prometheus Books.

Women with harmful mutations in either *BRCA1* or *BRCA2* have a risk of breast cancer that is about five times the normal risk, and a risk of ovarian cancer that is about ten to thirty times normal. The risk of breast and ovarian cancer is higher for women with a high-risk *BRCA1* mutation than with a *BRCA2* mutation.

*Morris, Joi L.; Gordon, Ora K. (2010). *Positive Results: Making the Best Decisions When You're at High Risk for Breast or Ovarian Cancer*. Amherst, N.Y.: Prometheus Books.

High-risk mutations, which disable an important error-free DNA repair process (homology directed repair), significantly increase the person's risk of developing breast cancer, ovarian cancer and certain other cancers.*

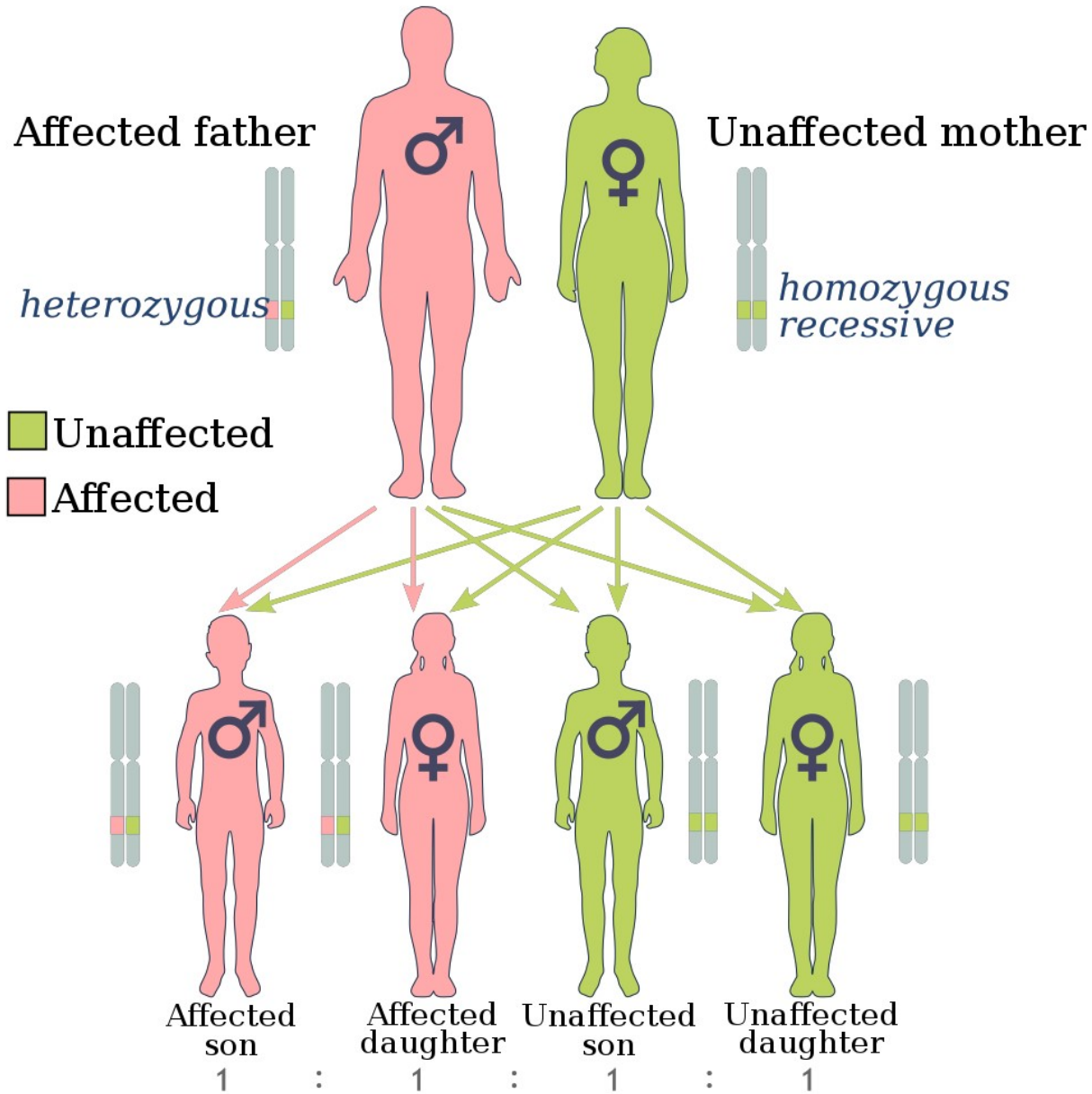
*Morris, Joi L.; Gordon, Ora K. (2010). *Positive Results: Making the Best Decisions When You're at High Risk for Breast or Ovarian Cancer*. Amherst, N.Y.: Prometheus Books.

Why *BRCA1* and *BRCA2* mutations lead preferentially to cancers of the breast and ovary is not known, but lack of *BRCA1* function seems to lead to non-functional X-chromosome inactivation.

Stadler, ZK.; Kauff, ND. (Jan 2010). "Weighing options for cancer risk reduction in carriers of *BRCA1* and *BRCA2* mutations". *J Clin Oncol*. 28 (2): 189–91

Mutations can be inherited from either parent and may be passed on to both sons and daughters. Each child of a genetic carrier, regardless of sex, has a 50% chance of inheriting the mutated gene from the parent who carries the mutation.

Stadler, ZK.; Kauff, ND. (Jan 2010). "Weighing options for cancer risk reduction in carriers of *BRCA1* and *BRCA2* mutations". *J Clin Oncol*. 28 (2): 189–91



***BRCA* mutations are inherited in a genetically dominant fashion, from either parent.**

As a result, half of the people with *BRCA* gene mutations are male, who would then pass the mutation on to 50% of their offspring, male or female.

Cui, J; Antoniou, AC; Dite, GS; Southey, MC; Venter, DJ; Easton, DF; Giles, GG; McCredie, MR; Hopper, JL (Feb 2001). "AfterBRCA1 and BRCA2-what next? Multifactorial segregation analyses of three-generation, population-based Australian families affected by female breast cancer". Am J Hum Genet. 68 (2): 420–31.

The risk of *BRCA*-related breast cancers for men with the mutation is higher than for other men, but still low.
However, *BRCA* mutations can increase the risk of other cancers, such as colon cancer, pancreatic cancer, and prostate cancer.*

*Friedenson B (2005). "*BRCA1* and *BRCA2* pathways and the risk of cancers other than breast or ovarian". *MedGenMed*. 7(2): 60.

72 previously unknown genes mutations have been recently found that lead to the development of breast cancer. BRCA1 mutation contains 125,950 base pairs. A mutation is a misspelling such that the gene cannot code the proper protein.

Holly Yan (2013-05-14). "What's the gene that led to Angelina Jolie's double mastectomy?. Health. CNN.

According to the National Cancer Institute 55% - 65% of women who inherit the BRCA1 mutation and around 45% of women who inherit the BRCA2 mutation will develop breast cancer by the age of 70. However only 1% of women have these mutations which is only a small fraction of all inherited breast cancer.

Holly Yan (2013-05-14). "What's the gene that led to Angelina Jolie's double mastectomy?. Health. CNN.

Only about 10% of breast cancers are hereditary.
Most of the newly identified variants are in regions of the genome that regulate nearby genes.

Holly Yan (2013-05-14). "What's the gene that led to Angelina Jolie's double mastectomy?. Health. CNN.

HER2 (from human epidermal growth factor receptor 2) is a member of the human epidermal growth factor receptor family. Over-expression of
this **oncogene** has been shown to play an important role in the development and progression of certain aggressive types of breast cancer. *

** "ERBB2 erb-b2 receptor tyrosine kinase 2 [Homo sapiens (human)] - Gene - NCBI". www.ncbi.nlm.nih.gov. Retrieved 2016-06-14.*

In recent years the protein has become an important biomarker and target of therapy for approximately 30% of breast cancer patients.*

**Mitri Z, Constantine T, O'Regan R (2012). "The HER2 Receptor in Breast Cancer: Pathophysiology, Clinical Use, and New Advances in Therapy". Chemotherapy Research and Practice. 2012:*

HER2 is so named because it has a similar structure to human epidermal growth factor receptor, or HER1. It is so named because it was derived from a rodent glioblastoma cell line, a type of neural tumour.*

* Mitri Z, Constantine T, O'Regan R (2012). "The HER2 Receptor in Breast Cancer: Pathophysiology, Clinical Use, and New Advanc in Therapy". Chemotherapy Research and Practice. 2012: 743193. PMC 3539433. PMID 23320171.

An **oncogene** is a gene that has the potential to
cause cancer. In tumour cells, theyareoften mutated and/or expressed at high levels.
Activated oncogenes can cause mutant cells designated for apoptosis to survive and proliferate instead.*

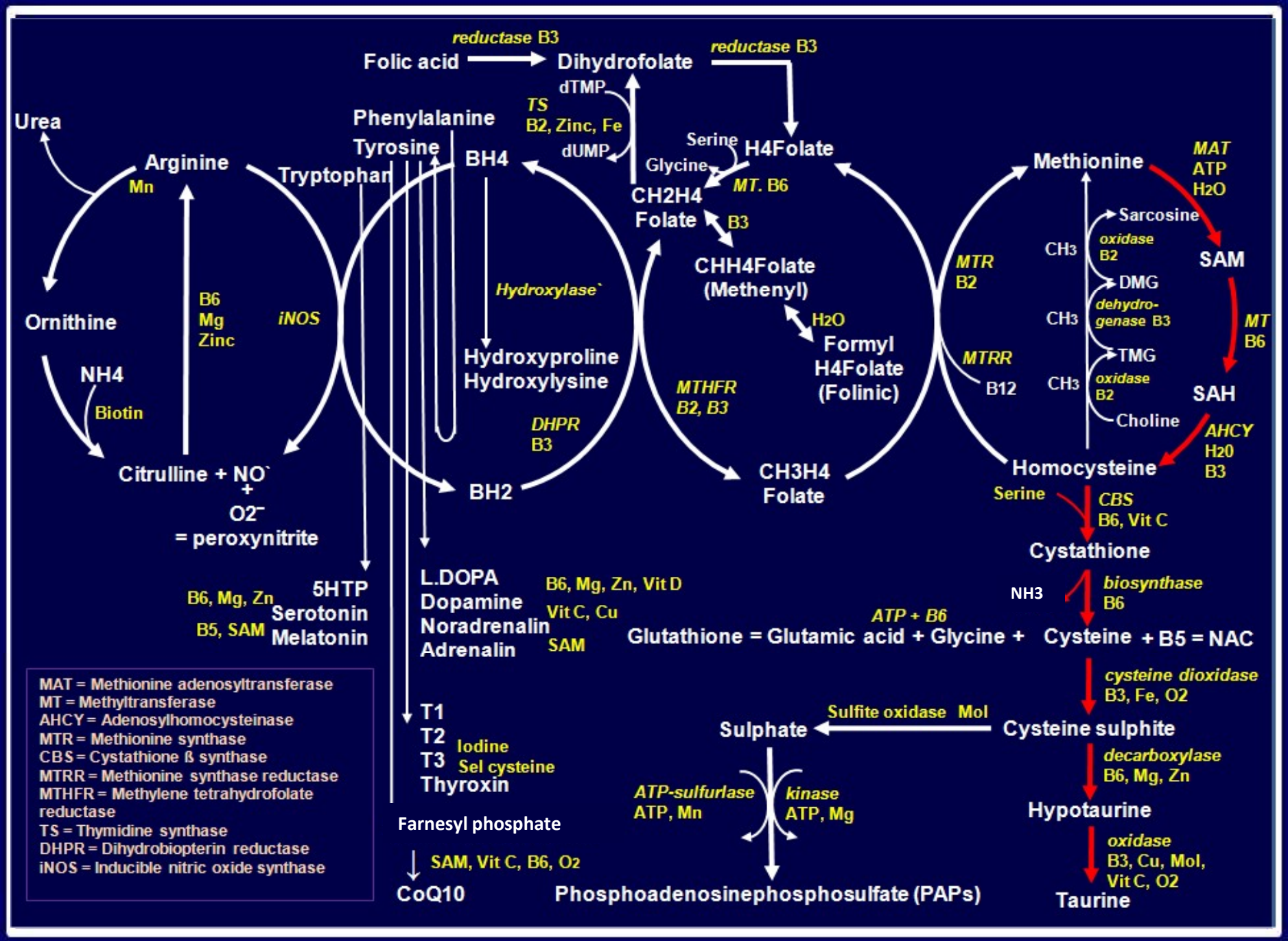
*Wilbur, Beth, editor. The World of the Cell, Becker, W.M., et al., 7th ed. San Francisco, CA; 2009.

Methylation

Methylation

Amines, phenols, thiols (isothiocyanates), noradrenalin, adrenalin, L.DOPA, dopamine, melatonin, histamine, serotonin, pyridine, sulfites and hypochlorites, heavy metals, caffeine, solanene.

"HNMT histamine N-methyltransferase". NCBI Genetic Testing Registry. Retrieved 18 February 2014.
COMT catechol-O-methyltransferase". NCBI Genetic Testing Registry. Retrieved 18 February 2014.
Ragsdale, S.W. "Catalysis of methyl group transfers involving tetrahydrofolate and B12" *Vitamins and Hormones*, 2008


reductase B3
Folic acid
Dihydrofolate
reductase B3
dTMP
TS
B2, Zinc, Fe
dUMP
Urea
Arginine
Mn
Phenylalanine
Tyrosine
Tryptophan
BH4
Serine
H4Folate
Glycine
MT. B6
CH2H4
Folate
B3
CHH4Folate
(Methenyl)
H2O
Formyl
H4Folate
(Folinic)
Methionine
MAT
ATP
H2O
Sarcosine
oxidase
B2
SAM
CH3
DMG
dehydro-
genase B3
CH3
MT
B6
TMG
CH3
oxidase
B2
SAH
Choline
AHCY
H20
B3
MTR
B2
MTRR
B12
Ornithine
B6
Mg
Zinc
iNOS
Hydroxylase`
Hydroxyproline
Hydroxylysine
NH4
Biotin
MTHFR
B2, B3
DHPR
B3
Citrulline + NO`
+
O2⁻
= peroxynitrite
BH2
CH3H4
Folate
Homocysteine
Serine
CBS
B6, Vit C
Cystathione
B6, Mg, Zn
5HTP
Serotonin
B5, SAM
Melatonin
L.DOPA
Dopamine
Noradrenalin
Adrenalin
B6, Mg, Zn, Vit D
Vit C, Cu
SAM
NH3
biosynthase
B6
ATP + B6
Glutathione = Glutamic acid + Glycine + Cysteine + B5 = NAC
cysteine dioxidase
B3, Fe, O2
Sulfite oxidase Mol
Sulphate
Cysteine sulphite
decarboxylase
B6, Mg, Zn
T1
T2
T3
Iodine
Sel cysteine
Thyroxin
ATP-sulfurlase
ATP, Mn
kinase
ATP, Mg
Hypotaurine
Farnesyl phosphate
SAM, Vit C, B6, O2
oxidase
B3, Cu, Mol,
Vit C, O2
CoQ10
Phosphoadenosinephosphosulfate (PAPs)
Taurine
MAT = Methionine adenosyltransferase
MT = Methyltransferase
AHCY = Adenosylhomocysteinase
MTR = Methionine synthase
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MTRR = Methionine synthase reductase
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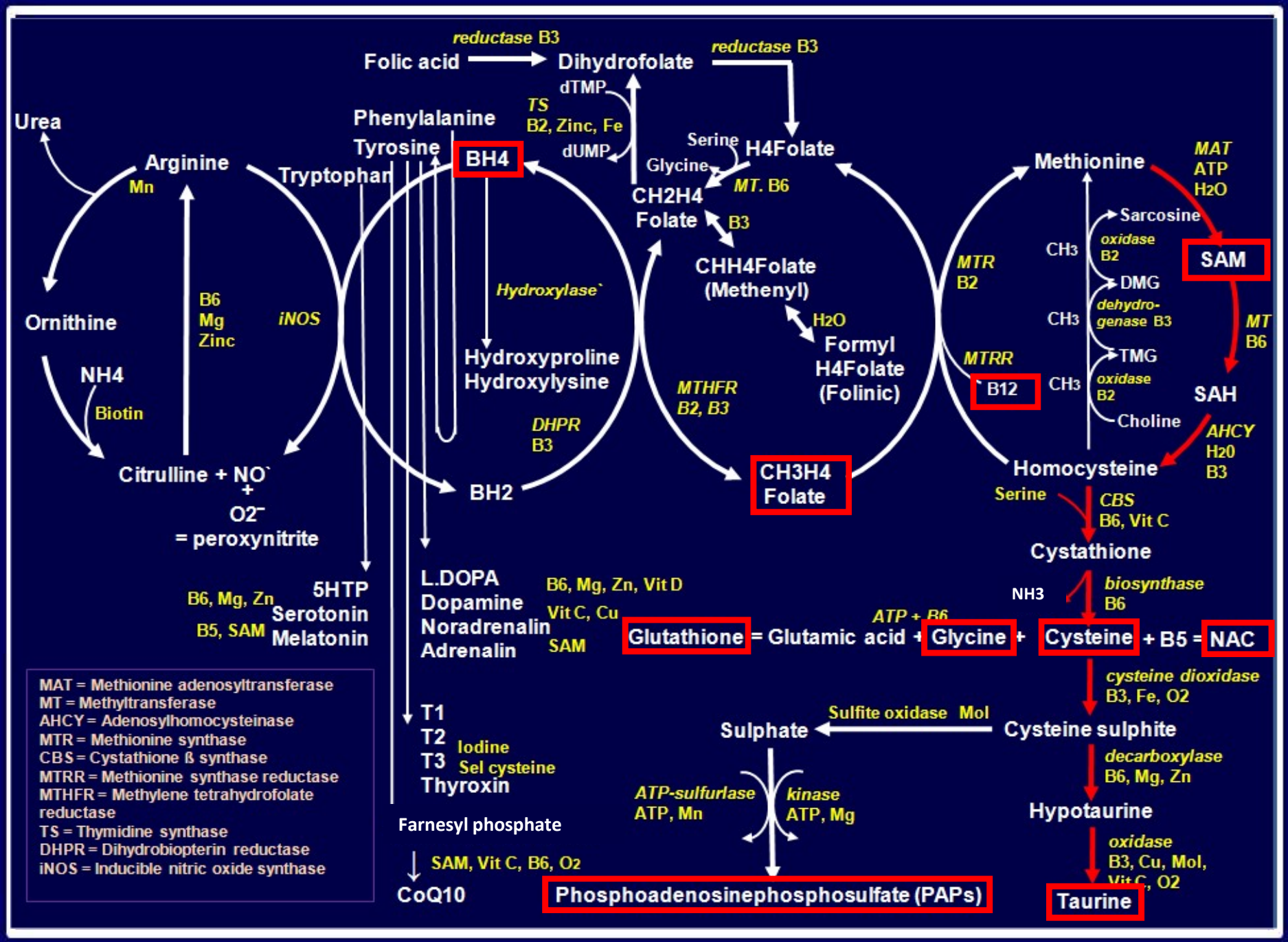
iNOS = Inducible nitric oxide synthase


Folic acid
reductase B3
Dihydrofolate
reductase B3
dTMP
TS
B2, Zinc, Fe
dUMP
Urea
Arginine
Mn
Phenylalanine
Tyrosine
Tryptophan
BH4
Serine
Glycine
H4Folate
MT. B6
CH2H4
Folate
B3
CHH4Folate
(Methenyl)
H2O
Formyl
H4Folate
(Folinic)
Methionine
MAT
ATP
H2O
Sarcosine
oxidase
B2
DMG
dehydro-
genase B3
TMG
oxidase
B2
Choline
CH3
CH3
CH3
SAM
MT
B6
SAH
AHCY
H20
B3
MTR
B2
MTRR
B12
Ornithine
B6
Mg
Zinc
iNOS
NH4
Biotin
Hydroxylase`
Hydroxyproline
Hydroxylysine
DHPR
B3
MTHFR
B2, B3
CH3H4
Folate
BH2
Citrulline + NO`
+
O2⁻
= peroxynitrite
Homocysteine
Serine
CBS
B6, Vit C
Cystathione
NH3
biosynthase
B6
B6, Mg, Zn
5HTP
Serotonin
B5, SAM
Melatonin
L.DOPA
Dopamine
Noradrenalin
Adrenalin
B6, Mg, Zn, Vit D
Vit C, Cu
SAM
Glutathione = Glutamic acid + Glycine + Cysteine + B5 = NAC
ATP + B6
cysteine dioxidase
B3, Fe, O2
Sulfite oxidase Mol
Sulphate
Cysteine sulphite
decarboxylase
B6, Mg, Zn
Hypotaurine
oxidase
B3, Cu, Mol,
Vit C, O2
Taurine
T1
T2
T3
Iodine
Sel cysteine
Thyroxin
Farnesyl phosphate
SAM, Vit C, B6, O2
CoQ10
ATP-sulfurlase
ATP, Mn
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ATP, Mg
Phosphoadenosinephosphosulfate (PAPs)
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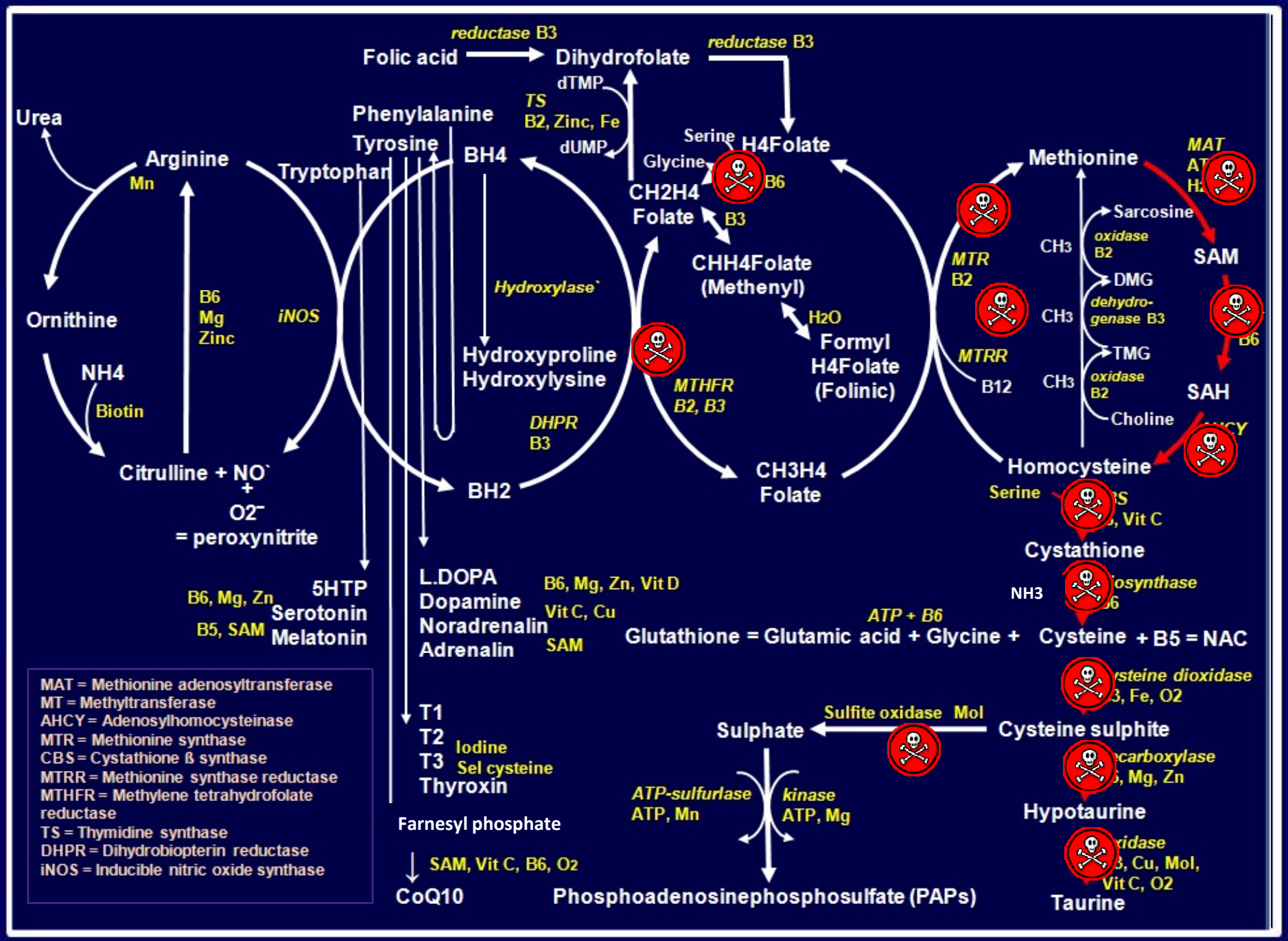
reductase B3
Folic acid
Dihydrofolate
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dTMP
TS
B2, Zinc, Fe
dUMP
Urea
Arginine
Mn
Phenylalanine
Tyrosine
Tryptophan
BH4
Serine
H4Folate
Glycine
B6
CH2H4
Folate
B3
CHH4Folate
(Methenyl)
H2O
Formyl
H4Folate
(Folinic)
Methionine
MAT
Sarcosine
oxidase
B2
SAM
CH3
DMG
dehydro-
genase B3
TMG
oxidase
B2
Choline
SAH
MTR
B2
MTRR
B12
Ornithine
B6
Mg
Zinc
iNOS
NH4
Biotin
Hydroxylase`
Hydroxyproline
Hydroxylysine
MTHFR
B2, B3
DHPR
B3
Citrulline + NO`
+
O2⁻
= peroxynitrite
BH2
CH3H4
Folate
Homocysteine
Serine
Vit C
Cystathione
NH3
ATP + B6
Glutathione = Glutamic acid + Glycine +
Cysteine + B5 = NAC
B6, Mg, Zn
5HTP
Serotonin
B5, SAM
Melatonin
L.DOPA
Dopamine
Noradrenalin
Adrenalin
B6, Mg, Zn, Vit D
Vit C, Cu
SAM
T1
T2
T3
Thyroxin
Iodine
Sel cysteine
Farnesyl phosphate
SAM, Vit C, B6, O2
CoQ10
Sulfite oxidase
Mol
Sulphate
Cysteine sulphite
Fe, O2
Mg, Zn
Hypotaurine
Cu, Mol,
Vit C, O2
Taurine
ATP-sulfurlase
ATP, Mn
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ATP, Mg
Phosphoadenosinephosphosulfate (PAPs)
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Glutathione

Glutathione

Xenobiotics such as aromatic disulfides, phenol, napthalene, anthracene, phenanthacin compounds, aliphatic disulfides and the regeneration of endogenous thiols from disulfides.

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 679

Hayes JD, Flanagan JU, Jowsey IR (2005). "Glutathione transferases". *Annu. Rev. Pharmacol. Toxicol*. 45: 51–88. doi:10.1146/annurev.pharmtox.45.120403.095857. PMID 15822171

Cysteine

Glutamic acid

ATP → ADP

γ- glutamylcysteine ligase

Mg, Mn, Zn 1p 370nm

γ- Glutamylcysteine

Glycine

ATP → ADP

glutathione synthetase

Mg, S 20q 397nm

GSSG

GSH

Glutathione

Xenobiotics
Toxic metals

40%

GST

Glutamate Cysteine Ligase (GCL) is the first enzyme of the cellular glutathione (GSH) biosynthetic pathway.GSH, and by extension GCL, is critical to cell survival. Nearly every eukaryotic cell, from plants to yeast to humans, expresses a form of the GCL protein for the purpose of synthesizing GSH. *

**Dalton TP, et al. (2004). "Genetically altered mice to evaluate glutathione homeostasis in health and disease". Free Radic Biol Med. 37 (10): 1511–26.*

To further highlight the critical nature of this enzyme, genetic knockdown of GCL results in embryonic lethality.* Furthermore, dysregulation of GCL enzymatic function and activity is known to be involved in the vast majority of human diseases, such as diabetes, Parkinson's disease, Alzheimers disease, COPD, HIV/AIDS, and cancer. **

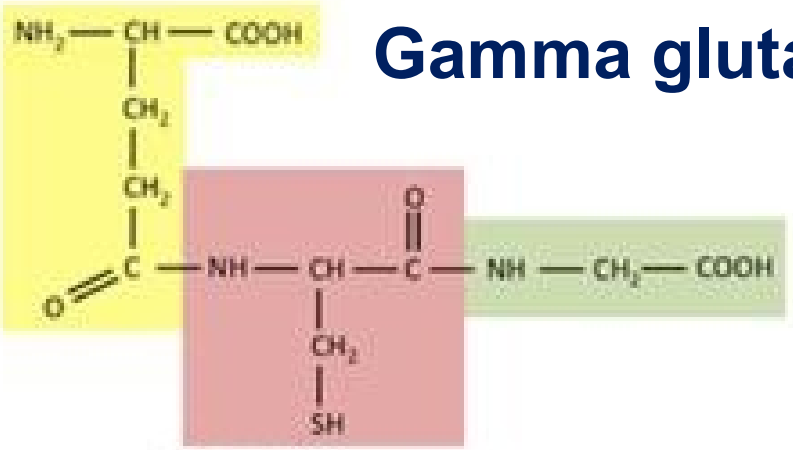
*Dalton TP, et al. (2004). "Genetically altered mice to evaluate glutathione homeostasis in health and disease". *Free Radic Biol Med*. 37 (10): 1511–26.

.**"Regulation of glutathione synthesis". *Mol Aspects Med*. 30 (1–2): 42–59.

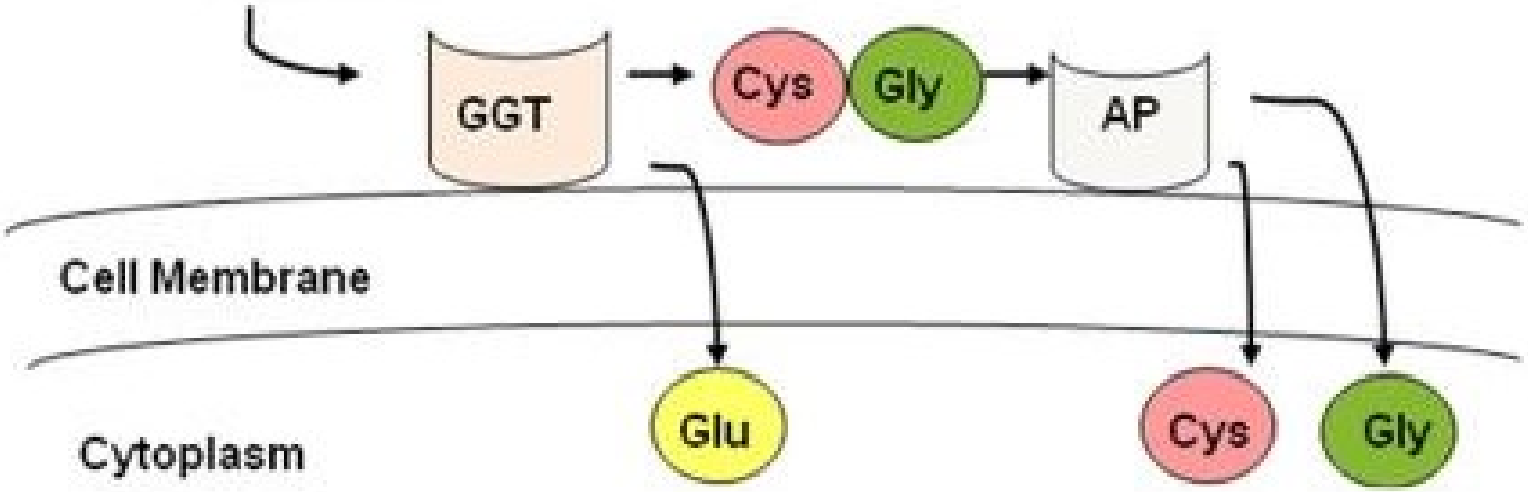
This typically involves impaired function leading to decreased GSH biosynthesis, reduced cellular antioxidant capacity, and the induction of oxidative stress. However, in cancer, GCL expression and activity is enhanced, which serves to both support the high level of cell proliferation and confer resistance to many chemotherapeutic agents.***

*** Backos DS, et al. (2012). "The role of glutathione in brain tumor drug resistance". *Biochem Pharmacol*. 83 (8): 1005–12.

Gamma glutamyltransferase (GGT)



Glutathione



Hydrolysis of extracellular glutathione by GGT. GGT releases glutamate and cysteinyl-glycine. Cysteinyl-glycine hydrolysed by aminopeptidase (AP) releasing cysteine and glycine. All three amino acids can then be taken up into the cell to synthesise glutathione but process not very efficient. Glutathione cannot be taken up intact in most cells.

Gamma-glutamyltransferase (GGT)

High in

Alcohol abuse, Barbituates, NSAIs, Aspirin, St John's wort.

Biliary, liver and pancreas diseases

CVD and Atherosclerosis

Metabolic syndrome. High body mass index is associated with type 2 diabetes only in persons with high serum GGT.

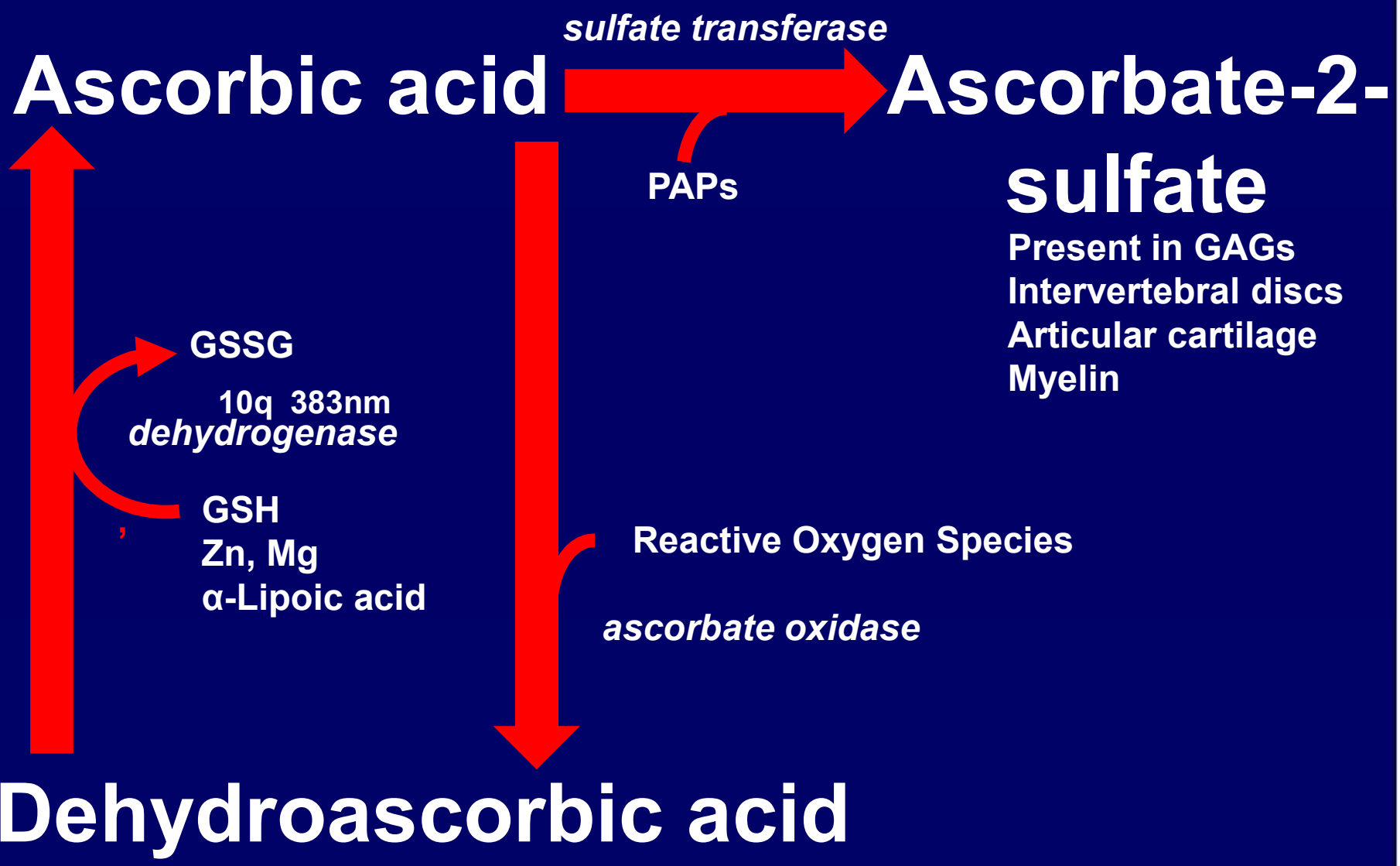
Lim JS, Lee DH, Park JY, Jin SH, Jacobs DR (June 2007). "A strong interaction between serum gamma-glutamyltransferase and obesity on the risk of prevalent type 2 diabetes: results from the Third National Health and Nutrition Examination Survey". Clinical Chemistry. 53 (6): 1092–8. doi:10.1373/clinchem.2006.079814. PMID 17478563.

Glutathione dehydrogenase (ascorbate) is an enzyme that catalyzes the chemical reaction

2 glutathione + dehydroascorbate > glutathione disulfide + ascorbate. *

*Savita Gangwar, ... Jagat Narayan Maurya, in Emerging Technologies and Management of Crop Stress Tolerance, Volume 2, 2014

Vitamin C


sulfate transferase
Ascorbic acid
Ascorbate-2-sulfate
PAPs
Present in GAGs
Intervertebral discs
Articular cartilage
Myelin
GSSG
10q 383nm
dehydrogenase
GSH
Zn, Mg
α-Lipoic acid
Reactive Oxygen Species
ascorbate oxidase
Dehydroascorbic acid

Sulfation

Sulfation

Neurotransmitters, steroid hormones, certain drugs, many xenobiotic and phenolic compounds such as estrogens, aliphatic alcohols, aryl amines and alicyclic hydroxysteroids, paracetamol (acetaminophen), Bisphenol A, cyanide, oxalates

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 679
The Detoxification System Part III: Sulfoxidation and Sulfation by Mark J Donohue
file:///E:/Users/Chris%20Astill-Smith/Downloads/Report%20%2311%20-%20Sulfoxidation.pdf

Taurine

Taurine

Bile acids,

Hypochlorites

The Detoxification System Part III: Sulfoxidation and Sulfation by Mark J Donohue
file:///E:/Users/Chris%20Astill-Smith/Downloads/Report%20%2311%20-%20Sulfoxidation.pdf

Cysteine

O2, NADPH, Fe

cysteine dioxygenase 5q 377nm

Cysteine sulfinate

P-5-P

CO2

cysteine sulfinate decarboxylase

12q 385nm

Hypotaurine

NAD, Fe, Mol

NADH+H

hypotaurine dehydrogenase

12q 385nm

Taurine

Metabolic Pathways -
http://smpdb.ca/search