Epigenetics

Heritable Acquired Traits

What do I want to achieve by this presentation?

1. Evolution is an ongoing process.
2. Freedom of discussion has to be applied in science.
3. Health and happiness for everybody!
4. Life is worth for protection!
5. Theories of evolution themselves are under the process of evolution.

The Theories of Evolution underlie Evolution

Lamarck:

Natural environment – desire – use / neglect (of organs or limbs) – change – heritability of the acquired traits - Evolution

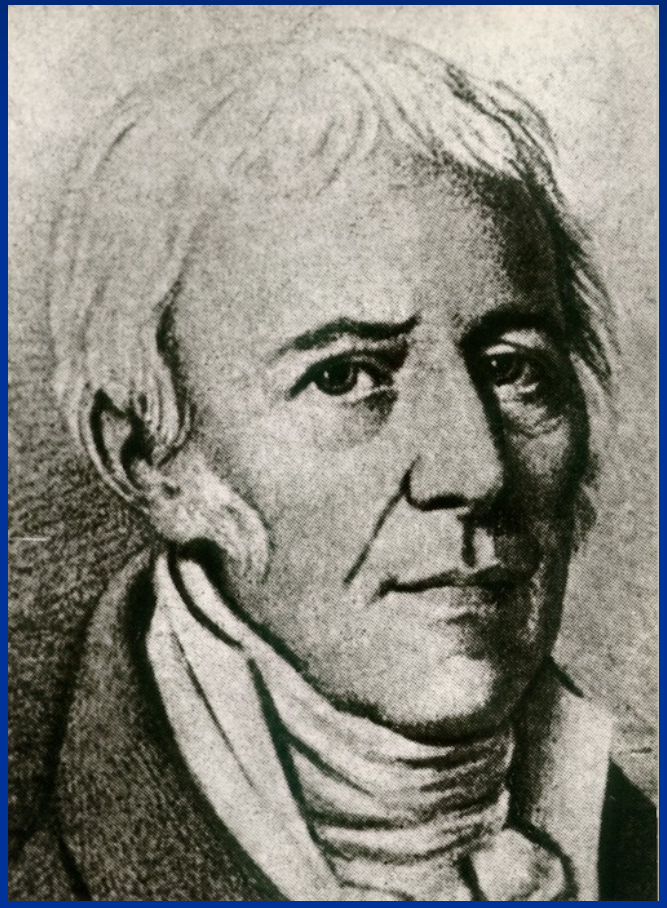
Darwin:

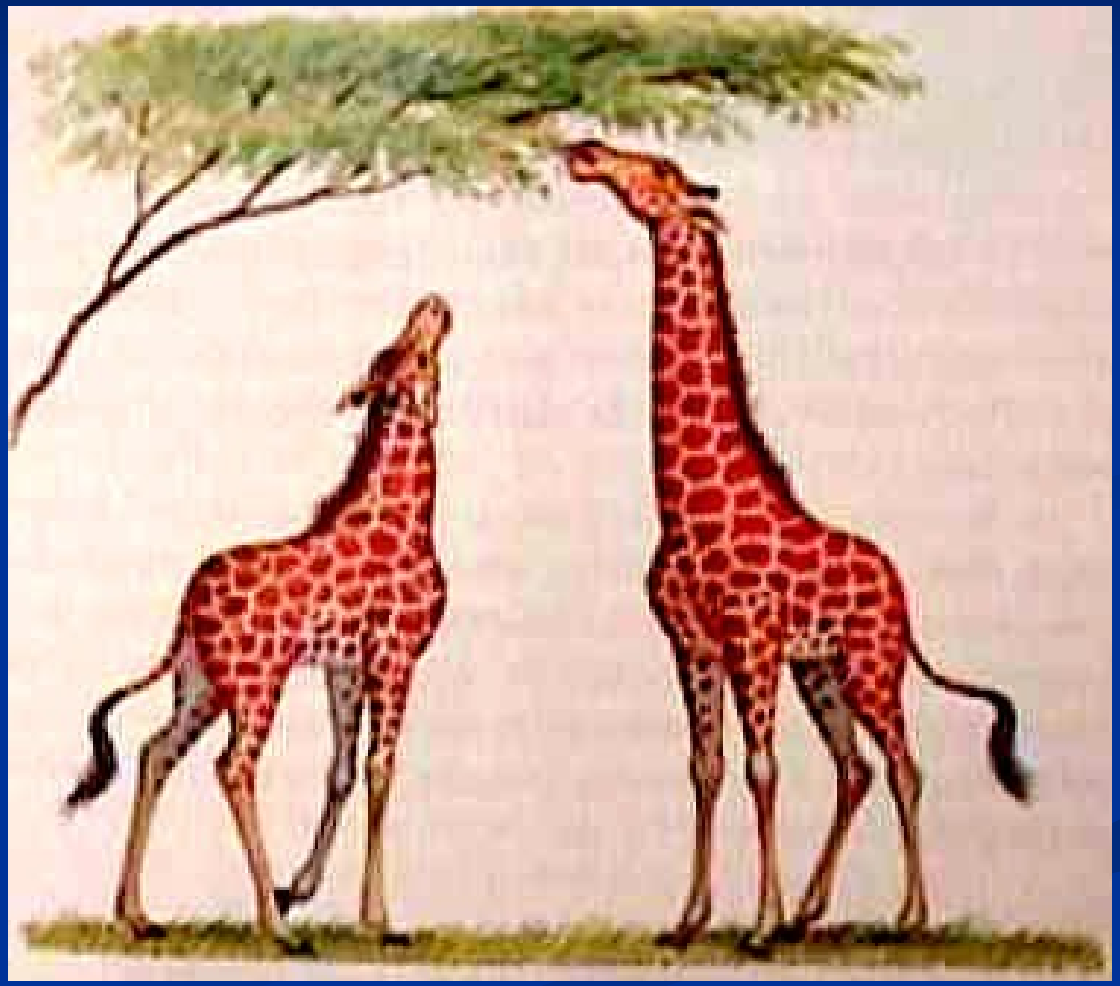
Over-population with high variability – condition of the environment – „struggle for life“ - „survival of the fittest“- Evolution

E. Mayr: Synthetic Theory (modern Darwinian Theory):

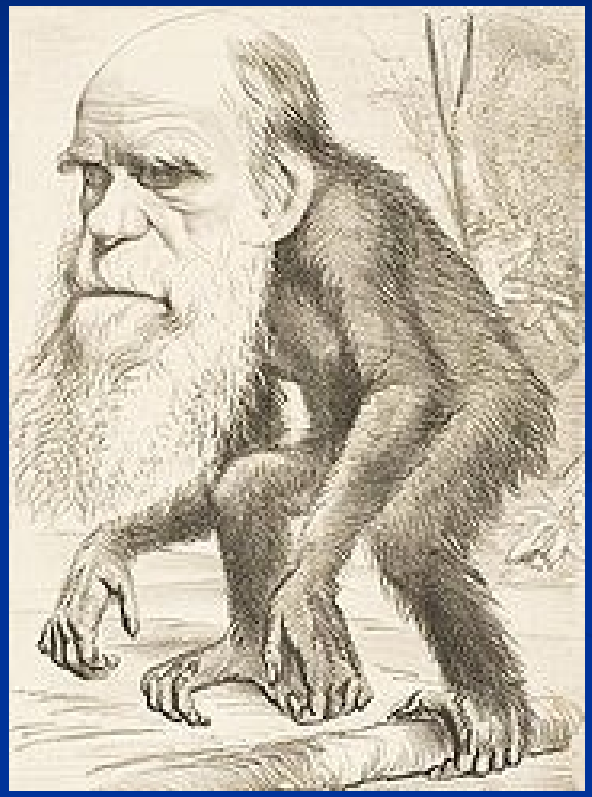
Genotype + Mutations – Phenotype – Selection – Isolation - Evolution

Was Lamarck wrong?



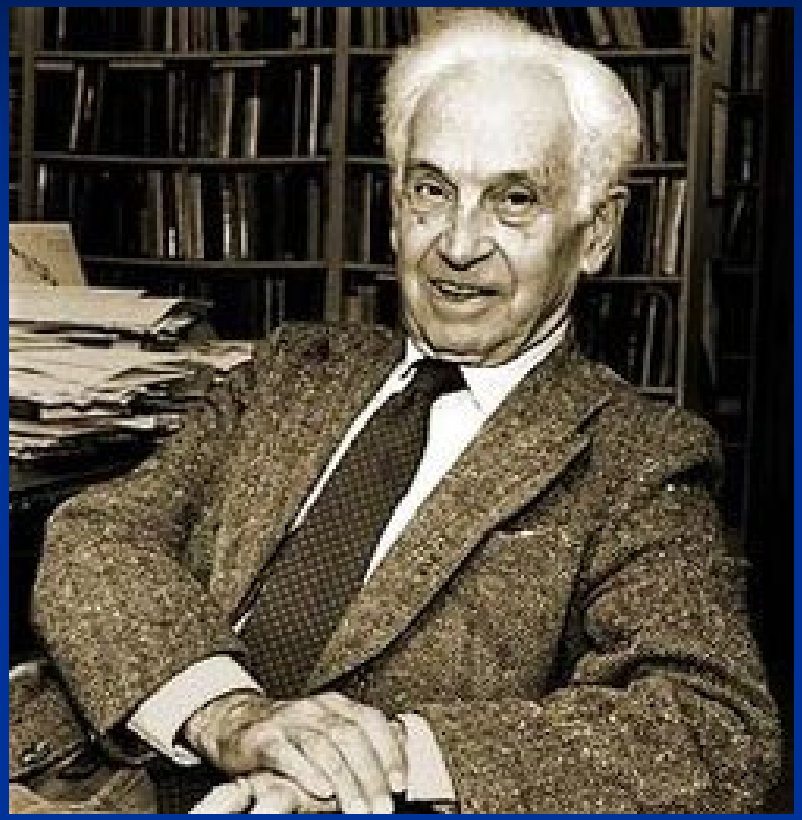


Defamation of scientists: Darwin



1859: „The origin of species“

Ernst Mayr – the famous scientist on evolution



1904 (Allgäu) – 2005 (Massachusetts)

1998 and 2001 publication of: *This is Biology* and *What Evolution is.*

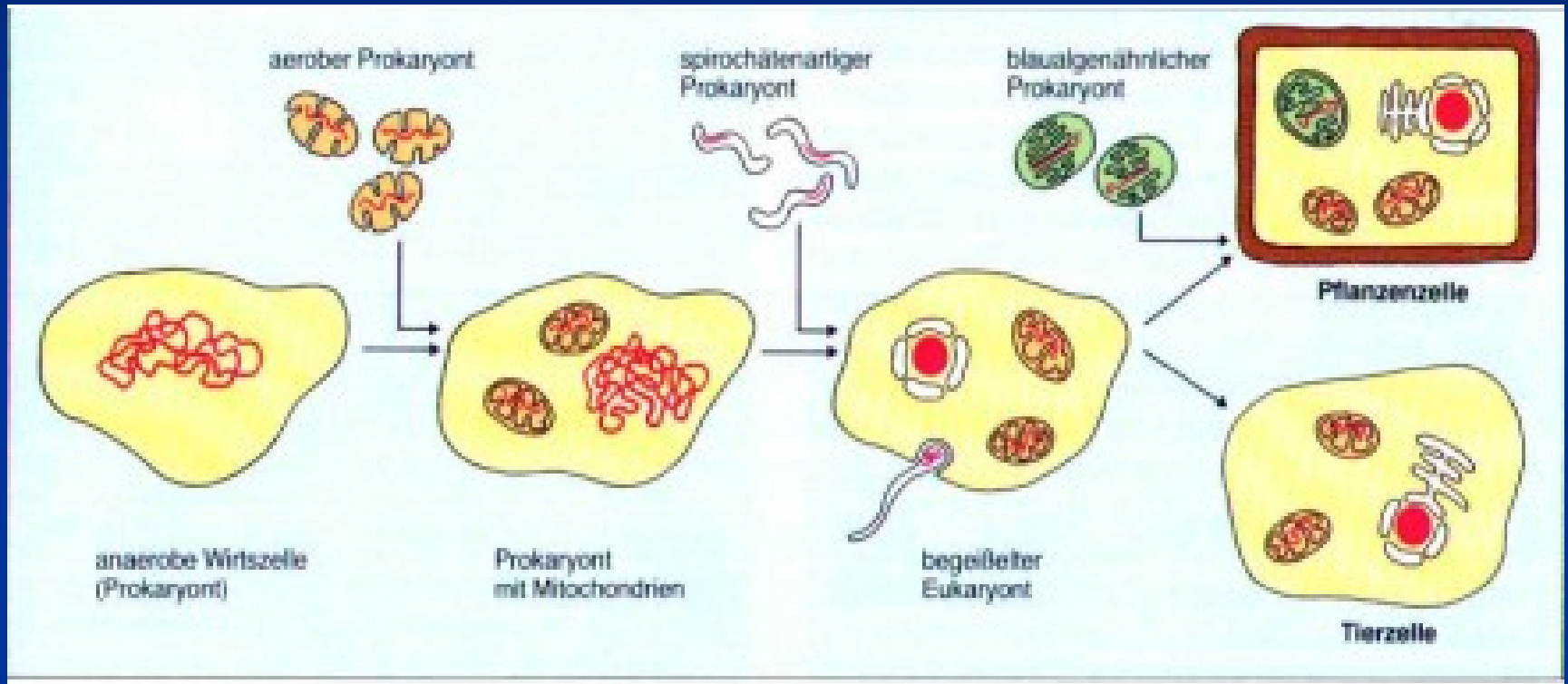
Darwin: „Survival of the fittest"

Meaning:...?

Best adapted

The sense changes depending on the environment (culture and meaning) in the course of time!

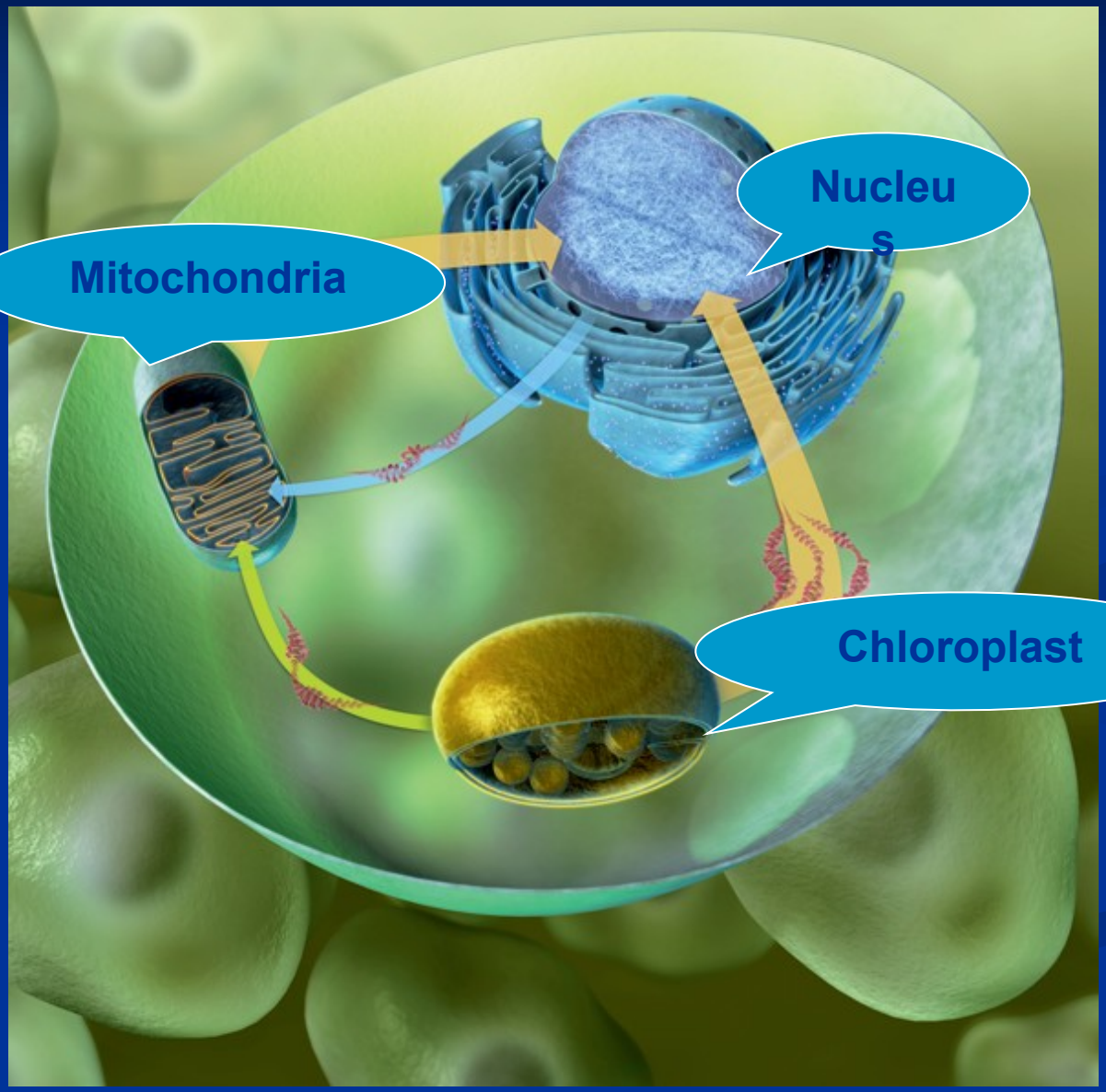
Symbiogenesis



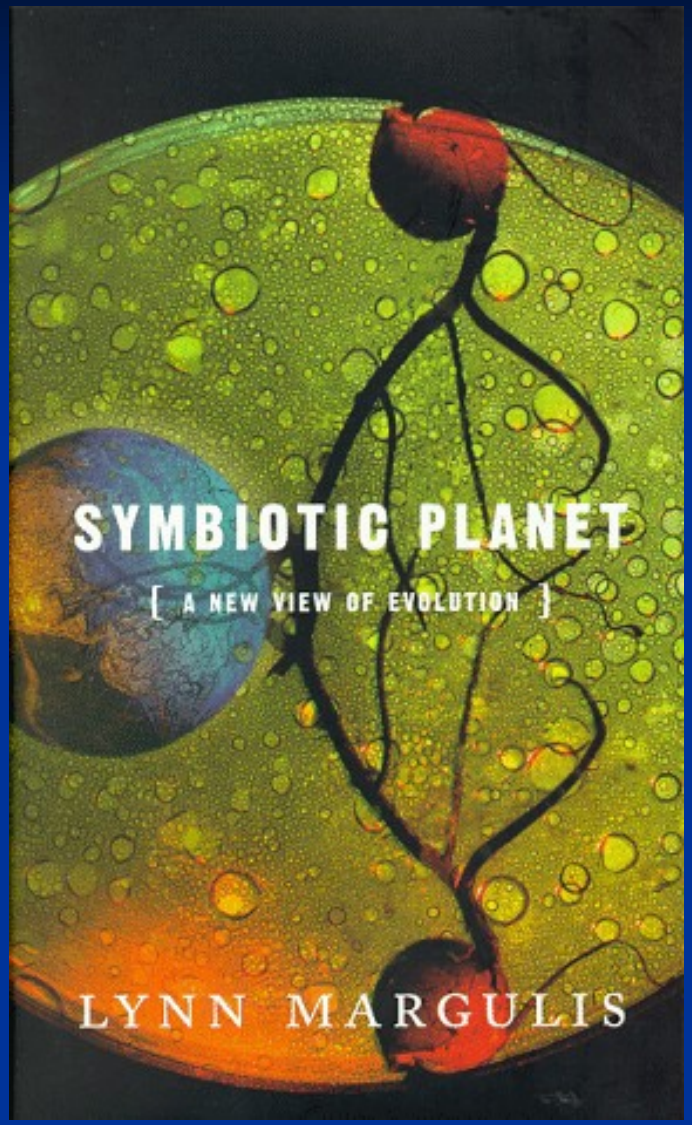
315.1. Möglicher Ablauf der Entstehung von Zellorganellen

How cell-organelles could have been evolved!

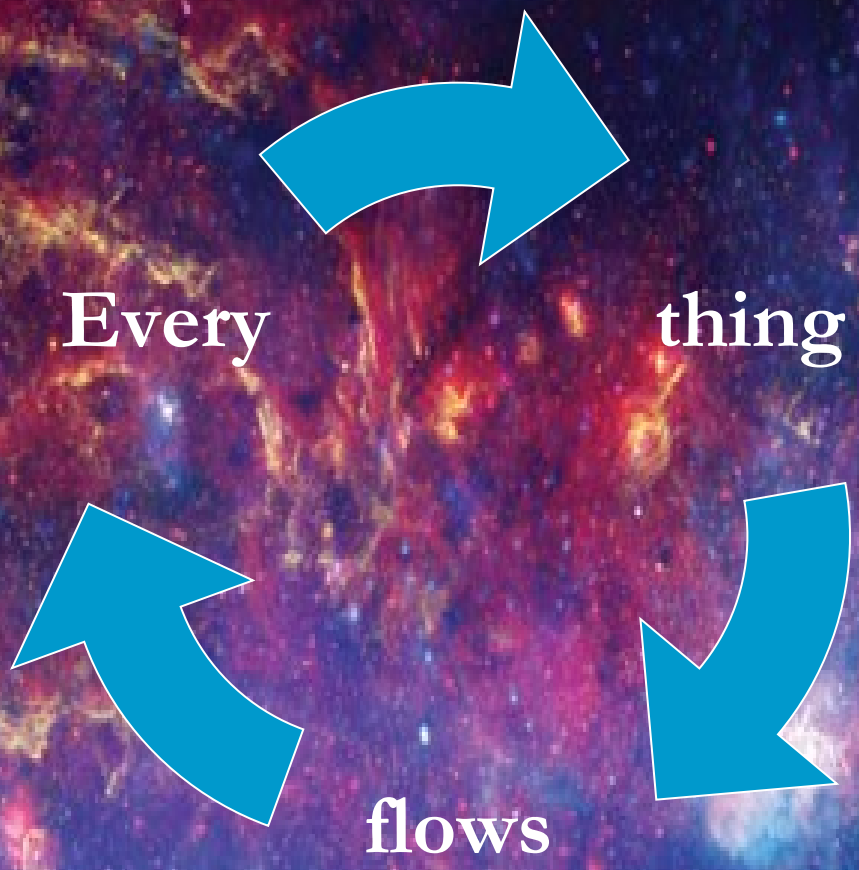
Evolution and Symbiosis



Lynn Margulis



Cooperation and Symbiosis



Evolution as a never-ending process

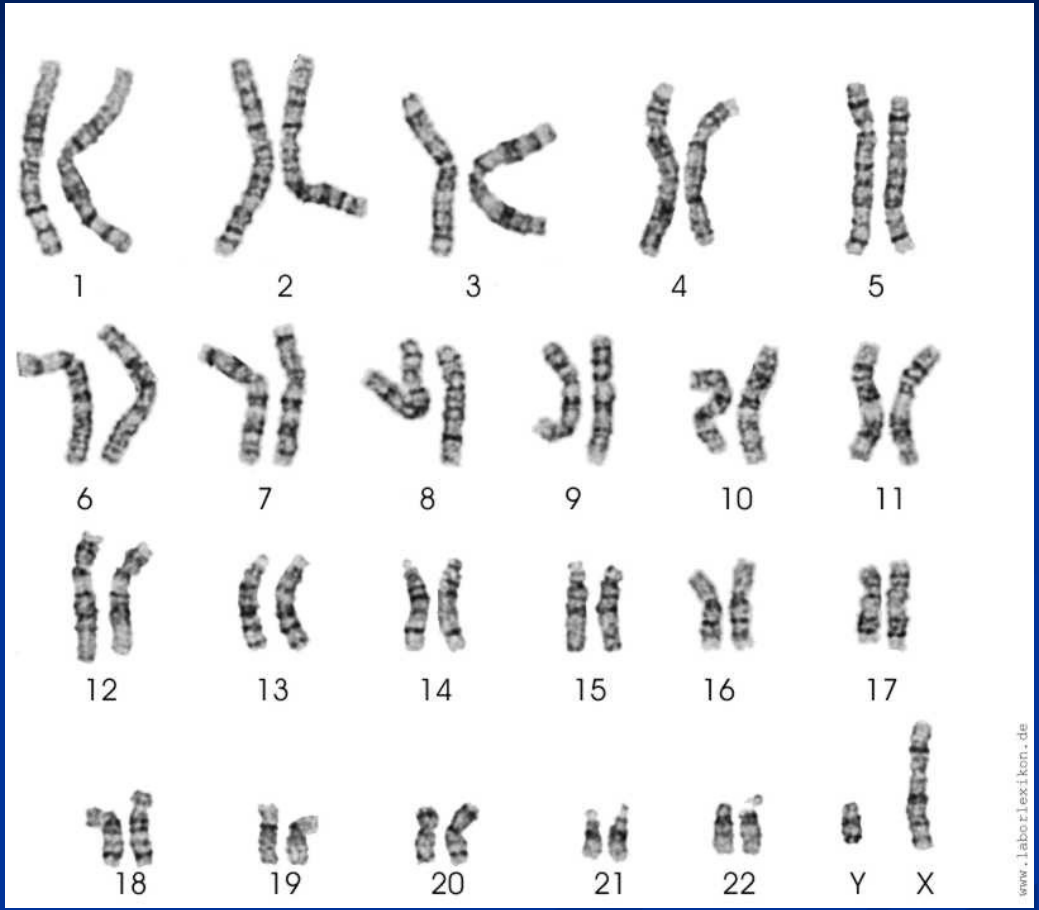
Systems Biology

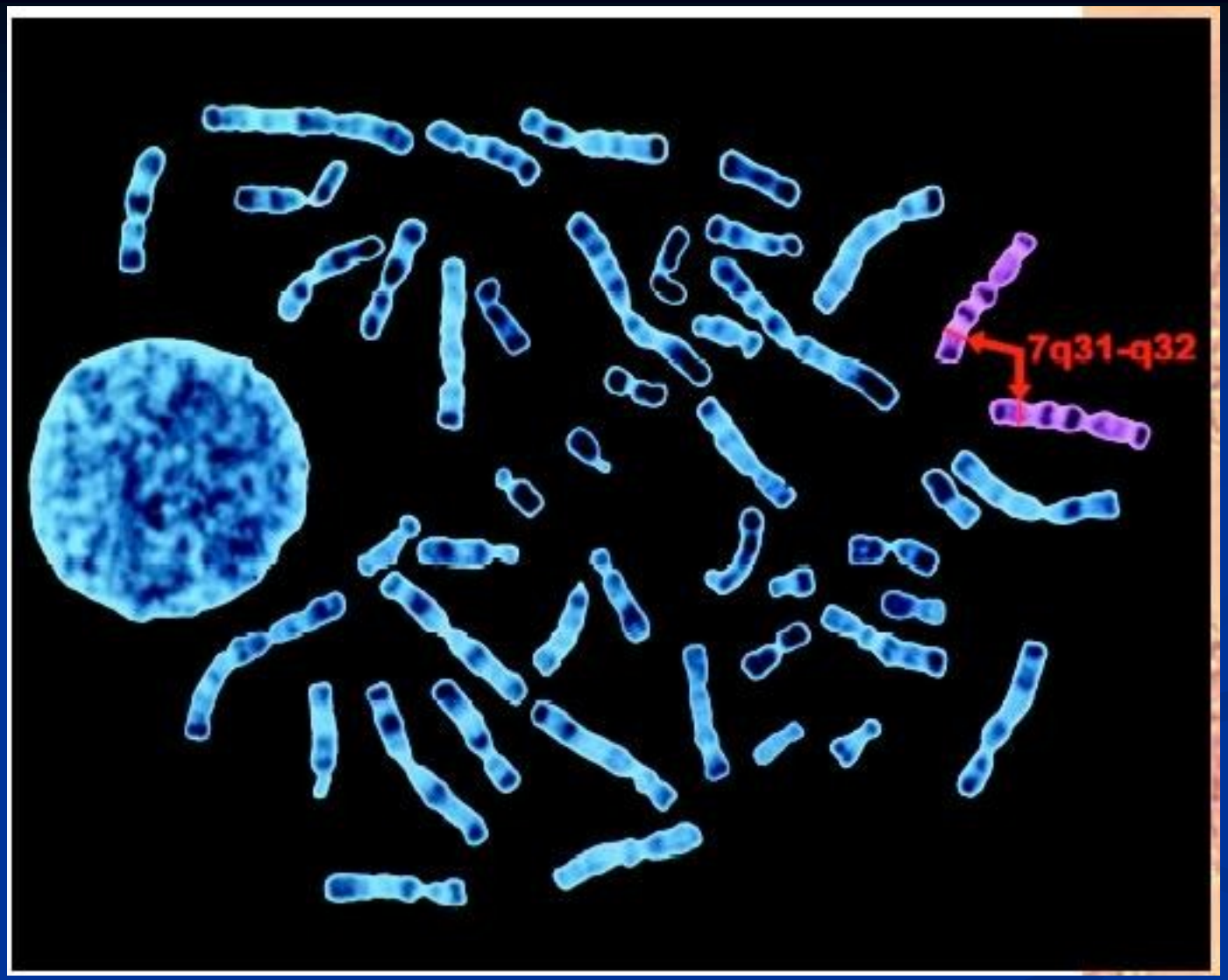
To study biochemical processes in cells, organs and organisms as a whole entity –is the ambitious aim of Systems Biology!

These special fields are interacting in solving scientific and social problems:

- ***Physiology,***
- ***Mathematics,***
- ***Informatikcs and***
- ***Medical Sciences***

Karyotyping the Human Being



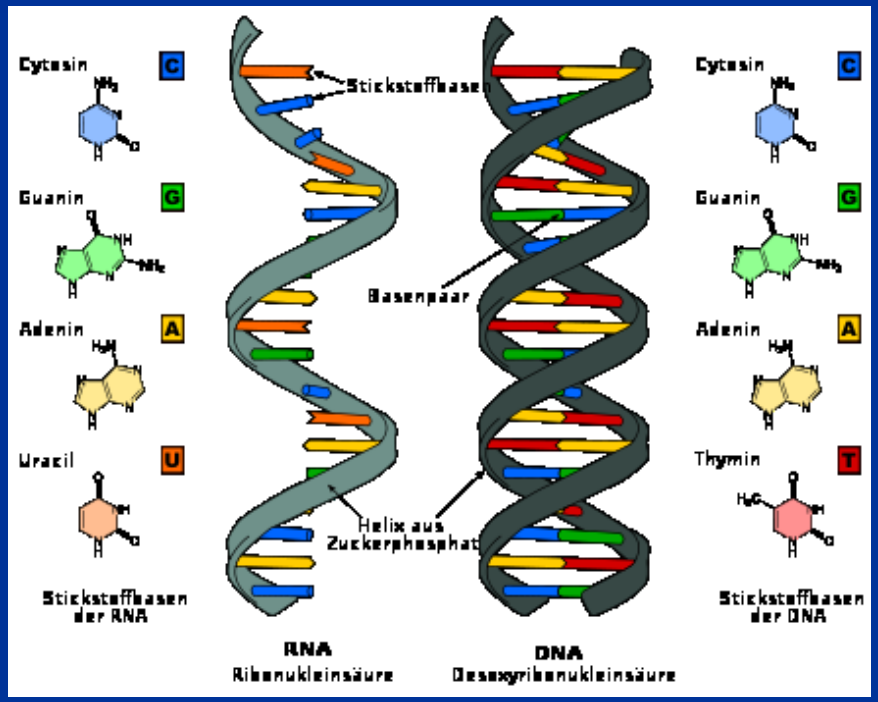


A photomicrograph of human chromosomes showing a mutation on gene 7, which is responsible for cystic fibrosis.

The Tasmanian Devil: Disease by Inbreeding!

Who was first - RNA or DNA?

Structural Model of a Ribozym, feature of the **RNA-World-Hypothesis***



*Renee´Schroeder, Max F. Perutz Laboratories, University of Vienna / RNA-Biology

The Central Dogma of molecular Biology is no Dogma any more:

DNA => RNA => PROTEIN

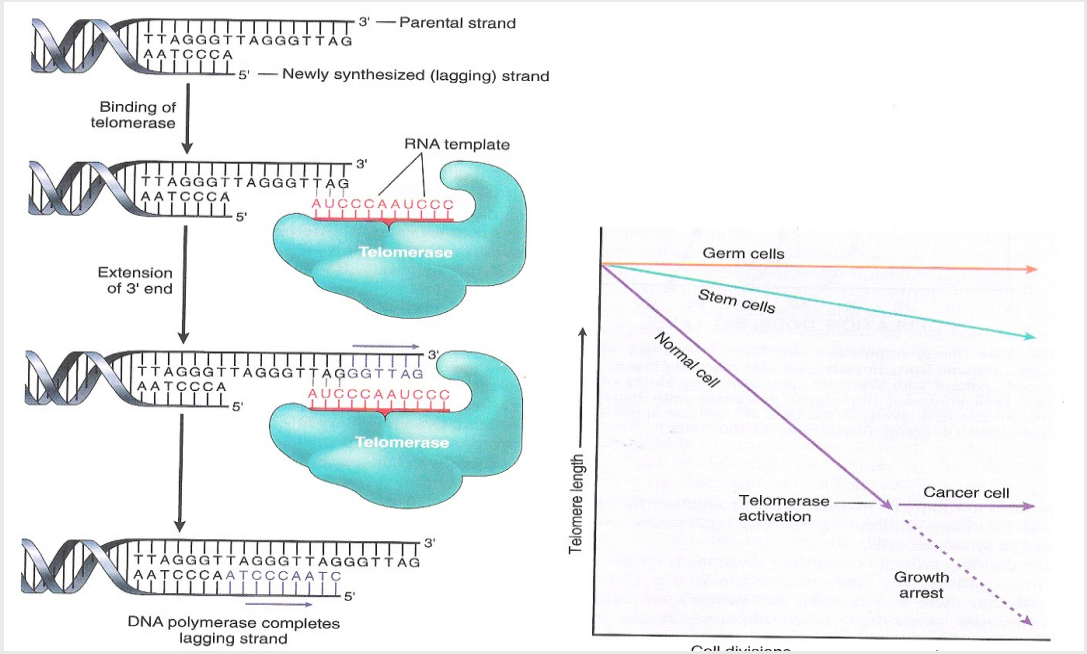
DNA <=> RNA

PROTEIN => PROTEIN (PRIONS)

Prusiner, S. B., U.S.A., University of California, School of Medicine, San Francisco, CA, geb. 1942: Nobelpreis 1997: "for his discovery of prions - a new biological principle of infection"

Transcription of RNA in DNA is an evolutionary Standard in all Cells

The role of telomerase in different cells



Connection between length of telomers and life expectancy

Telomerase of the cell is as well a reverse transcriptase and necessary after each mitosis.
(Nobelprice for Medicine 2009 to E. Blackburn, C. Greider, J. W. Szostak /USA)

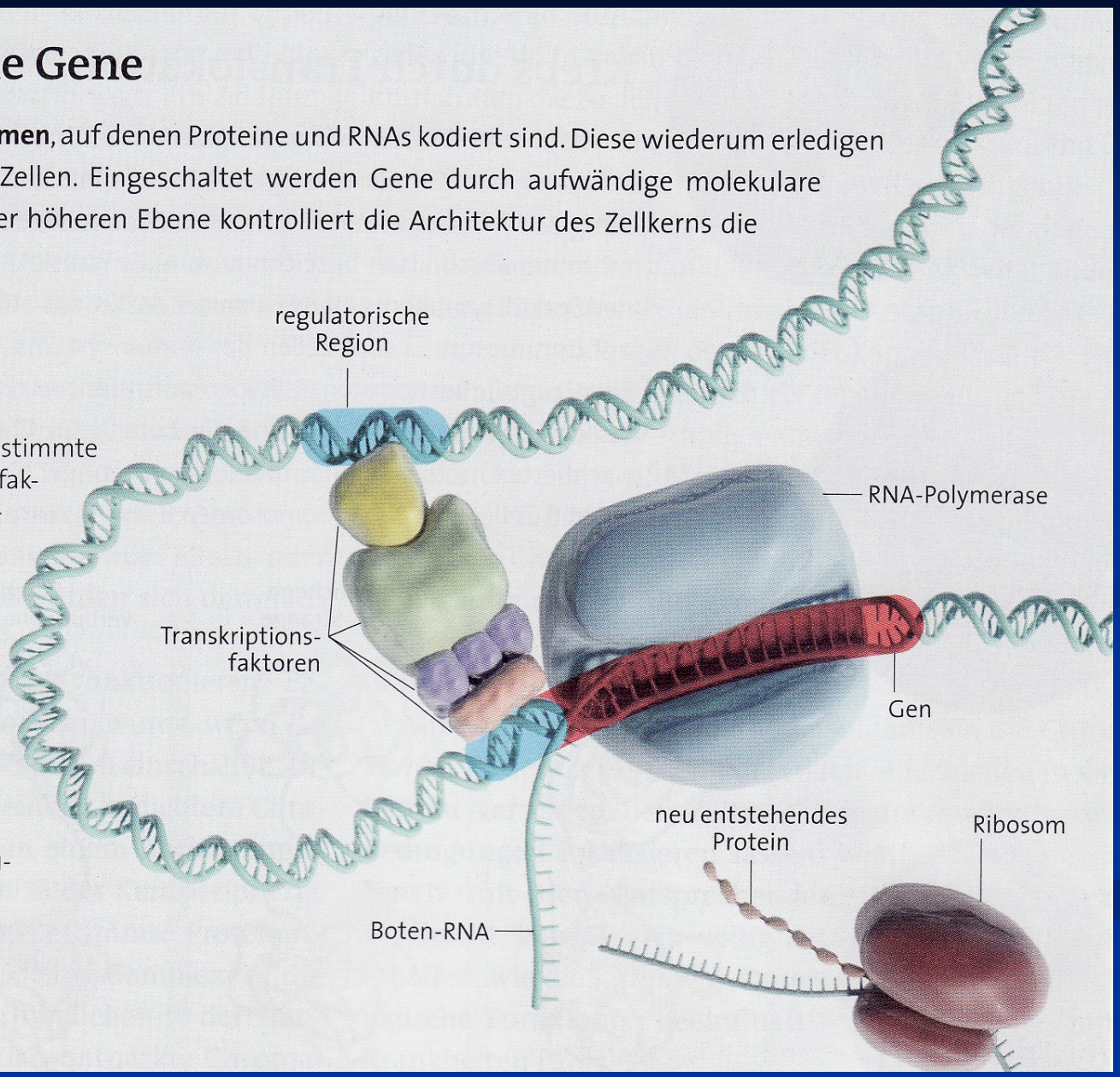
Gene-Activation

So aktiviert die Zelle Gene

Gene sind die Teile der Chromosomen, auf denen Proteine und RNAs kodiert sind. Diese wiederum erledigen den Großteil der Arbeit in den Zellen. Eingeschaltet werden Gene durch aufwändige molekulare Maschinen (oberes Bild). Auf einer höheren Ebene kontrolliert die Architektur des Zellkerns die Genaktivität (unten).

Von der DNA zum Protein

Ein Gen wird aktiviert, wenn sich bestimmte Proteine, die man als Transkriptionsfaktoren bezeichnet, an seine regulatorischen Regionen binden. Sie ermöglichen den RNA-Polymerasen, die Buchstabenabfolge (Nukleotidsequenz) der DNA abzulesen und in Form von RNA zu vervielfältigen. Wenn es sich um ein proteinkodierendes Gen handelt, wandern die RNA-Moleküle (Boten-RNAs) aus dem Zellkern ins Zellplasma, wo die Ribosomen gemäß den auf ihnen kodierten Bauplänen die Proteine herstellen.



Cloning: Genetic identity but different!

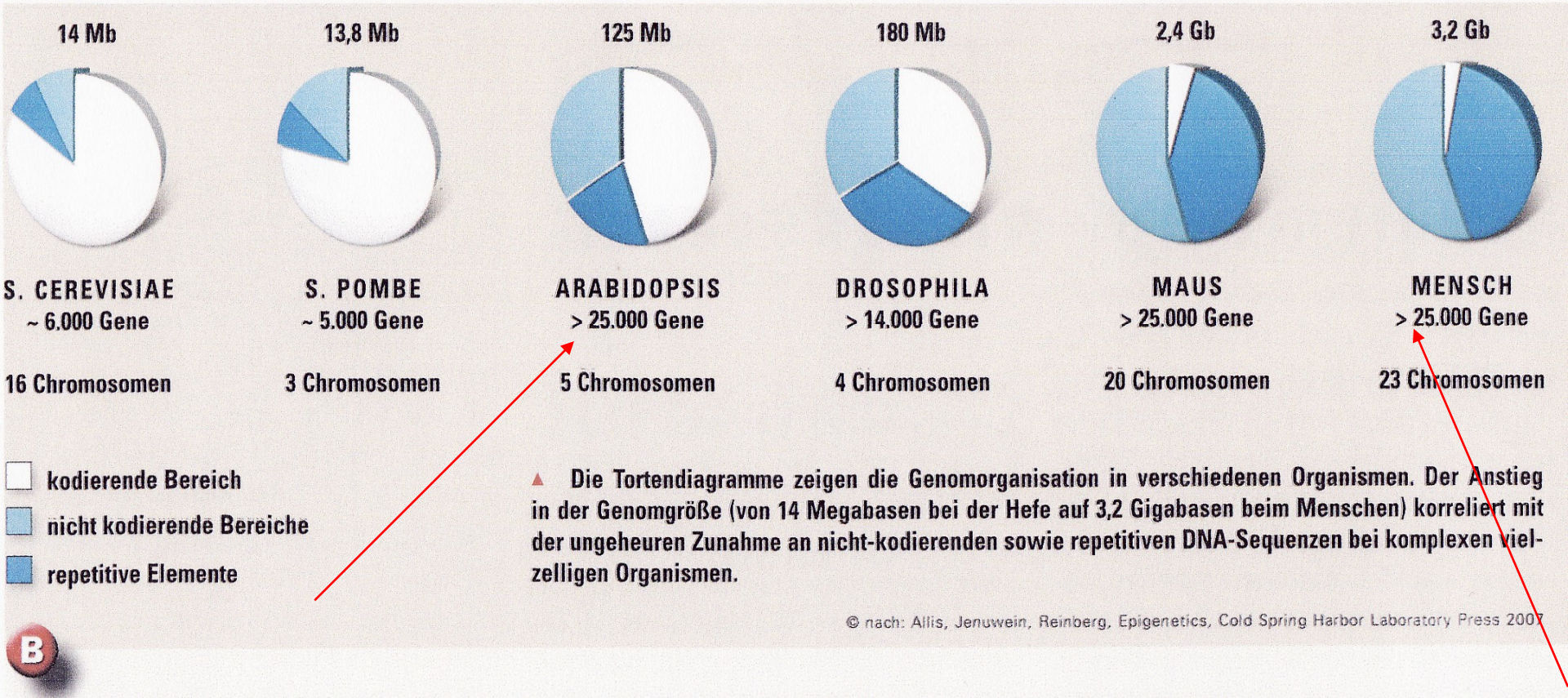
Copycat

Why?

CC was born at the College of Veterinary Medicine at Texas A&M University, under the direction of Dr. Mark Westhusin, in collaboration with Dr. Taeyoung Shin. Her existence was announced publicly on February 14, 2002, in conjunction with the publication by the scientific journal Nature of a paper about the accomplishment.

Evolution of the genes from yeast to humans:

Only about 2% of the DNA from humans codes for proteins.
The other 98 % match to our „Dark Matter"!



Coding means, related to genes (proteins).

„Dark matter“ of the genome may play a major biological role in cell development and metabolism including diseases like cancer.

Involved are
many different
Non coding RNA genes
that have recently been detected.

What are pathogens?

The human being has about 3 – 5 kg of microbes on and in his body (gut, skin, mucous membranes).
They are harmless or necessary in symbiosis.
If the immune system becomes weak, there might be an imbalance or an ineffective fight against invaders from the environment. Harmless bacteria might increase (i. e. Helicobacter pylori, Candida and other species in the stomach, throat or lung).

The Neuroscience of the Gut

Autismus and Mikrobiom – a Connection?

Microbiom and Vaccination – do we need an evaluation?

Human Being:
30.000 human genes but 3.000.000 microbial genes!
10 times more microorganisms than own cells.

Princeton University scientist Bonnie Bassler compared the approximately 30,000 human genes found in the average human to the more than 3 million bacterial genes inhabiting us, concluding that we are at most one percent human. We are only beginning to understand the sort of impact our bacterial passengers have on our daily lives.

http://www.scientificamerican.com/article.cfm?id=the-neuroscience-of-gut

Our body is part of the microbial world; the human being exists in more than 90% in microbial genes and organisms.

The air contains more than1800 different species of bacteria.

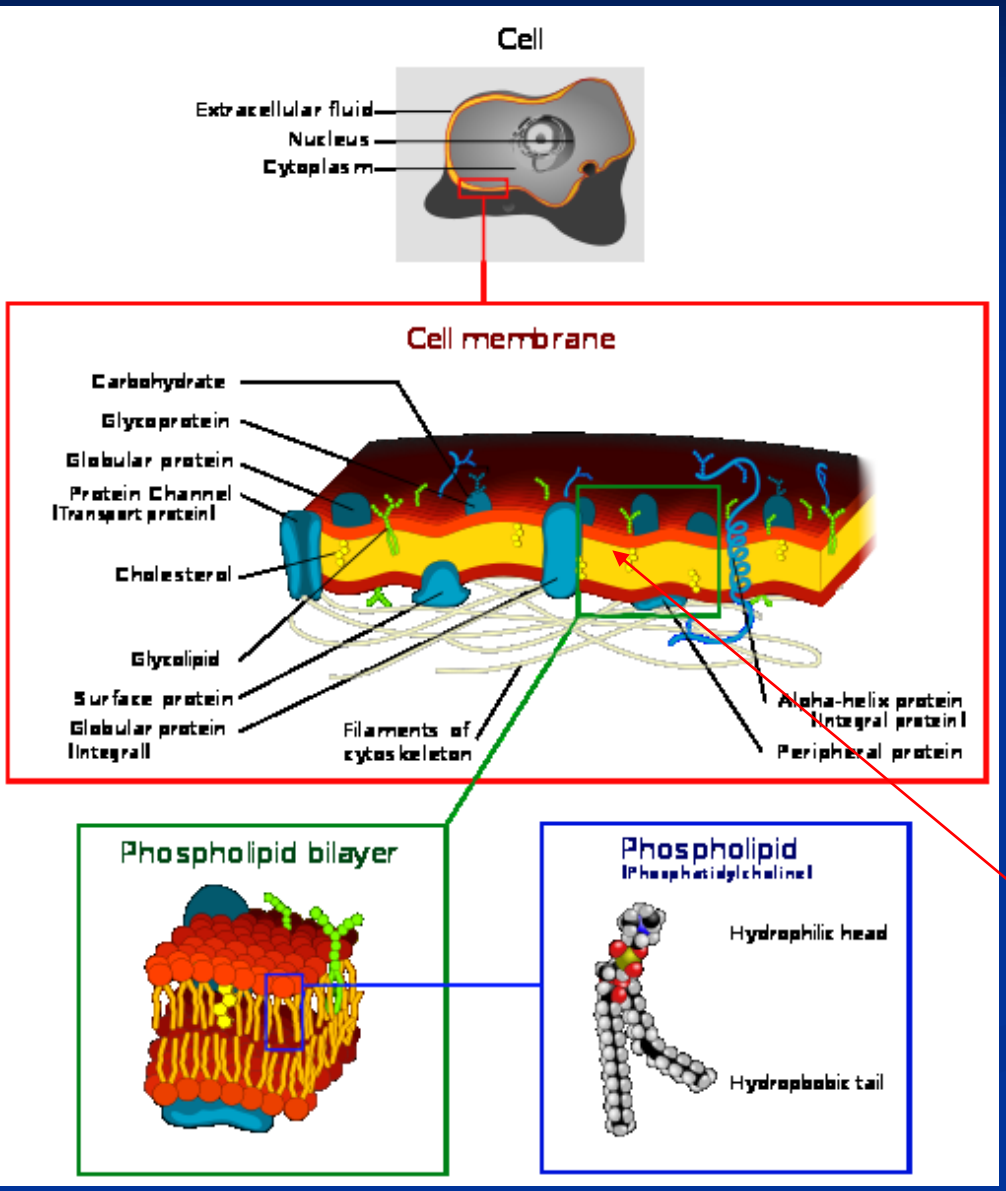
This flower-like image is the work of Eshel Ben-Jacob, a professor of physics at Tel Aviv University in Israel.

- Working with colleagues at the Center for Theoretical Biological Physics at the University of California, San Diego, he wants to unravel what it is that makes bacteria so adept at survival by looking at pattern formation in complex dynamic systems alongside the molecular biology and biophysics of bacteria.

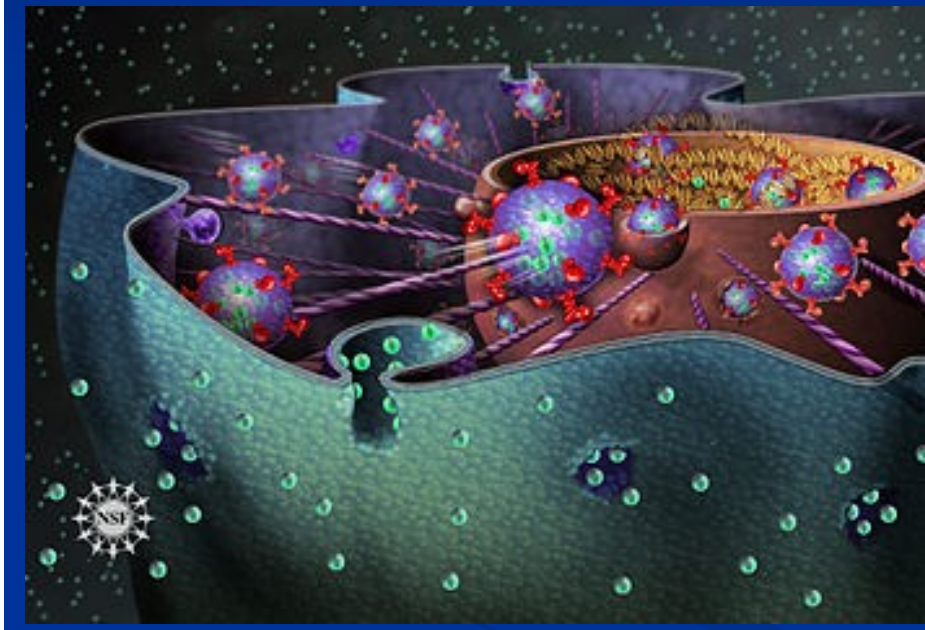
  Ben-Jacob's work is artificially coloured, but the pattern is produced by the

- *Bacteria responding to stresses* put upon them. For example, by limiting the food source, the colony can be made to reorganise itself into long tendrils, increasing its surface area to find more nutrients.

Cell-Communication



Nucleus



Cell- membrane

Why is Cell Communication Interesting?

...and what does it deal with?

It is about interaction and communication, about health and disease. The stimili come from

- **outside**
- **inside**
- **organisms**
- **organs**
- **cells**
- **organels**
- **genes**
- **molecules**

The Cell is the smallest Entity of Life!

Cell-communication

Is transmitted by different RNAs, proteins, exo- and endosomes, informosomes,clathrins, to mention only some of them.

The Journal of Immunology, 2005, 174: 4779–4788.

HIV Type 1 Can Act as an APC upon Acquisition from the Host Cell of Peptide-Loaded HLA-DR and CD86 Molecules1

Jocelyn Roy, Genevie`ve Martin, Jean-Franc¸ois Gigue`re, Dave Be´langer, Myriam Pe´trin,and Michel J. Tremblay

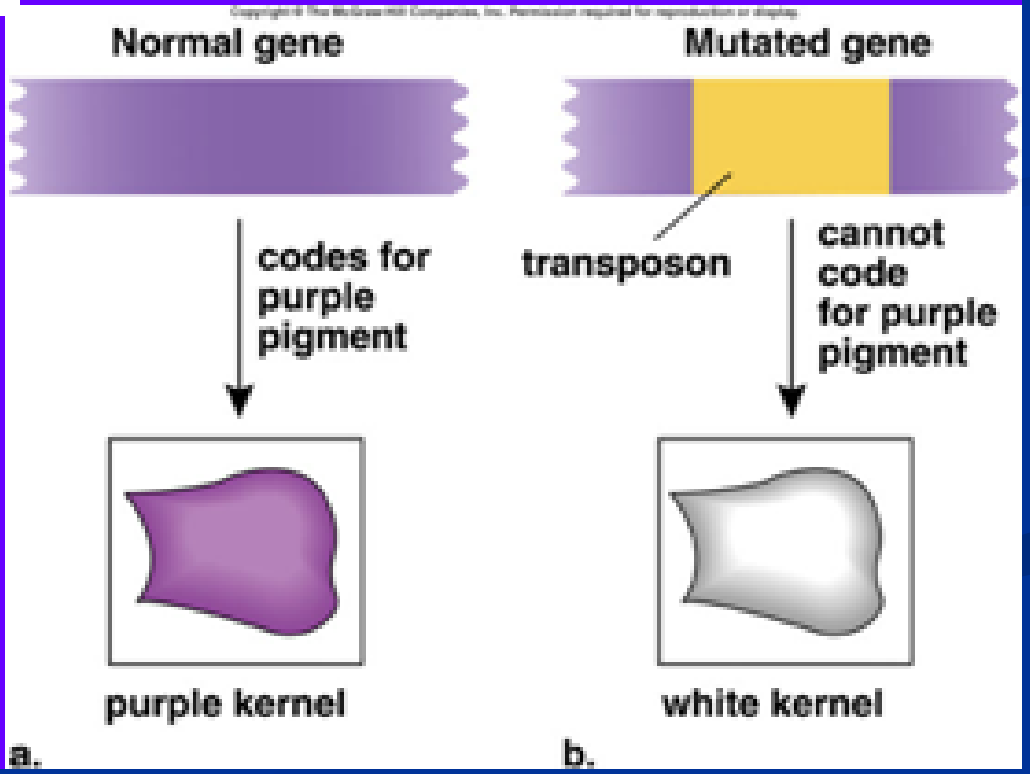
Till now science was not able to explain the speed of Evolution.

The following factors give hints:

1. Transposons
2. Retro-transposons
3. Gen-duplications
4. Horizontal Gen-transfer

Transposons are jumping genes!

Transposons are small pieces of DNA that get cut from one spot and spliced into an inappropriate spot– often right in the middle of a gene. The gene's sequence is altered and it can no longer be used to produce the protein it codes for.

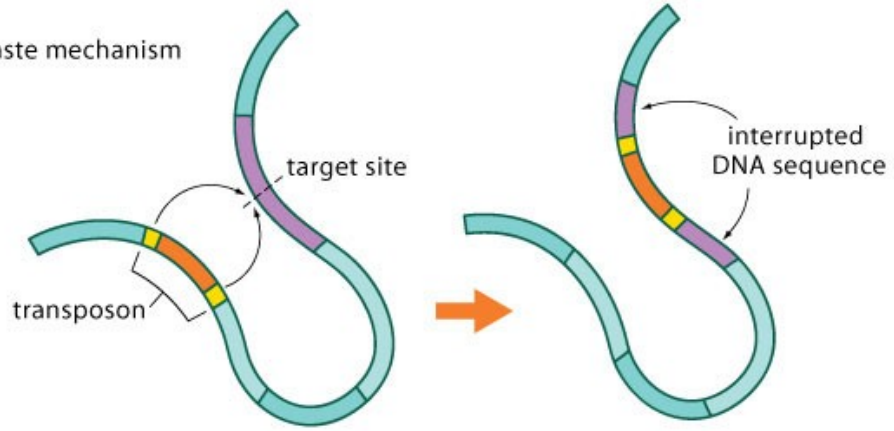


Barbara Mc. Clintock (Nobelprice for Physiology and Medicine 1983)

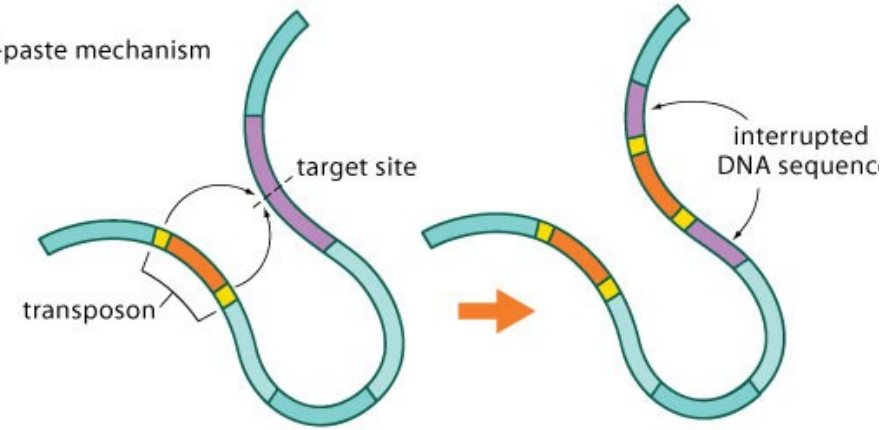
Transposons „jumping genes“

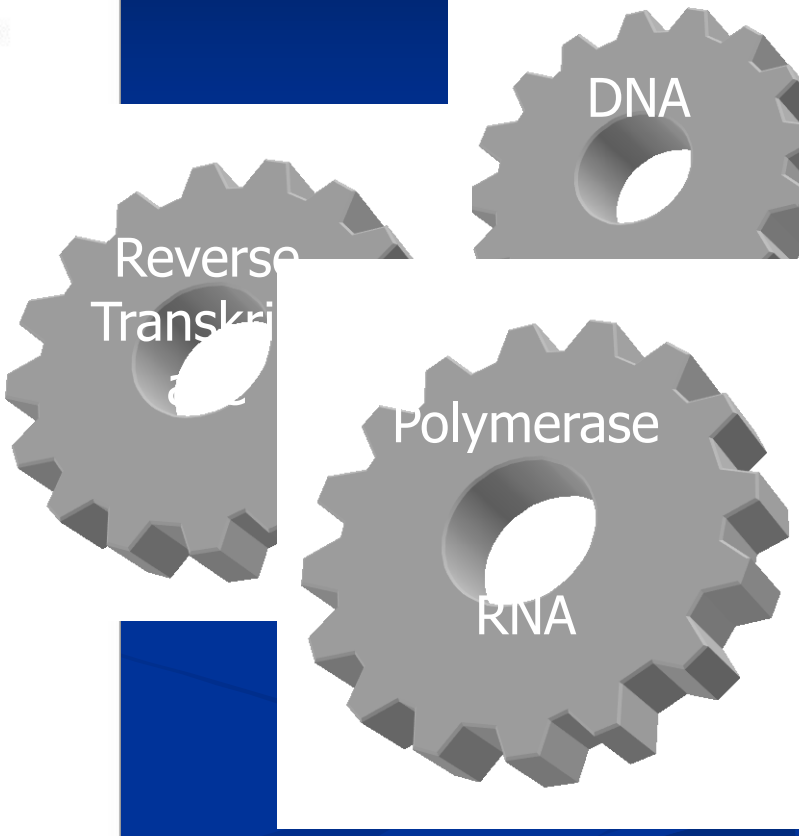
Two methods of transposition:

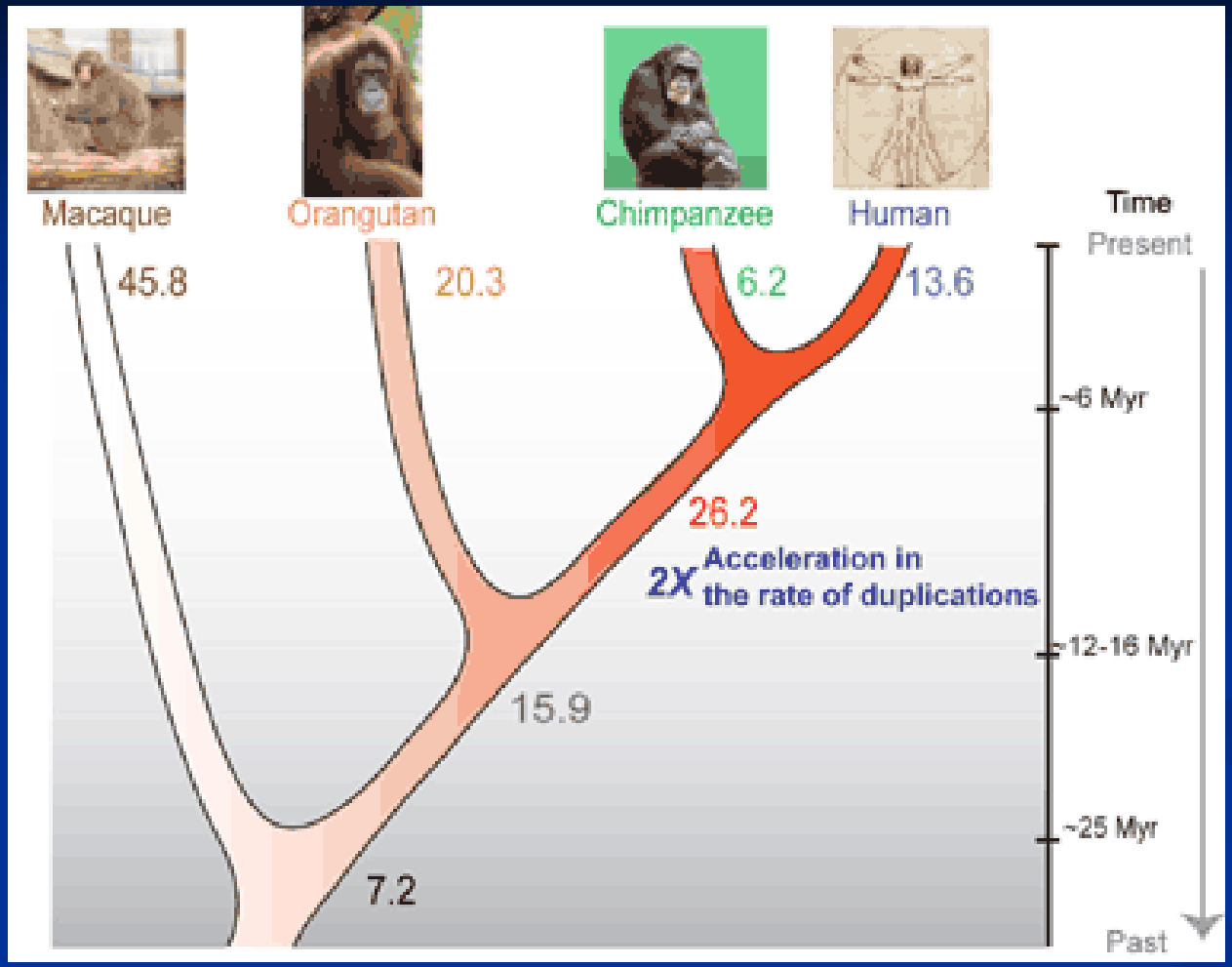
1. Cut-and-paste mechanism



2. Copy-and-paste mechanism







Gen-Duplication as a driving Force in Evolution

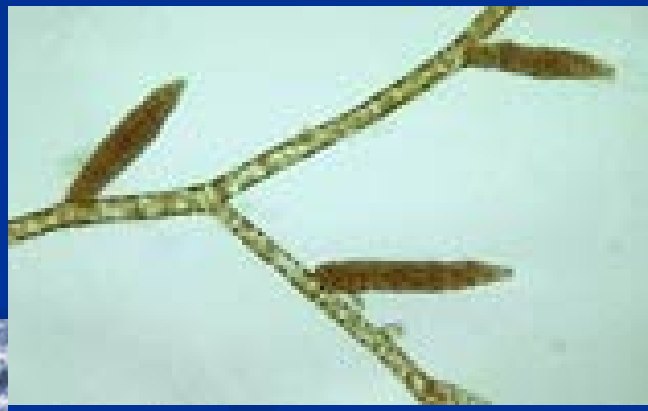
Virus „fertilizes" ancient-cells

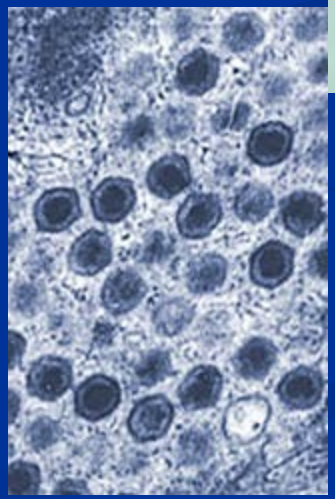
Study confirms hypothesis for evolution of the cell.

Ectocarpus siliculosus and viral genes.

Horizontal Gen-transfer

Journal of BMC Evolutionary Biology.





Elektron mikroscope photograph of „ EsV-1 virus partikels“
© MPI for Chemcal Ecology/Delaroque

(DLO.idw - Max-Planck-Institut for chemical Ecology, 2008, April 30)

There is proof for absorption of foreign (from other species) molecules like DNA, RNA, proteins.
By this action the nucleic acids can be transfered into the own genome or be degraded in the cell.

This explains

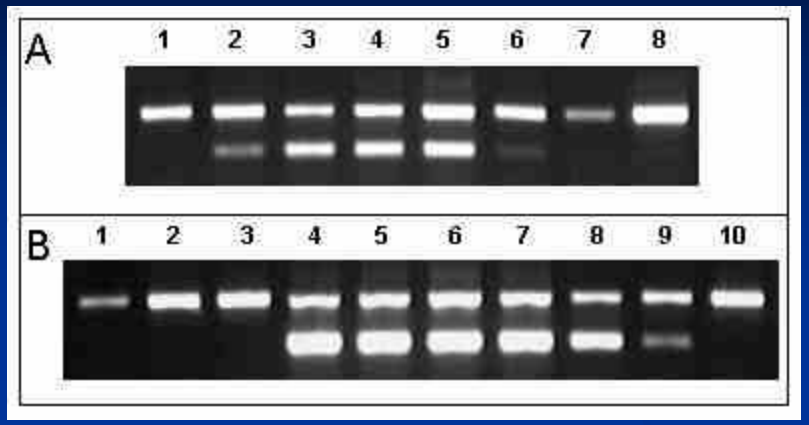
- Health
- Disease
- Allergies
- (accelerated) evolution.

Without this process of interaction and learning of the immune system the living organism is not able to develop.

The „Fluid Genome“ –
Change of the Immune System

By the re-arrangement of the genome in correspondence to stimulations from inside and from the environment in active and passive manner, specifically in T-cells (lymphocytes) of the human species, we have to agree to author Mae Wan Ho, who calls this the *„fluid genome“*.

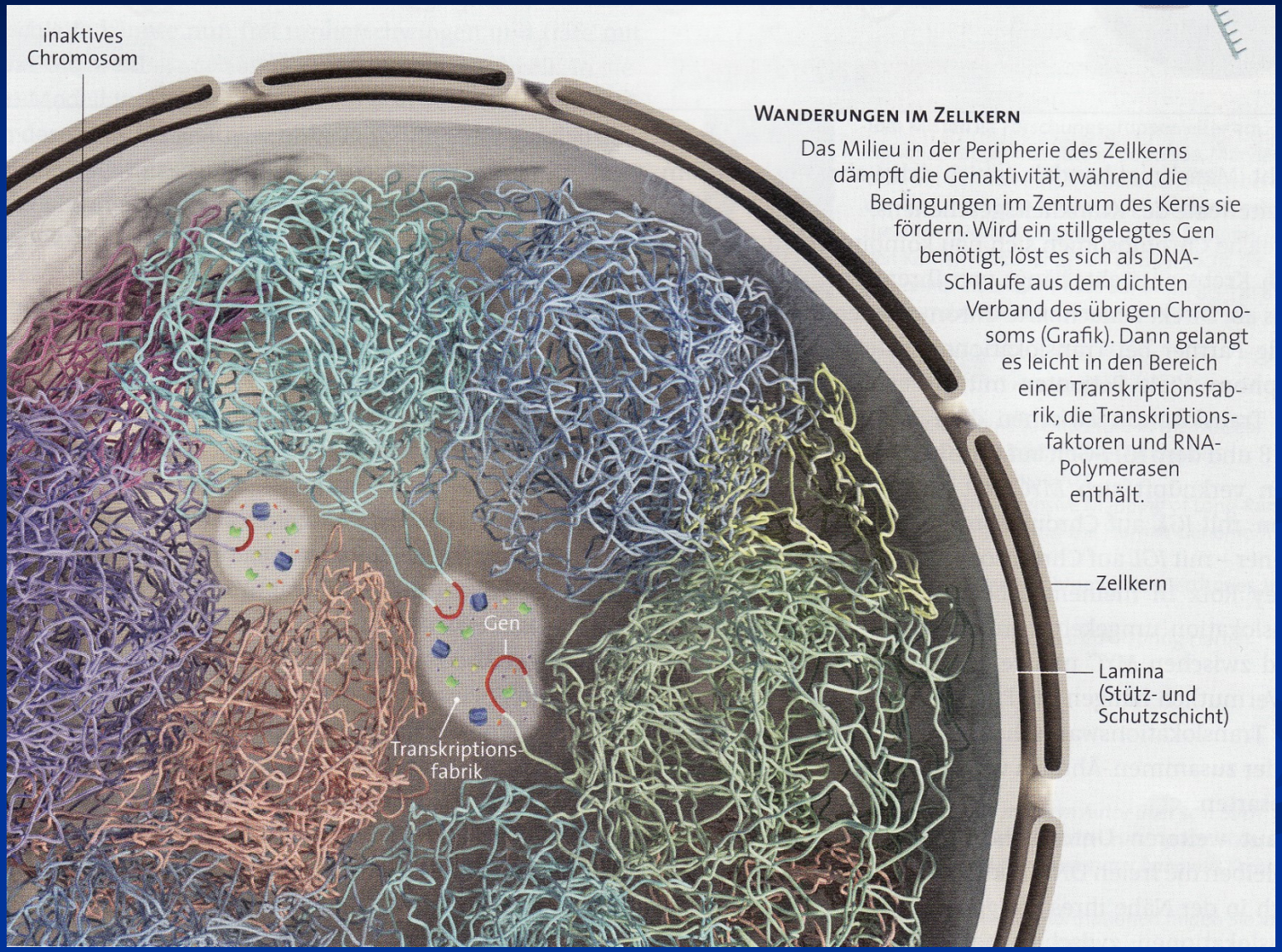
Gen-Expression



DNA = > RNA = > PROTEIN

Generation of Enzymes (Proteins)

Gen activity in relation to the chromosomal position in the nucleus



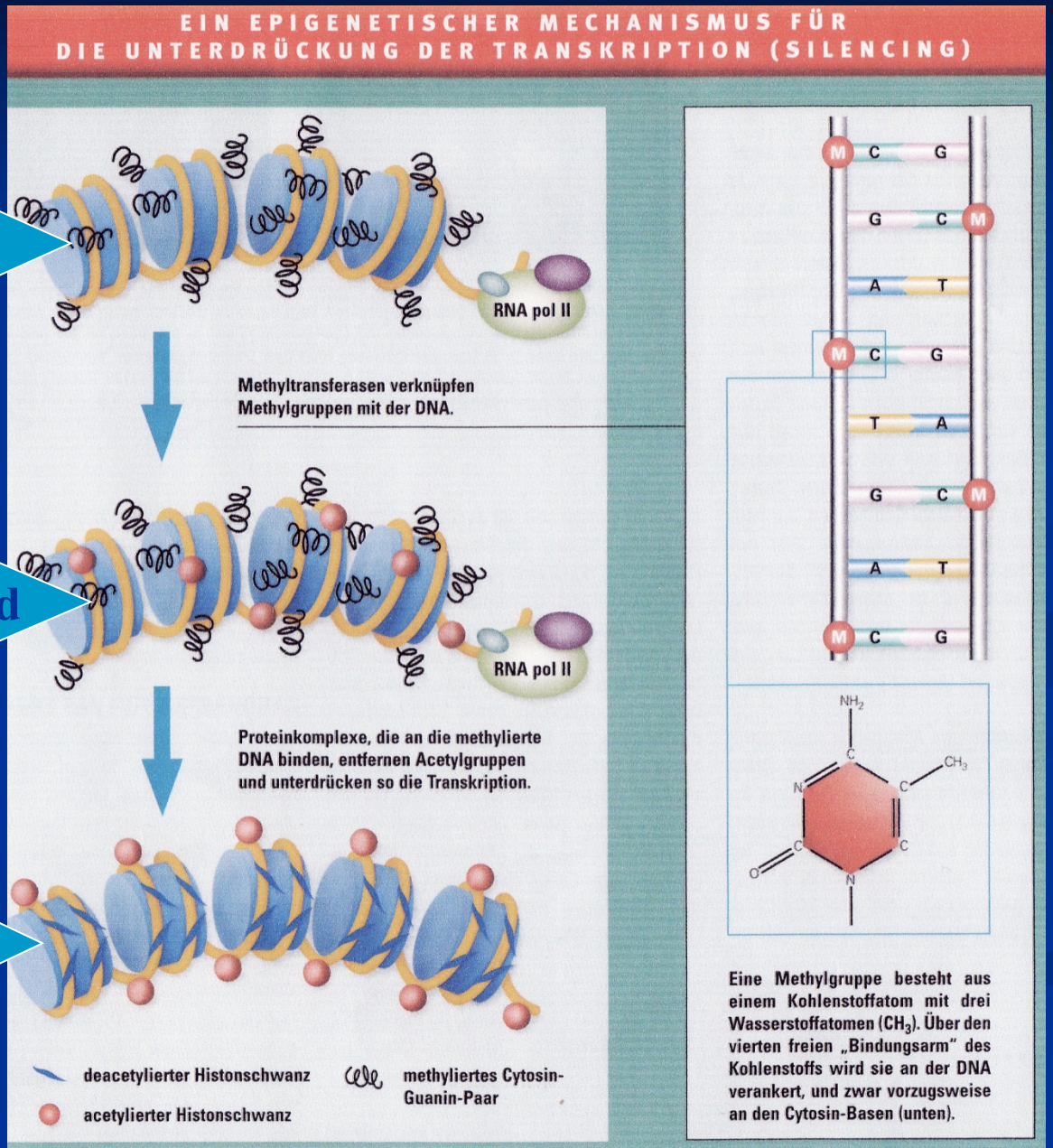
Scientific America

Gene Expression: An Epigenetic Mechanism

Histones

DNA methylated

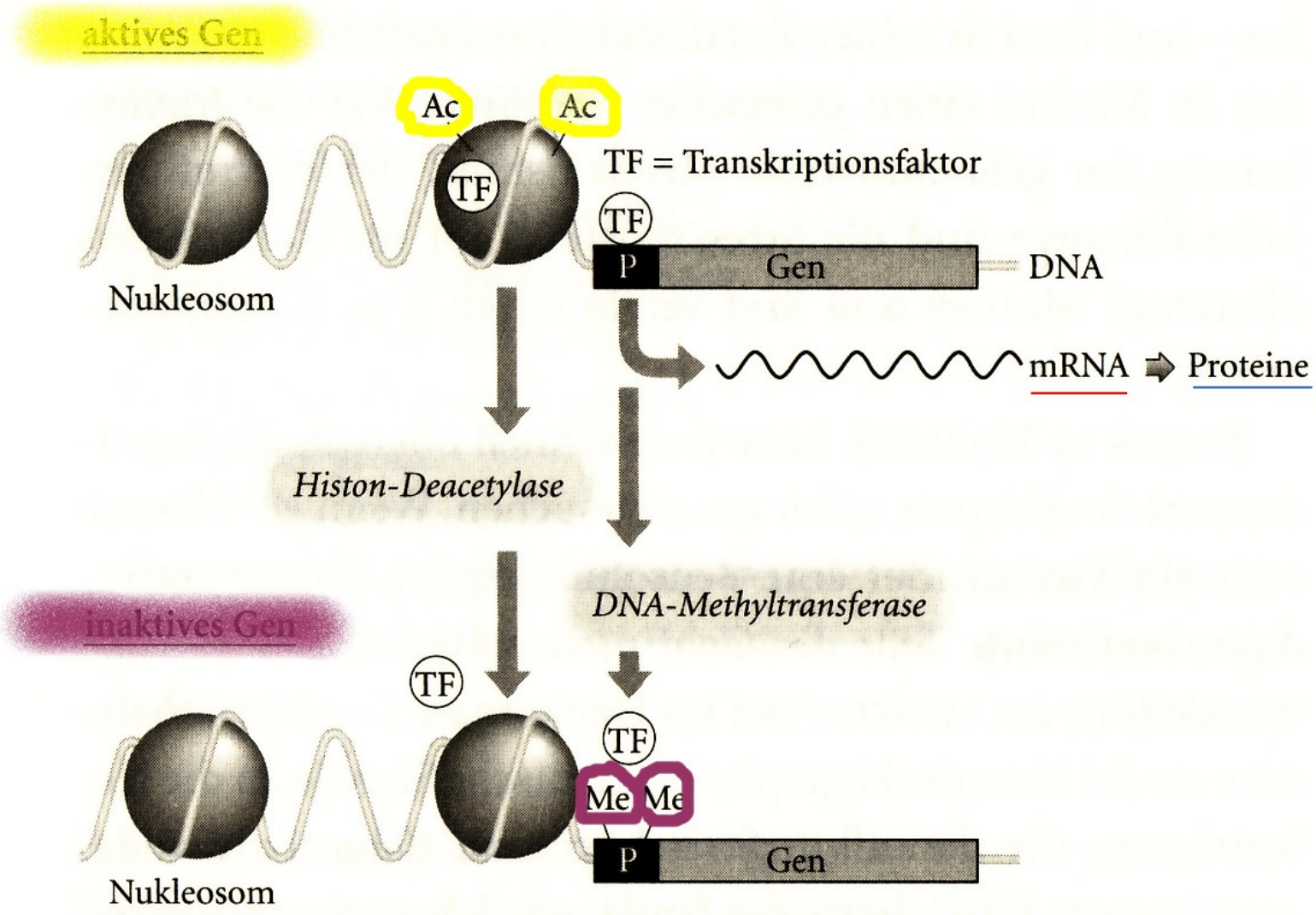
Deacetylation



Many important enzymes of the cell need the *element Selenium – best if organic* –to unroll their activity, specifically those that are involved in fighting oxidative stress and infections!

The cell gets methyl-groups from the amino acid methionine.

Example: Activated and Deactivated genes

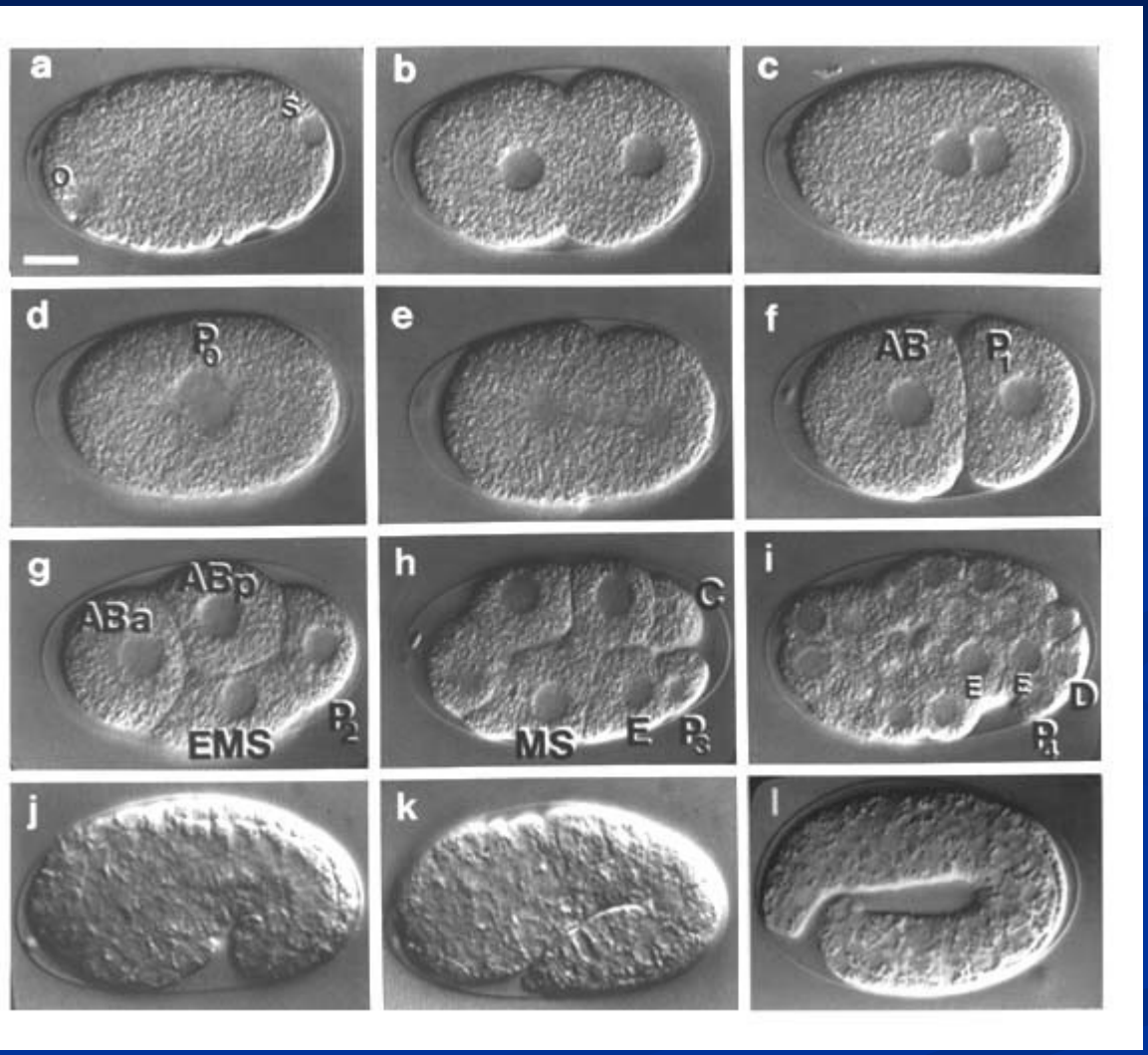


Das Anhängen von Methylgruppen (Me) und das Entfernen von Acetylgruppen (Ac) beeinflusst, ob ein bestimmtes Gen in Proteine überschrieben wird oder nicht.

Im 2006 the US-citizens Craig C. Mello und Andrew Z. Fire received the Nobel Price for Medicine for the detection of RNA – interference (RNA-i) in *Caenorhabditis elegans*.

These molecules are very important in gene regulation on DNA in all living species including humans.

Embryonic development of *C. elegans*

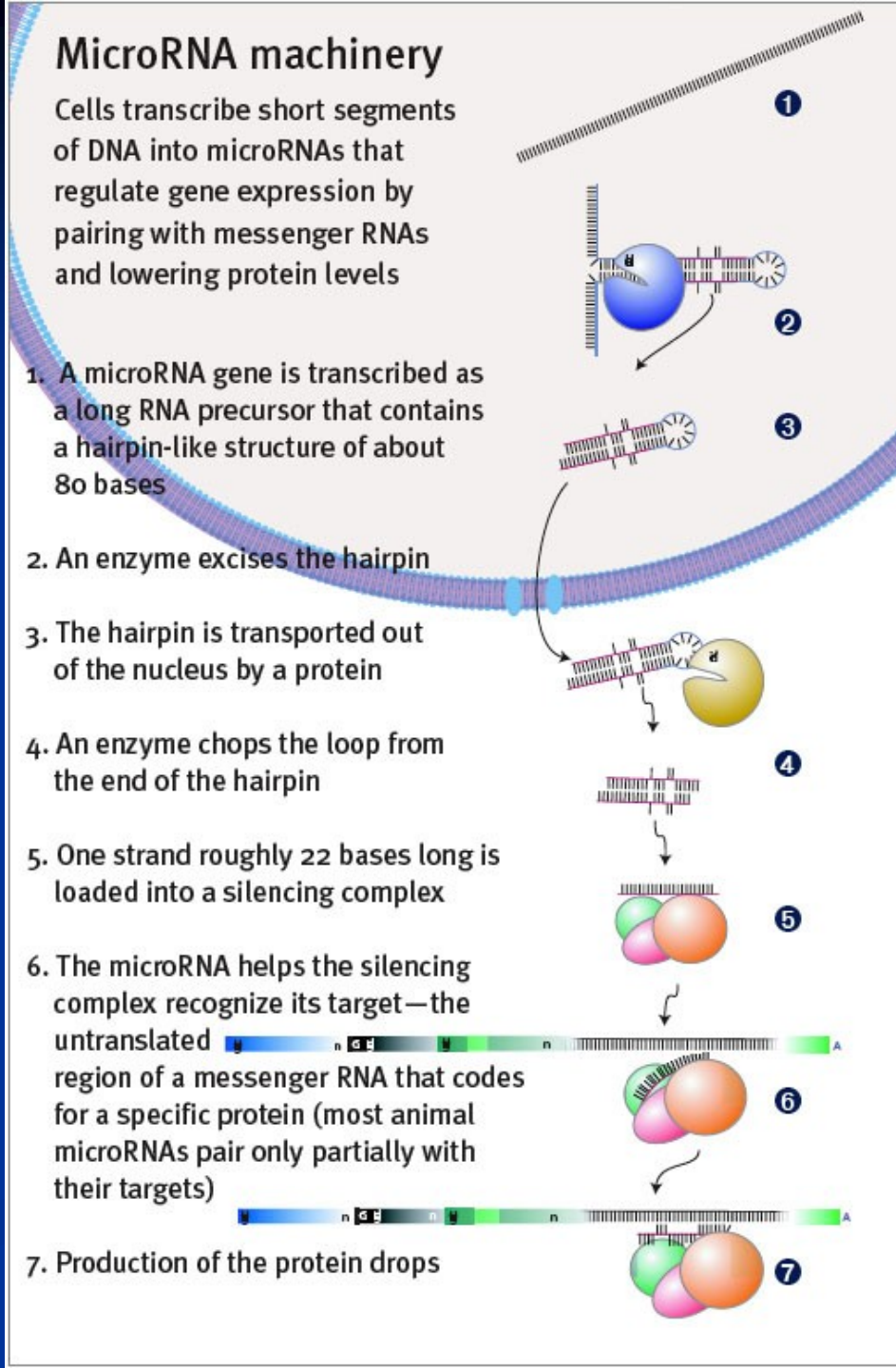


Now many different types of RNA are detected!

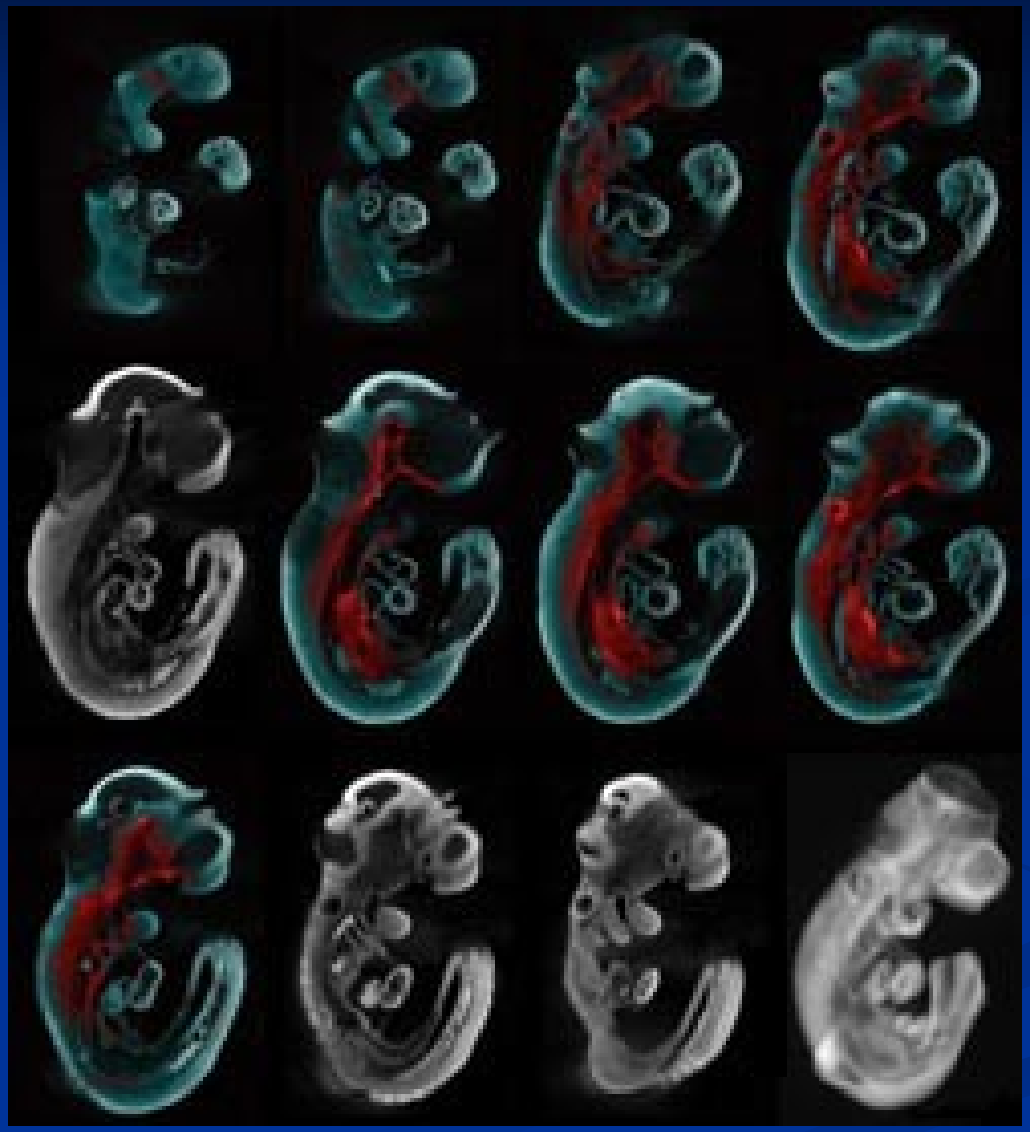
Micro-RNA or RNA-i regulates Gen-expression of m-RNA.

This takes place in the RISC-Complex. (Argonaute-Protein)

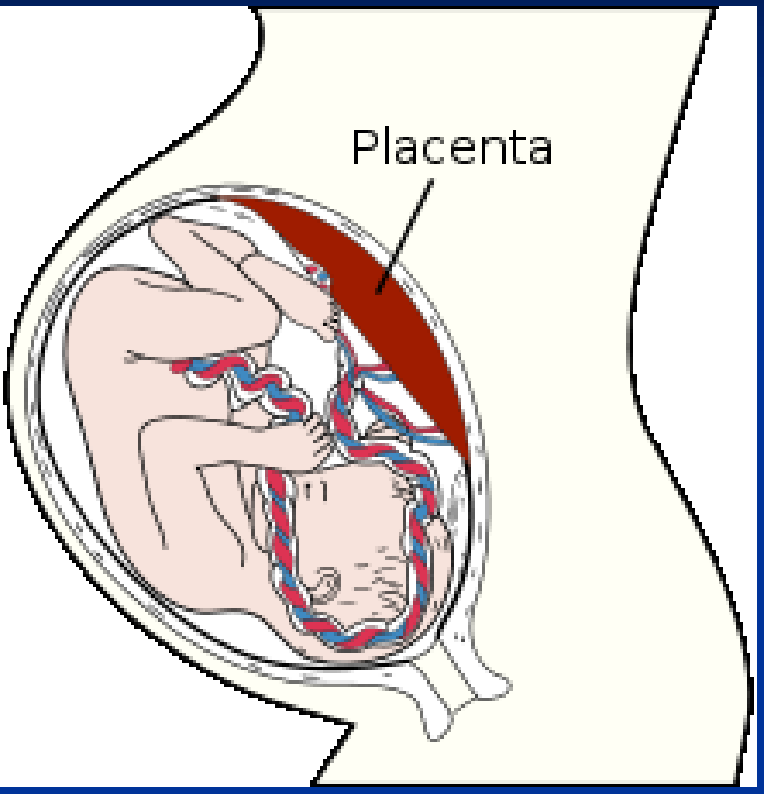
Creation of endosomes, transport to the cell-membrane for receptors or other structures

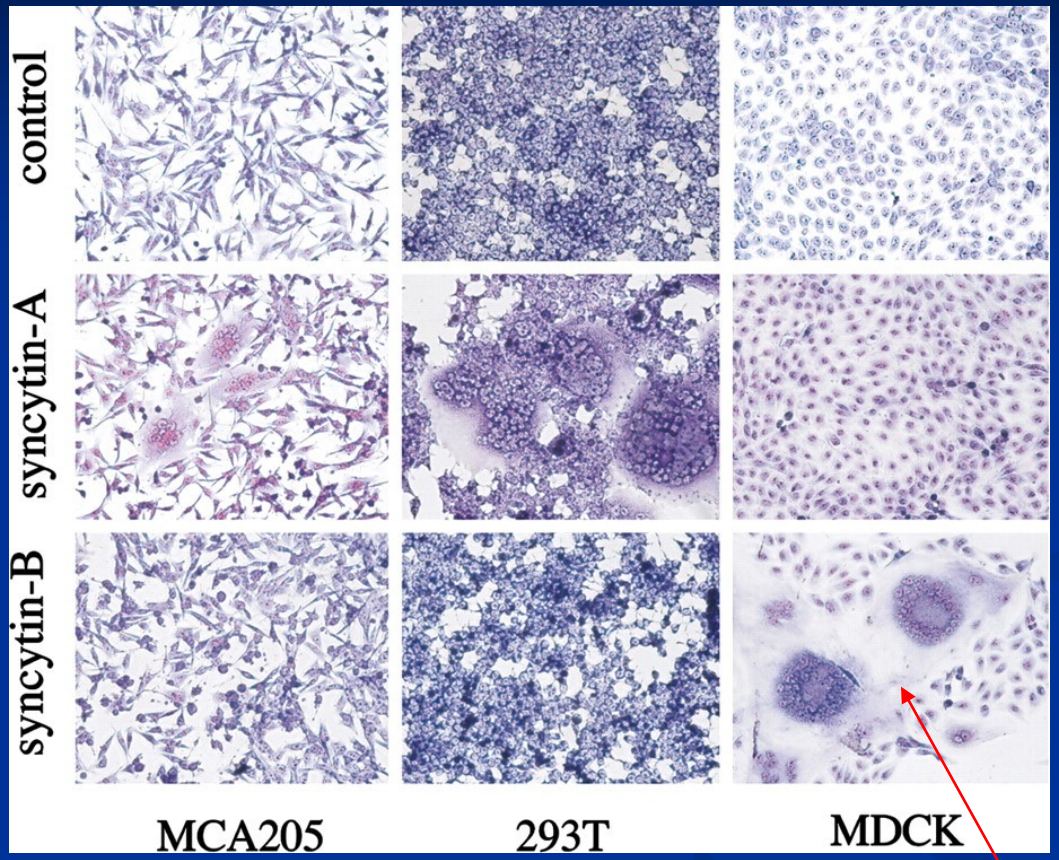


Embryogenesis



Syncytin, which is expressed from „endogenous retrovirus" of humans, is involved in cell merging of the placena by natural processes.





Humans have more than 400% more of „retroviral" genes than „human genes"

Dupressoir A et al. PNAS 2005;102:725-730

PNAS

Placenta

Plazental animals are able to carry out long during pregnancies, which is due to an „accident“:
The invasion of genetical parasites.

Success: Symbiosis

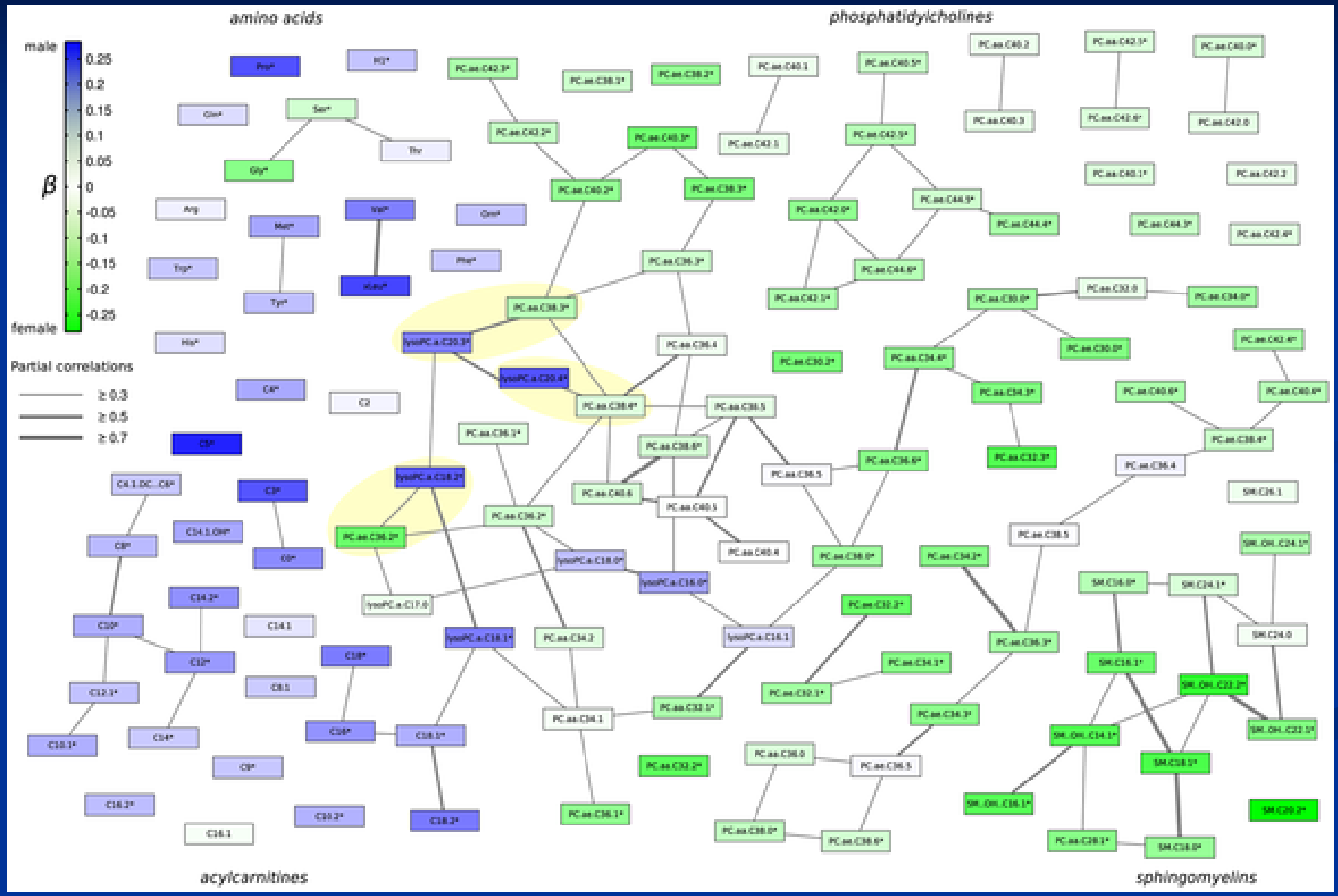
- **13 % of the genes of the placenta belong to the transposable element MER 20.**
- **They react on stimulation by progesterone.**
- **MER20 has allowed to grow the placenta.**
- **MER 20 is involved and necessary in gene expression and regulation.**

These transposons have the epigenetic signatures of enhancers, insulators and repressors, directly bind transcription factors essential for pregnancy and coordinately regulate gene expression in response to progesterone and cAMP. We conclude that the transposable element, MER20, contributed to the origin of a novel gene regulatory network dedicated to pregnancy in placental mammals, particularly by recruiting the cAMP signaling pathway into endometrial stromal cells.

Transposon-mediated rewiring of gene regulatory networks contributed to the evolution of pregnancy in mammals

Vincent J Lynch,,1 Robert D Leclerc,,1 Gemma May1 & & Günter P Wagner1 **Yale Uniuversity/Ecology and Evolutionary Biology (EEB)**
Nature Genetics (2011) doi:10.1038/ng.917 Received 04 November 2010 Accepted 01 August 2011 Published online 25 September 2011

Genexpression differs in both sexes men, women, both:



Affection triggers genes

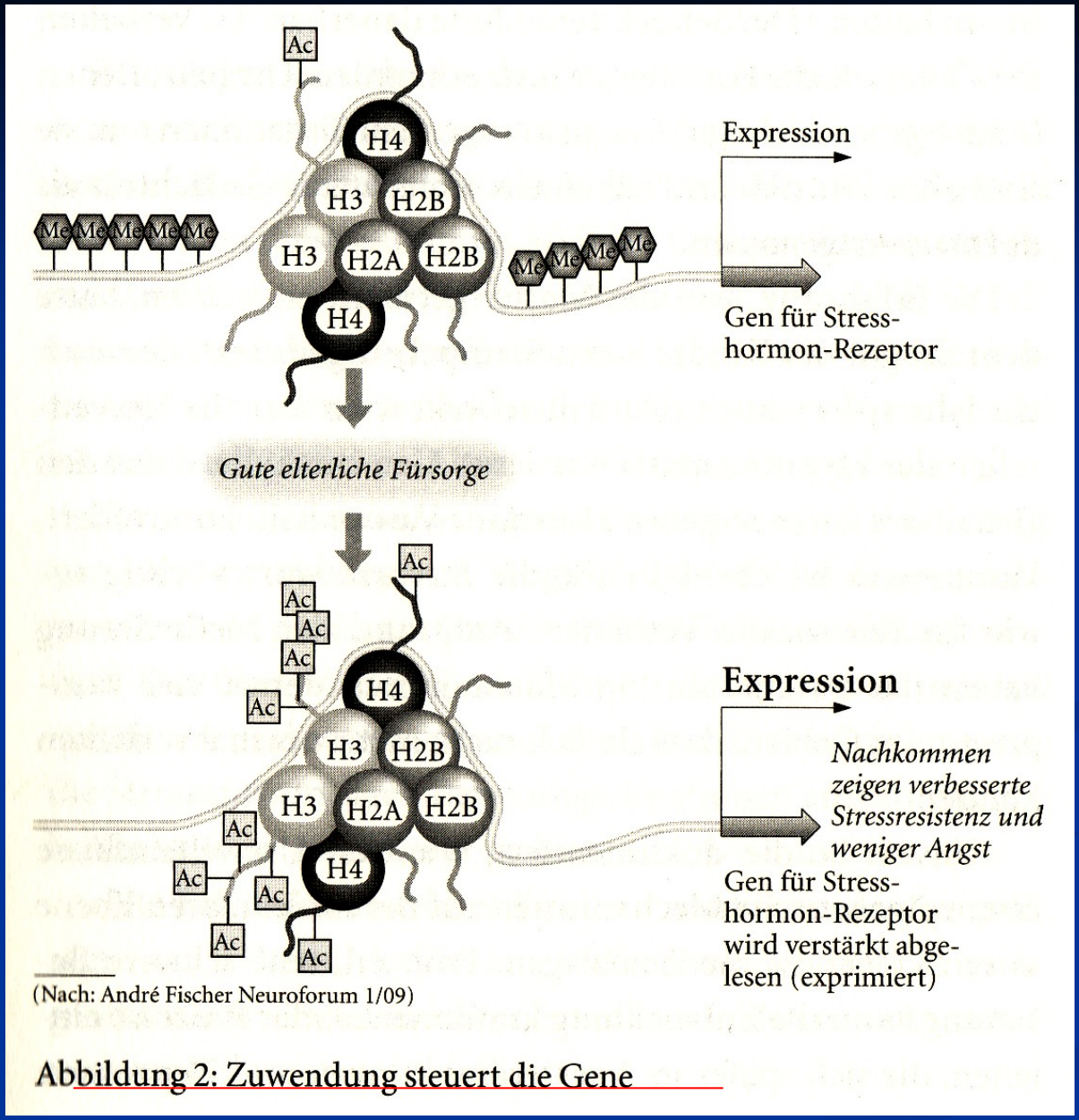
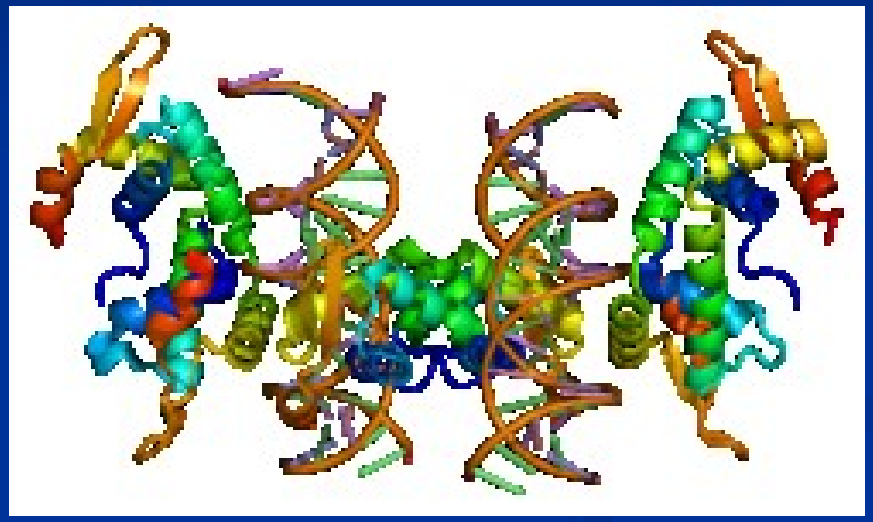


Abbildung 2: Zuwendung steuert die Gene

Literature: Jörg Blech: Gene sind kein Schicksal S. Fischer-Verlag

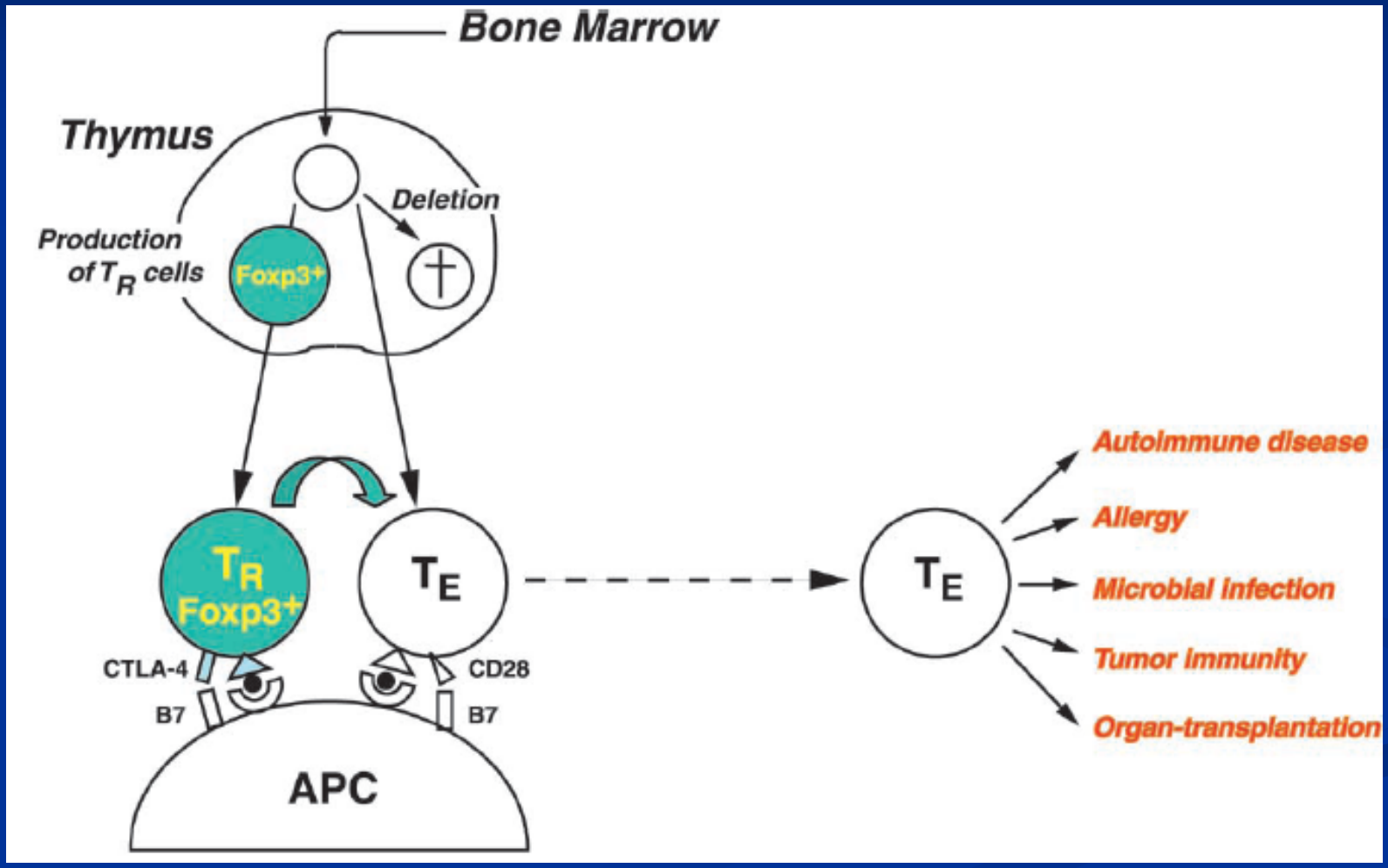
Transcription Factors:

The Forkhead-Box-Protein P2 (FOXP2) is a transcription factor and belongs to the Forkhead-Box-Protein family.



The mass media call the *FOXP2*-Gene **„language -gene"**. After knock-down of the gene in mice (Knockout-Mouse) or by mutation in human cells, it reacts in a pleiotropic way. This results in the change of many phenotypic traits.

Transkription Factors:
Foxp3 in regulatory T-cells



Sakaguchi S, 2005

Chemical Substances might decrease Gene Expression!

2,6-dichloro-4-nitrophenol,C015802,618-80-4,ACO2,50,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in decreased expression of ACO2 mRNA",decreases expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,CASP3,836,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in increased activity of CASP3 protein",increases^activity,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,CASP3,836,Homo sapiens,9606,"benzyloxycarbonyl-valyl-alanyl-aspartyl-fluoromethane analog inhibits the reaction [2,6-dichloro-4-nitrophenol results in increased activity of CASP3 protein]",decreases^reaction|increases^activity,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,DLSTP1,1744,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in decreased expression of DLSTP1 mRNA",decreases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,FH,2271,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in decreased expression of FH mRNA",decreases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,GAPDH,2597,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in increased expression of GAPDH mRNA",increases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,H2AFX,3014,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in decreased expression of H2AFX mRNA",decreases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,IDH3A,3419,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in decreased expression of IDH3A mRNA",decreases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,MDH1,4190,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in decreased expression of MDH1 mRNA",decreases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,PDHA1,5160,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in decreased expression of PDHA1 mRNA",decreases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,RPL13A,23521,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in increased expression of RPL13A mRNA",increases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,RPS3,6188,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in increased expression of RPS3 mRNA",increases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,SDHA,6389,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in decreased expression of SDHA mRNA",decreases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,SDHB,6390,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in decreased expression of SDHB mRNA",decreases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,SDHD,6392,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in decreased expression of SDHD mRNA",decreases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,SULT1A1,6817,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol inhibits the reaction [SULT1A1 protein results in increased sulfation of 4-nitrophenol]",decreases^reaction|increases^sulfation,15531517|11425650

2,6-dichloro-4-nitrophenol,C015802,618-80-4,SULT1A3,6818,Homo sapiens,9606,"[2,6-dichloro-4-nitrophenol co-treated with SULT1A3 protein] results in decreased sulfation of Ethinyl Estradiol",affects^cotreatment|decreases^sulfation,15483196

2,6-dichloro-4-nitrophenol,C015802,618-80-4,SULT1A3,6818,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol inhibits the reaction [SULT1A3 protein results in increased sulfation of Dopamine]",decreases^reaction|increases^sulfation,11425650|15531517

2,6-dichloro-4-nitrophenol,C015802,618-80-4,SULT1E1,6783,Homo sapiens,9606,"[2,6-dichloro-4-nitrophenol co-treated with SULT1E1 protein] results in decreased sulfation of Ethinyl Estradiol",affects^cotreatment|decreases^sulfation,15483196

2,6-dichloro-4-nitrophenol,C015802,618-80-4,TUBA1B,10376,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in increased expression of TUBA1B mRNA",increases^expression,11227219

2,6-dichloro-4-nitrophenol,C015802,618-80-4,UBC,7316,Homo sapiens,9606,"2,6-dichloro-4-nitrophenol results in increased expression of UBC mRNA",increases^expression,11227219

2,6-dihydroxyanthraquinone,C034889,84-60-6,UGT1A1,54658,Homo sapiens,9606,"UGT1A1 protein results in increased glucuronidation of 2,6-dihydroxyanthraquinone",increases^glucuronidation,14557274|12756209

2,6-dihydroxyanthraquinone,C034889,84-60-6,UGT1A10,54575,Homo sapiens,9606,"UGT1A10 protein results in increased glucuronidation of 2,6-dihydroxyanthraquinone",increases^glucuronidation,14557274

2,6-dihydroxyanthraquinone,C034889,84-60-6,UGT1A7,54577,Homo sapiens,9606,"UGT1A7 protein results in increased glucuronidation of 2,6-dihydroxyanthraquinone",increases^glucuronidation,14557274

2,6-dihydroxyanthraquinone,C034889,84-60-6,UGT1A8,54576,Homo sapiens,9606,"UGT1A8 protein results in increased glucuronidation of 2,6-dihydroxyanthraquinone",increases^glucuronidation,14557274

2,6-dihydroxyanthraquinone,C034889,84-60-6,UGT1A9,54600,Homo sapiens,9606,"UGT1A9 protein results in increased glucuronidation of 2,6-dihydroxyanthraquinone",increases^glucuronidation,14557274

2,6-diisocyanatotoluene,C026942,91-08-7,ALB,213,Homo sapiens,9606,"2,6-diisocyanatotoluene binds to ALB protein",affects^binding,9124697

2,6-diisocyanatotoluene,C026942,91-08-7,HBB,3043,Cavia porcellus,10141,"2,6-diisocyanatotoluene binds to HBB protein",affects^binding,8728499

2,6-diisocyanatotoluene,C026942,91-08-7,TAC1,6863,Rattus norvegicus,10116,"[Toluene 2,4-Diisocyanate co-treated with 2,6-diisocyanatotoluene] results in increased expression of TAC1 mRNA",affects^cotreatment|increases^expression,10673198

2,6-diisocyanatotoluene,C026942,91-08-7,TAC1,6863,Rattus norvegicus,10116,"[Toluene 2,4-Diisocyanate co-treated with 2,6-diisocyanatotoluene] results in increased expression of TAC1 protein",affects^cotreatment|increases^expression,10673198

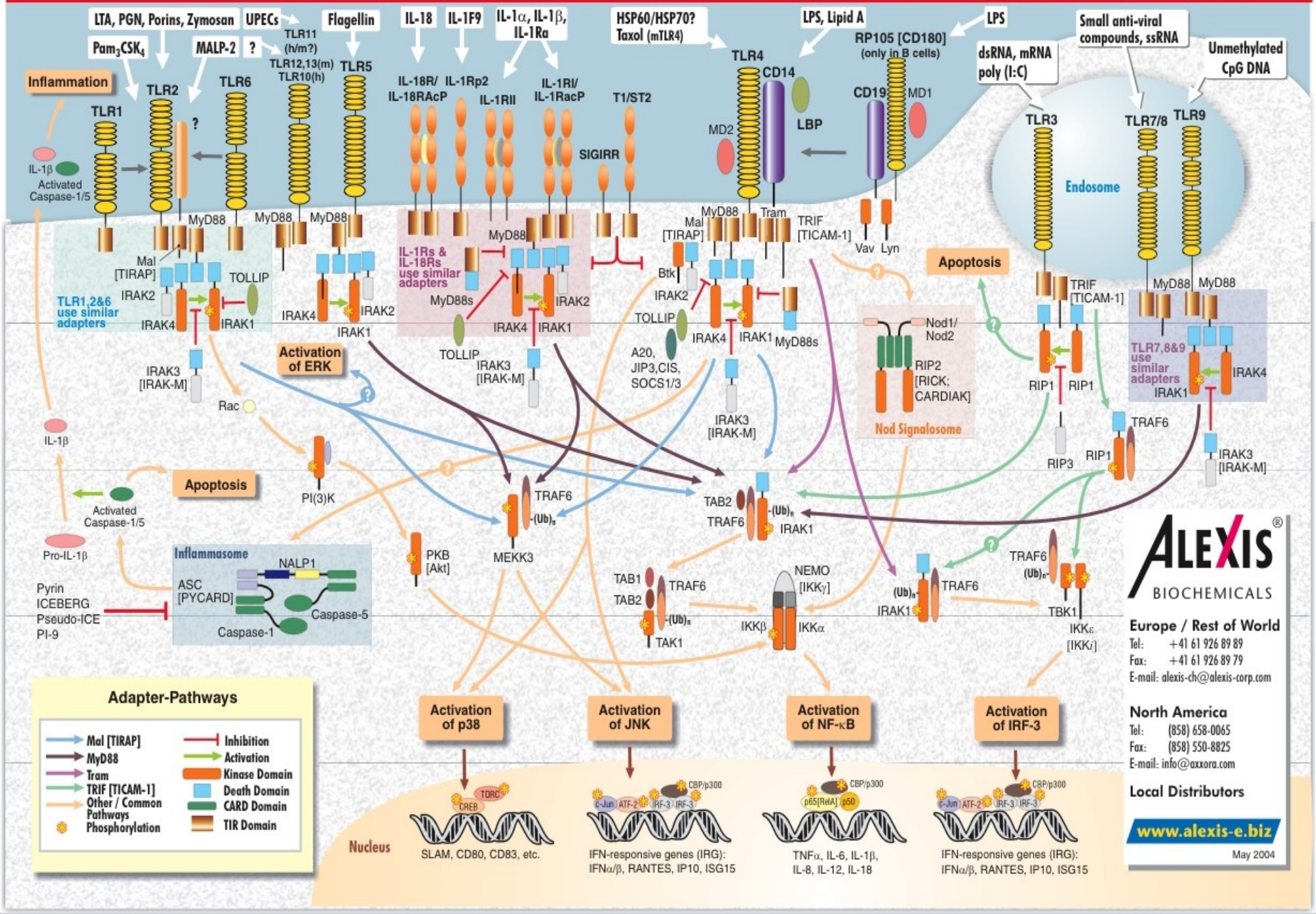
2,6-dimethylnaphthalene,C028519,581-42-0,CYP1A2,1544,Homo sapiens,9606,"2,6-dimethylnaphthalene results in decreased activity of CYP1A2 protein",decreases^activity,15916432

2,6-dimethylnaphthalene,C028519,581-42-0,CYP2A6,1548,Homo sapiens,9606,"CYP2A6 protein results in increased oxidation of 2,6-dimethylnaphthalene",increases^oxidation,17156750

2,6-dimethylnaphthalene,C028519,581-42-0,CYP2E1,1571,Homo sapiens,9606,"CYP2E1 protein results in increased oxidation of 2,6-dimethylnaphthalene",increases^oxidation,17156750

2,6-dinitrotoluene,C023514,606-20-2,A2M,2,Rattus norvegicus,10116,"2,6-dinitrotoluene affects the expression of A2M mRNA",affects^expression,21346803

Inflammation Signaling Pathways of the Interleukin-1 & Toll-like Receptor Superfamily



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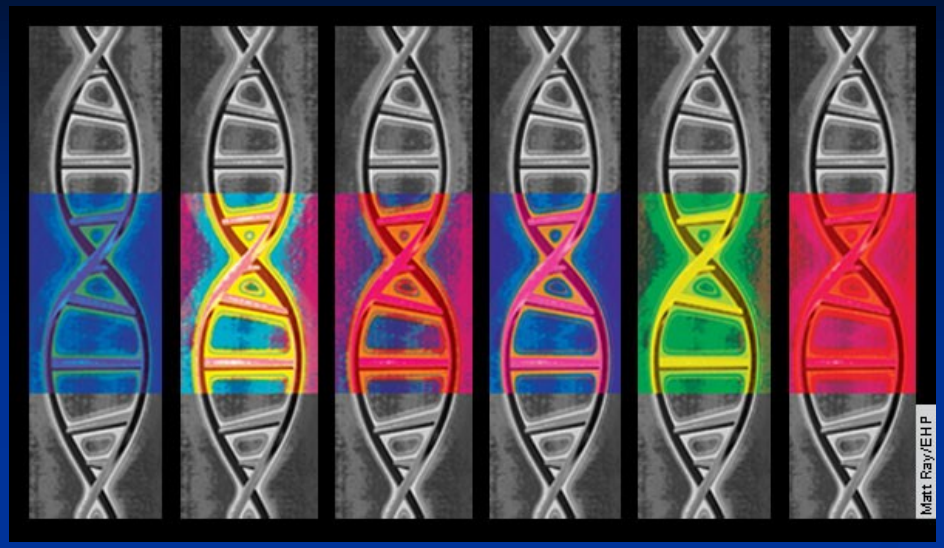
Epigenetics:



Environmental stimuli change gene expression.

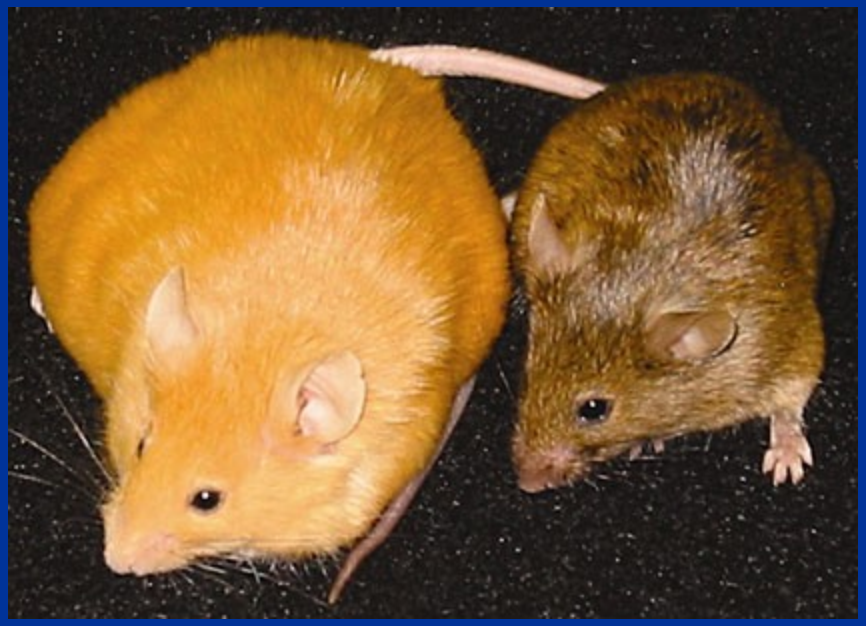
This effect is heritable.

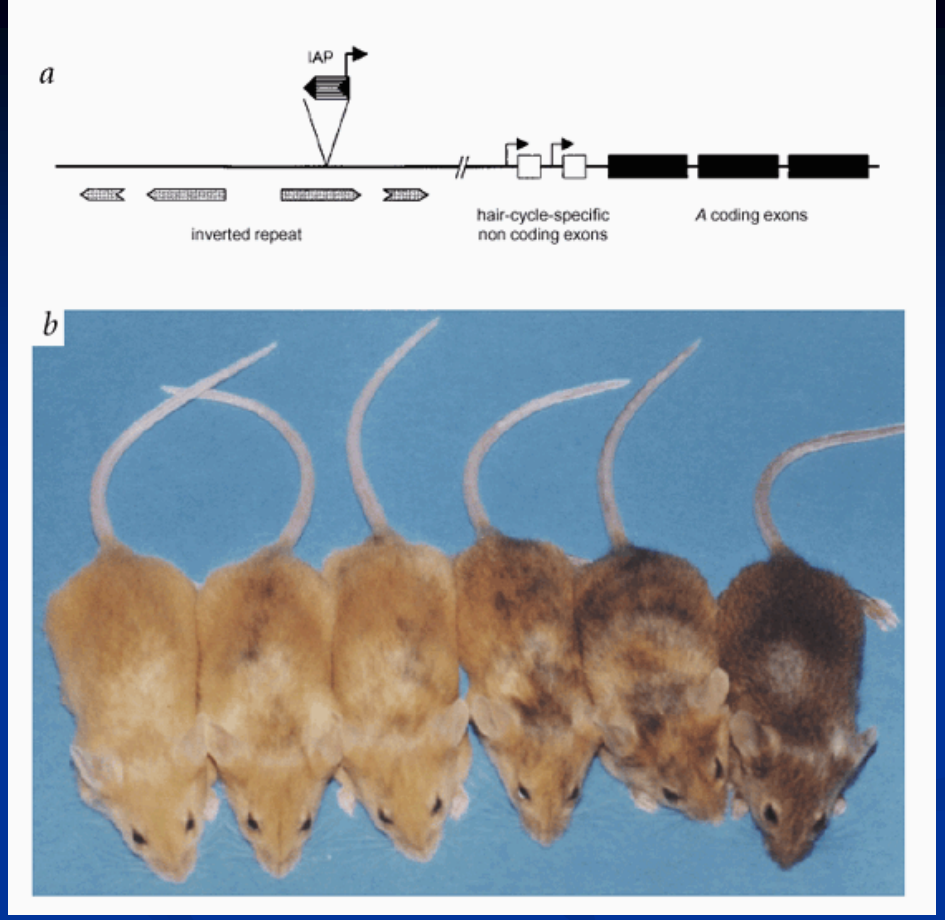
At the „*Eidgenössische Hochschule Basel“ e*pigeneticist Renato Paro heated the eggs of Drosophila flies up to 37° Celsius.

White eyes changed to red.

This trait was epigenetic because the next generation did also show it.

•**Folic acid and ist effect during pregnancy but NOT after it.**

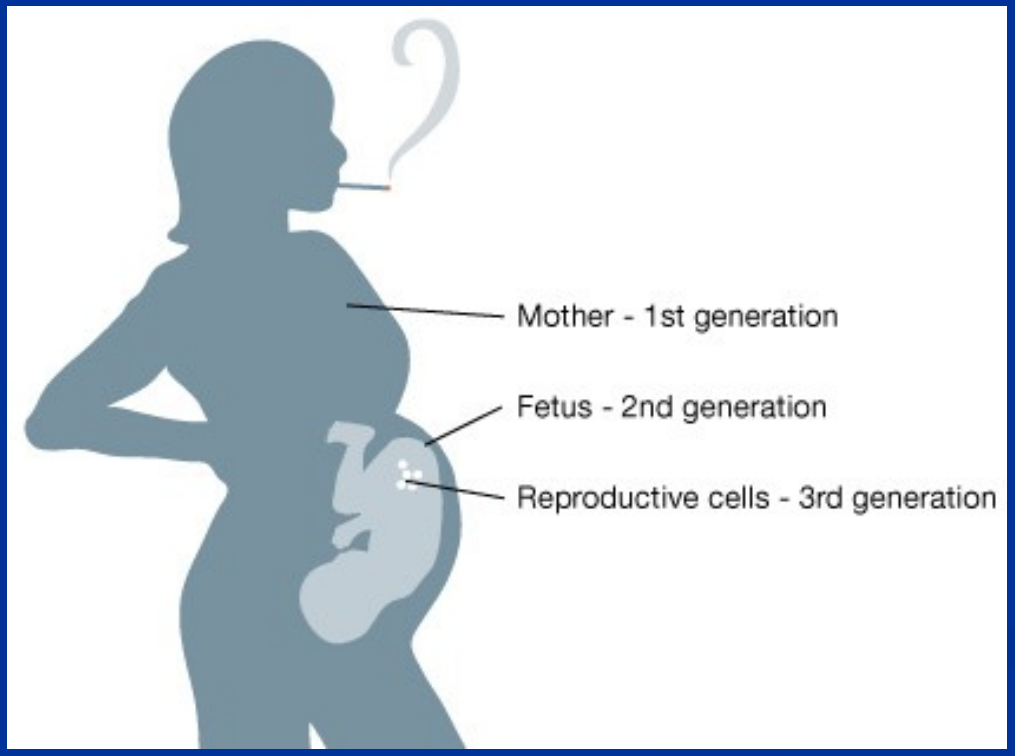


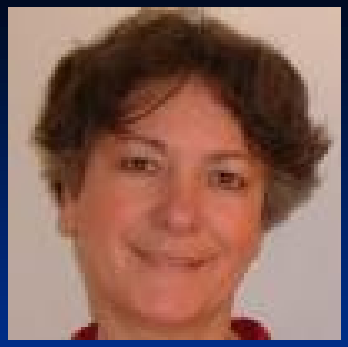


Folic acid starts off a chain reaction that leads to methlyation (silencing) of DNA, leading to different fur colors due to differential 'silencing' of a retroviral promoter and the 'agouti' gene.

Waterland and Jirtle : Transposable elements: targets for early nutritional effects on epigenetic gene regulation. *Mol Cell Biol* 23:5293-5300, 2003

Pregnancy and the future of children and grand-children:





Eva Jablonka and Marion Lamb

2009-02-05

Eva Jablonka is Professor at the Cohn Institute for the History and Philosophy of Science and Ideas, Tel-Aviv University.

Marion Lamb was Senior Lecturer at Birkbeck College, University of London.

A good example from the work of Michael Skinner and collegues:
They stated, that pregnant rats who got an injection that suppresses androgens, will lead to diseases in their descendants, which are heritable over several generations.
„... 101 cases of epigenetic inheritance..."

Ethnics / Indivuals and Gene Expression:

- Northern Europeans and drinking of milk (lactose intolerance)
- Inuit / Asians (Alcohol degradation)
- Smokers and lung cancer

  (Vitamin A promotes the absorption in lung and intestines and thus is not recommended with uptake of nocious substances.)

Der Standard: 20.10.2011: Brunet et. al /Stanford, Calif.

Nachkommen von Fadenwürmern, die epigenetisch auf Langlebigkeit getrimmt wurden, leben zum Teil noch in der dritten Generation länger als ihre normalen Kollegen.

Foto: P. Phillips

Caenorhabditis and epigenetic longevity!

Genetical predisposition for cardiovascular disease disease and risik reduction with uptake of raw vegetables.

Cardiovascular disease (CVD) is linked with diet and other lifestyle factors, but there is also an association with SNP (single nucleotide polymorphism) variants in genes on chromosome 9, in the 9p21 region.

PLoS Medicine, 9 (10) DOI: 10.1371/journal.pmed.1001106

Most epigenetic changes in the germ cells will be neutralized by reprogramming, but some changes are transmitted to the next generation.

A vaccination against HIV means an attack against the own bodily structures and thus is contradictive!

After a vaccination agaist HIV one tests HIV-positive!

Who does want this?

"Primum nil nocere"
„First – do no harm!"
(Hippokrates)

Gene activation can be triggered by certain (toxic) environmental agents like:

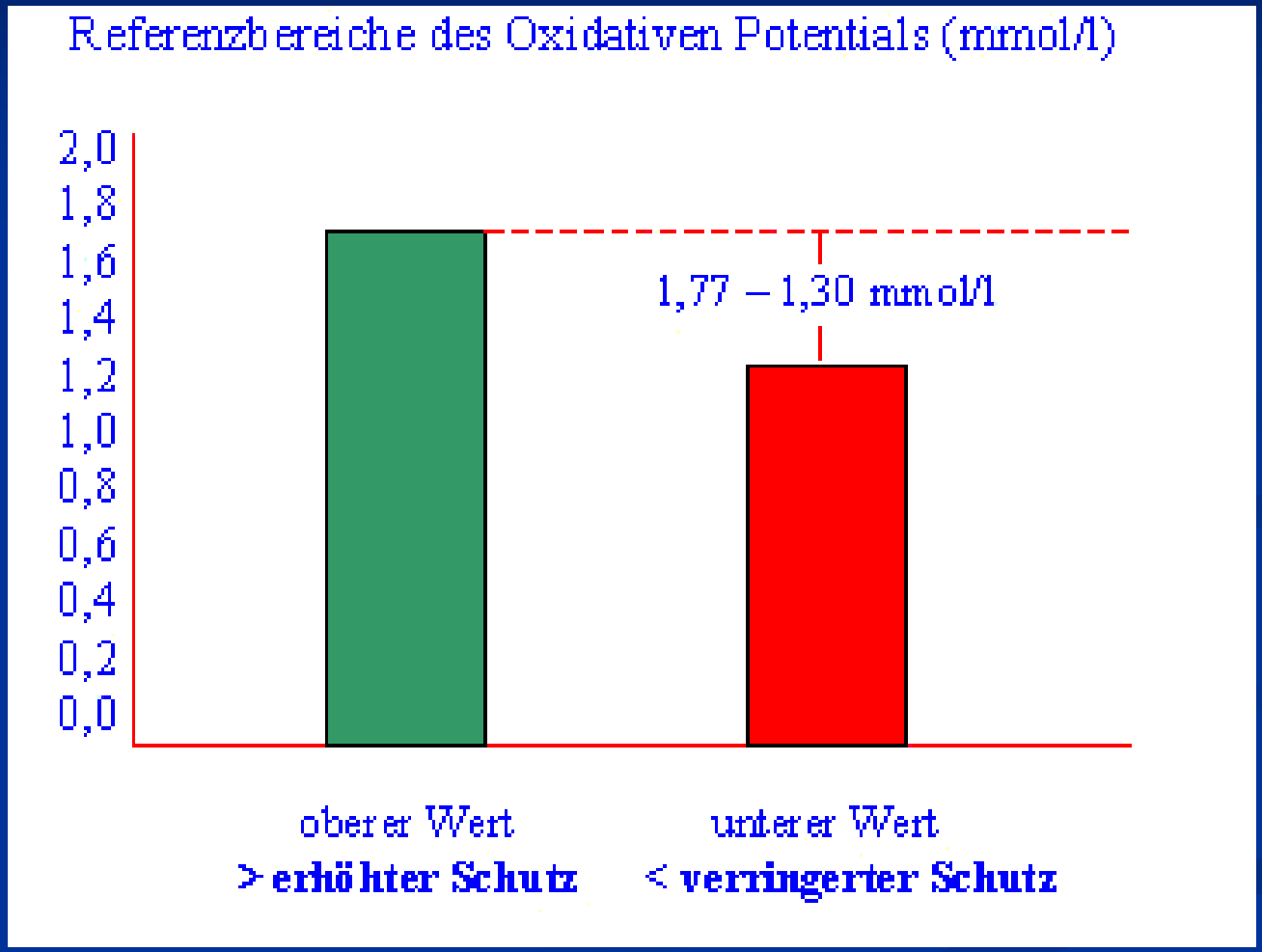
- **Severe starvation or undernutrition**
- **Overwhelming infections,**
- **Legal and illegal drugs,**

to name only some of them.

The medical term is

„OXIDATIVE STRESS“

Stress can alter the oxidative potential of the cell by producing „free radicals“ .



Lowering can also occur through „empty nutrition“ (only calories, no information).

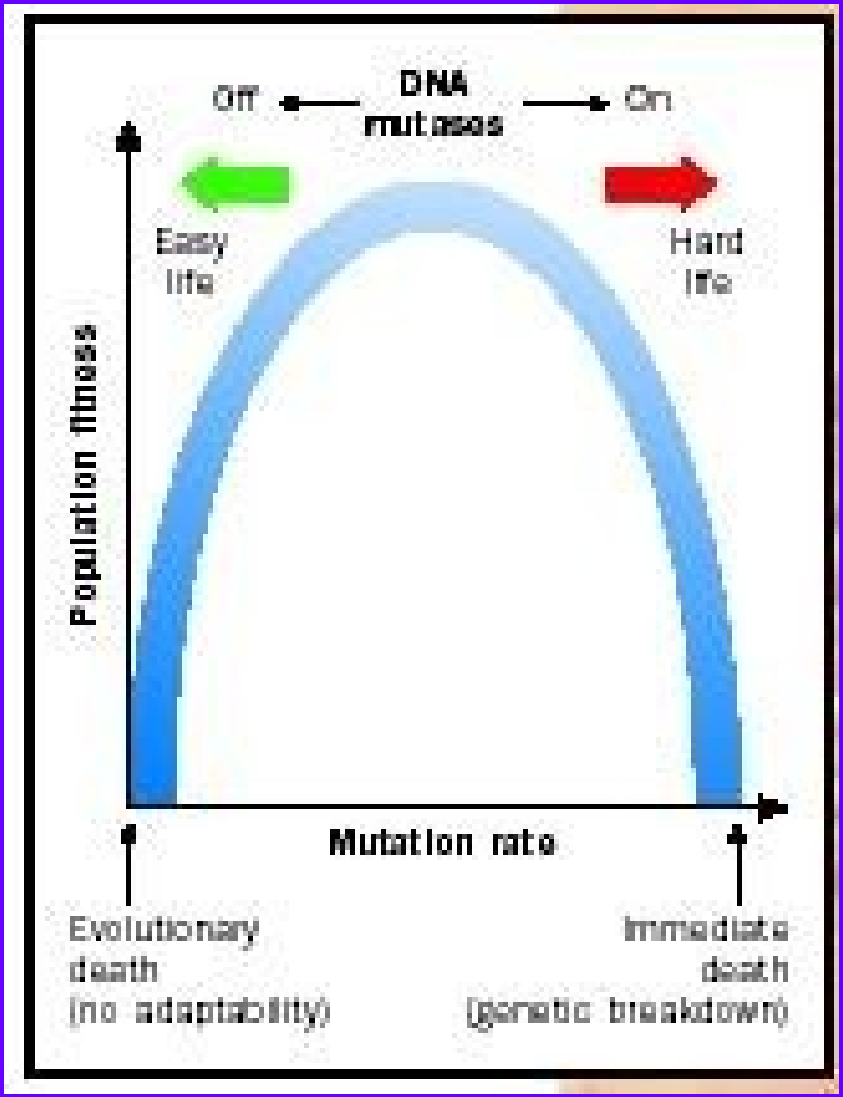
Remember:

The diagnosis (prognosis) of a severe disease alone can induce illness and death, without any symptoms of disease.

NOCEBO-Effekt!

The opposite is the well studied PLACEBO effect.

EVOLUTION and MUTATION



Extinction of the population

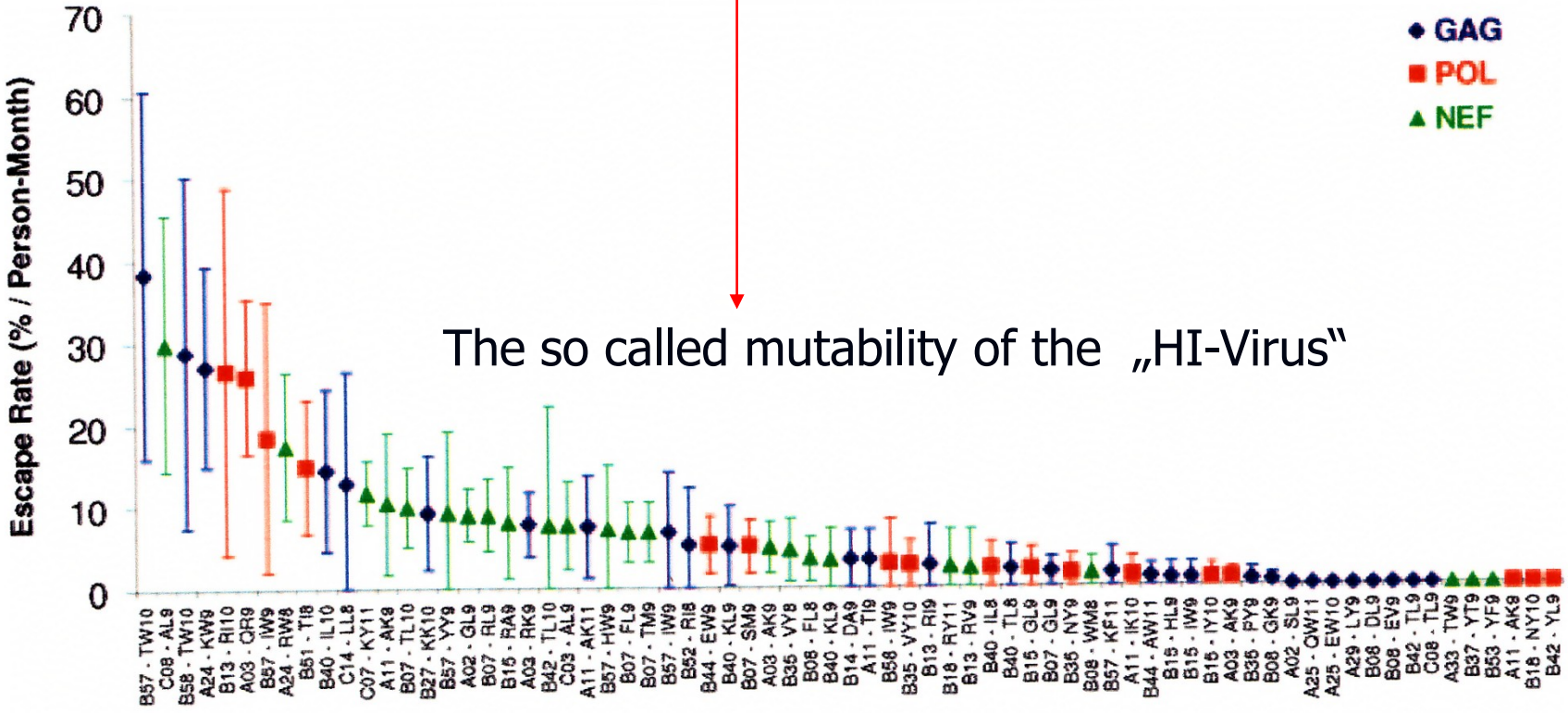
Extinction of the individual

Result:

The more Stress
The more Mutations.

Marked Epitope- and Allele-Specific Differences in Rates of Mutation in Human Immunodeficiency Type 1 (HIV-1) Gag, Pol, and Nef Cytotoxic T-Lymphocyte Epitopes in Acute/Early HIV-1 Infection

Zabrina L. Brumme et al. *Partners AIDS Research Center, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts*



JOURNAL OF VIROLOGY, Sept. 2008, p. 9216–9227 Vol. 82, No. 18 0022-538X/08/$08.000
doi:10.1128/JVI.01041-08

Genvariations in the HLA-System of Human Chromosom 6: Nef, PR, RT, VPR adaption

Supplementary Table 1a: Full list of HLA allele-associated HIV polymorphisms in Nef

Gene	Codon	HLA	Escape	Reversion
Nef	5	A11	C	
Nef	7	B57		K
Nef	7	B83	-	
Nef	8	A02		G
Nef	8	A24	M	
Nef	8	C04		L
Nef	11	A68		A
Nef	11	B57	A	V
Nef	11	C03		K
Nef	11	C06		V
Nef	12	B40		G
Nef	14	B08	Y	
Nef	15	A31	D, T	A
Nef	15	B51		A
Nef	15	B57		A
Nef	21	A11		R
Nef	21	A33	T	
Nef	21	B46		R
Nef	21	B58	T	
Nef	23	A34	Q	
Nef	23	B13	-	
Nef	24	B54	-	
Nef	24	C02		E
Nef	24	C06		E
Nef	28	A11		D
Nef	28	B14		D
Nef	28	C05		D
Nef	28	C08		D
Nef	30	A31		V
Nef	33	A11		A
Nef	33	A68	A	V
Nef	38	B37	G	E
Nef	39	A24	K	
Nef	39	B37		R
Nef	39	B44		T
Nef	39	C06		K
Nef	40	B37	R	
Nef	43	B55	V	I
Nef	43	C03		I
Nef	45	B38		S
Nef	49	B57	P	
Nef	50	B14	T	
Nef	50	B35		T
Nef	50	B53	G	A
Nef	50	B57	E	
Nef	50	B58	D, E	A
Nef	51	B58	N	T
Nef	53	B14	P	A
Nef	53	B81	S	
Nef	53	C08	P	A
Nef	54	B14	A	D
Nef	54	C08	A	D
Nef	56	B54	C	
Nef	58	A33	V	L
Nef	61	C05		Y
Nef	62	A74	S	
Nef	65	B35		D
Nef	65	B40		E
Nef	65	B45	D	E
Nef	65	C06	D	E
Nef	71	A03	K	R
Nef	71	B07	K	R
Nef	71	B14	R	K
Nef	71	B35	R	K
Nef	71	C04	R	K
Nef	71	C07	K	R
Nef	71	C08	R	K
Nef	71	C16	R	
Nef	73	A69	R	Q
Nef	74	B45		V
Nef	76	B81		L
Nef	81	A29		F
Nef	81	A30		F
Nef	81	A32		F
Nef	81	A33		F
Nef	81	A66		F
Nef	81	B07		F
Nef	81	B13		F
Nef	81	B14	S	
Nef	81	B18		F
Nef	81	B35	F	Y
Nef	81	B40	Y	F
Nef	81	B41		F
Nef	81	B42		F
Nef	81	B44		F
Nef	81	B45		F
Nef	81	B46		F
Nef	81	B49		F
Nef	81	B52		F
Nef	81	B55		F
Nef	81	C04	F	Y
Nef	81	C16		F
Nef	82	A03	R	
Nef	82	B14		K
Nef	82	B15		R
Nef	83	A03	G	A
Nef	83	A11	G	A
Nef	83	B15	G	A
Nef	83	B40	G	A
Nef	83	B44		G
Nef	83	B55	G	A
Nef	83	C03	G	A
Nef	83	C07	A	G
Nef	85	A02		L
Nef	85	A11	L	V
Nef	85	A68	L	V
Nef	85	B07	V	L
Nef	85	B14	F, M, R	L
Nef	85	B15	L	V
Nef	85	B55	L	V
Nef	85	C03	L	V
Nef	85	C07	V	L
Nef	85	C08	F, M, R	L, V
Nef	87	B08		L
Nef	89	B14	F	H
Nef	89	C08	F	H
Nef	91	B14	I	L
Nef	91	C08	I	L
Nef	92	A11	R	K
Nef	92	B55		K
Nef	94	A01	E, N, Q	K
Nef	94	B08	E, M, N, Q	K
Nef	94	B15	K	
Nef	94	C03		N
Nef	94	C07	E, Q	K
Nef	98	B40	D	E
Nef	100	A03		I
Nef	100	B40	M	L
Nef	100	C03		L
Nef	101	B14	I	V
Nef	101	B40	I	V
Nef	101	C01	V	
Nef	101	C08	I	
Nef	102	A29	H	Y
Nef	102	B14	H	
Nef	102	B44	H	Y
Nef	102	C08	H	
Nef	102	C16	H	Y
Nef	105	A01	R	K
Nef	105	A02	K	
Nef	105	A03	Q	
Nef	105	B07	Q	
Nef	105	B08	R	K
Nef	105	B15	K	
Nef	105	B44	Q	
Nef	105	B49	K	
Nef	105	C07	Q, R	K
Nef	105	C16	Q	
Nef	107	A30	Q	
Nef	107	B13	R	Q
Nef	107	C06	R	
Nef	114	A30	I	
Nef	114	B08	V	
Nef	114	B13	V	I
Nef	114	B57		I
Nef	114	C06	V	I
Nef	114	C07	I	V
Nef	115	B18	H	Y
Nef	115	C07	H	Y
Nef	116	B57	N	H
Nef	116	B58		H
Nef	116	C06	N	H
Nef	120	B51	F	Y
Nef	120	C14	F	Y
Nef	125	A30	H	Q
Nef	125	B51		Q
Nef	125	C07		H
Nef	125	C14		Q
Nef	126	A26	S	
Nef	126	B51	C	N
Nef	126	C14	C	N
Nef	133	A24	T	I
Nef	133	A26		T
Nef	133	B35	T	I
Nef	133	B38	I	T
Nef	133	B57	I	T
Nef	133	C02	P	
Nef	135	A02	Y	F
Nef	135	A03	Y	F
Nef	135	A11		F
Nef	135	A24	F	Y
Nef	135	C01	F	Y
Nef	139	A24	L	
Nef	143	A23	Y	F
Nef	143	B58		F
Nef	150	B51		Q
Nef	151	B39		E
Nef	151	B41	S	
Nef	153	A02	I	V
Nef	153	B37		I
Nef	156	A30	D	
Nef	158	B40		E
Nef	161	B15		D
Nef	163	C16		C
Nef	168	A31		I
Nef	168	C06	L	
Nef	169	B18		C
Nef	173	A03	T	
Nef	173	B18	I	M
Nef	174	B40	D	E
Nef	175	B44		S
Nef	176	B44	T	
Nef	177	C12		E
Nef	178	B40	R	K
Nef	182	A68		I
Nef	182	A69	Q	
Nef	182	B18		V
Nef	182	B27		E
Nef	182	B37		V
Nef	182	C03	K	
Nef	182	C06		V
Nef	184	A02		K
Nef	184	A36	E	K
Nef	184	B14	K	R
Nef	184	B27		R
Nef	184	B57	R	K
Nef	187	B39		S
Nef	188	A31		R
Nef	188	B27	H	R
Nef	188	C16	R	
Nef	191	B07		Y
Nef	191	B14		F
Nef	191	C08		F
Nef	192	B39	R	H
Nef	194	A01		R
Nef	194	A31	M	V
Nef	194	B08	M	V
Nef	194	B35	V	M
Nef	194	B48		M
Nef	194	C04	V	
Nef	194	C06	V	
Nef	196	A02	R	
Nef	196	A31	K	R
Nef	198	B15	L	
Nef	198	B35		Q
Nef	198	B57	M	L
Nef	198	C04		Q
Nef	198	C14	K, Q	L
Nef	201	A33		E
Nef	201	B58		E
Nef	202	B50		Y
Nef	206	C02		C
Nef	206	C03	*	C
Nef	206	C07	C	

Supplementary Table 1b: Full list of HLA allele-associated HIV polymorphisms in Protease, Reverse Transcriptase and VPR

Gene	Codon	HLA	Escape	Reversion
PR	10	B15	I	L
PR	12	B51		T
PR	12	B52	A	T
PR	14	A68	R	K
PR	14	B51	R	K
PR	14	C14	R	K
PR	14	C15	R	K
PR	15	B51	V	I
PR	35	B44	D	E
PR	35	C05	D	E
PR	35	C16		E
PR	37	C16	S	
PR	63	B13	S	P, C
PR	64	B13	M	
PR	93	B15	L	I
RT	11	B40	R	K
RT	11	C03	R	K
RT	35	B57		I
RT	102	B48	R	K
RT	102	C08	R	
RT	123	B35	E	D
RT	123	B44	D	E
RT	123	C04		D
RT	135	A02		V
RT	135	A25		T
RT	135	A29		T
RT	135	B13		T
RT	135	B51	T	I
RT	135	B58		T
RT	135	C08		T
RT	135	C14	T	I
RT	135	C15	T	I
RT	162	B07	C	S
RT	165	B07	I	T
RT	173	C07		T
RT	174	B15	R	Q
RT	177	B35	E	D
RT	200	B08	T	
RT	200	B40	I	
RT	203	A29	D	E
RT	207	B15	E, R	Q
RT	211	B44		R
RT	245	B57	E	V
RT	245	B58	E	V
RT	245	C06		V
RT	250	B53		D
RT	275	C17		K
RT	277	A02	K	R
RT	277	A03	R	K
RT	309	A31		I
RT	321	A66		P
RT	321	B81		P
RT	329	C05		I
RT	335	C02	D	
RT	345	A11		P
RT	369	A30		T
RT	369	B13		T
RT	376	C12	S	
RT	379	B38	G	
RT	379	B58	G	S
RT	386	B53	I	T
RT	399	A32	D	E
VPR	28	B40	H	
VPR	32	B27	K	R
VPR	32	C01	K	R
VPR	32	C02	K	R
VPR	37	B51	A	V
VPR	37	C14	T	
VPR	48	A25		E
VPR	55	A33	T	A
VPR	63	A02	T	
VPR	63	A26		I
VPR	63	B38	V	
VPR	84	A29		T
VPR	84	B50		I
VPR	84	C16		T
VPR	85	A31		Q
VPR	86	C02		Q
VPR	86	C06	P	
VPR	87	C01		R
VPR	88	C01	G	
VPR	93	A25	S	

Source: The DNA-sequence and analysis of human chromosome 6, October 23rd, 2003
The Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge CB10 1SA, UK

Supplementary Table 1a: Full list of HLA allele-associated HIV polymorphisms in Nef

Gene	Codon	HLA	Escape	Reversion
Nef	5	A11	C	
Nef	7	B57		K
Nef	7	B83	-	
Nef	8	A02		G
Nef	8	A24	M	
Nef	8	C04		L
Nef	11	A68		A
Nef	11	B57	A	V
Nef	11	C03		K
Nef	11	C06		V
Nef	12	B40		G
Nef	14	B08	Y	
Nef	15	A31	D, T	A
Nef	15	B51		A
Nef	15	B57		A
Nef	21	A11		R
Nef	21	A33	T	
Nef	21	B46		R
Nef	21	B58	T	
Nef	23	A34	Q	
Nef	23	B13	-	
Nef	24	B54	-	
Nef	24	C02		E
Nef	24	C06		E
Nef	28	A11		D
Nef	28	B14		D
Nef	28	C05		D
Nef	28	C08		D
Nef	30	A31		V
Nef	33	A11		A
Nef	33	A68	A	V
Nef	38	B37	G	E
Nef	39	A24	K	
Nef	39	B37		R
Nef	39	B44		T
Nef	39	C06		K
Nef	40	B37	R	
Nef	43	B55	V	I
Nef	43	C03		I
Nef	45	B38		S
Nef	49	B57	P	
Nef	50	B14	T	
Nef	50	B35		T
Nef	50	B53	G	A
Nef	50	B57	E	
Nef	50	B58	D, E	A
Nef	51	B58	N	T
Nef	53	B14	P	A
Nef	53	B81	S	
Nef	53	C08	P	A
Nef	54	B14	A	D
Nef	54	C08	A	D
Nef	56	B54	C	
Nef	58	A33	V	L
Nef	61	C05		Y
Nef	62	A74	S	
Nef	65	B35		D
Nef	65	B40		E
Nef	65	B45	D	E
Nef	65	C06	D	E
Nef	71	A03	K	R
Nef	71	B07	K	R
Nef	71	B14	R	K
Nef	71	B35	R	K
Nef	71	C04	R	K
Nef	71	C07	K	R
Nef	71	C08	R	K
Nef	71	C16	R	
Nef	73	A69	R	Q
Nef	74	B45		V
Nef	76	B81		L
Nef	81	A29		F
Nef	81	A30		F
Nef	81	A32		F
Nef	81	A33		F
Nef	81	A66		F
Nef	81	B07		F
Nef	81	B13		F
Nef	81	B14	S	
Nef	81	B18		F
Nef	81	B35	F	Y
Nef	81	B40	Y	F
Nef	81	B41		F
Nef	81	B42		F
Nef	81	B44		F
Nef	81	B45		F
Nef	81	B46		F
Nef	81	B49		F
Nef	81	B52		F
Nef	81	B55		F
Nef	81	C04	F	Y
Nef	81	C16		F
Nef	82	A03	R	
Nef	82	B14		K
Nef	82	B15		R
Nef	83	A03	G	A
Nef	83	A11	G	A
Nef	83	B15	G	A
Nef	83	B40	G	A
Nef	83	B44		G
Nef	83	B55	G	A
Nef	83	C03	G	A
Nef	83	C07	A	G
Nef	85	A02		L
Nef	85	A11	L	V
Nef	85	A68	L	V
Nef	85	B07	V	L
Nef	85	B14	F, M, R	L
Nef	85	B15	L	V
Nef	85	B55	L	V
Nef	85	C03	L	V
Nef	85	C07	V	L
Nef	85	C08	F, M, R	L, V
Nef	87	B08		L
Nef	89	B14	F	H
Nef	89	C08	F	H
Nef	91	B14	I	L
Nef	91	C08	I	L
Nef	92	A11	R	K
Nef	92	B55		K
Nef	94	A01	E, N, Q	K
Nef	94	B08	E, M, N, Q	K
Nef	94	B15	K	
Nef	94	C03		N
Nef	94	C07	E, Q	K
Nef	98	B40	D	E
Nef	100	A03		I
Nef	100	B40	M	L
Nef	100	C03		L
Nef	101	B14	I	V
Nef	101	B40	I	V
Nef	101	C01	V	
Nef	101	C08	I	
Nef	102	A29	H	Y
Nef	102	B14	H	
Nef	102	B44	H	Y
Nef	102	C08	H	
Nef	102	C16	H	Y
Nef	105	A01	R	K
Nef	105	A02	K	
Nef	105	A03	Q	
Nef	105	B07	Q	
Nef	105	B08	R	K
Nef	105	B15	K	
Nef	105	B44		Q
Nef	105	B49		K
Nef	105	C07	Q, R	K
Nef	105	C16		Q
Nef	107	A30		Q
Nef	107	B13	R	Q
Nef	107	C06	R	
Nef	114	A30		I
Nef	114	B08		V
Nef	114	B13	V	I
Nef	114	B57		I
Nef	114	C06	V	I
Nef	114	C07	I	V
Nef	115	B18	H	Y
Nef	115	C07	H	Y
Nef	116	B57	N	H
Nef	116	B58		H
Nef	116	C06	N	H
Nef	120	B51	F	Y
Nef	120	C14	F	Y
Nef	125	A30	H	Q
Nef	125	B51		Q
Nef	125	C07		H
Nef	125	C14		Q
Nef	126	A26	S	
Nef	126	B51	C	N
Nef	126	C14	C	N
Nef	133	A24	T	I
Nef	133	A26		T
Nef	133	B35	T	I
Nef	133	B38	I	T
Nef	133	B57	I	T
Nef	133	C02	P	
Nef	135	A02	Y	F
Nef	135	A03	Y	F
Nef	135	A11		F
Nef	135	A24	F	Y
Nef	135	C01	F	Y
Nef	139	A24	L	
Nef	143	A23	Y	F
Nef	143	B58		F
Nef	150	B51		Q
Nef	151	B39		E
Nef	151	B41	S	
Nef	153	A02	I	V
Nef	153	B37		I
Nef	156	A30	D	
Nef	158	B40		E
Nef	161	B15		D
Nef	163	C16		C
Nef	168	A31		I
Nef	168	C06	L	
Nef	169	B18		C
Nef	173	A03	T	
Nef	173	B18	I	M
Nef	174	B40	D	E
Nef	175	B44		S
Nef	176	B44	T	
Nef	177	C12		E
Nef	178	B40	R	K
Nef	182	A68		I
Nef	182	A69	Q	
Nef	182	B18		V
Nef	182	B27		E
Nef	182	B37		V
Nef	182	C03	K	
Nef	182	C06		V
Nef	184	A02		K
Nef	184	A36	E	K
Nef	184	B14	K	R
Nef	184	B27		R
Nef	184	B57	R	K
Nef	187	B39		S
Nef	188	A31		R
Nef	188	B27	H	R
Nef	188	C16	R	
Nef	191	B07		Y
Nef	191	B14		F
Nef	191	C08		F
Nef	192	B39	R	H
Nef	194	A01		R
Nef	194	A31	M	V
Nef	194	B08	M	V
Nef	194	B35	V	M
Nef	194	B48		M
Nef	194	C04	V	
Nef	194	C06	V	
Nef	196	A02	R	
Nef	196	A31	K	R
Nef	198	B15	L	
Nef	198	B35		Q
Nef	198	B57	M	L
Nef	198	C04		Q
Nef	198	C14	K, Q	L
Nef	201	A33		E
Nef	201	B58		E
Nef	202	B50		Y
Nef	206	C02		C
Nef	206	C03	*	C
Nef	206	C07	C	

Supplementary Table 1b: Full list of HLA allele-associated HIV polymorphisms in Protease, Reverse Transcriptase and VI

Gene	Codon	HLA	Escape	Reversion
PR	10	B15	I	L
PR	12	B51		T
PR	12	B52	A	T
PR	14	A68	R	K
PR	14	B51	R	K
PR	14	C14	R	K
PR	14	C15	R	K
PR	15	B51	V	I
PR	35	B44	D	E
PR	35	C05	D	E
PR	35	C16		E
PR	37	C16	S	
PR	63	B13	S	P, C
PR	64	B13	M	
PR	93	B15	L	I

Gene	Codon	HLA	Escape	Reversion
RT	11	B40	R	K
RT	11	C03	R	K
RT	35	B57		I
RT	102	B48	R	K
RT	102	C08	R	
RT	123	B35	E	D
RT	123	B44	D	E
RT	123	C04		D
RT	135	A02		V
RT	135	A25		T
RT	135	A29		T
RT	135	B13		T
RT	135	B51	T	I
RT	135	B58		T
RT	135	C08		T
RT	135	C14	T	I
RT	135	C15	T	I
RT	162	B07	C	S
RT	165	B07	I	T
RT	173	C07		T
RT	174	B15	R	Q
RT	177	B35	E	D
RT	200	B08	T	
RT	200	B40	I	
RT	203	A29	D	E
RT	207	B15	E, R	Q
RT	211	B44		R
RT	245	B57	E	V
RT	245	B58	E	V
RT	245	C06		V
RT	250	B53		D
RT	275	C17		K
RT	277	A02	K	R
RT	277	A03	R	K
RT	309	A31		I
RT	321	A66		P
RT	321	B81		P
RT	329	C05		I
RT	335	C02	D	
RT	345	A11		P
RT	369	A30		T
RT	369	B13		T
RT	376	C12	S	
RT	379	B38	G	
RT	379	B58	G	S
RT	386	B53	I	T
RT	399	A32	D	E

Gene	Codon	HLA	Escape	Reversion
VPR	28	B40	H	
VPR	32	B27	K	R
VPR	32	C01	K	R
VPR	32	C02	K	R
VPR	37	B51	A	V
VPR	37	C14	T	
VPR	48	A25		E
VPR	55	A33	T	A
VPR	63	A02	T	
VPR	63	A26		I
VPR	63	B38	V	
VPR	84	A29		T
VPR	84	B50		I
VPR	84	C16		T
VPR	85	A31		Q
VPR	86	C02		Q
VPR	86	C06	P	
VPR	87	C01		R
VPR	88	C01	G	
VPR	93	A25	S	

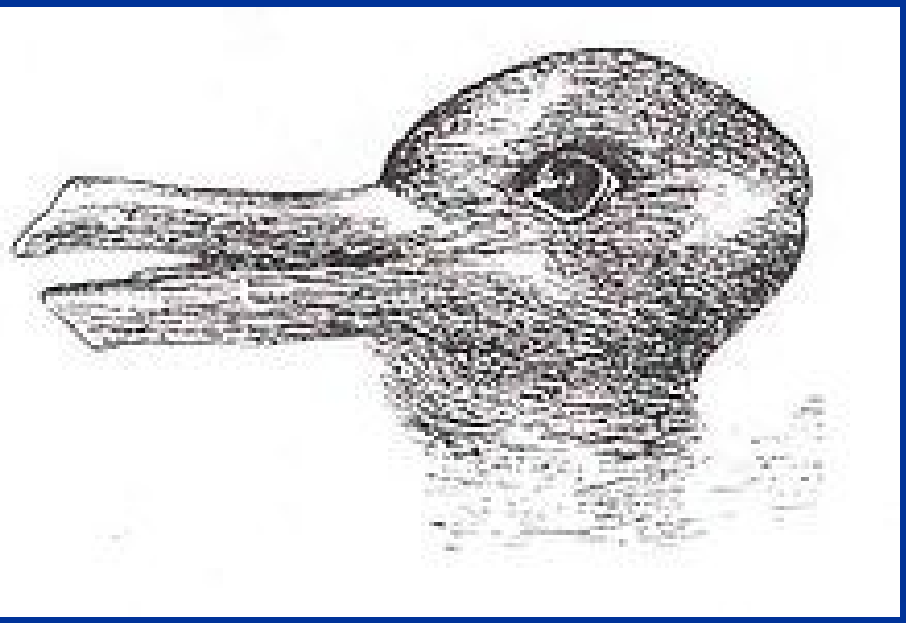
Chemical Substances (medications) can evoke mutations!

Mutation frequency in ribavirin-treated poliovirus populations

Population	G to A mutations	C to T mutations	Total mutation frequency[a]
Normal population	0.5	1.2	2.1
100 μM Ribavirin	—	1.3	2.5
400 μM Ribavirin	4.4	5.0	9.3
1000 μM Ribavirin	6.8	12.0	20.8

[a] Mutations per 10,000 nt sequenced (reprinted with permission from Crotty et al., 2001)

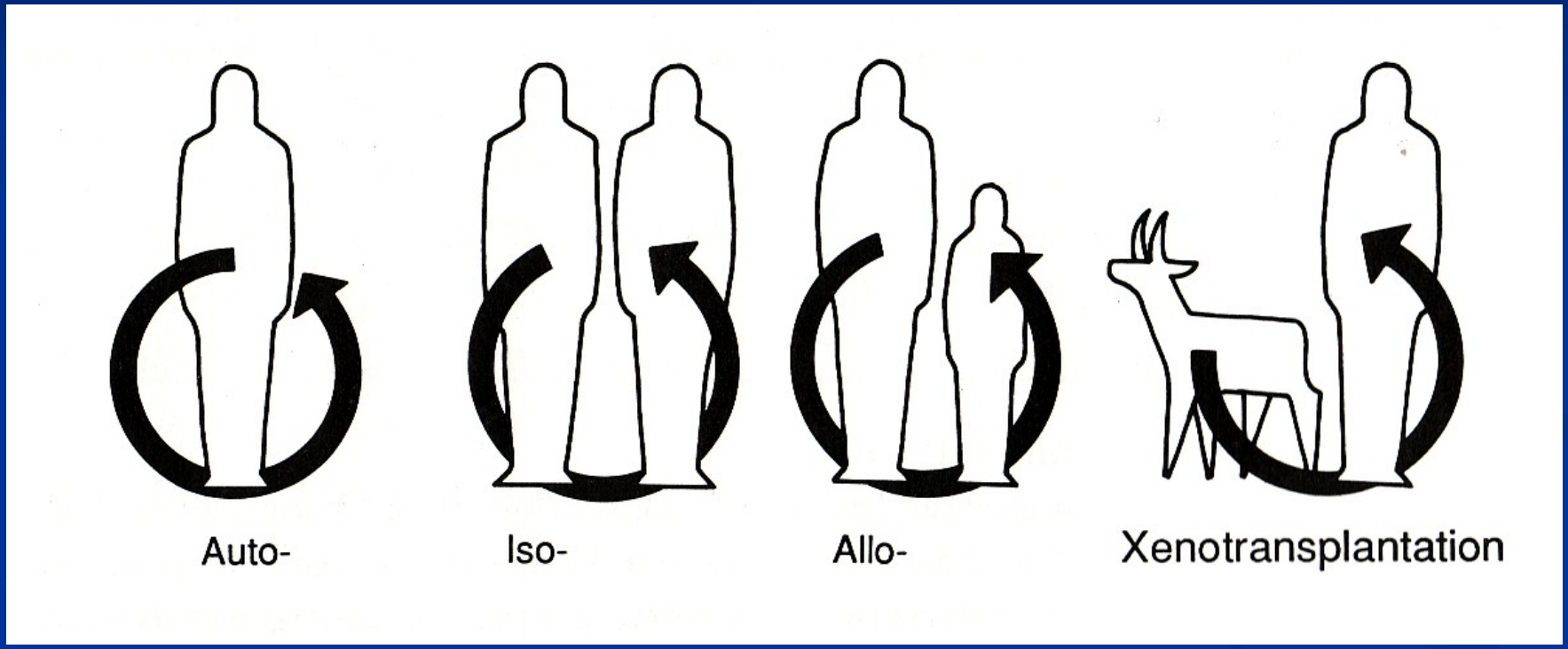
Thomas Samuel Kuhn was an US-American Scientist on Theory and History of Science.
In his main work „*The Structure of Scientific Revolutions*" Kuhn proposes a change in Paradigma over time.



Duck or rabbit?

Perception as a radical change!

Transplantation



A challenge for the immune system!

Example: Liver transplantation in cancer

Necessity of immune suppressive medications

(Drugs are similar to antiretrovirals.)

The differentiation betwee self and non-self is more difficult.

Drugs lead to mutations and transpositions
(The body defends itself by creating „new inventions")
Antibody Production!

HIV-positive!

Blood transfusions have to be controlled exactly for quality because this means:

A blood transfusion is comparable to an organ transplantation for 4 months.

Then the donor cells are degraded and replaced by own cells.

VIRUS = POISON

Infectus = infected

Infektion = communicable disease

Expectation:
The driving force comes from outside and is harmfull!

Fact:
The agent comes from inside and reacts to the environment!

We need a new evaluation of

- Exosomes
- Endosomes
- Virus
- Gene expression
- Epigenetics
- Lateral gene transfer (over generations)
- Horizontal gene transfer (from outside, between species)
- „Infection“ (sperms and pollen = male germ cells)
- Allergy (Ragweed)
- Disease and evolution

This is Evolution!

Fact: We take up molecules (DNA, RNA) from the environment (breast-feeding, nutrition) and might integra them into our genome!

Cell Research advance online publication 20 September 2011; doi: 10.1038/cr.2011.158

Exogenous plant MIR168a specifically targets mammalian LDLRAP1: evidence of cross-kingdom regulation by microRNA

Lin et al. Published online 20 September 2011.

Research on AIDS is Research in Gen-(technology) and Transcriptom.

***Paracelsus* said:**

„Everything is depending on the concentration“.

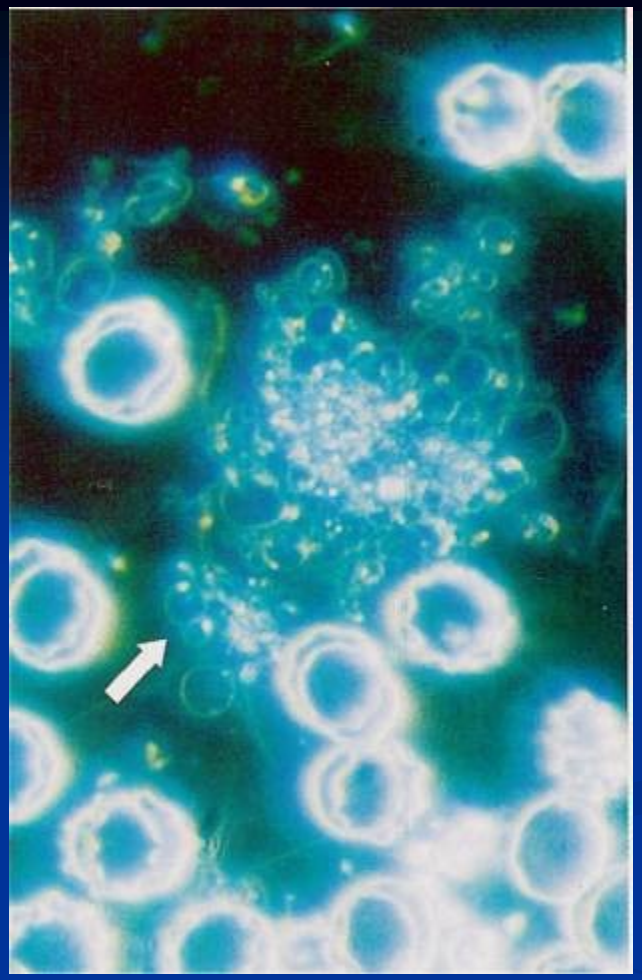
1958 J.Lederberg got the Nobel Price for the discovery of the Polymorphisms and the sexual reproduction of bacteria by fusion of the nuclei. *Lederberg, 1958*

Joshua Lederberg states that bacteria live with humans and all other species very often in a cooperative interaction.

Spontanous remissions of cancer are often associated with severe bacterial infections at the same time.

Scientists have detected a new form of Listeria. They are able to live without cell wall (L-Form) and replicate.

This disproves a hundred year old acceptance.



Cell free bacteria in human blood (dark field microscopy). The elements with the thick white rings are erythrocytes.

A study from
Markova et al. (2008)
indicates that the resistance to antibiotics in Staphylococcus aureus (MRSA) might be a result of cell free forms of bacteria.

The problem becomes more serious by recognizing the existence of multi-resistant tuberculosis germs, which are even dependent on the antibiotic Rifampicin, (Zhong et al., 2010). If the drug was given to patients the disease got worse. After quitting the antibiotic it became possible to heal the patient.

The dependence was confirmed in the lab!

Research changes more and more to become

„Personalized Medicine“

We have to reflect about the following arguments:

- **Costs / Advantage (Is prevention a better option?)**
- **Data protection („DNA-fingerprint“)**
- **Freedom of decision (Self-determination / Democracy)**
- **Ethics (Chances and decisions for life of the person)**

On the other hand „Personalized Medicine“ might lead to a more individual treatment.

G. Superti-Furga, Director of the Center of molecular Medicine in Vienna:

„Recenttly 50 % of the administered drugs do not act in the patient but show all side-effects.“

Everybody is unique – even in his genetic equipment!

Die Presse, 5. Oktober 2011

The new scientific findings and techniques (gene tests) mean a huge potential also in dangers.

Pharmacogenetics opens up a wide field, which can not be controlled by the lay people.

We have to respect the individual decisions concerning testing or not!

Respect the Human Rights!

Save freedom of all mankind!

If someone will get ill, depends mostly on the environment.

Which disease will manifest depends mostly on the genes.

But there exists also a cytoplasmatic inheritance!

The „perception“ is also depending on genes and environment.

What can we do already?

Investment in a humane society and health:

- Healthy nutrition
- Exercise, sports, yoga, meditation
- Stress reduktion
- Cooperation
- Self responsibility
- Good „starting conditions" (children, families)
- Social responsibility
- Life long learning and interest
- Holistic education / culture
- Free access to information
- Free choice for treatment, method or system
- Free, responsible research (balanced)
- Politics that are independent and act responsible

Giuseppe Arcimboldo 1527 - 1593

You are what you eat!

By ingesting nutrients we do not only acquire calories but also informations.

This includes nucleic acids (mikro-RNA) from nutrition.
RNA triggers metabolism and includes genetic informations.
This has to result in high responsibility including GMO and vaccinations!

This is Evolution!

You are , what you think!
You are, what you feel!

Communication between living creatures influences the communication of the cell.

(Nocebo-Effect)

Genes serve for the possibilities,
Life decides about realization!

Epigenetics and research on genes have to implement responsibility for us and the next generations!

The future of human beings
depends not any longer on what they do,
but on what they refrain from!

John Irving, writer

Our generation will not so much claim about the atrocities of bad humans rather than the dreadful silence of the good ones.
(Martin Luther King)

The error does not convert to truth even if it spreads and gets a good response.
(Mahatma Ghandi)

Science is only a pervesion of itself, if it yields not to the prosperity of the humanity.

Nicola Tesla, 1919
(Wireless energy transfer – how has it been used?)

Let theories die instead of humans!

Karl Popper: Austrian/ British Philosopher


Thank you for your attention!
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