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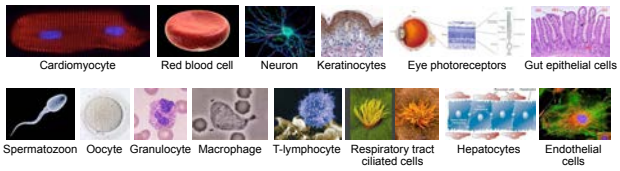
International Centre for Genetic Engineering and Biotechnology (ICGEB)

Trieste

Genetic Engineering

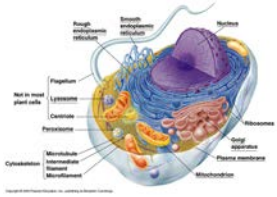
Our body is made up of cells



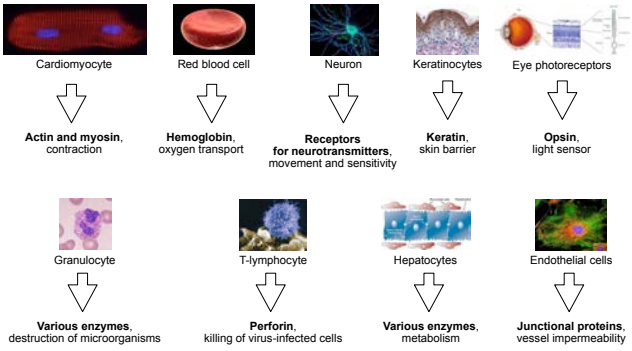
The human body:

~1x10^{14} (100 trillion) cells

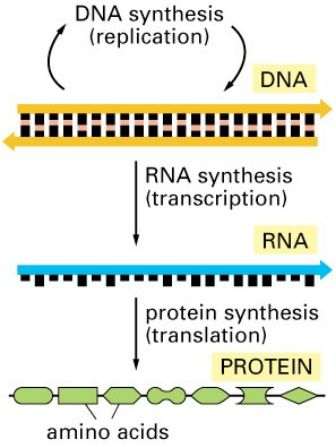
200+ different cell types

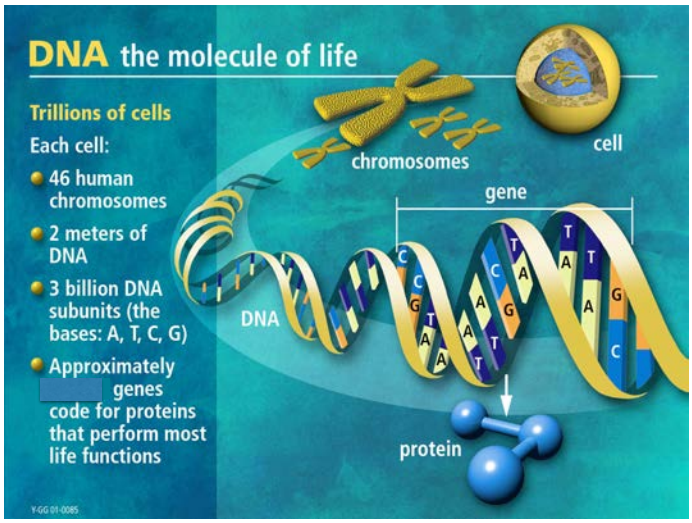


Cell function is exerted by proteins



Flow of genetic information



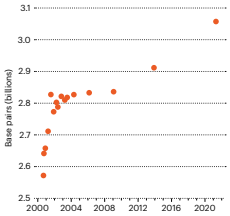


A COMPLETE HUMAN GENOME IS CLOSE: HOW THE GAPS WERE FILLED

Researchers added 200 million DNA base pairs and 115 genes — but they've yet to finish the Y chromosome.

COMPLETING THE HUMAN GENOME

Researchers have been filling in incompletely sequenced parts of the human reference genome for 20 years, and have now almost finished it, with 3.05 billion DNA base pairs.



0.3% of sequence might still have errors. Includes X but not Y chromosome. Count excludes mitochondrial DNA.

158 | Nature | Vol 594 | 10 June 2021

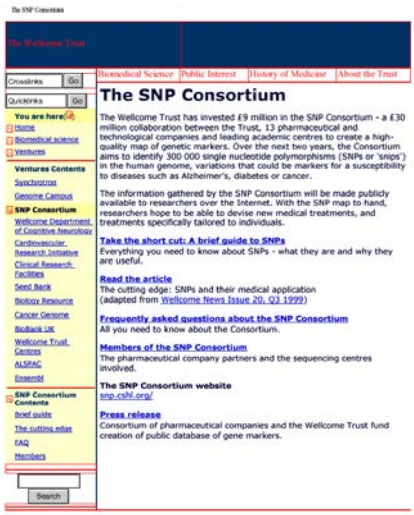
- Telomere-to-Telomere (T2T) Consortium, 30 institutions
- 115 new genes that code for proteins, for a total of 19,969
- cells from a hydatidiform mole, a tissue that forms in humans when a sperm inseminates an egg with no nucleus (chromosomes only from the father)
- new sequencing technology, which uses lasers to scan long stretches of DNA isolated from cells
- T2T-CHM13 represents only one person's genome

The human genome

Number of chromosomes:	46
Size of the human genome:	~3x10^9 bp
Number of genes:	~20.000
Genes:	30%
Extragenic DNA	70%
Coding regions	<2% (!)
Non coding regions	>98%

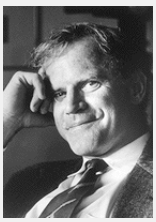
The main genomes sequenced before the human genome

		SIZE	NUMBER OF GENES
1984	Bacteriophage lambda	0.049	
1991	Smallpox virus	0.186	187
1995	Haemophilus infulenzae	1.8	1,740
1996	Saccharomyces cerevisiae	12.1	6,000
1997	Helicobacter pylori	1.67	1,590
1997	Escherichia coli	4.64	4,288
1998	Coenorabditis elegans	97	19,099
2000	Drosophyla melanogaster	180	13,061
2000	Pseudomonas aeruginosa	6.3	6,000 ?
2000	Arabidopsis thaliana	100	25,000
2001	Homo sapiens sapiens	2,910	26-36,000
	Mus musculum		
	Plasmodium falciparum (chr 2 and 3)		

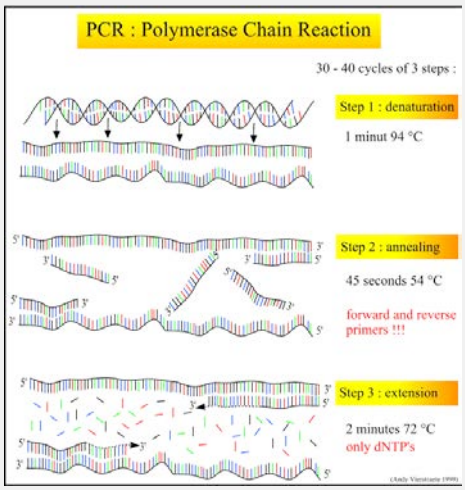


Confrontando il DNA di due individui sani si riconoscono circa 3 milioni di differenze (1 nucleotide ogni mille)

Approximately 3 x10^6 differences exist between the genomes of two healthy individuals (1 every 1000 nucleotides)

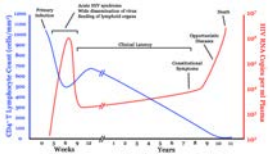


Kary B. Mullis



Applications of PCR:

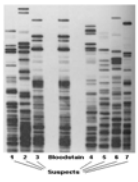
1. Detection of pathogens



2. Diagnosis of genetic diseases

3. Identification of criminals, forensic medicine, paternity test

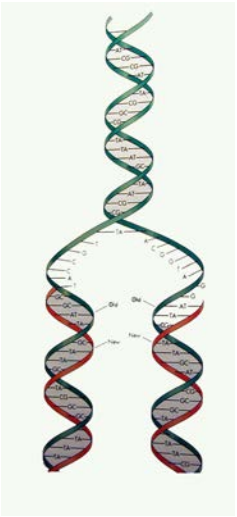
4. Monitoring gene expression



5. Evolutionary tracing

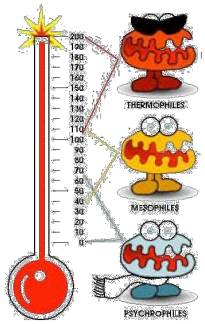
6. DNA cloning

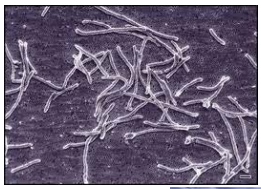
The molecular bases of DNA replication



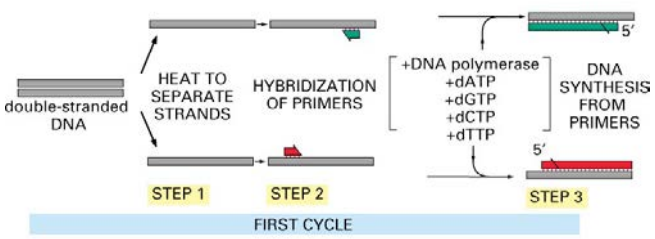
Taq polymerase is a DNA polymerase derived from Thermus Aquaticus

Thermus Aquaticus is a Gram Positive bacterium that is classified under a group called thermophiles. Thermophiles are defined as organisms that thrive and reproduce at temperatures that are above 45 Degrees Celsius. Specifically, Thermus Aquaticus optimally thrives and reproduces at 70 degrees celsius.

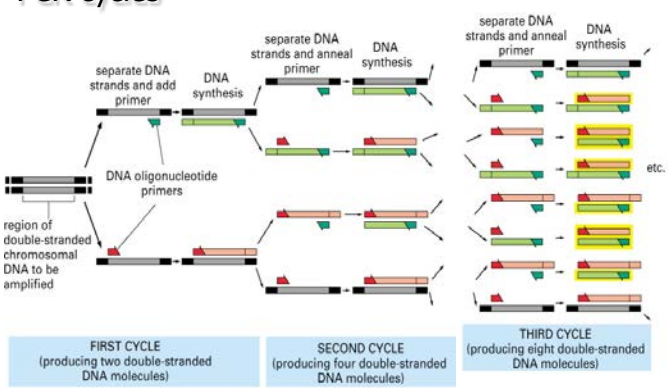


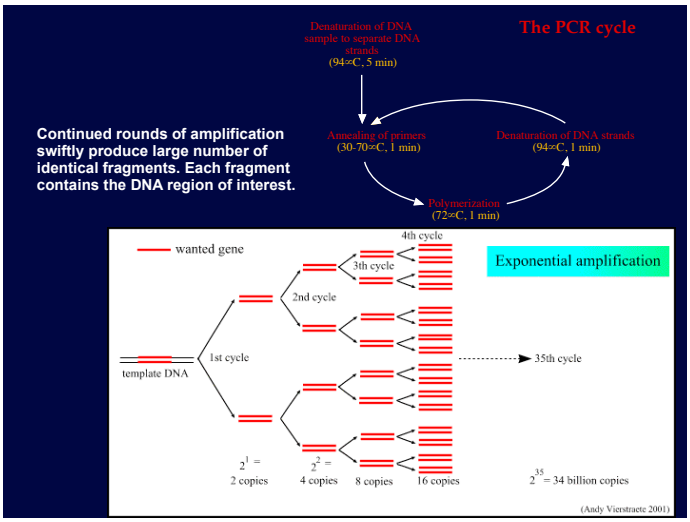


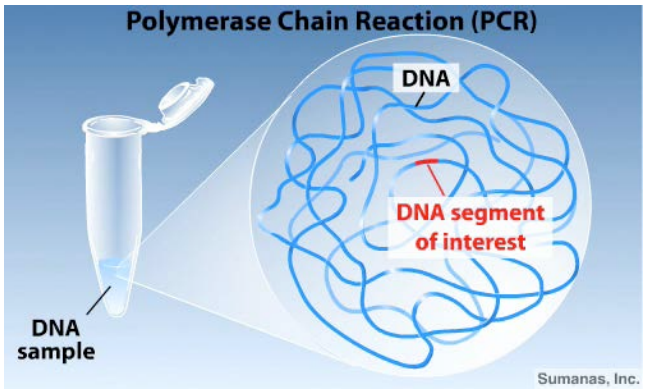
PCR amplification

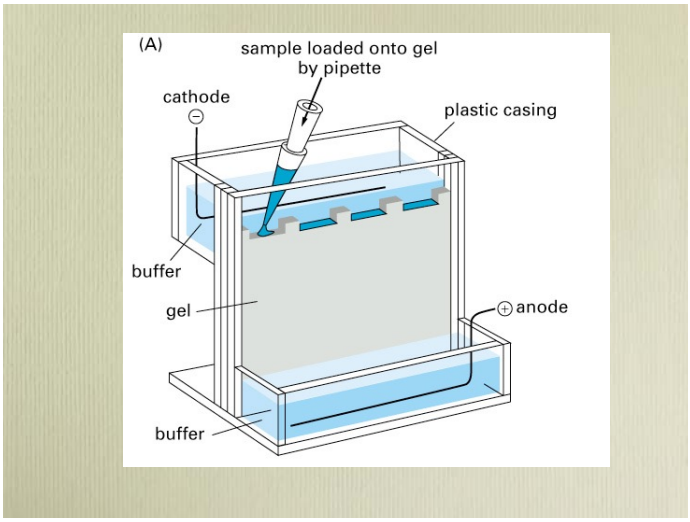


PCR cycles

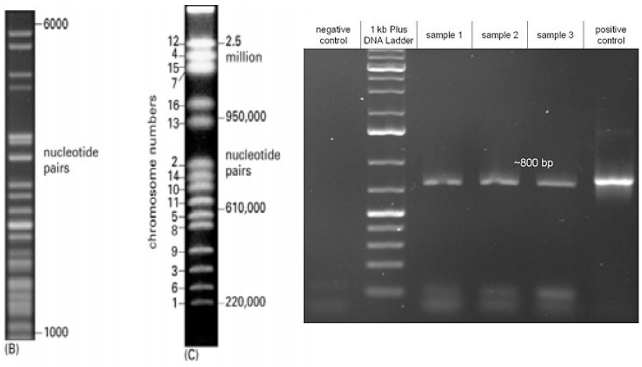




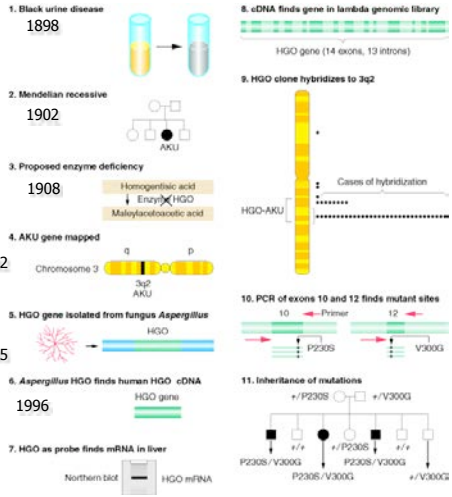




Gel Electrophoresis Separates DNA Molecules of Different Sizes

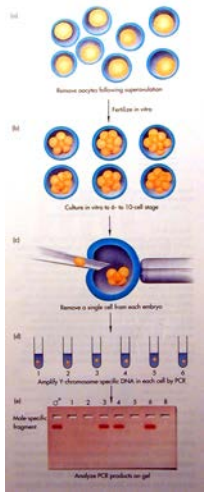


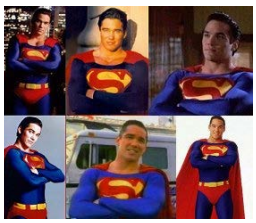
The story of the human gene defective in alkaptonuria



HGO: homogentisate 1,2-dioxygenase

Embryo selection





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Online Mendelian Inheritance in Man
Johns Hopkins University

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Links

ARM FOLDING PREFERENCE

TEXT

If in folding his arms the right arm is on top, the person is classed R. Hand clasping (139800) is a comparable trait. Falk and Ayala (1971) concluded that, although both traits are heritable to a significant extent, a simple mendelian hypothesis is not tenable. Ferronato et al. (1974) found no significant correlation between parents and children for arm folding preference, i.e., right arm or left arm on top.

REFERENCES

1. Falk, C. T.; Ayala, F. J. :
Genetic aspects of arm folding and hand clasping. *Jpn. J. Hum. Genet.* 15: 241-247, 1971.

2. Ferronato, S.; Thomas, D.; Sadava, D. :
Preferences for handedness, arm folding, and hand clasping in families. *Hum. Hered.* 24: 345-351, 1974.
PubMed ID : 4461659

CREATION DATE

Victor A. McKusick : 6/4/1986

EDIT HISTORY

mimadm : 4/9/1994
supermim : 3/16/1992
supermim : 3/20/1990
ddp : 10/26/1989
marie : 3/25/1988
root : 1/12/1988

OMIM
Online Mendelian Inheritance in Man
Johns Hopkins University

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EARS, ABILITY TO MOVE

TEXT

Linder (1949) found a frequency of the trait among parents and sibs of probands, leading to the idea that the ability is inherited as a somewhat irregular dominant. In 5 of 24 cases both parents lacked the trait. In Barcelona, Hernandez (1980) found that 19.9% of men and 9.57% of women could move their ears. In males, there was an association with tongue rolling (189300).

REFERENCES

1. Hernandez, M. :
La movilidad del pabellon auditivo. *Trab. Antropol.* XVIII(4): 199-203, 1980.

2. Linder, L. :
The ability to move the ears. *Hereditas* 35 (suppl.): 620-621, 1949.

CREATION DATE

Victor A. McKusick : 6/4/1986

EDIT HISTORY

mimadm : 6/25/1994
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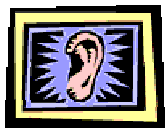
ddp : 10/26/1989
marie : 3/25/1988
reenie : 6/4/1986



news and views

Mapping genes for human personality

C. Robert Cloninger[1], Rolf Adolfsson[2] & Nenad M. Svrakic[1]

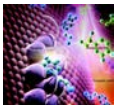
Nature Genetics 12, 3-4 (1996)

Temperament: dynamic organization of the psychobiological systems that regulate automatic responses to emotional stimuli

Four temperament domains:
- Novelty seeking
- Harm avoidance
- Reward dependence
- Persistence

e.g.: **extravert with mature creative character:**
HIGH Novelty seeking
LOW Harm avoidance (optimistic)
HIGH Reward dependence (sociable)
LOW Persistence

e.g.: **antisocial alcoholics:**
LOW Novelty seeking
~ Harm avoidance (optimistic)
LOW Reward dependence (sociable)
~ Persistence



10% of variation in Novelty seeking is accounted for by a polymorphism of the D4 dopamin receptor gene (D4DR)

Long alleles: HIGH Novelty seeking (exploratory, thrill seeking, excitable)
Short alleles: LOW Novelty seeking (deliberate, rigid, orderly)

Ebstein et al. Nature Genetics 12, 78-80 (1996)
Benjamin et al. Nature Genetics 12, 81-84 (1996)

Meeting American Association of Physical Anthropologists

Tracking the Evolutionary History of a "Warrior" Gene

TAMPA, FLORIDA—About 1200 researchers attended the 73rd Annual Meeting of the American Association of Physical Anthropologists here from 14 to 17 April to hear talks on primate genes, behavior, and fossils.

For males, a bit of aggression and risk-taking can earn rewards—just ask real-estate magnate Donald Trump. But inappropriate aggression can lead to violence, addiction, early death, and, the worst fate of all in evolutionary terms, no offspring.

Now, researchers have found signs of this balancing act in the genes of our primate cousins. At the meeting, a team of geneticists traced one genetic variant, an allele that predisposes men to aggressive, impulsive, and even violent behavior, to chimpanzees, gorillas, and other primates. They conclude that this and similar variants arose at least 25 million years ago as a monkey ancestor.

In order to be retained for so long, these variants must have conferred some selective advantage on the monkeys—and humans—who carried them, says author Tim Newman, a biological anthropologist at the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in Rockville, Maryland. What we see today as dangerously inappropriate behavior could be "simply out of context," says Newman. "Bold, aggressive males might have been quicker to catch prey or detect threats." Others agree: "If this [allele] has been around that long, then it must be maintained by balancing selection," says biological anthropologist Henry Harpending of the University of Utah in Salt Lake City.

The gene, found on the X chromosome, codes for an enzyme called monoamine oxidase A (MAOA), which breaks down several neurotransmitters in the brain, such as dopamine and serotonin, thus preventing excess neurotransmitters from interfering with communication among neurons. But the gene is polymorphic: A repeat sequence of 30 base pairs has been inserted from three to five times into the promoter region. Fewer repeats mean that less MAOA enzyme is produced and fewer neurotransmitters are removed.

The MAOA gene's effects have been linked to aggression. Lab mice that lack the enzyme are more aggressive, and one human family whose members do not produce the enzyme at all has been linked with violent behavior (*Science*, 18 June 1993, p. 1722). Men who carry the short allele, and so presumably produce a limited amount of enzyme, have been shown to be more likely to be aggressive, impulsive, and even violent if they were abused as children or drink alcohol. Men who had the short variant and were mistreated as boys were four times more likely than other men to have committed violent crimes such as rape, robbery, and assault, according to one study that tracked boys from birth in New Zealand (*Science*, 2 August 2002, p. 851). (Women also inherit the allele, but the effects are easier to study in men, who have only one X chromosome.)

Mad macaque. A genetic variant linked to violence in men has counterparts in primates and can make macaques like this one more aggressive.

These findings intrigued psychiatrist Klaus-Peter Lesch of the University of Würzburg in Germany, who works with the NIAAA group. His team first found, in macaques, a similar 18-base-pair repeat that also modulates MAOA enzyme activity. And macaques with less enzyme were more aggressive than other macaques when competing for food, says Lesch.

Newman then sampled all apes and many monkeys—almost 600 primates in all—and found the same 30-base-pair repeat seen in humans or the shorter 18-base-pair repeat, among other forms. He noted that apes and Old World (Asian and African) monkeys carried these alleles, whereas New World (South American) monkeys did not. That suggests that the allele arose after New World and Old World monkeys split, but before apes and Old World monkeys diverged about 25 million years ago.

During those 25 million years, aggressive and risk-taking behavior must have had reproductive payoffs for some males, says Newman. But the gene didn't sweep through populations, because if a male was too violent, he probably died before reproducing. Newman suggests that the MAOA gene may offer a rare example of so-called balancing selection, in which selection favors two or more forms of a gene and maintains all the forms in a population. "The human social environment required the development of all kinds of emotional and cognitive capabilities, and [it] demanded variation in impulsivity in humans," agrees David Goldman, a member of the NIAAA team. "It's what I call the warrior vs. the worrier." In other words, primate politics has long favored more than one route to success.

Chimpanzee Gang Warfare

Primatologists have long known that chimpanzees can be demonic: Bands of males routinely head to the borders of their territory to seek, and sometimes destroy, foreign chimpanzees. But what triggers these patrols, and why do males of the troop—who compete fiercely with one another most of the time—seem to cooperate while on patrol? The answer, it seems, may be a male mortality.

In a study of a group of 150 chimpanzees at Ngogo in the Kibale National Park in Uganda, researchers found that chimpanzees went on patrol only after they had assembled enough members to have overwhelming force. Patrols require "safety in numbers" because attacking a foreign chimpanzee is dangerous, explains primatologist John Mitani of the University of Michigan, Ann Arbor, co-author of the study with primatologist David Watts of Yale University.

Once a patrol formed, its members exhibited frequent displays of male bonding. "Cooperation among males is rare among animals," says Watts. "It is conspicuous that closely related chimpanzees and humans demobilization to engage in this coalitional aggression against outsiders."

PNAS

Genetic variation in the vasopressin receptor 1a gene (*AVPR1A*) associates with pair-bonding behavior in humans

Hasse Walum*†‡, Lars Westberg†§, Susanne Henningsson§, Jenae M. Neiderhiser¶, David Reiss‖, Wilmar Igl*, Jody M. Ganiban**, Erica L. Spotts††, Nancy L. Pedersen*, Elias Eriksson§, and Paul Lichtenstein*

*Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Box 281, S-171 77 Stockholm, Sweden; †Department of Pharmacology, Institute of Neuroscience and Physiology, University of Gothenburg, Box 431, S 405 30 Gothenburg, Sweden; ‡Department of Psychology, Pennsylvania State University, University Park, PA 16802; §Yale Child Study Center, Yale University, New Haven, CT 06520; **Department of Psychology, The George Washington University, Building GG 2125 G St NW, Washington, DC 20052; and ††Behavioral and Social Research Program, National Institute on Aging, Bethesda, MD 20892-9205

Edited by Solomon H. Snyder, Johns Hopkins University School of Medicine, Baltimore, MD, and approved July 14, 2008 (received for review March 28, 2008)

RS3 allele "334" present in 2 our 5 men

PARTNER BONDING: Renders men distant and disagreeable rather than emotionally close and available

MARITAL STATUS: Is predictive of men not getting married (32% of the man with two alleles were living to women without getting married vs. 17% of men without any allele)

PERCEIVED MARITAL PROBLEMS: Men with two copies of the allele had twice the risk of experiencing marital dysfunction with a threat of divorce

Table 3. Effect of 0, 1 or 2 334 alleles on male reports on the Partner Bonding Scale, marital crisis, and marital status

Measure	Number of 334 alleles 0	1	2	*df*	*F*	*P*
Mean score for the Partner Bonding Scale in the three groups						
Partner Bonding Scale	48.0 (6.50)	46.3 (6.16)	45.5 (6.71)	2, 143	8.40	0.0004
Frequency and column-wise percentage of subjects reporting marital crisis/threat of divorce in the three groups						
Have you experienced marital crisis or threat of divorce during the last year?						
No	469 (85%)	277 (84%)	27 (66%)	2, 143	5.00	0.008
Yes	81 (15%)	51 (16%)	14 (34%)			
Frequency and column-wise percentage of subjects being married or cohabiting in the three groups						
Marital status						
Married	457 (83%)	275 (84%)	28 (68%)	2, 143	4.36	0.01
Cohabiting	96 (17%)	52 (16%)	13 (32%)			

Values for the Partner Bonding Scale are means with standard deviation in brackets.

SMITTEN

DAILY SEX & RELATIONSHIPS BLOG

See all blog posts

Does Your Man Have "The Cheating Gene?"

Thursday, 09/ 4/2008 at 11:02 AM Comments (12)

V1aR gene RS3 allele 334

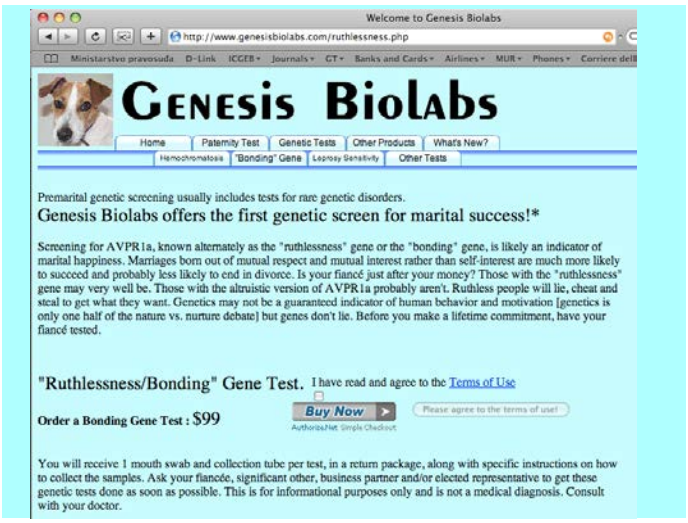
the "cheating gene"
the "infidelity gene"
the "divorce gene"

the "committment gene"
the "bonding gene"
the "monogamy gene"

My grandfather just wasn't "the cheating type." Although he was a tall, dark and handsome fighter pilot in WWII, he wouldn't have cheated on my grandmother in a million years. I figured he was just a great guy. But new research shows that his good behavior might have been in his genes. And other men, because of their genes, may cheat more often!

Swedish scientists have just made a shocking discovery: Two out of every five men (that's a lot!) carry a gene variant, known as an allele. Men with one or two of the alleles were found in the study to be more likely to have marital problems and get divorced than other men. Women involved with these men were also more likely describe their partners as distant and disagreeable.

Yikes, that's pretty heavy news. Have you met guys who seem like the "cheating type"? On the flip, have you met guys who seem destined to be faithful? If you're dating someone, would you want to test him for the gene before walking down the aisle? And what if you found out he had it--would that change your mind about marrying him? Tell me your thoughts, ladies!



The heritability of happiness

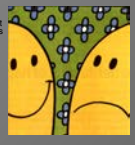
Dean H. Hamer

Nature Genetics 14, 125-126 (1996)

Longitudinal study of 1,380 pairs of twins born between 1936-1955. Measure of happiness by the Well Being scale of the Multidimensional Personality Questionnaire

"Hello, said Mr. Happy. "I'm Mr. Happy." "Oh, are you indeed", sniffed the person who looked like Mr. Happy but wasn't. "Well, my name is Mr. Miserable, and I'm the most miserable person in the world." "Why are you so miserable?" asked Mr. Happy. "Because I am." replied Mr. Miserable.

Happy Talk



Correlation for Well Being scale:

If twins grew up together:
0.44 for monozygotic twins
0.08 for dizygotic twins

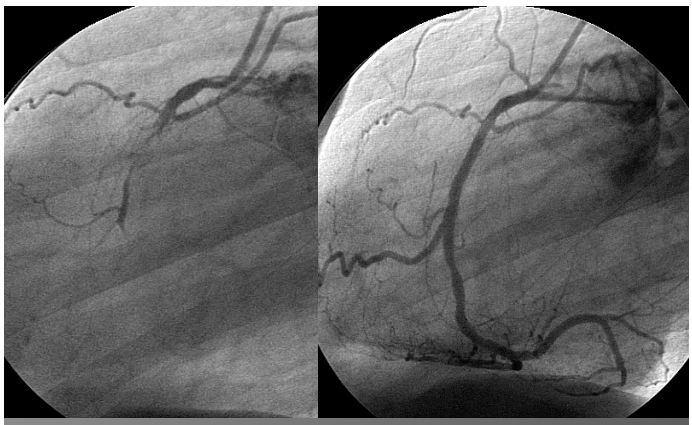
If twins were separated at infancy:
0.52 for monozygotic twins
0.02 for dizygotic twins

40-50% of happiness hereditable
0% due to shared environment
including parenting style, socioeconomic status and educational system
50-60% due non shared environment
including unique life experiences

After 5 years:
cross-time correlation: **0.5 for both type of twins**
cross-time
cross-twin correlation: **0.40 for monozygotic twins**
0.07 for dizygotic twins

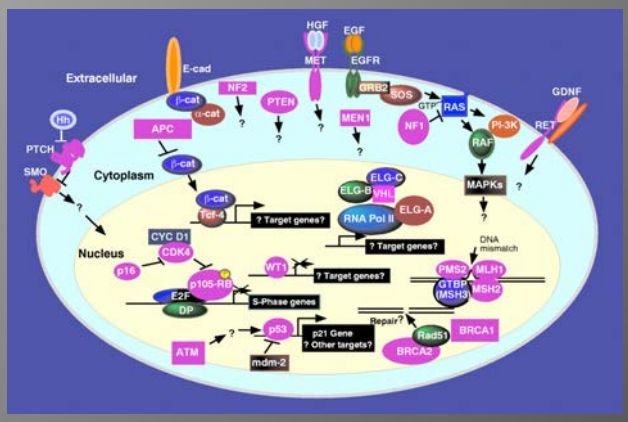
0.4/0.5 = 80% of stable happiness is genetic

Lykken and Tellegen. Psychol. Sci. 7, 186-189 (1996)



L'infarto del miocardio in soggetti giovani (prima dei 40 anni)

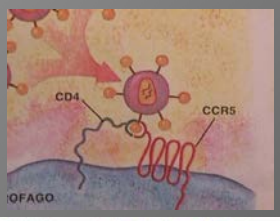
Meccanismi molecolari della crescita tumorale



POLIMORFISMI/ MUTAZIONI PROTETTIVI:

CCR5 E HIV

ANEMIA FALCIFORME E MALARIA



Human Identity Testing

- Forensic cases -- **matching suspect with evidence**
- Paternity testing -- **identifying father**
- Historical investigations
- Missing persons investigations
- Mass disasters -- **putting pieces back together**
- Convicted felon DNA databases

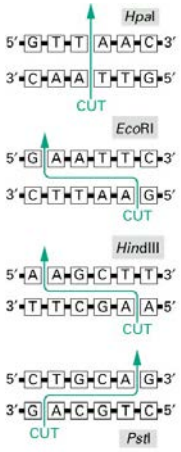
Sources of Biological Evidence

- **Blood**
- **Semen**
- **Saliva**
- **Urine**
- **Hair**
- **Teeth**
- **Bone**
- **Tissue**

Brief History of Forensic DNA Typing

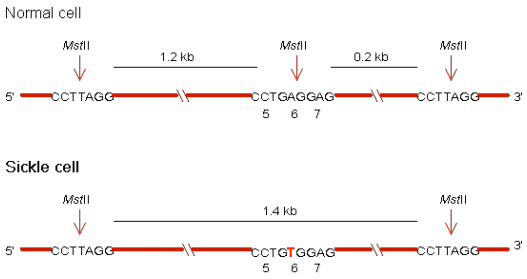
- 1980 - Ray White describes first polymorphic RFLP marker
- 1985 - Alec Jeffreys discovers multilocus VNTR probes
- 1985 - first paper on PCR
- 1988 - FBI starts DNA casework
- 1991 - first STR paper
- 1995 - FSS starts UK DNA database
- 1998 - FBI launches CODIS database

Restriction nucleases

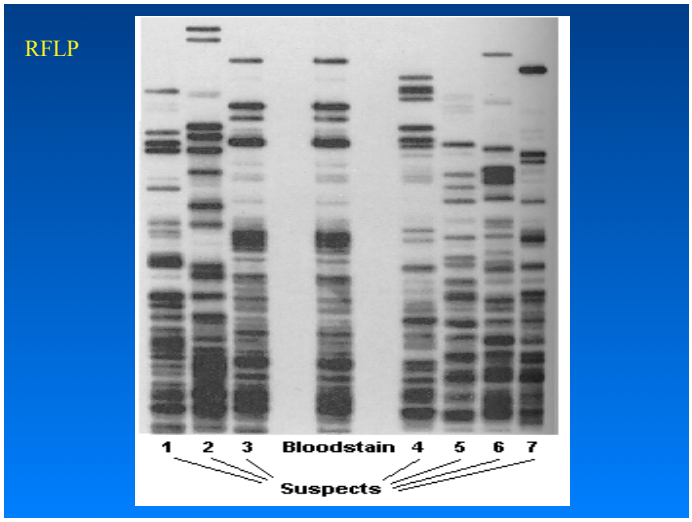


Restriction Fragment Length Polymorphism (RFLP)

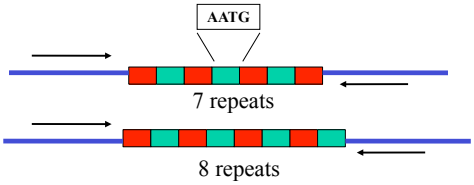
Polymorphism refers to the DNA sequence variation between individuals of a species. If the sequence variation occurs at the restriction sites, it could result in RFLP. The most well known example is the RFLP due to b globin gene mutation.



Restriction Fragment Length Polymorphism (RFLP) resulting from b-globin gene mutation. In the normal cell, the sequence corresponding to 5th to 7th amino acids of the b-globin peptide is CCTGAGGAG, which can be recognized by the restriction enzyme *Mst*II. In the sickle cell, one base is mutated from A to T, making the site unrecognizable by *Mst*II. Thus, *Mst*II will generate 0.2 kb and 1.2 kb fragments in the normal cell, but generate 1.4 kb fragment in the sickle cell.



Short Tandem Repeats (STRs)

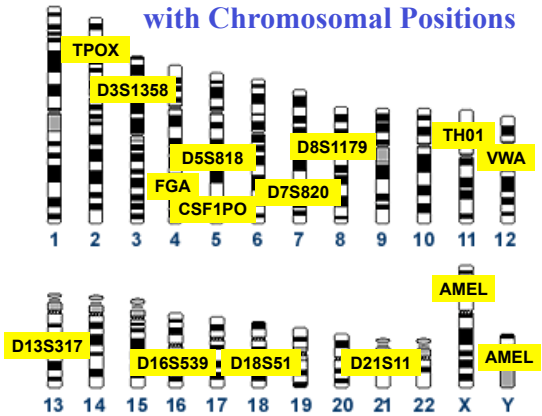


the repeat region is variable between samples while the flanking regions where PCR primers bind are constant

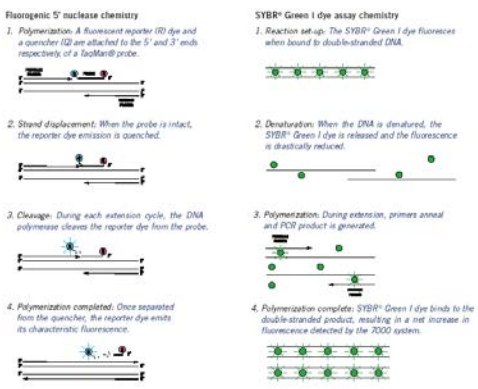
Homozygote = both alleles are the same length

Heterozygote = alleles differ and can be resolved from one another

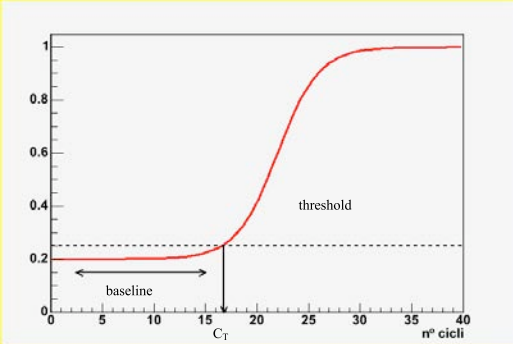
13 CODIS Core STR Loci with Chromosomal Positions



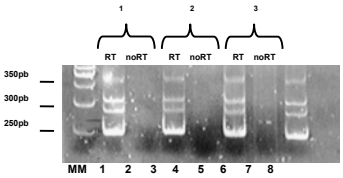
Real Time PCR



The amplification plot

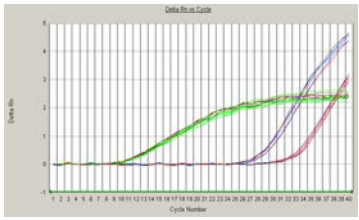


Gene expression analysis



Traditional PCR

Real Time PCR



Multiplex PCR

- Over 10 Markers Can Be Copied at Once
- Sensitivities to levels less than 1 ng of DNA
- Ability to Handle Mixtures and Degraded Samples
- Different Fluorescent Dyes Used to Distinguish STR Alleles with Overlapping Size Ranges

DNA Use in Forensic Cases

- Most are rape cases (>2 out of 3)
- Looking for match between evidence and suspect
- Must compare victim's DNA profile

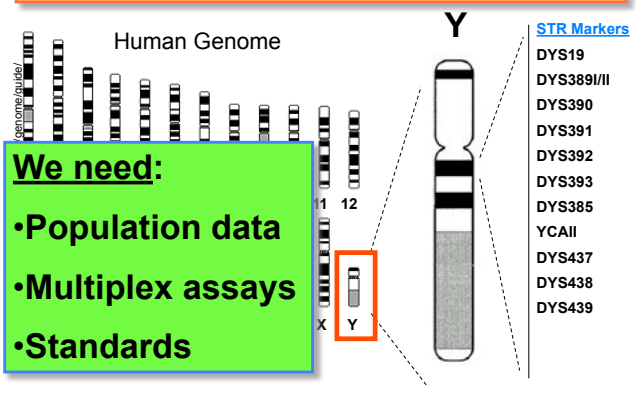
Challenges

- Mixtures must be resolved
- DNA is often degraded
- Inhibitors to PCR are often present

Highly Multiplexed Assays for Measuring Polymorphisms on the Y-Chromosome

International Society of Forensic Genetics
August 30, 2001
John Butler Rich Schoske Pete Vallone

There is a growing interest in the Y-chromosome to aid forensic and paternity testing…
(>50 presentations here at ISFG on Y markers)



We need:

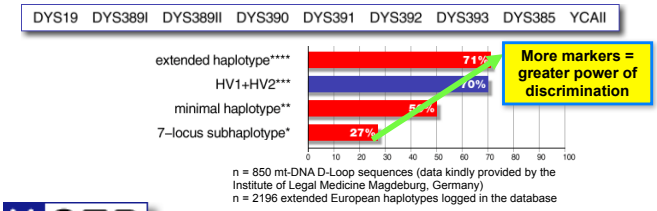
- **Population data**
- **Multiplex assays**
- **Standards**

European Y-STR Haplotype Reference Database

Created by Sascha Willuweit and Lutz Roewer
Institute of Legal Medicine, Humboldt-Universität Berlin, Germany
in cooperation with Michael Krawczak (Cardiff), Manfred Kayser (Leipzig) and Peter de Knijff (Leiden)

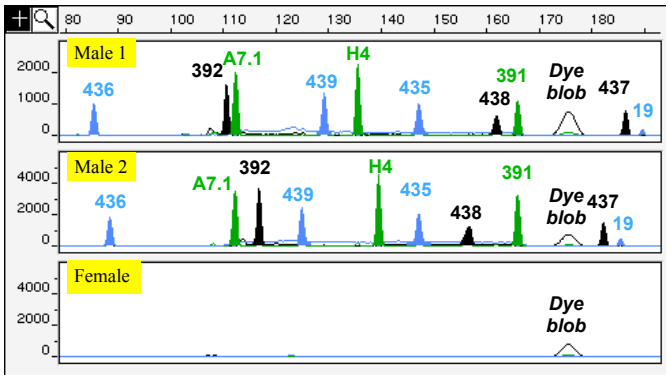
This database has been accessed **14809** times since 01/01/2000. Last haplotype entry **3/26/2001**

Current state of the database: **45** European population samples
5529 minimal haplotypes, **2196** of these are extended haplotypes

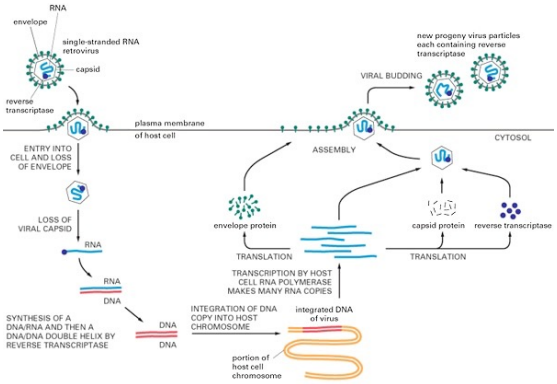


n = 850 mt-DNA D-Loop sequences (data kindly provided by the Institute of Legal Medicine Magdeburg, Germany)
n = 2196 extended European haplotypes logged in the database

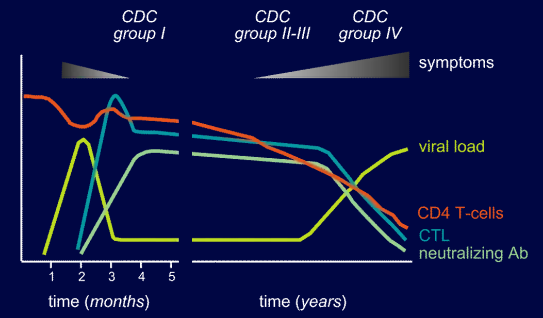
http://www.ystr.org/europe/



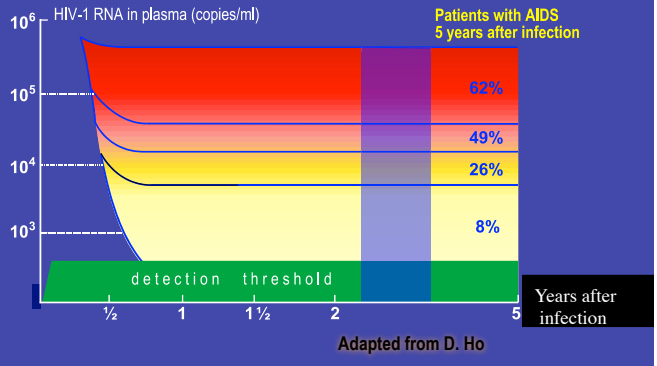
HIV life cycle



Natural history of HIV infection

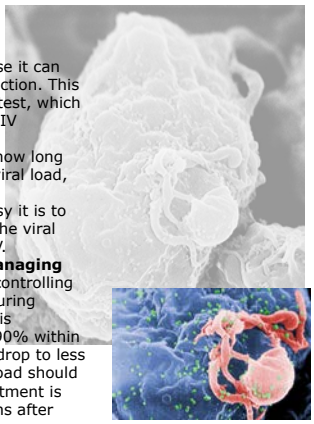


Correlation between HIV load in plasma and progression to AIDS

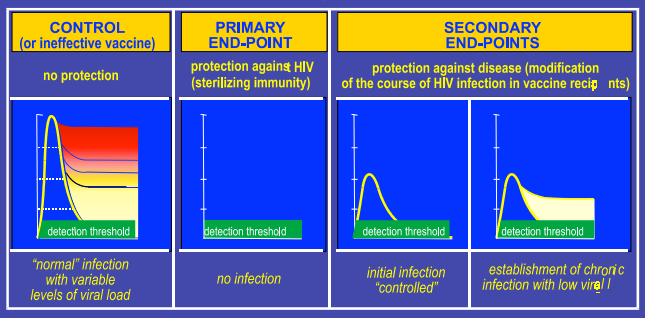


The HIV viral load is helpful in several areas:

- The test can be used for **diagnosis**, because it can detect a viral load a few days after HIV infection. This is better than the standard HIV (antibody) test, which can be "negative" for 2 to 6 months after HIV infection.
- For **prognosis**, viral load can help predict how long someone will stay healthy. The higher the viral load, the faster HIV disease progresses.
- For **prevention**, viral load predicts how easy it is to transmit HIV to someone else. The higher the viral load, the higher the risk of transmitting HIV.
- Finally, the viral load test is valuable for **managing therapy**, to see if antiretroviral drugs are controlling the virus. Current guidelines suggest measuring baseline (pre-treatment) viral load. A drug is "working" if it lowers viral load by at least 90% within 8 weeks. The viral load should continue to drop to less than 50 copies within 6 months. The viral load should be measured within 2 to 8 weeks after treatment is started or changed, and every 3 to 4 months after that.

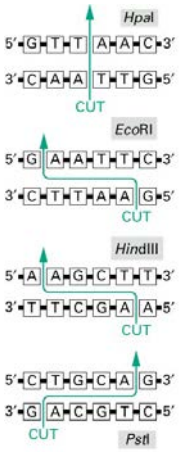


Potential end-points of HIV-vaccine efficacy trials

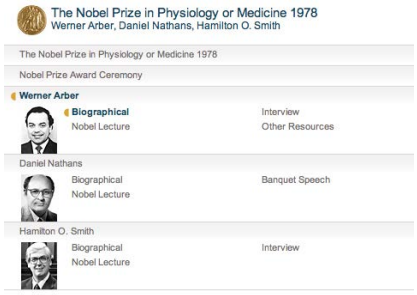


Genetic Engineering

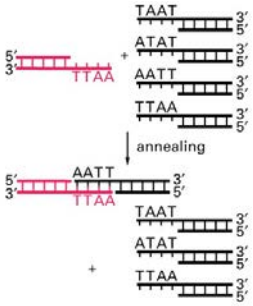
- Recombinant proteins
- Genetically modified plants
- Genetically modified animals
- Gene therapy
- Gene editing



Restriction enzymes



Recombinant DNA molecules



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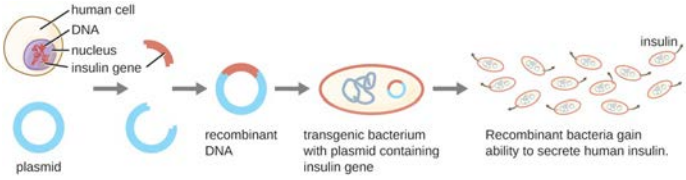
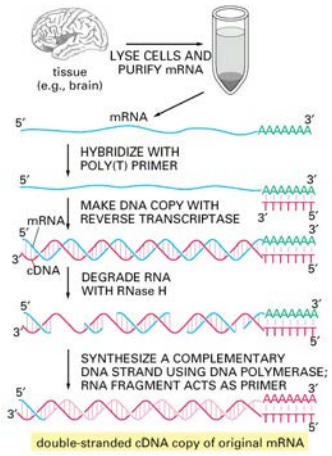
Recombinant DNA technology



cDNA

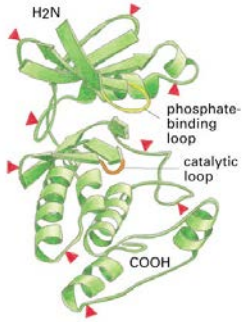


Biopharmaceutical Products

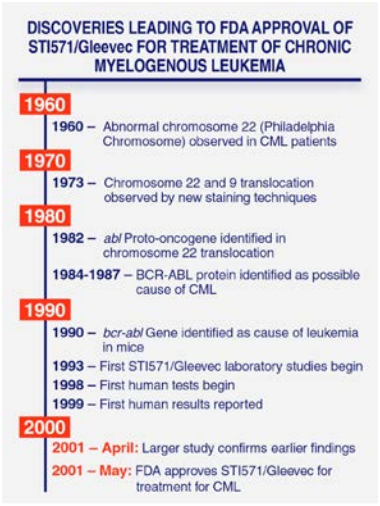
Product	Product
Insulin	1982
Human Growth Hormone (hGH)	1985
α–Interferon	1986
Hepatitis B Vaccine	1986
Tissue Plasminogen Activator (TPA)	1987
Erythropoietin-α	1989
γ-Interferon	1990
Granulocyte Colony Stimulating Factor (G-CSF)	1991
Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF)	1991
Interleukin 2	1992
Factor VIII	1992
β-Interferon	1993
DNase (Pulmozyme®)	1993
Glucocerebrosidase (Cerezyme®)	1994
ReoPro®	1994

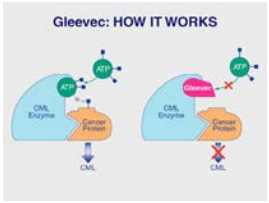
Source: Consulting Resources Corp.

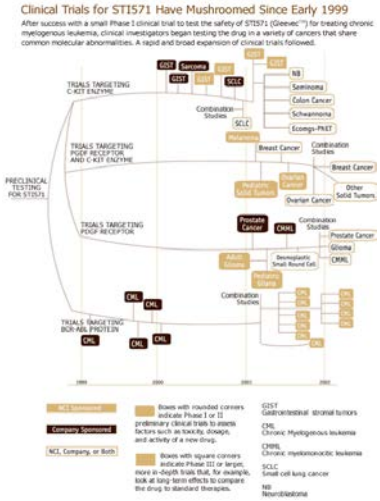
The 3D structure of a protein kinase



The ATP (which donates the P group) and the substrate are held in the active site, between the orange and yellow loops

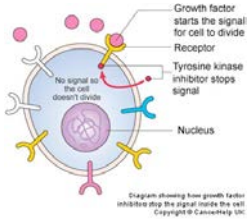


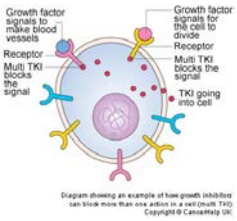


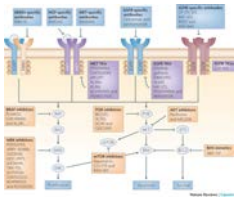


Tyrosine kinase inhibitors

Tyrosine kinase inhibitors are also called TKIs. They block chemical messengers (enzymes) called tyrosine kinases. Tyrosine kinases help to send growth signals in cells. So blocking them stops the cell growing and dividing. Cancer growth blockers can block one type of tyrosine kinase or more than one type. TKIs that block more than one type of tyrosine kinase are called multi-TKIs.







TKIs Approved for Clinical Use

- Herceptin (trastuzumab) - metastatic breast cancer
- Glivec (imatinib) - chronic myeloid leukaemia and GIST
- Iressa (gefitinib) - NSCLC
- Erbitux (cetuximab) - metastatic colorectal cancer
- Tarceva (erlotinib) - NSCLC

Genetic Engineering

- Recombinant proteins
- Genetically modified plants
- Genetically modified animals
- Gene therapy
- Gene editing

Many crops never existed in nature

Fragraria chiloensis
Chile

X

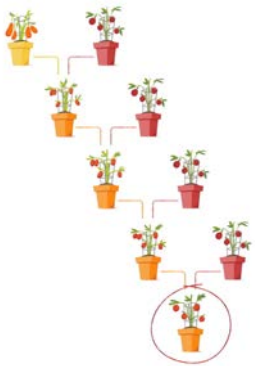
Fragraria virginiana
Eastern North America

Fragraria ananassa
Paris Botanical Garden, 1766

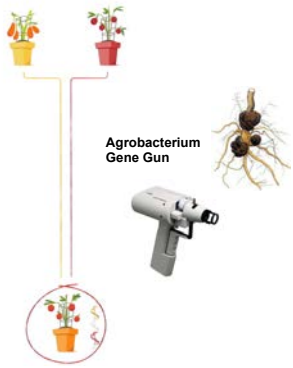
Seedless fruits are not natural

More than one way to alter a plant

Traditional Plant Breeding



Genetic Engineering

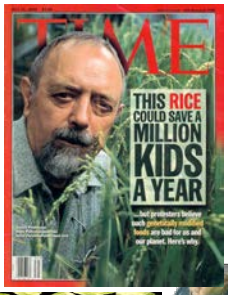


Nutritionally Enhanced: Golden Rice

Vitamin A deficiency is a leading cause of blindness often leading to mortality throughout the developing world.

Without vitamin A proper development does not take place and 2 million children die by the age of 4 or 5 every year.

Many more children dye from vitamin A deficiency than from AIDS, tuberculosis or malaria.



The solution: golden rice, engineered to [?] produce beta-carotene, the precursor of vitamin A

La patata in Australia

PLRV (Potato Leaf Roll Virus) e' il principale problema per le coltivazioni di patate in Australia

Inserendo un gene di PLRV la patata diventa resistente all'infezione

Trasporto e lavorazione innescano un processo di ossidazione che conferisce alle patate uno sgradevole colore brunastro

Tale processo può essere prevenuto inserendo una copia antisenso del gene responsabile, la PPO (polifenol-ossidasi)

Le patate geneticamente modificate, resistenti all'infezione da PRLV e all'ossidazione, sono disponibili sul mercato australiano dall'anno 2000

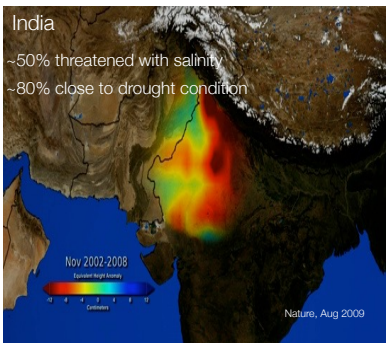
In Europa ad un acceso dibattito intorno ai rischi degli OGM non corrisponde una adeguata conoscenza del problema dal punto di visto scientifico

- **35% della persone intervistate ritiene che i pomodori non contengano geni, mentre li contengono soltanto quelli geneticamente modificati**
- **il 24% ritiene che "Se una persona mangia OGM I geni si trasferiscano a lui"**

Eurobarometer Survey, 2000

Salinity and drought: two serious threats to agricultural yield

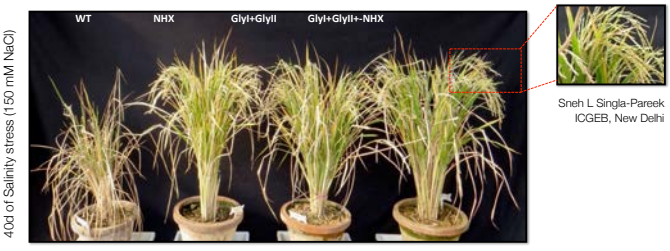
NASA satellites unlock secret to Northern India's vanishing water



Haryana, Punjab, Rajasthan and Delhi (the grain baskets of India) lost 109 cubic km of ground water in last 6 yrs (2002-08)

Sneh L Singla-Pareek
ICGEB, New Delhi

Triple transgenic rice plants for durable stress tolerance

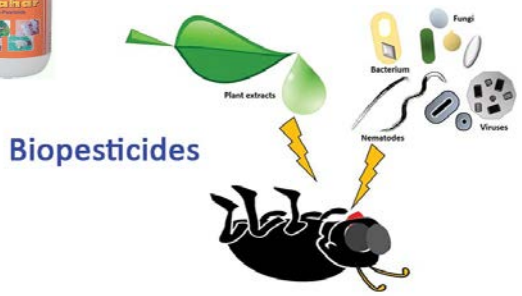


Sneh L Singla-Pareek
ICGEB, New Delhi

Triple (Gly+GlyII+NHX) transgenic rice plants show better reproductive growth as compared to double (GlyI+GlyII) or single (NHX1) transgenic lines and WT plants under salinity stress conditions

Biological pesticides for pest control

Biopesticide based on insect symbiont bacteria for agriculture and horticultural crops developed and commercialised, over 300,000 litres /year

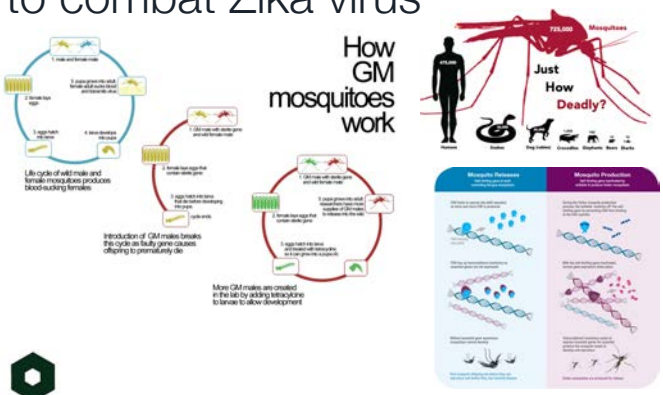


Genetic engineering for biofuel production

Biofuels provide a potential route to avoiding the global political instability and environmental issues that arise from reliance on petroleum. Currently, most biofuel is in the form of **ethanol** generated **from starch or sugar** (Brazil supplies one quarter of its ground transportation fuel with ethanol from the fermentation of sugarcane sugar), but this can meet only a limited fraction of global fuel requirements. In addition, starch and sugar that are used for for the production of ethanol compete with food supplies.

Conversion of **cellulosic biomass**, which is both abundant and renewable, is a promising alternative. However, the cellulases and pretreatment processes involved are very expensive. **Genetically engineering plants to produce cellulases and hemicellulases**, and to reduce the need for pretreatment processes through lignin modification, are promising paths to solving this problem, together with other strategies, such as increasing plant polysaccharide content and overall biomass.

Genetically modified mosquitoes to combat Zika virus



OXITEC

Aedes mosquito transmits Zika, dengue, yellow fever and chikungunya

Big companies and GMOs

Mixed Messages

Faced with protests over genetically modified foods, some major food companies are divided over how to deal with the controversy.

GENETICALLY MODIFIED CROPS ARE NOW WIDELY GROWN . .

Soybeans **52%** genetically modified
38 million acres out of 73 million total acres in the United States

Corn **25%** genetically modifi
19 million acres out 78 million total acres in the United States

. . . AND COMPANIES FACE MORE CONFLICTS

NOVARTIS

ONE SIDE Gerber Products, a unit of the company, has banned genetically modified ingredients from its baby-food formulas.

THE OTHER SIDE Novartis is a Swiss pharmaceutical giant that makes and sells genetically modified corn and soybean seeds.

McDONALD'S

ONE SIDE Asked suppliers to stop shipping genetically modified potatoes.

THE OTHER SIDE In its restaurants, French fries are cooked in vegetable oil made from genetically modified corn and soybeans.

PEPSICO

ONE SIDE The Frito-Lay division announced in January that it would stop using genetically modified corn in its chips.

THE OTHER SIDE The company's flagship soft drink uses corn syrup made from genetically modified corn.

The New York Times

Conceptual paper

The Nobel Laureates' Campaign Supporting GMOs

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ABSTRACT

More than 800 million people suffer from hunger in the world. Using modern plant breeding methods to generate so-called GMOs (Genetically Modified Organisms), agricultural scientists have shown that crop yields and nutritional quality can be greatly improved. Many GMO varieties have been specifically developed with the aim of being resistant to pests, tolerant to drought and containing beneficial nutrients. This leads to a reduction in the use of insecticides in water and on land. If anything, the GMO varieties are safer than traditionally bred varieties because they are made in a very precise manner. However, the scientific evidence on this issue is being ignored by the Green Parties such as Greenpeace who continue to deny the science and mislead the public. 129 Nobel Laureates have joined in a campaign to convince the Green Parties and the public that they should support the use of GMOs, especially for the sake of the developing world.

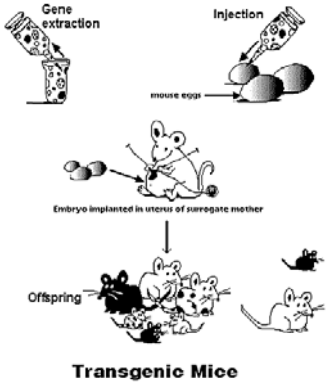
Genetic Engineering

- Recombinant proteins
- Genetically modified plants
- Genetically modified animals
- Gene therapy
- Gene editing

Genetic manipulation of animals to discover gene function

Drosophila melanogaster
When flies have a mutation wherein the *Antennapedia* gene is expressed in the head (as well as in the thorax), legs rather than antennae grow out of the head sockets

How to make a transgenic mouse

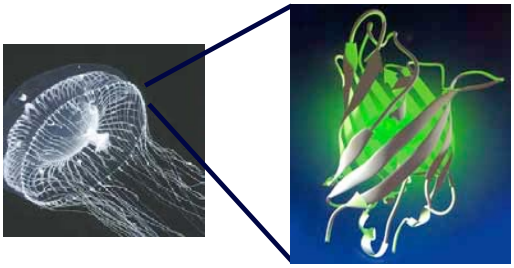


Transgenic Mice

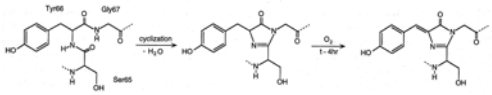
Transgenesis involves transfer of foreign DNA into totipotent or pluripotent embryo cells (either **fertilized oocytes**, **cells of the very early embryo** or **cultured embryonic stem cells**) followed by insertion of the transferred DNA into host chromosomes

Transgenic mouse for growth hormone

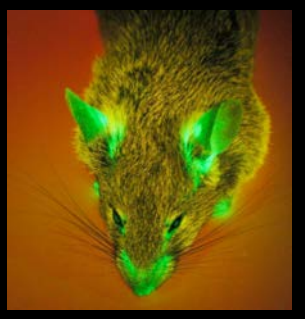
Green fluorescent protein

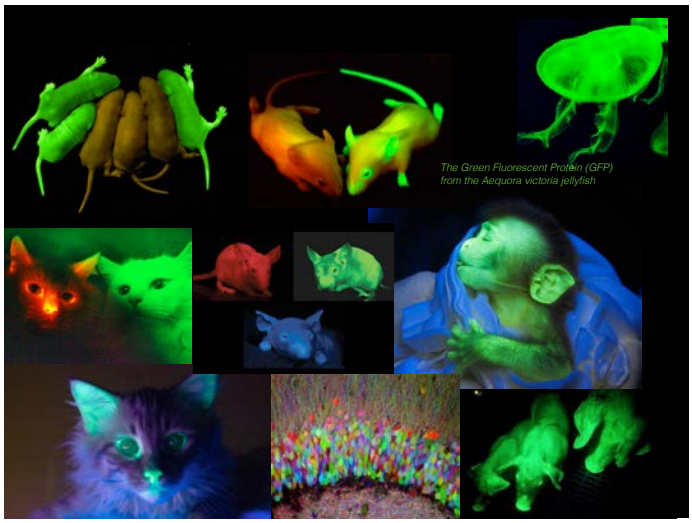


238-amino-acids 27-kD protein containing a photoexcitable greenish-light-emitting chromophore



The GFP transgenic mouse





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la Repubblica

L'Aifa approva il medicinale più caro della storia: lo Zolgensma contro la Sma
di Michele Bocci

Negli Usa ha avuto il via libera per 2,1 milioni di dollari. In Italia si sarebbe raggiunto un accordo con Novartis, per riconoscere circa 1,5 milioni di euro a trattamento ma prevedendo un pagamento dilazionato nel tempo

10 MARZO 2021 · 1 MINUTI DI LETTURA

Currently approved gene therapy products

Drug	Company	Disease	Prevalence	Price (USD)
Glybera	UniQure	Lipoprotein lipase deficiency (LPLD)	1:1,000,000	1M
Strimvelis	GlaxoSmithKline	ADA-SCID	1:100,000	665K (money-back
Yescarta	Gilead/Kite Pharma	CAR-T for Diffuse Large B-cell NHL	4:100,000 per year	373K
Kymriah	Novartis	CAR-T for B-cell ALL	1,7:100,000	475K
Luxturna	Spark Therapeutics	LCA due to RPE65 defects	<1:100,000	435K per eye
Zynteglo	Bluebird bio	Beta thalassaemia	60K symptomatic individuals born annually	1.78M (over 5 years)
Zolgensma	Avexis/Novartis	SMA	1-2:100,000	2.1M

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Genetic engineering: fear and worry