



---

---

---

---

---

---

---

---

### Causes of Aging

1. Degradation of your “cellular timekeepers”, known as telomeres.
2. Progressive death over time to your body’s main “power source”, your mitochondria.
3. Free radical exposure and resulting oxidative damage (i.e. the “rusting” of your body’s cells).

---

---

---

---

---

---

---

---

1. Gene damage - DNA polymerase
2. SNIPs – 380nm
3. Gene regulation
  1. Methylation - SAM
  2. Citrullination - Citrulline
  3. Acetylation - AcetylCoA
  4. Phosphorylation - ATP
  5. SUMOylation - Ubiquitin
  6. Ubiquitination - Ubiquitin
  7. ADP-ribosylation - Adenosine 5 diphosphoribose
4. Codon challenge – 400nm

---

---

---

---

---

---

---

---

**Identifying the Subconscious (Definitive) Meridian**

---

---

---

---

---

---

---

---

**Identifying the Subconscious meridian**  
**1. With eyes looking down TL around al the B&E points.**

**The one that weakens is the subconscious meridian.**

---

---

---

---

---

---

---

---

**Yang points indicate neurotransmitter deficiencies.**

**Yin points indicate neurotransmitter excesses**

**B and E Points**

---

---

---

---

---

---

---

---

**2. Patient TLs positive B&E point(s) (or with subconscious meridian acetate on umbilicus) whilst looking down and practitioner taps Definitive Point 60x at 2 Hz.**

---

---

---

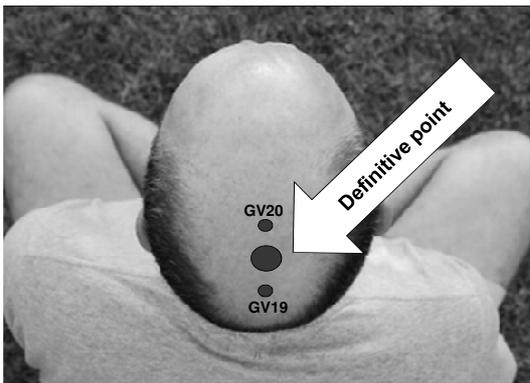
---

---

---

---

---



---

---

---

---

---

---

---

---

**3. Identify weak associated meridian muscle.  
Usually just one on the associated meridian.  
All other associated muscles will weaken when tested bilaterally.  
Use this muscle to test for priority when using any nutritional supplement(s).**

---

---

---

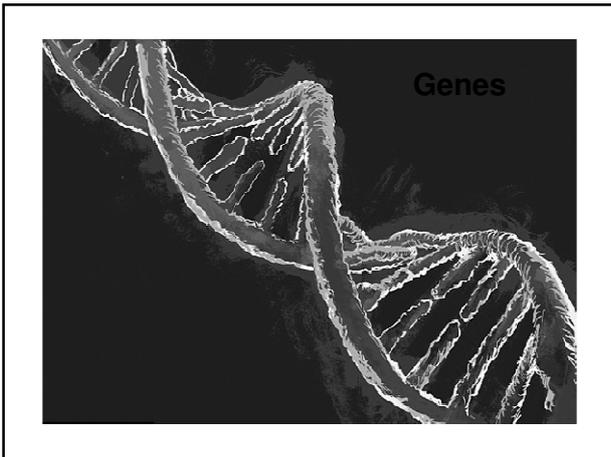
---

---

---

---

---



---

---

---

---

---

---

---

**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.**

---

---

---

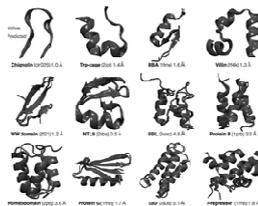
---

---

---

---

**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.**



---

---

---

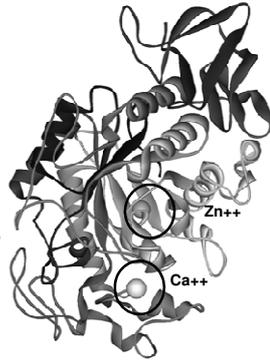
---

---

---

---

Enzymes require co-factors to function e.g. Amylase which requires Calcium and Zinc



---

---

---

---

---

---

---

---

Proteins are made of amino acids  
They -

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

---

---

---

---

---

---

---

---

Amino acids are biologically important organic compounds composed of amine (-NH<sub>2</sub>) 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, hydrogen, oxygen, and nitrogen.

---

---

---

---

---

---

---

---



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.

---

---

---

---

---

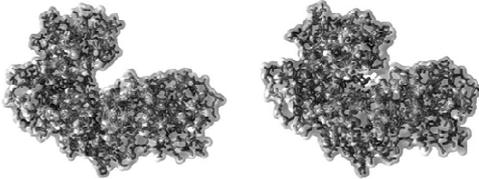
---

---

---

**Conformation A    Conformation B**

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



---

---

---

---

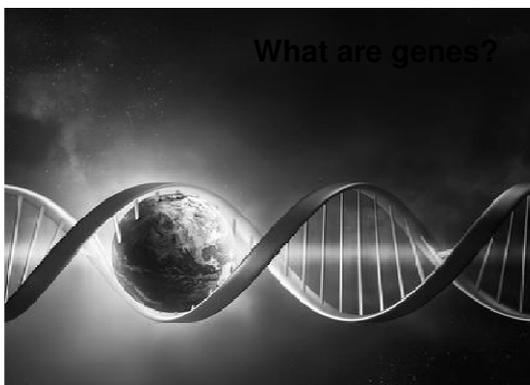
---

---

---

---

What are genes?



---

---

---

---

---

---

---

---

**Genes are build from chains of Deoxyribonucleic Acid (DNA)**

**Genes are modulated by primary and secondary messengers.  
“Turning the gene on” is known as gene expression.**

---

---

---

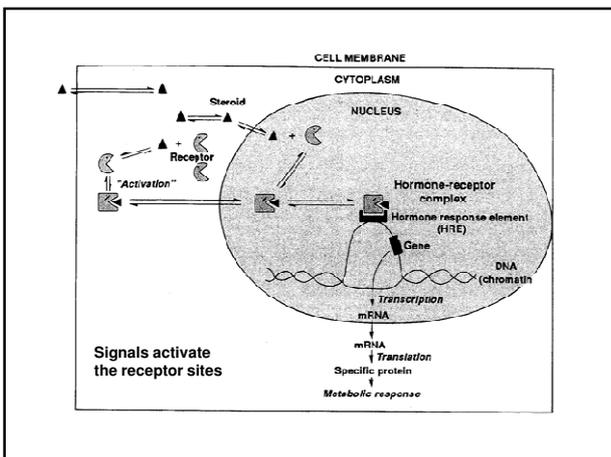
---

---

---

---

---



---

---

---

---

---

---

---

---

**Primarily, genes encode for the synthesis of proteins.**

**The human genome possesses about 24,000 genes.**

**Plants encode for about 18,000 genes.**

**Fruit flies encode for 20,000 genes.**

---

---

---

---

---

---

---

---

The message coded within the gene is first transcribed into a template mirror image of the coding strand of the DNA by messenger Ribonucleic Acid (mRNA).

RNA contains the same bases as DNA except that Uracil replaces Thymine.

---

---

---

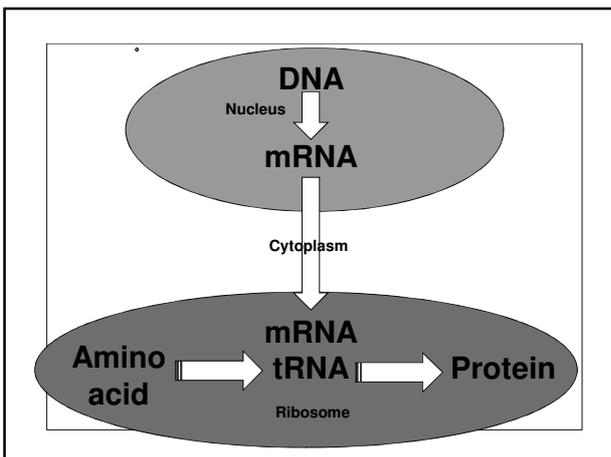
---

---

---

---

---



---

---

---

---

---

---

---

---

(Messenger) mRNA translates the gene expression from the gene to the ribosome to synthesise protein enzymes.



---

---

---

---

---

---

---

---

**(Transfer) tRNA serves as an adapter molecule for the translation of mRNA into protein sequences.**

---

---

---

---

---

---

---

---

**(Ribosomal) rRNA contributes to the formation of ribosomes.**

**Ribosomes are a mixture of RNA molecules and protein and can in themselves act as enzymatic catalysts.**

---

---

---

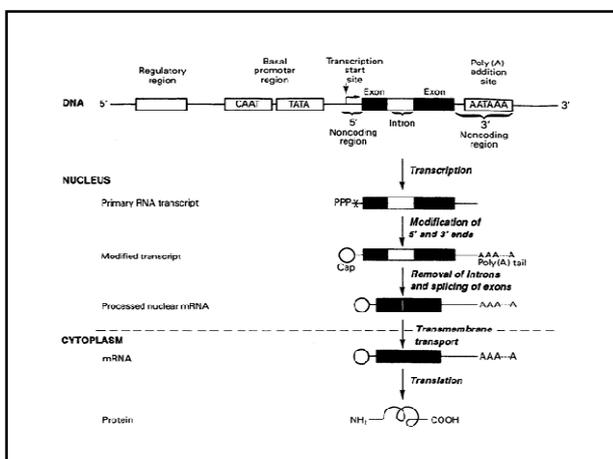
---

---

---

---

---




---

---

---

---

---

---

---

---

**Both DNA and RNA are composed of Nucleotides derived from either purine or pyrimidine bases.**

**The purine bases are Adenine and Guanine.**

**The pyrimidine bases are Cytosine, Uracil and Thymine.**

---

---

---

---

---

---

---

---

**Nucleosides are bases that have ribose or deoxyribose sugar linked via a covalent bond.**

**Nucleotides are mono-phosphorylated nucleosides.**

---

---

---

---

---

---

---

---

**Building Nucleic acids**

<b>Bases</b>	Adenine, Cytosine, Guanine, Thymine, Uracil
<b>Nucleosides</b>	Adenosine, Cytidine, Guanosine, Thymidin, Uridine
<b>Nucleotides</b>	AMP, CMP, GMP, TMP, UMP dAMP, dCMP, dGMP, dTMP,dUMP
<b>Nucleic acids</b>	RNA, DNA

---

---

---

---

---

---

---

---

Base Formula	Base	Nucleoside X = Ribose or Deoxyribose	Nucleotide X = Ribose phosphate
	<b>Adenine</b> A	<b>Adenosine</b> A	<b>Adenosine monophosphate</b> AMP
	<b>Guanine</b> G	<b>Guanosine</b> G	<b>Guanosine monophosphate</b> GMP
	<b>Cytosine</b> C	<b>Cytidine</b> C	<b>Cytidine monophosphate</b> CMP
	<b>Uracil</b> U	<b>Uridine</b> U	<b>Uridine monophosphate</b> UMP
	<b>Thymine</b> T	<b>Thymidine</b> T	<b>Thymidine monophosphate</b> TMP

---

---

---

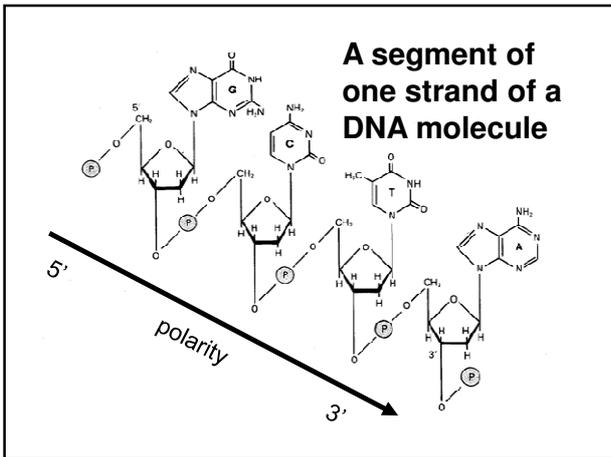
---

---

---

---

---




---

---

---

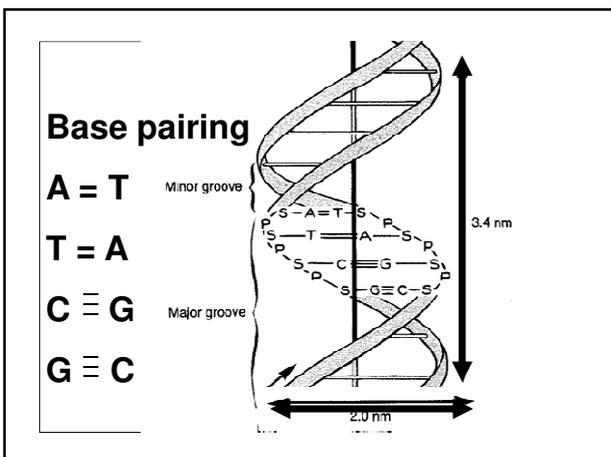
---

---

---

---

---




---

---

---

---

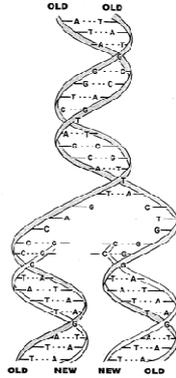
---

---

---

---

The double stranded structure of DNA and the template function of each old strand (shaded) on which a new complementary strand is synthesised.




---

---

---

---

---

---

---

---

**DNA Coding**

TTT	Phe	TCT	Ser	TAT	Tyr	TGT	Cys
TTC	Phe	TCC	Ser	TAC	Tyr	TGC	Cys
TTA	Leu	TCA	Ser	TAA	Stop	TGA	Stop
TTG	Leu	TCG	Ser	TAG	Stop	TGG	Trp
CTT	Leu	CCT	Pro	CAT	His	CGT	Arg
CTC	Leu	CCC	Pro	CAC	His	CGC	Arg
TTA	Leu	CCA	Pro	CAA	Gln	CGA	Arg
CTG	Leu	CCG	Pro	CAG	Gln	CGG	Arg
ATT	Ile	ACT	Thr	AAT	Asn	AGT	Ser
ATC	Ile	ACC	Thr	AAC	Asn	AGC	Ser
ATA	Ile	ACA	Thr	AAA	Lys	AGA	Arg
ATG	Met	ACG	Thr	AAG	Lys	AGG	Arg
GTT	Val	GCT	Ala	GAT	Asp	GGT	Gly
GTC	Val	GCC	Ala	GAC	Asp	GGC	Gly
GTA	Val	GCA	Ala	GAA	Glu	GGA	Gly
GTG	Val	GCG	Ala	GAG	Glu	GGG	Gly

---

---

---

---

---

---

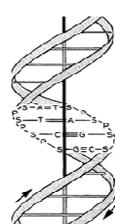
---

---

DNA strands:  
 Coding → 5'—TGBAA TTGTACGGGATAACAATTTACACAGGAAACAGCTATGACCATG—3'  
 Template → 3'—ACCTTAACACTCGCCTATTGTTAAAGTGTGTCTTTGTGATACTGGTAC—5'  
 RNA transcript: 5' → AUUGUAGCGGAUAACA AUUUCACACAGGAAACAGCUAUGACCAUG—3'

The relationship between the sequences of an RNA transcript and its gene, in which the coding and template strands are shown with their polarities. The RNA transcript with a 5' to 3' polarity is complementary to the template strand with its 3' to 5' polarity. Note that the sequence in the RNA transcript and its polarity is the same as that in the coding strand, except that the U of the transcript replaces the T of the gene.

e.g. DNA Coding – ATG  
 DNA Template – TAC  
 mRNA Coding – AUG



**DNA Coding and Template strands**

---

---

---

---

---

---

---

---

**DNA Template**

AAA	Phe	AGA	Ser	ATA	Tyr	ACA	Cys
AAG	Phe	AGG	Ser	ATG	Tyr	ACG	Cys
AAT	Leu	AGT	Ser	ATT	Stop	ACT	Stop
AAC	Leu (i)	AGC	Ser	ATC	Stop	ACC	Trp
GAA	Leu	GGA	Pro	GTA	His	GCA	Arg
GAG	Leu	GGG	Pro	GTG	His	GCG	Arg
AAT	Leu	GGT	Pro	GTT	Gln	GCT	Arg
GAC	Leu (i)	GGC	Pro	GTC	Gln	GCC	Arg
TAA	Ile	TGA	Thr	TTA	Asn	TCA	Ser
TAG	Ile	TGG	Thr	TTG	Asn	TCG	Ser
TAT	Ile	GTG	Thr	TTT	Lys	TCT	Arg
TAC	Met (i)	TGC	Thr	TTC	Lys	TCC	Arg
CAA	Val	CGA	Ala	CTA	Asp	CCA	Gly
CAG	Val	CGG	Ala	CTG	Asp	CCG	Gly
CAT	Val	CGT	Ala	CTT	Glu	CCT	Gly
CAC	Val	CGC	Ala	CTC	Glu	CCC	Gly

---

---

---

---

---

---

---

---

---

---

---

---

**mRNA Coding**

UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys
UUC	Phe	UCC	Ser	UAC	Tyr	UGC	Sel Cys
UUA	Leu	UCA	Ser	UAA	Stop	UGA	Stop
UUG	Leu (i)	UCG	Ser	UAG	Pyrrrolysine	UGG	Trp
CUU	Leu	CCU	Pro	CAU	His	CGU	Arg
CUC	Leu	CCC	Pro	CAC	His	CGC	Arg
UUA	Leu	CCA	Pro	CAA	Gln	CGA	Arg
CUG	Leu (i)	CCG	Pro	CAG	Gln	CGG	Arg
AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser
AUC	Ile	ACC	Thr	AAC	Asn	AGC	Ser
AUA	Ile	ACA	Thr	AAA	Lys	AGA	Arg
AUG	Met (i)	ACG	Thr	AAG	Lys	AGG	Arg
GUU	Val	GCT	Ala	GAU	Asp	GGU	Gly
GUC	Val	GCC	Ala	GAC	Asp	GGC	Gly
GUA	Val	GCA	Ala	GAA	Glu	GGA	Gly
GUG	Val	GCG	Ala	GAG	Glu	GGG	Gly

---

---

---

---

---

---

---

---

---

---

---

---

**Nucleotides are synthesised by**

- 1. De novo synthesis from amphibolic intermediates**
- 2. Ingestion from foods**
- 3. Repair of damaged molecules**

---

---

---

---

---

---

---

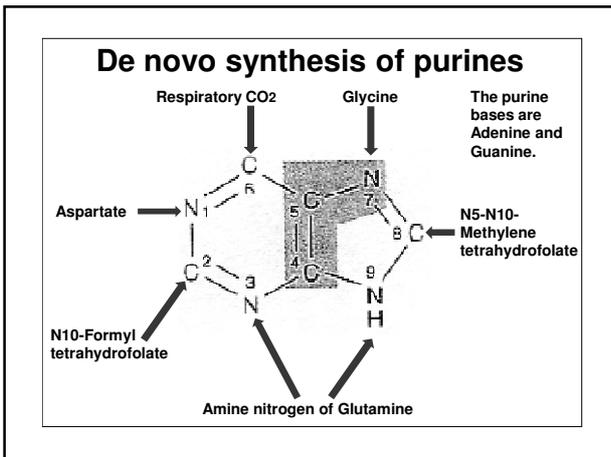
---

---

---

---

---




---

---

---

---

---

---

---

---

**Nucleotides are synthesised by**

1. De novo synthesis from amphibolic intermediates
2. Ingestion from foods
3. Repair of damaged molecules

---

---

---

---

---

---

---

---

**Nucleic acids released from ingested food and nuclear proteins in the intestinal tract are degraded to mononucleotides by ribonucleases, deoxyribonucleases and polynucleotidases.**

---

---

---

---

---

---

---

---

**Nucleotidases and phosphatases hydrolyze the mononucleotides to nucleosides, which either are absorbed or are further degraded by intestinal phosphorylase to purine and pyrimidine bases.**

---

---

---

---

---

---

---

---

**Nucleotides are synthesised by**

- 1. De novo synthesis from amphibolic intermediates**
- 2. Ingestion from foods**
- 3. Repair of damaged molecules**

---

---

---

---

---

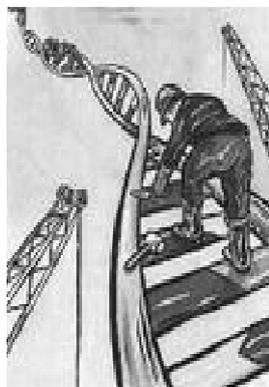
---

---

---

**DNA Repair**

**The initiation of DNA synthesis requires priming by a short length of RNA.**



---

---

---

---

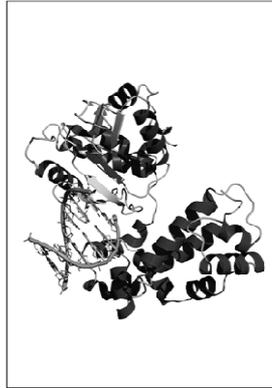
---

---

---

---

**The process is regulated by DNA polymerase which is a zinc dependant metallo-enzyme.**



---

---

---

---

---

---

---

---

**The selection of the entering deoxyribonucleotide is dependant upon proper base pairing with the other strand of the DNA molecule.**

---

---

---

---

---

---

---

---

**A deficiency in DNA polymerase may lead to the insertion of an incorrect base into the DNA sequence thus creating a single nucleotide polymorphism (SNIP).**

---

---

---

---

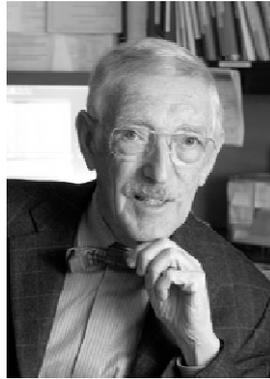
---

---

---

---

**According to Bruce Ames each cell in the body suffers between 25,000-100,000 oxidative hits per day.**



---

---

---

---

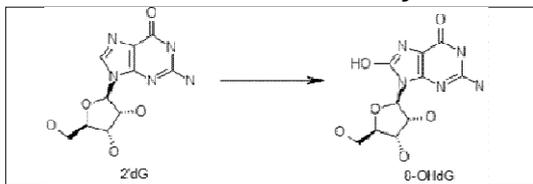
---

---

---

---

**This figure is obtained by measuring the quantity of oxidised deoxyguanosine in the urine per day and dividing by the number of cells in the body.**



---

---

---

---

---

---

---

---

**The same cofactors apply to RNA repair by RNA polymerase, also a zinc dependant enzyme.**

---

---

---

---

---

---

---

---

**So for optimal DNA / RNA repair there must be**

- 1. An adequate pool of nucleotide bases and**
- 2. Zinc for the dependant DNA polymerase and RNA polymerase enzymes.**

---

---

---

---

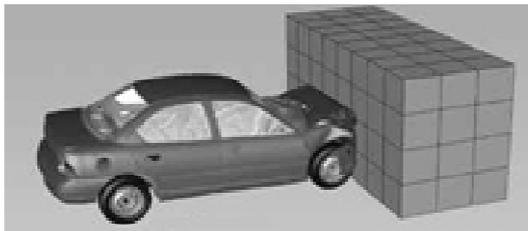
---

---

---

---

**Think of DNA polymerase as the cement needed to repair the wall**



**and think of DNA as needed to replace the broken bricks**

---

---

---

---

---

---

---

---

**Optimal forms of zinc**

**Colloidal zinc**

**Zinc ascorbate**

**Zinc bisglycinate**

**Zinc citrate**

**Zinc picolinate**

**Triple zinc**

---

---

---

---

---

---

---

---

**The single food most capable of repairing DNA is the Beetroot. Can repair chromosome abnormalities.**



---

---

---

---

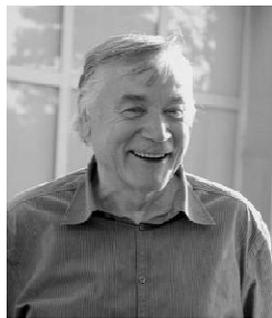
---

---

---

---

**SNIP's**



**Fritz Albert Popp**

---

---

---

---

---

---

---

---

**Popp chose to work specifically with UV light because of the experiments of a Russian biologist named Alexander Gurwitsch who, while working with onions in 1923, discovered that roots could stimulate a neighbouring plant's roots if the two adjacent plants were in quartz glass pots but not if they were in silicon glass pots. The only difference being that the silicon filtered UV wavelengths of light while the quartz did not. Gurwitsch theorized that onion roots could communicate with each other by ultraviolet light.**

---

---

---

---

---

---

---

---

What Popp discovered was that benzo[a]pyrene (the cancer producing molecule) absorbed the UV light, then re-emitted it at a completely different frequency -- it was a light "scrambler". The benzo[e]pyrene (harmless to humans), allowed the UV light to pass through it unaltered. Popp was puzzled by this difference, and continued to experiment with UV light and other compounds. He performed his test on 37 different chemicals, some cancer-causing, some not. After a while, he was able to predict which substances could cause cancer. In every instance, the compounds that were carcinogenic took the UV light, absorbed it and changed or scrambled the frequency. Each of the carcinogens reacted only to light at a specific frequency -- 380 nm (nanometres) in the ultra-violet range.

---

---

---

---

---

---

---

---

---

---

**Genotoxicity**

In genetics, genotoxicity describes the property of chemical agents that damages the genetic information within a cell causing mutations, which may lead to cancer.

While genotoxicity is often confused with mutagenicity, all mutagens are genotoxic, however, not all genotoxic substances are mutagenic.

---

---

---

---

---

---

---

---

---

---

In genetics, a mutagen is a physical or chemical agent that changes the genetic material, usually DNA, of an organism and thus increases the frequency of mutations above the natural background level. As many mutations can cause cancer, mutagens are therefore also likely to be carcinogens.

---

---

---

---

---

---

---

---

---

---



---

---

---

---

---

---

---

---

**There are normal variations of DNA sequences known as polymorphisms.**

**They occur once in every 500 nucleotides, or about 107 times per genome.**

**They occur mostly in the non-coding regions of DNA.**

---

---

---

---

---

---

---

---

**CELL MUTATIONS**

**Result when changes occur in the nucleotide sequence due to**

- 1. Nutritional deficiencies.**
- 2. By Pathogens, Chemicals, Mycotoxins, Ultra-violet and ionizing Radiation induced oxidative damage.**
- 3. Depurination from thermal lability.**

---

---

---

---

---

---

---

---

Once of the most dangerous chemicals is benzene as it may cause chromosome breaks 5-30 years after exposure on chromosome 2 and 5 causing portions of 2 to fuse with 5. The result is multiple myeloma or lymphoma

---

---

---

---

---

---

---

---

According to Bruce Ames

As many as one third of mutations in a gene result in the corresponding enzyme having an increased Michaelis constant or  $K_m$  (decreased binding affinity) for a coenzyme, resulting in a lower rate of reaction.

---

---

---

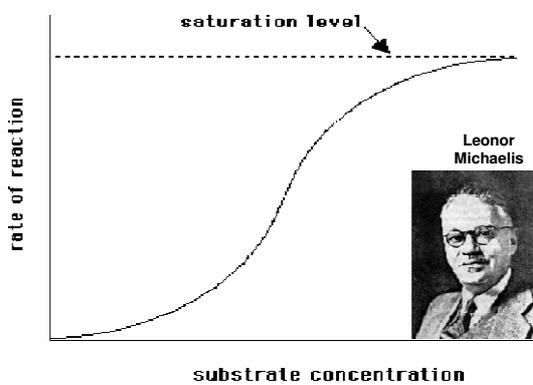
---

---

---

---

---



---

---

---

---

---

---

---

---

**The  $K_m$  is a measure of the binding affinity of an enzyme for its ligand (i.e. substrate or coenzyme) and is defined as the concentration of ligand required to fill one half of the ligand binding sites.**

---

---

---

---

---

---

---

---

**About 50 human genetic diseases due to defective enzymes can be remedied or ameliorated by the administration of high doses of the corresponding vitamin coenzyme, which at least partially restores enzymatic activity.**

---

---

---

---

---

---

---

---

**Many Single Point Mutations (SNIPs), in which the variant amino acid reduces coenzyme binding and thus enzymatic activity, are likely to be remediable by raising cellular concentrations of the vitamin coenzyme.**

---

---

---

---

---

---

---

---

**Mutations maybe**

- 1. Single Point Mutations (SNIPs).**
- 2. Deletions, Insertions and Rearrangements of DNA (Cut and Pastes).**

---

---

---

---

---

---

---

---

**Single base point mutations (SNIPs) maybe**

- 1. Transitions where a given purine is changed to the other purine or a given pyrimidine is changed to the other pyrimidine.**

---

---

---

---

---

---

---

---

**PURINES**

**ADENINE ↔ GUANINE**

**PYRIMIDINE**

**CYTOSINE ↔ THYMINE**

---

---

---

---

---

---

---

---

or where Uracil from (dUMP) is incorporated into the Thymine (dTMP) position in DNA.

**URACIL → THYMINE**

---

---

---

---

---

---

---

2. Transversions are changes from a purine to either of the two pyrimidines or the change of a pyrimidine into either of the two purines.

---

---

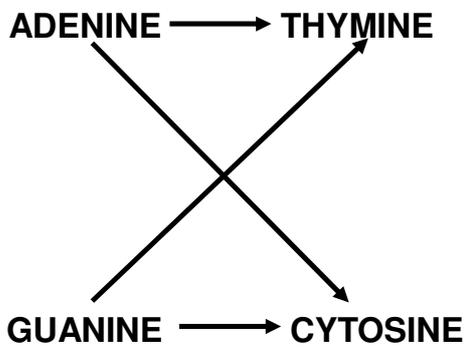
---

---

---

---

---



---

---

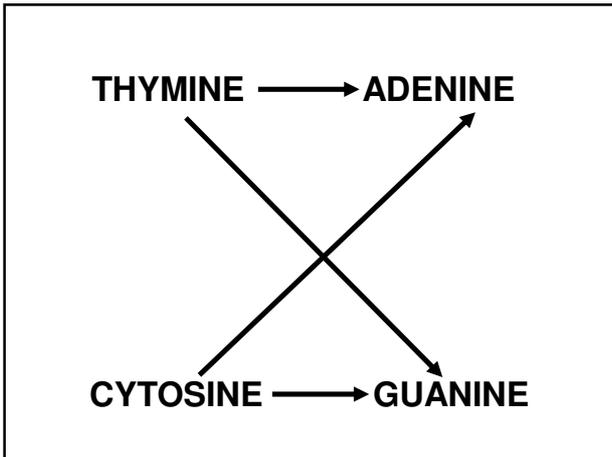
---

---

---

---

---



---

---

---

---

---

---

---

---

Single base changes will be replicated within the mRNA transcription.

There maybe

1. No detectable effect.
2. A mis-sense effect
3. A nonsense codon effect.

---

---

---

---

---

---

---

---

**SNIP Challenge**

1. Challenge each vial of nucleotide bases from strength to weakening over lower abdomen.
2. Note which one weakens.

---

---

---

---

---

---

---

---

- 1. Adenine
- 2. Cytosine
- 3. Guanine
- 4. Thymine
- 5. Uracil

---

---

---

---

---

---

---

**3. Challenge weakening nucleotide base against each of the other nucleotide bases to identify which negates.  
e.g. G>T**

**This will indicate the specific single nucleotide polymorphism (SNIP).**

---

---

---

---

---

---

---

**There is always an associated co-enzyme with each SNIP.**

**This indicates that a greater than normal amount of the coenzyme is required to bring an enzyme up to a more correct rate of reaction.**

---

---

---

---

---

---

---

**Each SNIP defect maybe  
apparent to Nutritional  
deficiency of the  
necessary substrates and  
Cofactors to activate the vitamin  
to become a coenzyme.**

---

---

---

---

---

---

---

---

- Each SNIP defect is caused by**
- 1. Inherited polymorphism (Miasm)**
  - 2. Acquired – Due to Zinc deficiency leading to reduced DNA / RNA polymerase function for the repair caused by ROS as a result of exposure to pathogens especially viruses, toxic metals, mycotoxins, chemicals and / or ionising radiation.**

---

---

---

---

---

---

---

---

Coding DNA Coding							
TTT	Phe	TCT	Ser	TAT	Tyr	TGT	Cys
TTC	Phe	TCC	Ser	TAC	Tyr	TGC	Cys
TTA	Leu	TCA	Ser	TAA	Stop	TGA	Stop
TTG	Leu (i)	TCG	Ser	TAG	Stop	TGG	Trp
CTT	Leu	CCT	Pro	CAT	His	CGT	Arg
CTC	Leu	CCC	Pro	CAC	His	CGC	Arg
TTA	Leu	CCA	Pro	CAA	Gln	CGA	Arg
CTG	Leu (i)	CCG	Pro	CAG	Gln	CGG	Arg
ATT	Ile	ACT	Thr	AAT	Asn	AGT	Ser
ATC	Ile	ACC	Thr	AAC	Asn	AGC	Ser
ATA	Ile	ACA	Thr	AAA	Lys	AGA	Arg
ATG	Met (i)	ACG	Thr	AAG	Lys	AGG	Arg
GTT	Val	GCT	Ala	GAT	Asp	GGT	Gly
GTC	Val	GCC	Ala	GAC	Asp	GGC	Gly
GTA	Val	GCA	Ala	GAA	Glu	GGA	Gly
GTG	Val	GCG	Ala	GAG	Glu	GGG	Gly

---

---

---

---

---

---

---

---

SNIP	COENZYME	FUNCTION	FRUIT / SEED	INFECTION
A>C	Methylcobalamin	Methylation	Orange pepper	Rubella
A>G	Thiamine pyro	Decarboxylation	Pea	Morbillinum, HG
A>T	SAM	Methylation	Kiwi, Papaya	Influenza
A>U	FAD(H)	Oxidation-reduction	Blueberry	Hepatitis
C>A	Adenosylcobalamin	Alkylation	Yellow pepper	Poliomyelitis
C>G	Thiamine triphos	Acetylation	Beans	Tuberculosis CMV
C>T	CH3H4Folate (Methyl)	Methylation	Broccoli	Varicella
C>U	Vit C	Oxidation-reduction	Rosehips	Herpes simplex
G>A	NAD(H)	Oxidation-reduction	Blackcurrant	Parotitis
G>C	Carboxybiotin	Carboxylation	Pumpkin	Chlamydia
G>T	P5P	Decarboxylation, Transamination	Red pepper	Gonorrhea
G>U	H4Biotin	Hydroxylation	Broad bean	Coxsackie
T>A	NADP(H)	Oxidation-reduction	Blackberry	Pertussis
T>C	FMN(H)	Oxidation-reduction	Bilberry	Hepatitis
T>G	Lipoamide	Acyl transfer	Watermelon	Herpes Zoster
T>U	CoQ10	Oxidation-reduction	Black grape	Mononucleosis
U>A	CH H4Folate (Methenyl or Folinic acid)	One carbon transfer	Raspberry	Syphilis
U>C	H4 Folate (Folic acid + NADH)	One carbon transfer	Gooseberry	Adeno virus
U>G	CoA	Acyl transfer	Elderberry	Salmonella, Varicella
U>T	CH2 H4 Folate (Methylene)	Methylation of uracil	Green pepper	Human Papilloma

---

---

---

---

---

---

---

---

---

---

---

---

**Assessing the optimal nutrient(s)**  
**With the weakening nucleotide**  
**base on the patient challenge with**  
**the appropriate co-enzyme.**  
**Should strengthen.**

---

---

---

---

---

---

---

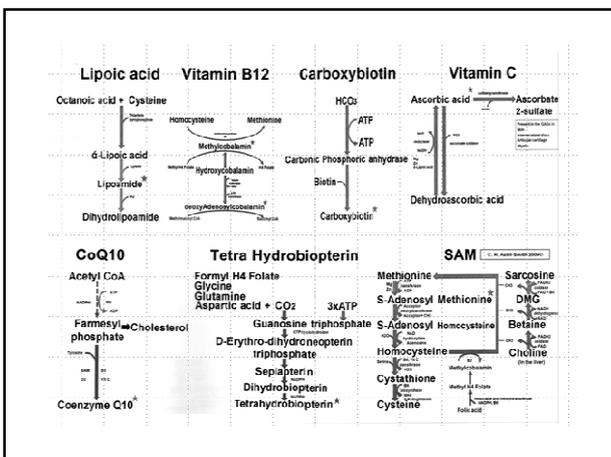
---

---

---

---

---




---

---

---

---

---

---

---

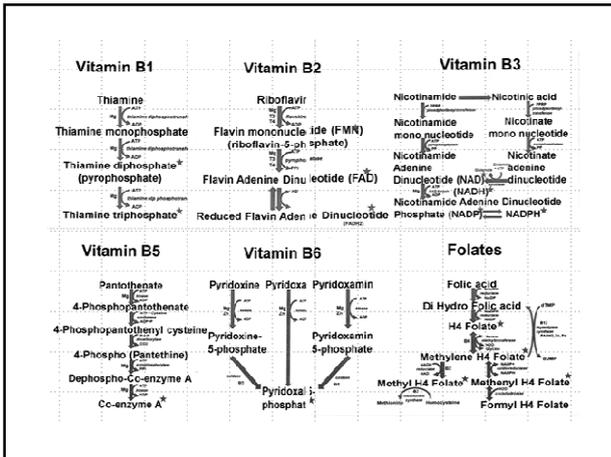
---

---

---

---

---




---

---

---

---

---

---

---

---

**Epigenetics is the study of cellular and physiological phenotypic trait variations that result from external or environmental factors that switch genes on and off and affect how cells express genes.**

---

---

---

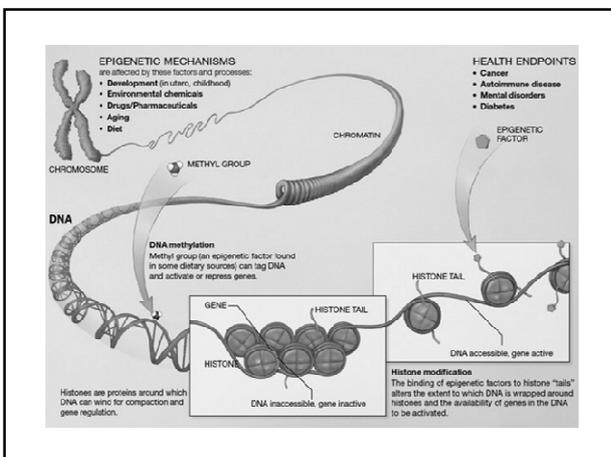
---

---

---

---

---




---

---

---

---

---

---

---

---

Hence, epigenetic research seeks to describe dynamic alterations in the transcriptional potential of a cell. These alterations may or may not be heritable.

---

---

---

---

---

---

---

---

Unlike genetics based on changes to the DNA sequence (the genotype), the changes in gene expression or cellular phenotype of epigenetics have other causes, thus use of the prefix *epi-*.

---

---

---

---

---

---

---

---

†Histones

---

---

---

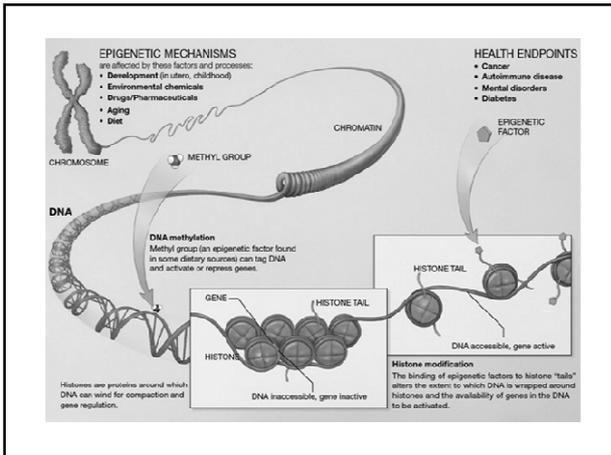
---

---

---

---

---




---

---

---

---

---

---

---

---

---

---

**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).**

---

---

---

---

---

---

---

---

---

---

**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.**

---

---

---

---

---

---

---

---

---

---

**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,**

---

---

---

---

---

---

---

---

**Five major families of histones proteins exist:**

**H1/H5, H2A, H2B, H3, and H4.**

**Histones H2A, H2B, H3 and H4 are known as the core histones, while histones H1 and H5 are known as the linker histones.**

---

---

---

---

---

---

---

---

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

---

---

---

---

---

---

---

---

**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.**

---

---

---

---

---

---

---

---

**Such modifications include**

- 1. Methylation**
- 2. Citrullination**
- 3. Acetylation**
- 4. Phosphorylation**
- 5. SUMOylation**
- 6. Ubiquitination**
- 7. ADP-ribosylation**

**This affects their function of gene regulation.**

---

---

---

---

---

---

---

---

**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.**

---

---

---

---

---

---

---

---

### 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.

---



---



---



---



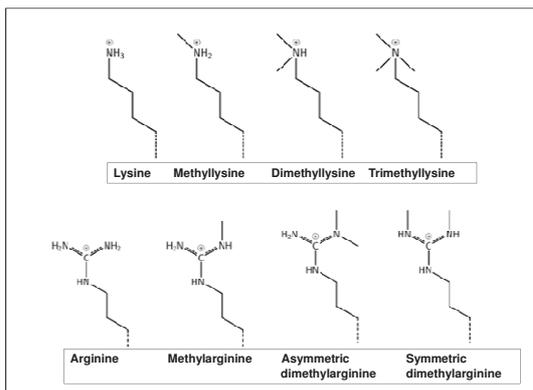
---



---



---




---



---



---



---



---



---



---

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.

---



---



---



---



---



---



---



**Main methylators are**  
**S. Adenosylmethionine (SAM)**  
**Methylcobalamin**  
**5MTHF**  
**Choline, Betaine (TMG), DMG**  
**MSM, DMSO?**

**Cofactors Zn**

---

---

---

---

---

---

---

---

**Demethylation**  
**Alpha-ketoglutarate-dependent**  
**non-heme enzymes are active**  
**for demethylation of DNA.**  
**Vitamin C**  
**Iron**  
**Hydroxycobalamin**

---

---

---

---

---

---

---

---

**2. Citrullination**  
**Enzymes called peptidylarginine**  
**deiminases (PADs) hydrolyze the**  
**imine group of arginines and**  
**attach a keto group, so that there**  
**is one less positive charge on the**  
**amino acid residue.**

---

---

---

---

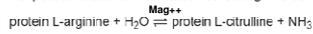
---

---

---

---

In enzymology, a **protein-arginine deiminase** (EC 3.5.3.15~~9~~) is an enzyme that catalyzes a form of post translational modification called arginine de-amination or **citrullination**:



Thus, the two substrates of this enzyme are protein L-arginine and H<sub>2</sub>O, whereas its two products are protein L-citrulline and NH<sub>3</sub>.

**Present in**  
**Lactobacillus brevis**  
**Lactobacillus plantarum**  
**Lactococcus lactis**

**Cofactors Ba and Ca**

---

---

---

---

---

---

---

---

**This process has been involved in the activation of gene expression by making the modified histones less tightly bound to DNA and thus making the chromatin more accessible.**

---

---

---

---

---

---

---

---

**PADs can also produce the opposite effect by removing or inhibiting mono-methylation of arginine residues on histones and thus antagonizing the positive effect arginine methylation has on transcriptional activity.**

---

---

---

---

---

---

---

---

### 3. 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.

---

---

---

---

---

---

---

---

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.

---

---

---

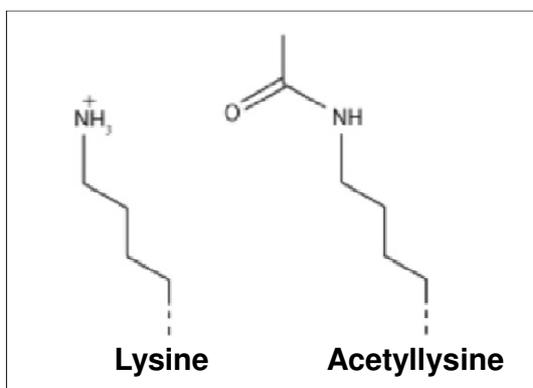
---

---

---

---

---



---

---

---

---

---

---

---

---

**Histone acetyltransferases are enzymes that acetylate lysine amino acids on histone proteins by transferring an acetyl group from acetyl CoA to form  $\epsilon$ -N-acetyl-lysine.**

---

---

---

---

---

---

---

---

**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.**

---

---

---

---

---

---

---

---

**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  
Co-enzyme NAD+  
Cofactors Zn and Na**

---

---

---

---

---

---

---

---

**4. Phosphorylation**

**Addition of a negatively charged phosphate group to serine, threonine and tyrosine can lead to major changes in protein structure, leading to the well-characterised role of phosphorylation in controlling protein function.**

---

---

---

---

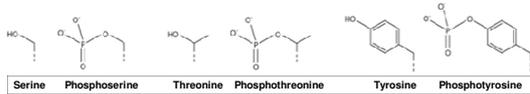
---

---

---

---

**It is not clear what structural implications histone phosphorylation has, but histone phosphorylation has clear functions as a post-translational modification. Co-factors ATP, Mg, Zn**




---

---

---

---

---

---

---

---

**5. SUMOylation**

**Small Ubiquitin-like Modifier (or SUMO) proteins are a family of small proteins that are covalently attached to and detached from other proteins in cells to modify their function.**

---

---

---

---

---

---

---

---

**SUMOylation is a post-translational modification involved in various cellular processes, such as nuclearcytosolic transport, transcriptional regulation, apoptosis, protein stability, response to stress, and progression through the cell cycle.**

---

---

---

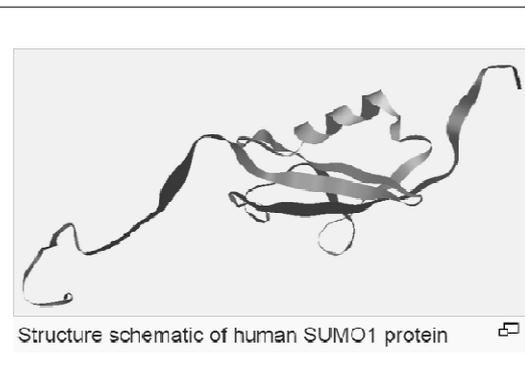
---

---

---

---

---



---

---

---

---

---

---

---

---

**6. Ubiquitination is an enzymatic post-translational modification in which a ubiquitin protein is attached to a substrate protein. This process most commonly binds the last amino acid of ubiquitin (glycine 76) to a lysine residue on the substrate.**

---

---

---

---

---

---

---

---

**Histones can be ubiquitinated and this is usually in the form of monoubiquitination (although polyubiquitinated forms do occur). Histone ubiquitination alters chromatin structure and allows the access of enzymes involved in transcription of genes.**

---

---

---

---

---

---

---

---

**Ubiquitin on histones also acts as a binding site for proteins that either activate or inhibit transcription and also can induce further post-translational modifications of the protein. These effects can all modulate the transcription of genes.**

---

---

---

---

---

---

---

---

**7. ADP-ribosylation is the addition of one or more ADP-ribose moieties to a protein. It is a reversible post-translational modification that is involved in many cellular processes, including cell signaling, DNA repair, gene regulation and apoptosis.**

---

---

---

---

---

---

---

---

**Improper ADP-ribosylation has been implicated in some forms of cancer.**  
**The source of ADP-ribose for most enzymes that perform this modification is the redox Cofactor NAD<sup>+</sup>.**

---

---

---

---

---

---

---

---

**NAD<sup>+</sup> a substrate of enzymes that add or remove chemical groups from proteins, in post translational modifications.**  
**Poly-(ADP-ribose) polymerases (PARPs) are found in most cells and catalyze the transfer of multiple ADP-ribose molecules to target proteins.**

---

---

---

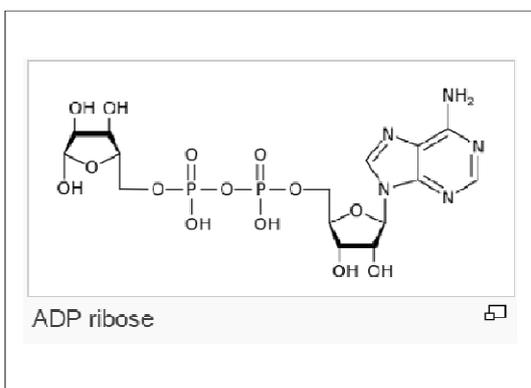
---

---

---

---

---



---

---

---

---

---

---

---

---

**Catalytic Triad**

---

---

---

---

---

---

---

---

**A catalytic triad refers to the three amino acid residues that function together at the centre of the active site of some hydrolase and transferase enzymes (e.g. proteases, amidases, esterases, acylases, lipases and  $\beta$ -lactamases).**

---

---

---

---

---

---

---

---

**ADP-ribosyltransferases have been shown to modify proteins that bind mRNA, which can cause silencing of that gene transcript.**

---

---

---

---

---

---

---

---

**Epithalamin**

---

---

---

---

---

---

---

---

**According to the peptide theory of ageing, ageing is an evolutionary determined biological process of changes in gene expression resulting in impaired synthesis of regulatory and tissue-specific peptides in organs and tissues, which provokes their structural and functional changes and the development of diseases.**

---

---

---

---

---

---

---

---

**Correspondingly, correction of such disorders by means of stimulation of peptide production in the organism or through their delivery can promote the normalisation of disturbed body functions.**

---

---

---

---

---

---

---

---

**Based on the data about the amino acid compositions of peptide preparations, novel principles of the design of biologically active short peptides possessing tissue-specific activities has been developed.**

---

---

---

---

---

---

---

---

**Dipeptides specific for the thymus and tetrapeptides specific for the heart, liver, brain cortex, and pineal glands stimulate the in vitro outgrowth of explants of respective organs.**

---

---

---

---

---

---

---

---

**Interestingly, for eye retina and the pineal gland, a common tetrapeptide Ala-Glu-Asp-Gly (Epitalon) has been designed, probably reflecting the common embryonal origin of these two organs. Epitalon reproduces the effects of Epithalamin including those related to its geroprotector activity.**

---

---

---

---

---

---

---

---

**In particular, Epitalon increases the lifespan of mice and fruit flies and restores the circadian rhythms of melatonin and cortisol production in old rhesus monkeys.**

---

---

---

---

---

---

---

---

**At the same time, Epitalon prolongs the functional integrity of the eye retina in Campbell rats with hereditary Retinitis Pigmentosa and improves the visual functions in patients with pigmental retinal degeneration. Changes in gene expression were observed to be produced by the short peptide preparations.**

---

---

---

---

---

---

---

---

**Therefore, the effects of Epitalon are suggested to be mediated by transcriptional machinery common for the pineal gland and the retina and, probably, for regulation of melatonin production**

---

---

---

---

---

---

---

---

**Melatonin, the hormone that regulates our daily cycle, is found to prolong life span in mice.**

**Melatonin in the blood is very sensitive to light exposure, and melatonin disappears with the dawn's early light**

---

---

---

---

---

---

---

---

**Anisimov found that sleeping in total darkness is better for longevity than exposure to light during the night.**

**(A recent study also suggests sleeping in the cold helps preserve insulin sensitivity.)**

---

---

---

---

---

---

---

---

**We know that gene expression is quite different in old and young people. The body times its life cycle using gene expression. When we're young, we express genes that make us grow. When we're middle-aged, we express genes that keep us healthy. When we're old, we express genes that destroy us.**

---

---

---

---

---

---

---

---

**“Gene expression” is the translation of DNA into proteins. Proteins are the signals and the workhorses of body chemistry. The translation is well understood since Francis Crick discovered the Genetic Code in the 1960s.**

---

---

---

---

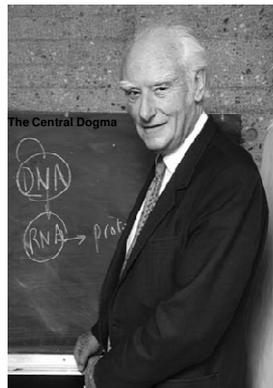
---

---

---

---

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



---

---

---

---

---

---

---

---

**But the language for determining which gene gets expressed when, is apparently much more complicated, and it is just beginning to be decoded in the 21st Century. This is the science of *Epigenetics*.**

---

---

---

---

---

---

---

---

**Among the signals that can locate a particular stretch of DNA, and turn it ON or OFF are short stretches of RNA called pi-RNAs, methyl transferases and histone de-acetylases.**

---

---

---

---

---

---

---

---

**But the point is that these short peptides that Anisimov has been studying for 20 years work also as gene promoters and repressors – epigenetic signals that are more specific than the methyl transferases and less specific than pi-RNAs. Apparently they can affect whole categories of genes.**

---

---

---

---

---

---

---

---

### Peptide bioregulation of aging: results and prospects

Vladimir N. Anisimov , Vladimir Ph. Khavinson

Research Article

First Online: 25 October 2009  
DOI: 10.1007/s10522-009-9249-8

Cite this article as:  
Anisimov, V.N. & Khavinson, V.P.  
Biogerontology (2010) 11: 138.  
doi:10.1007/s10522-009-9249-8

 45  3  145  
Citations Shares Views

#### Abstract

The review comprises the results of author's long-term investigation in the mechanisms of aging and a role of peptide bioregulators in prevention of age-related pathology. A number of small peptides have been isolated from different organs and tissues and their analogues (di-, tri-, tetrapeptides) were synthesized from the amino acids. It was shown that long-term treatment with some peptide preparations increased mean life span by 20–40%, slow down the age-related changes in the biomarkers of aging and suppressed development of spontaneous and induced by chemical or radiation carcinogens tumorigenesis in rodents. Possible mechanisms of the biological effects of small peptides are discussed in the paper. The results of clinical applications of peptide preparation during the period of 6–12 years are presented as well.

---

---

---

---

---

---

---

---

**Table 1** Effect of peptide bioregulators on life span of rodents

Peptide preparations	Species, strain of rodents	Sex	Age at the start of treatment, months	Life span, % to the control		Effect on spontaneous tumor	Reference	
				Mean	Maximum			
Epithalamin	Rats	Female	3.5	+25*	+6	↓	Dilman et al. (1979), 1978)	
			15	+6	+9	↓	Avsimov and Khavinson (1991)	
	SHR mice	Female	3.5	+31*	+14	↓	Avsimov et al. (1982a, 1982b)	
			3.5	+13	+5	↓	Avsimov et al. (1987)	
			3.5	+11*	-2	↓	Avsimov et al. (1989)	
Thymalin	CHFSn mice	Female	3.5	+28*	+11	↓	Avsimov et al. 1982a, 1982b	
			3.5	+12*	0	↓	Avsimov et al. 1987	
	SHR mice	Female	3.5	+2	-6	↓	Avsimov et al. (1989)	
			12	+13*	0	↓	Avsimov et al. (1989)	
Glu-Trp	Rats	Female	4	-2	+14	↓	Avsimov et al., 2000	
			Lys-Glu	6	+3*	+7	↓	Avsimov et al. 2001a, 2001b, 2002a, 2002b
Ala-Glu-Asp-Gly	HER-Zinc mice	Female	2	-7	0	↑	Avsimov et al. (2002a, 2002b)	
			Rats	4	-8	-6	↓	Vinogradova et al. (2007)
	SHR mice	Female	3	+7*	+5	↓	Vinogradova et al. (2008)	
			6	+17*	+12	↓	Avsimov et al. (2003)	
	CBA mice	Female	6	+5*	+42	↓	Avsimov et al. (2001a, 2001b, 2002a, 2002b)	
			SAMR1 mice	2	-5	-8	=	Avsimov et al. (2005)
	SAMP1 mice	Female	2	+7*	+8	=	Avsimov et al. (2005)	
			HER-Zinc mice	2	+13*	+14	↓	Avsimov et al. (2002a, 2002b)
	ESIP	SHR mice	Female	3	+17*	+24	↓	Popovich et al. (2003)
				3	+20*	+2	=	Votenzov et al. (2008)

ESIP delta-sperg inducing peptide, Trp-Ala-Gly-Asp-Ala-Ser-Gly-Glu

**The thymus trains the immune cells in our blood to attack invading cells, but to lay off our own body's cells. As we get older, the thymus shrinks. This may be a basic cause of aging immune function, auto-immune disease, and increased susceptibility to infection.**

**Thymalin was found to stimulate thymus re-growth and to rejuvenate immune function.**

Khavinson VKh , Morozov VG  
 St. Petersburg Institute of Bioregulation and Gerontology, 3,  
 Dynamo Prospect, 197110, St. Petersburg, Russia.  
 khavinson@gerontology.ru  
 Advances in Gerontology = Uspekhi Gerontologii /  
 Rossijskaia Akademiia Nauk, Gerontologicheskoe  
 Obschestvo [2002, 10:74-84]

**Thymalin is an immunomodulator polypeptide derived from the thymus and is a basic polypeptide made up of 4 amino acids residues.**



---

---

---

---

---

---

---

---

**Epithalamin was discovered in extracts from a region of the brain called the epithalamus. This region contains the pineal gland, or "third eye", which controls wake/sleep cycles and is the body's source of melatonin. Like thymalin, epithalamin is a string of four amino acids.**

---

---

---

---

---

---

---

---

**Thymalin generated excitement in the 1980s, until epithalamin stole its thunder. Not only did it extend life more consistently, but its effect on thymic growth was found to be superior to thymalin.**

---

---

---

---

---

---

---

---

**In the table, epithalamin has been the best-studied short peptide, and it has the best record for life extension in rodents. In a separate table, the same paper shows that epithalamin and thymalin suppress cancer. There is also evidence of large reductions in mortality when epithalamin was given to older humans**

---

---

---

---

---

---

---

---

**Table 3** Effect of treatment with peptide preparation on mortality rate in elderly and old subjects

Group of subjects	Indices	Control (administration of polyvitamins)	Administration of the pineal gland preparation	Administration of the complex of thymus and pineal gland preparations
Elderly people (60-74 years)	Number of subjects	48	46	No studies
	Initial mean age (years)	69.3 ± 2.2	71.1 ± 1.4	
	Mortality rate in the course of 6 years (%)	13.6	8.5*	
	Mortality rate in the course of 12 years (%)	41.1	22.3*	
Old people (75-89 years)	Number of subjects	25	24	20
	Initial mean age (years)	80.2 ± 1.6	81.5 ± 2.1	82.1 ± 2.3
	Mortality rate in the course of 6 years (%)	81.8	45.8*	31.3*

\* P < 0.05 as compared to the control

---

---

---

---

---

---

---

---

**In addition, it has recently been reported that epithalamin is a telomerase activator. Skeptics (Spindler in particular) point out that caloric restriction is such a strong influence on life span that many treatments will appear to show benefit only because they affect appetite.**

---

---

---

---

---

---

---

---

Some of the studies do measure food intake, and find that epithalamin is able to increase lifespan without decreasing food consumption.

---

---

---

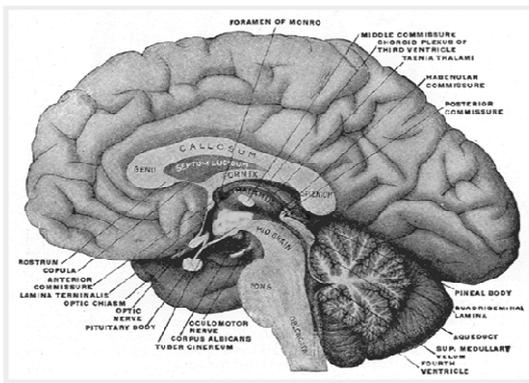
---

---

---

---

---



---

---

---

---

---

---

---

---

The epithalamus is shown in cherry. It includes the pineal gland, the so-called “third eye” which is responsible for the body’s light-sensitive clock, and where melatonin comes from. The hypothalamus is shown in lime.

---

---

---

---

---

---

---

---

**It includes various “nuclei”, notably the suprachiasmatic nucleus, which is the closest thing science has found to a developmental clock. The pituitary secretes hormones involved in the life cycle and the menstrual cycle: HGH, LH, FSH, TSH and sex hormones.**

---

---

---

---

---

---

---

---

**Thymic involution is one way in which the immune system is made incompetent with age – another is the proclivity of hematopoietic stem cells (blood-cell forming) to differentiate mostly to myeloid lineage cells (which produce the red blood cells, white blood cells and platelets-**

---

---

---

---

---

---

---

---

**except for lymphocytes which are lymphoid lineage cells, both b and t -lymphocytes), disturbing the normal balance lymphoid to myeloid cells.  
So the thymus normally ‘trains’ t-lymphocytes (they aren’t functional without such training),**

---

---

---

---

---

---

---

---

**but without enough lymphocytes to bring to maturity it's not that important that the thymus involutes – there aren't enough trainees to worry about. It's already been learned that factors carried in the blood are responsible for the change in HSC potency.**

---

---

---

---

---

---

---

---

**The restoration of the thymic functions and the thymic re-growth may be achieved in old mice by some endocrinological (melatonin) or nutritional interventions (arginine or zinc), suggesting that the thymic involution in old age is a phenomenon secondary to**

---

---

---

---

---

---

---

---

**age-related alterations occurring in neuroendocrine-thymus interactions. The targets for the thymic restoration may be hormone receptors and cytokines, strictly related to the presence of two nutritional factors, such as arginine and zinc, which are in turn essential for the efficiency of neuroendocrine -**

---

---

---

---

---

---

---

---

**immune network both in ontogeny and ageing.**

**The effect of melatonin is largely due to the presence of its specific receptors on cell membrane of thymocytes and Thymic Epithelial Cells (TECs).**

---

---

---

---

---

---

---

---

**TECs synthesize thymulin peptide that is required for T-cell differentiation and maturation within the thymus gland. In this context, the role of zinc is pivotal because it is involved, through “zinc finger motifs”, in the gene expression of melatonin receptors, in cell proliferation, apoptosis and thymulin reactivation.**

---

---

---

---

---

---

---

---

**Zinc is also required for the biological action of arginine, via Nitric Oxide pathway. Therefore, the beneficial effect of melatonin or arginine on neuroendocrine-thymus interaction in ageing can also occur via a better zinc pool redistribution within the body where the capability of the zinc-binding proteins -**

---

---

---

---

---

---

---

---

**- Metallothioneins (MT) in zinc release has a key role. These findings suggest that zinc, via MT buffering, can be a single mediator in modulating neuroendocrine-thymus interaction in ageing.**

---

---

---

---

---

---

---

---

**Epithalamin studies**

---

---

---

---

---

---

---

---

**Experimental Studies of the Pineal Gland Preparation Epithalamin**

Vladimir Kh. Khavinson  
, V. G. Morozov  
, Vladimir N. Anisimov

**Twenty-five years of study have shown a wide spectrum of high biological activity of the pineal peptide preparation epithalamin.**

---

---

---

---

---

---

---

---

**Long-term exposure to epithalamin was followed by an increase in the mean and maximum life spans and slower rates of aging of rats, mice, and *D. melanogaster*. Epithalamin increases pineal synthesis of serotonin, N-acetylserotonin, and melatonin and night pineal secretion of melatonin in adult and old rats.**

---

---

---

---

---

---

---

---

**The pineal preparation decreases the luteinizing hormone and prolactin levels in adult male rats as well as the threshold of the hypothalamopituitary complex to feedback inhibition by estrogens in old female rats; it slows down age-related cessation of estrous function in rats and induces the recurrence of estrous cydes -**

---

---

---

---

---

---

---

---

**- and fertility in old, persistently estrous rats. Epithalamin increases the levels of triiodothyronine and decreases thyroxine in serum of adult rats. It further decreases the levels of corticosterone in the serum of mice and increases the susceptibility of the hypothalamo-pituitary complex to**

---

---

---

---

---

---

---

---

**the homeostatic inhibition of adrenocorticotrophic function by glucocorticoids in old rats. Serum insulin and triglyceride levels in rabbits are decreased by epithalamin and the tolerance to glucose and diuresis are increased.**

---

---

---

---

---

---

---

---

**It was found that T and B cell-mediated immunity in adult and old mice as well as the titre of thymic serum factor and the titre of thymosin-like compounds in old mice are stimulated by the pineal peptide preparation in the same way as the colony-forming activity of splenocytes in pinealectomized rats.**

---

---

---

---

---

---

---

---

**Epithalamin inhibits spontaneous and induced carcinogenesis and is a potent antioxidant, decreasing lipid peroxidation and stimulating the activity of Cu/Zn superoxide dismutase.**

---

---

---

---

---

---

---

---

**The obtained results demonstrate a high efficiency of epithalamin therapy for prophylaxis of age-related pathology, including cancer, showing a new physiological way to slow down pathological processes and to extend human life spans.**

---

---

---

---

---

---

---

---

**Telomeres and Telomerase**

---

---

---

---

---

---

---

---

**There are many theories of aging, one of which is the shortening of telomeres in our DNA. A *telomere* is like the plastic tip on the end of your shoe lace. It protects the DNA from unraveling during each cell division.**

---

---

---

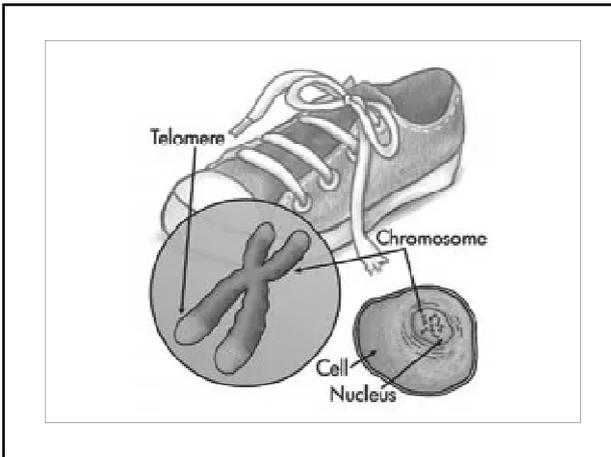
---

---

---

---

---



---

---

---

---

---

---

---

---

**Each cell division results in a slightly shorter telomere length, and eventually, the cell can no longer divide. This is called the *Hayflick Limit*, after Dr. Leonard Hayflick's discovery that cells have a limited number of times that they can divide.**

---

---

---

---

---

---

---

---

**In mammals, the telomeres are protected from shortening until the onset of sexual maturity. After that, they begin to shorten with each cell division, eventually leading to an inability to divide any more in order to replace worn out, damaged or diseased cells.**

---

---

---

---

---

---

---

---

There is an enzyme called *telomerase* that is produced in the cells which stimulates the lengthening of the telomeres. The pineal gland produces a hormone called *epithalamin* that tells the cells to produce telomerase which in turn results in longer telomeres in our DNA.

---

---

---

---

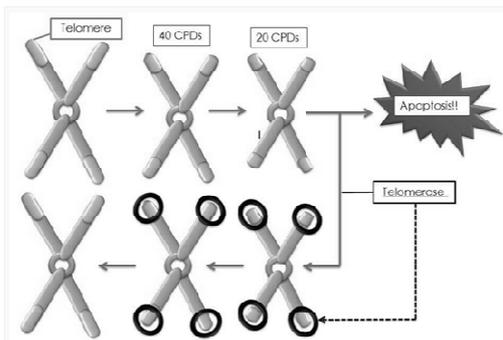
---

---

---

---

**Telomere Elongation**



---

---

---

---

---

---

---

---

The functionality of the pineal gland declines with age, and is partly responsible for age related diseases. What Dr. Khavinson found was that introducing epithalamin into mammals resulted in a reversal of age related diseases, and a reversal of the signs of aging.

---

---

---

---

---

---

---

---

**He was able to take geriatric female mice, who were no longer fertile, give them epithalamin, and after about two weeks of treatment, the mice became fertile again, got pregnant and had pups.**

---

---

---

---

---

---

---

---

**He showed that Epitalon induces telomerase activity in human somatic cells, proving that telomeres were lengthened by the peptide.**

---

---

---

---

---

---

---

---

**Telomerase, also called terminal transferase, is a ribonucleoprotein that adds a species-dependent telomere repeat sequence to the 3' end of telomeres.**

---

---

---

---

---

---

---

---

**A telomere is a region of repetitive sequences at each end of a eukaryotic chromatid, which protects the end of the chromosome from deterioration or from fusion with neighbouring chromosomes.**

---

---

---

---

---

---

---

---

**Telomerase, active in normal stem cells, is normally absent from, or at very low levels in, most somatic cells.**

---

---

---

---

---

---

---

---

**Telomerase is a reverse transcriptase enzyme that carries its own RNA molecule (e.g., with the sequence "CCCAAUCCC" in vertebrates) which is used as a template when it elongates telomeres.**

---

---

---

---

---

---

---

---

**Mothers caring for very sick children have shorter telomeres when they report that their emotional stress is at a maximum and that telomerase was active at the site of blockages in coronary artery tissue, possibly accelerating heart attacks.**

Epel, ES; Lin, J; Dhabhar, FS; Wolkowitz, OM; Puterman, E; Karan, L; Blackburn, EH (2010). "Dynamics of telomerase activity in response to acute psychological stress". *Brain Behav Immun*. 24

---

---

---

---

---

---

---

---

**In 2009, it was shown that the amount of telomerase activity significantly increased following psychological stress. Across the sample of patients telomerase activity in increased peripheral blood mononuclear cells by 18% one hour after the end of the stress.**

---

---

---

---

---

---

---

---

**Telomerase (RNA-directed DNA polymerase)  
Co-factors Mg and Mn**

---

---

---

---

---

---

---

---

**Telomere protectors and telomerase stimulants**  
**Ashwagandha**  
**Turmeric**  
**Glutathione**  
**CoQ10**  
**Magnesium ascorbate**

---

---

---

---

---

---

---

---

**The results of research are startling: for example, the application of Epithalamin diminished mortality in aged humans by 1.8 times over a 6 year period of observation.**

---

---

---

---

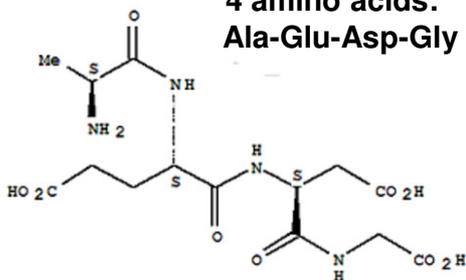
---

---

---

---

**Epithalamin is a small peptide of 4 amino acids: Ala-Glu-Asp-Gly**




---

---

---

---

---

---

---

---

**On the level of gene activity regulation it was established that administration of peptides Lys-Glu and Ala-Glu-Asp-Gly to transgenic mice caused a 2–3.6-fold suppression of HER-2/neu gene expression (human breast cancer) as compared to the control group.**

---

---

---

---

---

---

---

---

**It was revealed that addition of tetrapeptide Ala-Glu-Asp-Gly to the cultural medium of human lung fibroblasts induces telomerase gene expression and contributes to a 2.4-fold lengthening of telomeres. Activation of gene expression is accompanied by a growing number of cellular divisions (by 42.5%), which is the evidence of Hayflick's limit being overcome.**

---

---

---

---

---

---

---

---

**The effect of di- and tetrapeptides Lys-Glu, Glu-Trp, Ala-Glu-Asp-Gly, Ala-Glu-Asp-Pro on the expression of 15 247 murine heart and brain genes before and after peptides administration was studied with the employment of DNA-microarray technology. In this experiment, there were used clones from the library of the National Institute on Ageing, USA.**

---

---

---

---

---

---

---

---

**This experiment provided unique data on alteration in the expression of different genes under the effect of peptide preparations. An important conclusion driven from the experiment was that every peptide specifically regulates particular genes.**

---

---

---

---

---

---

---

---

**Results of this experiment testify to the existing mechanism of peptide regulation of gene activity. It was also registered that dipeptide Lys-Glu, showing immunomodulating activity, regulates gene interleukin-2 expression in blood lymphocytes.**

---

---

---

---

---

---

---

---

**From RNA to Protein**

---

---

---

---

---

---

---

---

**The translation of the nucleotide sequence of an mRNA molecule into protein takes place in the cytoplasm on a large ribonucleoprotein assembly called a ribosome.**

---

---

---

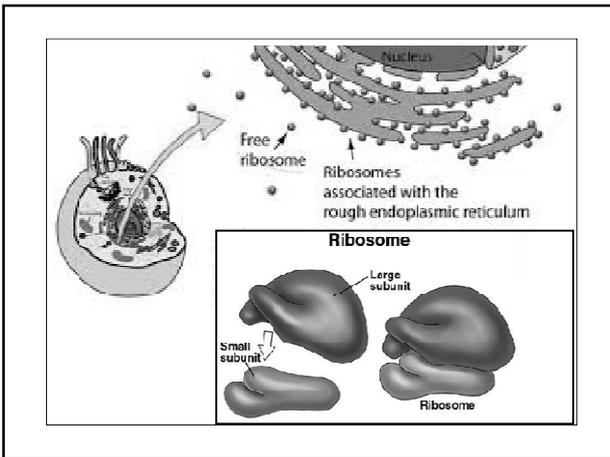
---

---

---

---

---



---

---

---

---

---

---

---

---

**The amino acids used for protein synthesis are first attached to a family of tRNA molecules, each of which recognizes, by complementary base-pair interactions, particular sets of three nucleotides in the mRNA (codons).**

---

---

---

---

---

---

---

---

1 CUC AGC GUU ACC AU  
—Leu—Ser—Val—Thr—

2 C UCA GCG UUA CCA U  
—Ser—Ala—Leu—Pro—

3 CU CAG CGU UAC CAU  
—Gln—Arg—Tyr—His—

The three possible reading frames in protein synthesis

---

---

---

---

---

---

---

---

The sequence of nucleotides in the mRNA is then read from one end to the other in sets of three according to the genetic code. To initiate translation, a small ribosomal subunit binds to the mRNA molecule at a start codon (AUG) that is recognized by a unique initiator tRNA molecule.

---

---

---

---

---

---

---

---

attached amino acid (Phe)

**A tRNA molecule**

5' end 3' end

D loop T loop

anticodon loop anticodon

a clover leaf

---

---

---

---

---

---

---

---

During this phase, aminoacyl tRNAs—each bearing a specific amino acid bind sequentially to the appropriate codon in mRNA by forming complementary base pairs with the tRNA anticodon.

---

---

---

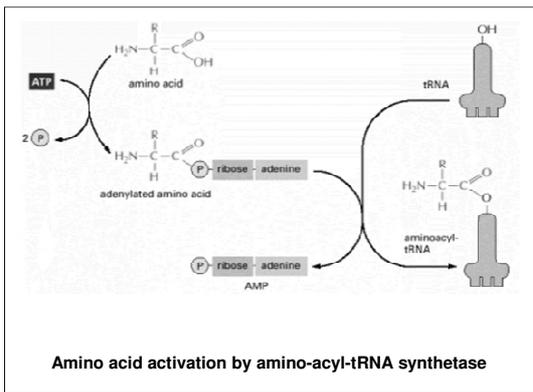
---

---

---

---

---



Amino acid activation by amino-acyl-tRNA synthetase

---

---

---

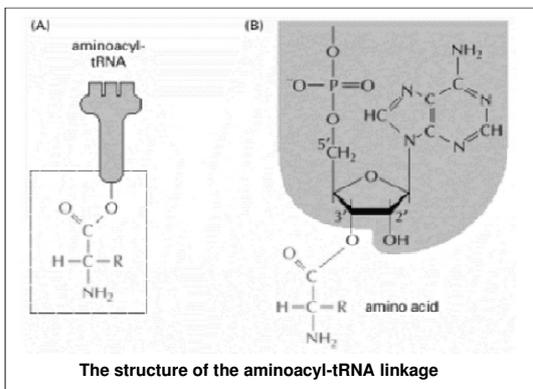
---

---

---

---

---



The structure of the aminoacyl-tRNA linkage

---

---

---

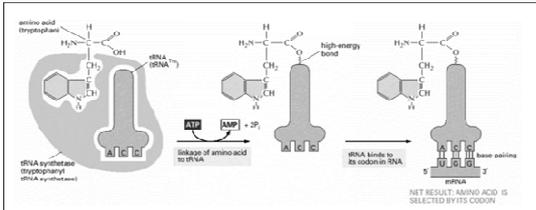
---

---

---

---

---



**The genetic code is translated by means of two adaptors that act one after another.**

---

---

---

---

---

---

---

---

**Each amino acid is added to the C-terminal end of the growing polypeptide by means of a cycle of three sequential steps: aminoacyl-tRNA binding, followed by peptide bond formation, followed by ribosome translocation.**

---

---

---

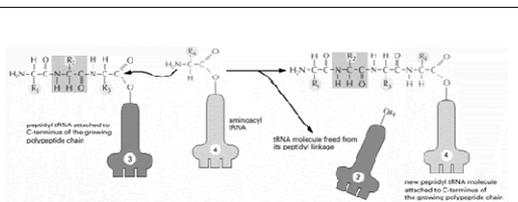
---

---

---

---

---



**The incorporation of an amino acid into a protein.**

---

---

---

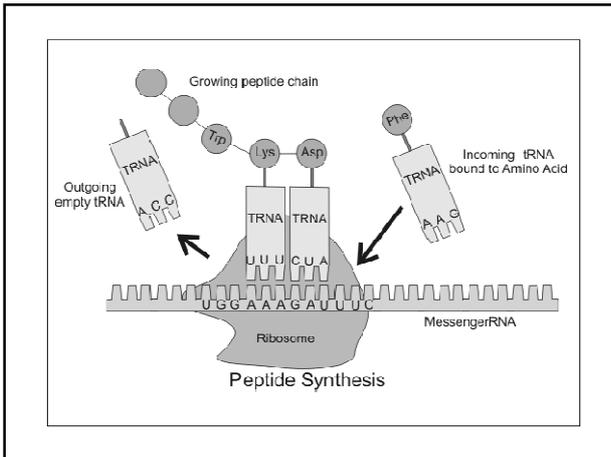
---

---

---

---

---



---

---

---

---

---

---

---

---

**The mRNA molecule progresses codon by codon through the ribosome in the 5'-to-3' direction until one of three stop codons is reached. A release factor then binds to the ribosome, terminating translation and releasing the completed polypeptide.**

---

---

---

---

---

---

---

---

**Superimposing the Genetic Code over the Periodic Table**

---

---

---

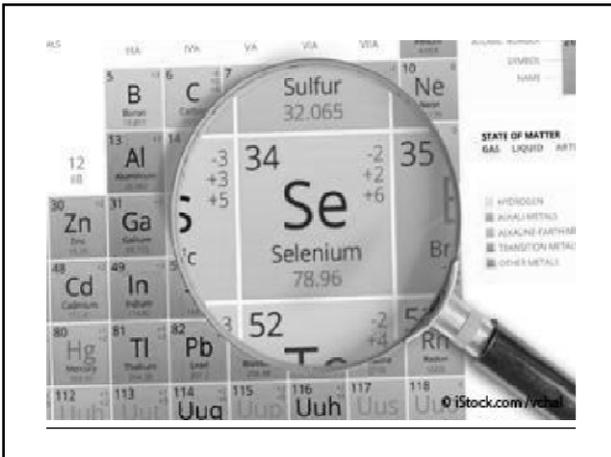
---

---

---

---

---




---

---

---

---

---

---

---

---

**The tumour suppressing gene p53 found on chromosome 17 is a selenium based gene that suppresses the formation of tumours.**

---

---

---

---

---

---

---

---

**↳ Codon Challenge**

- 1. Using the 400nm acetate from weakness challenge with each nucleotide base for strengthening.**
- 2. Leave positive nucleotide base on and wait 5 seconds for weakening.**
- 3. Repeat for next nucleotide base to strengthen**

---

---

---

---

---

---

---

---

4. Leave second positive nucleotide base on and wait 5 seconds for weakening.
5. Repeat for third nucleotide base to strengthen.

This is the positive codon

---

---

---

---

---

---

---

---

- The Codon Chart will tell you the
1. Associated Amino acid
  2. Spinal level
  3. Regulating element
  4. Valence
  5. Genetic meridian
  6. Optimal nutrient(s)

---

---

---

---

---

---

---

---

NUMBER	CODON	AMINO ACID	SPINE	REGULATOR	VALENCE	MERIDIAN	NUTRIENTS
1	CGC	Glycine	C1		-3	LI	S
2	AAA	Lysine	C2		-2	SI	S, Se
3	UAU	Tyrosine	C2D		-1	SI	
4	CAC	Histidine	C3		0	Sp	
5	GJU	Valine	C3D		+1	Sp	Na / K
6	CCG	Proline	C4		+2	HI	Ca, Mg
7	CAA	Glutamine	C4D		+3	HI	
8	AAU	Asparagine	C6		+4	SI	SI
9	GUG	Valine	C6D		-3	SI	
10	GCG	Alanine	C6		-2	BI	
11	GJA	Valine	C6D		-1	BI	I
12	ACG	Threonine	C7		0	Kid	K
13	UGG	Tryptophan	C7D		+1	Kid	I
14	GGC	Glycine	T1		+2	Cx	Mg
15	AUA	Isoleucine	T1D		+3	Cx	B
16	ACA	Threonine	T2		-4+	TW	SI, Co, I

---

---

---

---

---

---

---

---



**The associated Amino acid will display as making the test muscle go hypertonic in the clear. (You will need to cross TL to Kidney 27 on the same side to elicit weakness). Similarly the regulating element will do this also.**

---

---

---

---

---

---

---

---

**Using the hypertonic weakness obtained from the amino acid cross check against all the essential mineral Spectroscopic emission acetates for which one(s) strengthen.**

**This is the mineral the amino acid requires to activate the codon.**

---

---

---

---

---

---

---

---

**Challenge for the optimal form of the mineral from your Product Kit against the Subconscious Meridian's weak associated muscle. (e.g. Tensor fascia lata for the Large Intestine meridian)**

---

---

---

---

---

---

---

---

**You can next cross check in the clear for any toxic elements using the toxic metal Spectroscopic emission acetates.**

---

---

---

---

---

---

---

---

**Lastly using the 400nm acetate cross check for strengthening amino acids to elicit any mono, di, tri, quad peptide required to activate the gene(s).  
Prescribe positive amino acid(s) in organic apple juice 15 minutes before breakfast or at alternative time as tested.**

---

---

---

---

---

---

---

---

**T**

---

---

---

---

---

---

---

---

T

---

---

---

---

---

---

---

---

T

---

---

---

---

---

---

---

---

T

---

---

---

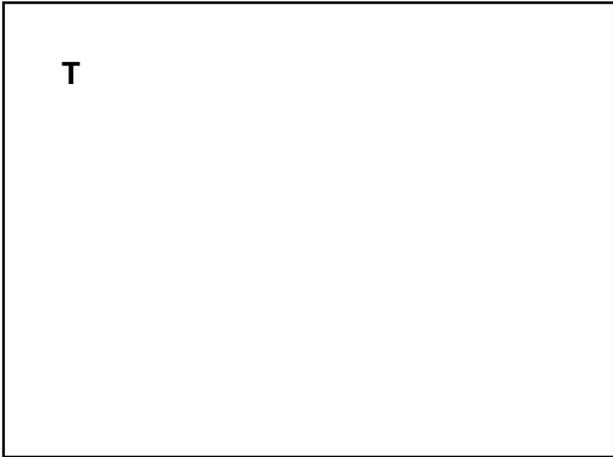
---

---

---

---

---



---

---

---

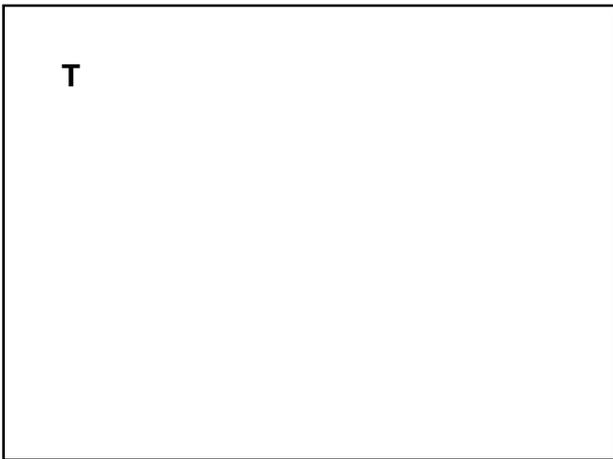
---

---

---

---

---



---

---

---

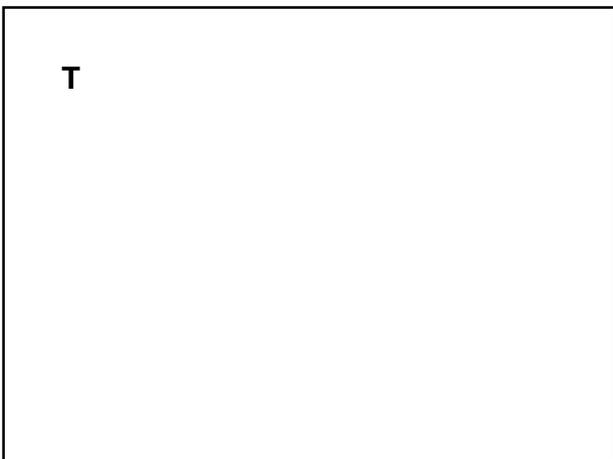
---

---

---

---

---



---

---

---

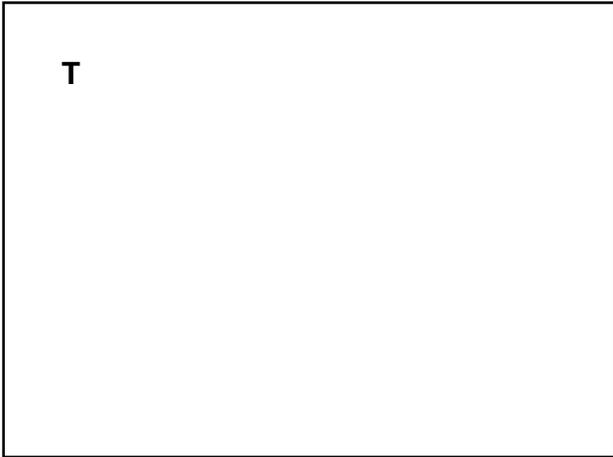
---

---

---

---

---



---

---

---

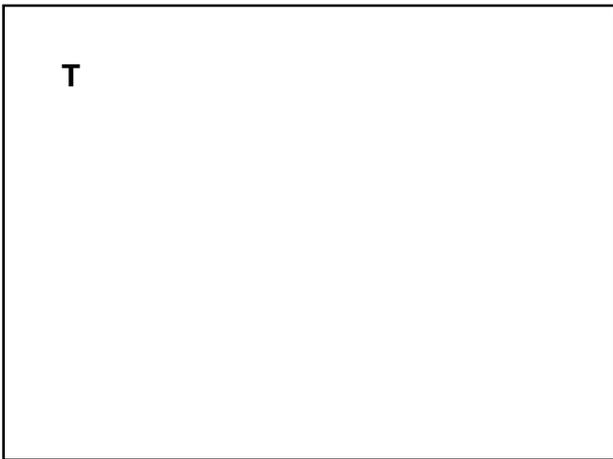
---

---

---

---

---



---

---

---

---

---

---

---

---