Chemical Biology

DNA ⇆ RNA ⇆ Proteins

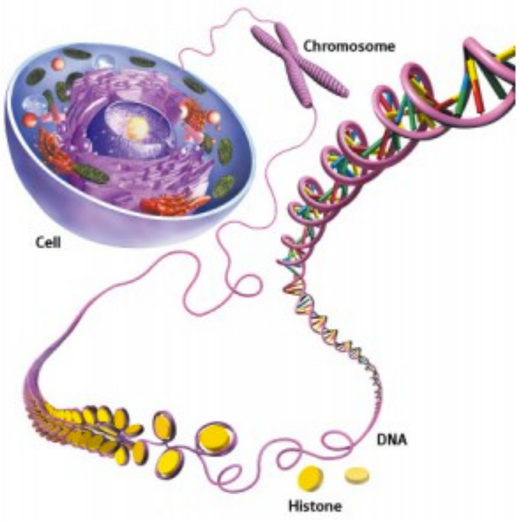
Molecular Engineering

Dr. Ron Rusay

https://www.youtube.com/watch?v=gG7uCskUOrA

DNA & RNA: Nucleic Acids

- Store & carry genetic information.

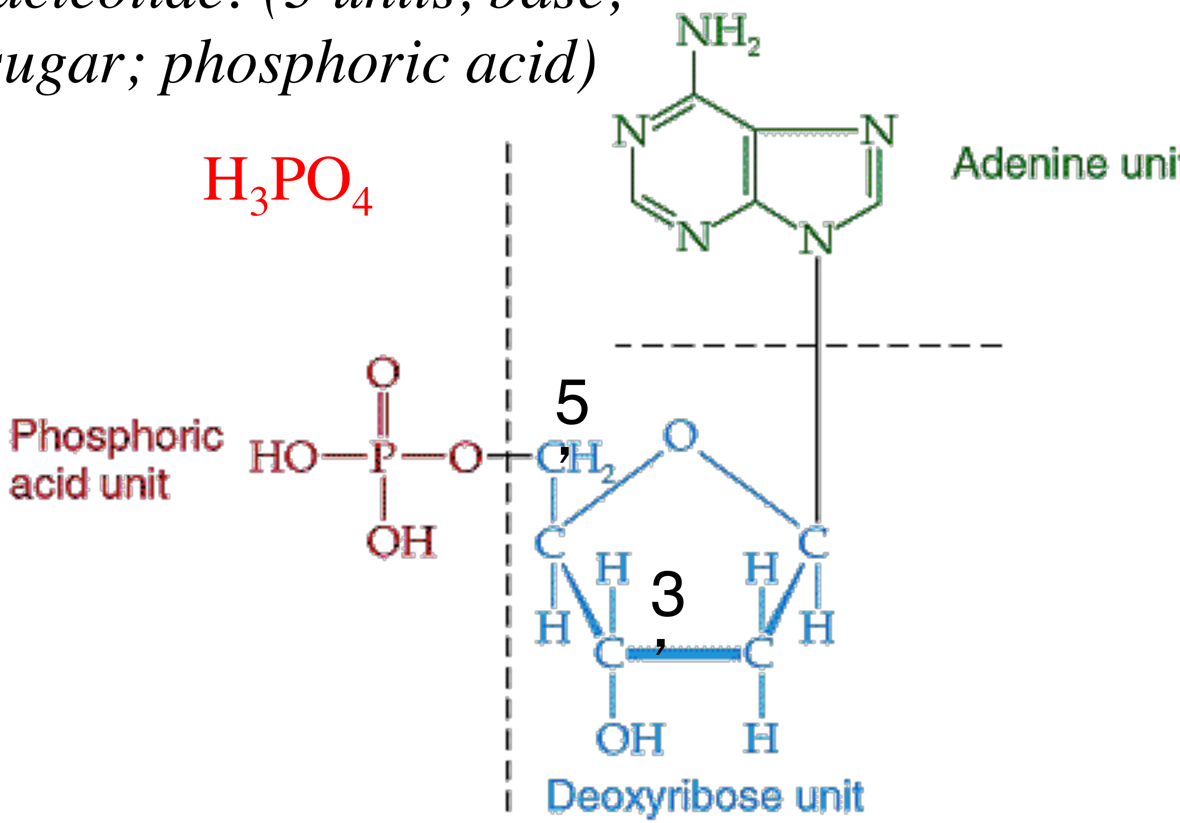


- DNA (deoxyribonucleic acids) have molecular weights ~ 6×10^6 to 16×10^6 daltons (amu) and are found inside the nucleus of the cell.
- RNA (ribonucleic acids) have molecular weights ~ 20,000 to 40,000 amu and are found in the cytoplasm outside the nucleus of the cell.

Nucleic "Acids"

Nucleotide: (3 units, base; sugar; phosphoric acid)

Organic base: $R\text{-}NH_2$



five carbon sugar

Nucleoside: does not include the phosphoric acid

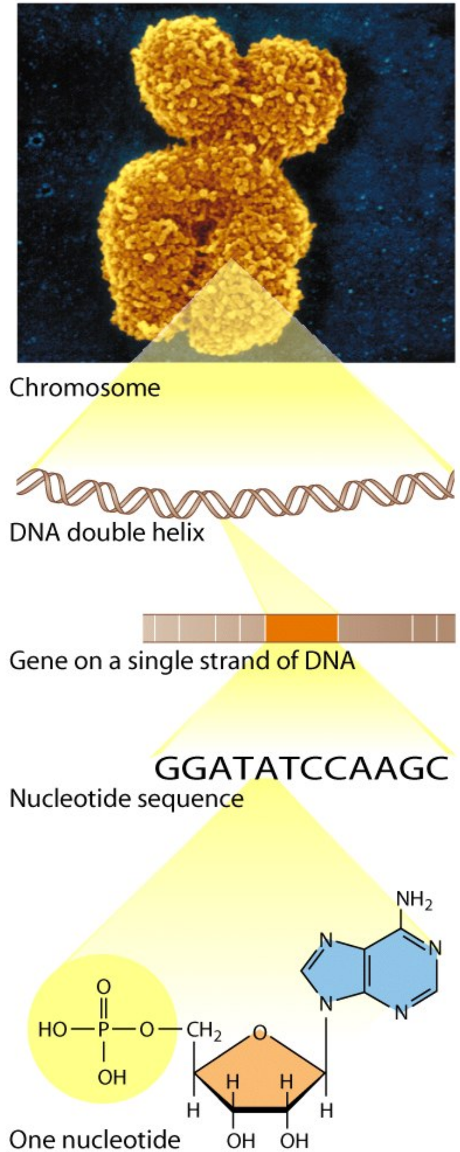
Nucleic Acids (DNA & RNA)

- DNA and RNA have different sugars (dexoyribose vs. ribose).
- There are only five bases found in DNA and RNA:
  - adenine (A),
  - guanine (G),
  - cytosine (C),
  - thymine (T found in DNA only), and
  - uracil (U found in RNA only).

Genetics & DNA

♀

XX



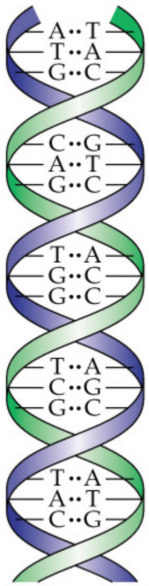
♂

XY

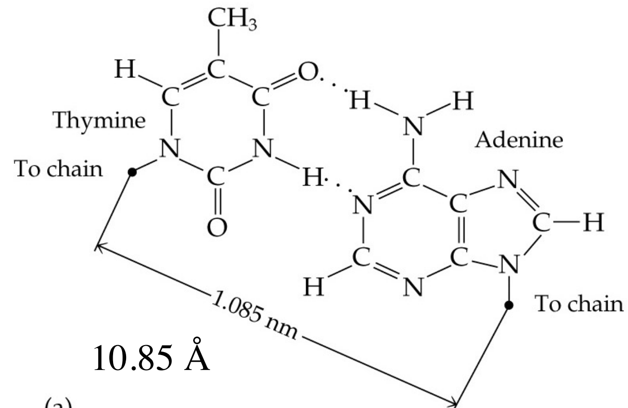
DNA: Size, Shape & Self Assembly

http://www.umass.edu/microbio/chime/beta/pe_alpha/atlas/atlas.htm

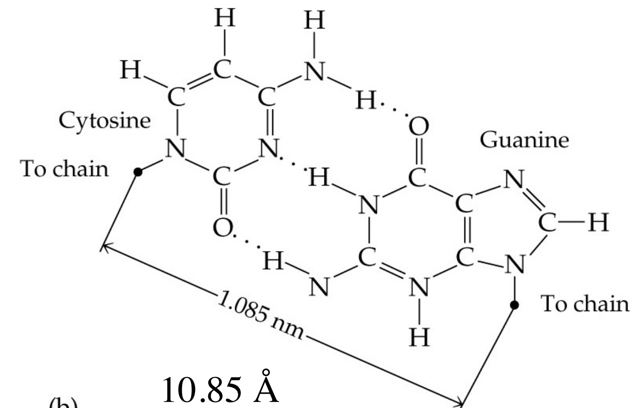
Views & Algorithms



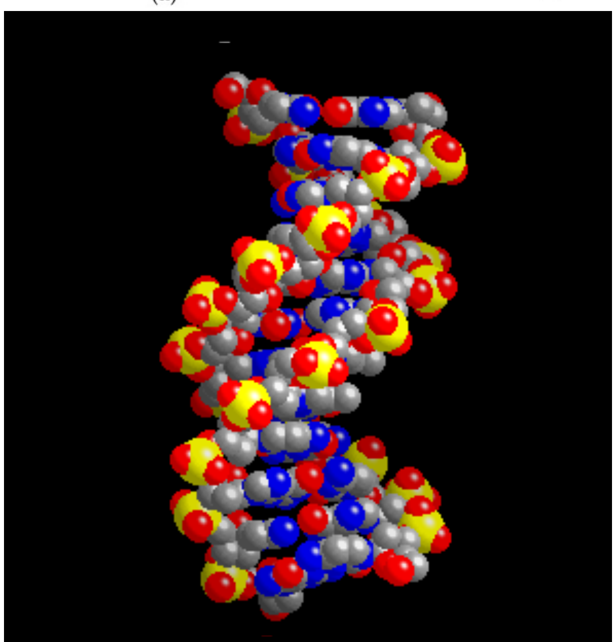
(a)

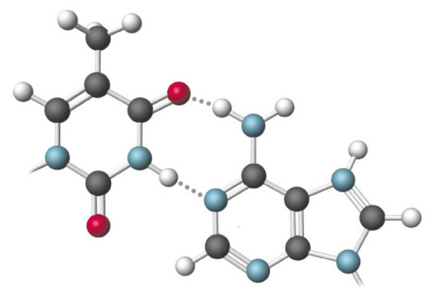


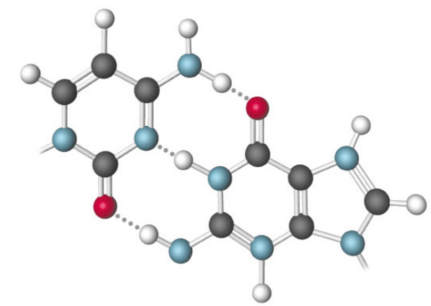
(a)



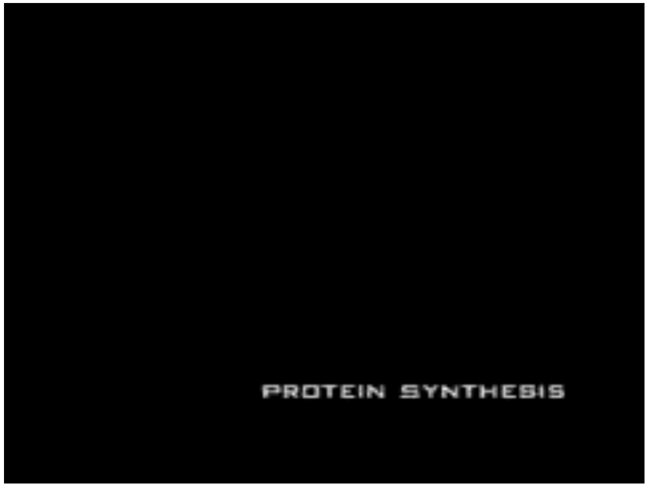
(b)



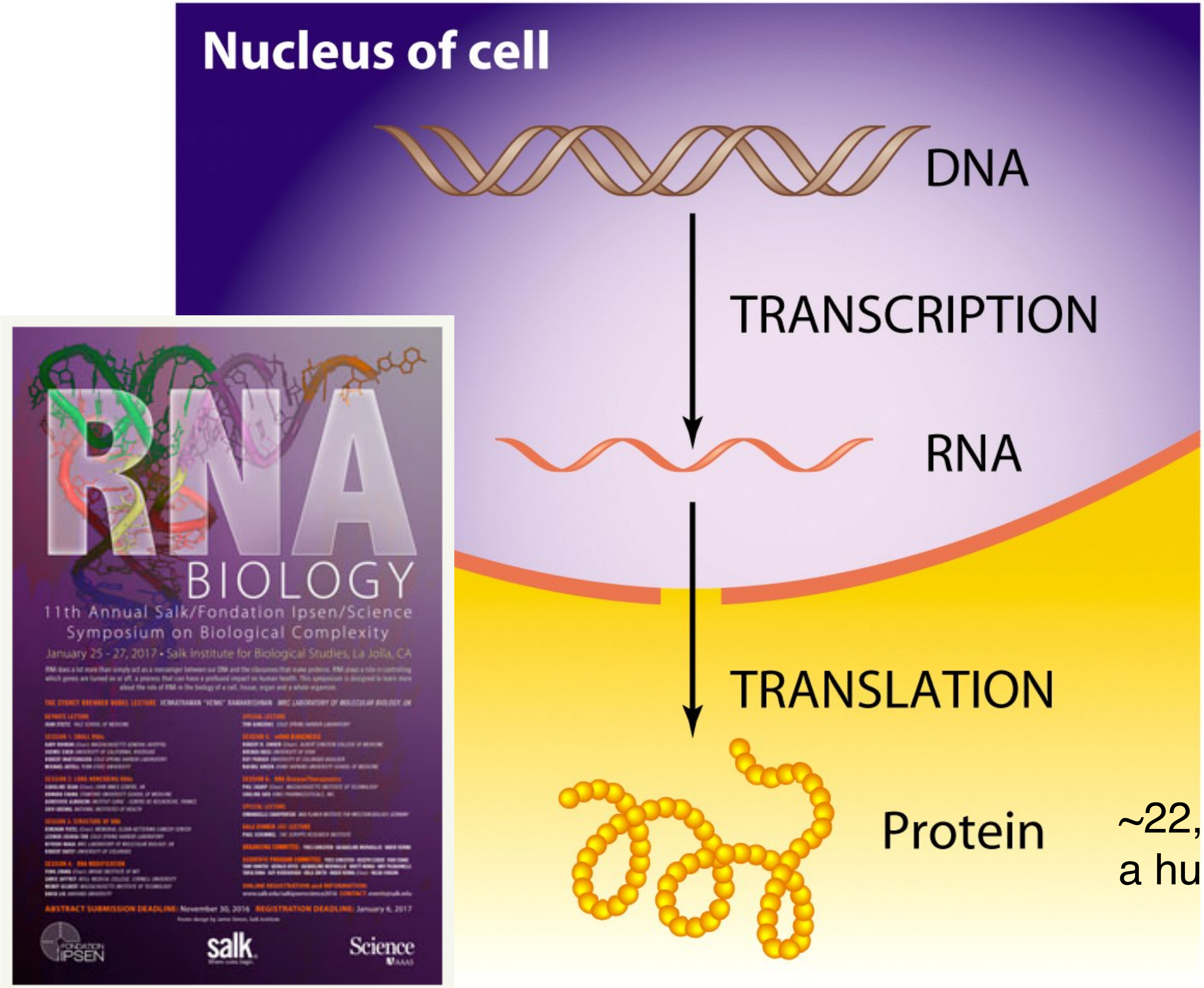




Protein Biosynthesis



https://www.dnalc.org/resources/3d/09-how-much-dna-codes-for-protein.html



~22,000 define
a human

Central Dogma

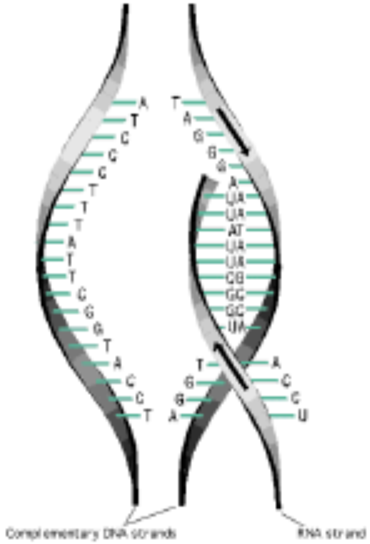
DNA

Transcription

mRNA

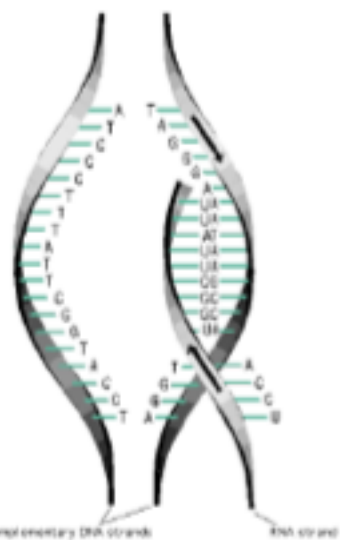
Translation

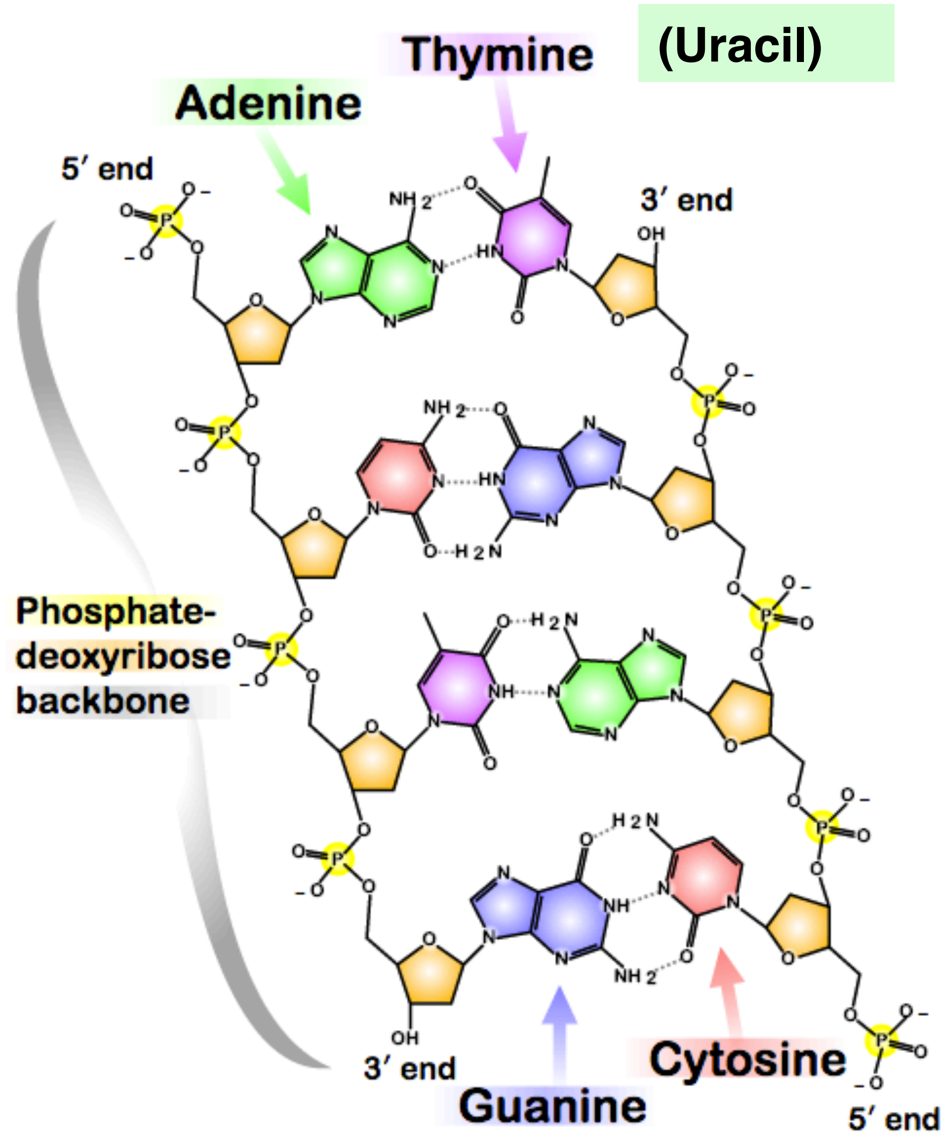
Protein



Amanda Ruby

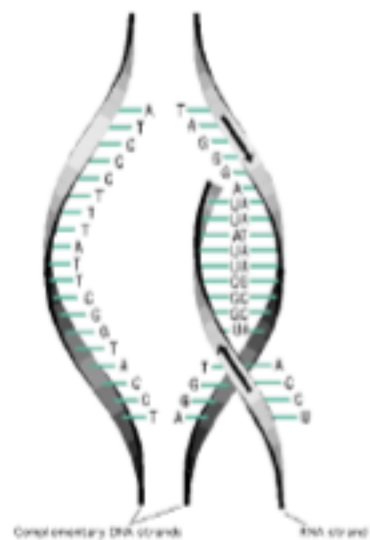
mRNA





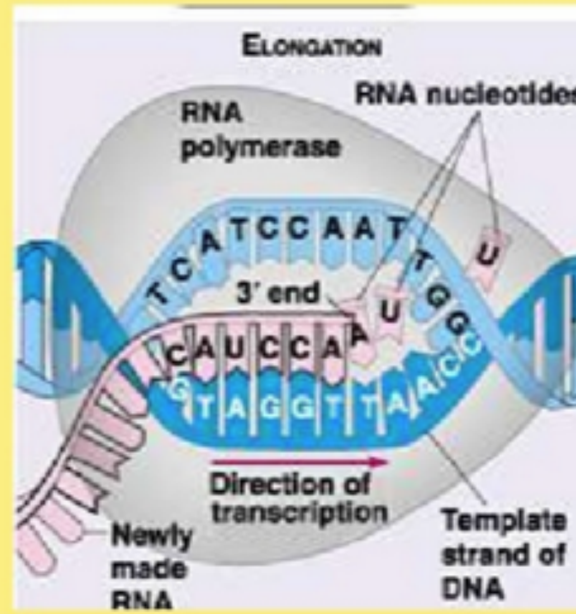
(Uracil)
Thymine
Adenine
5′ end
3′ end
Phosphate-
deoxyribose
backbone
3′ end
Cytosine
Guanine
5′ end

mRNA



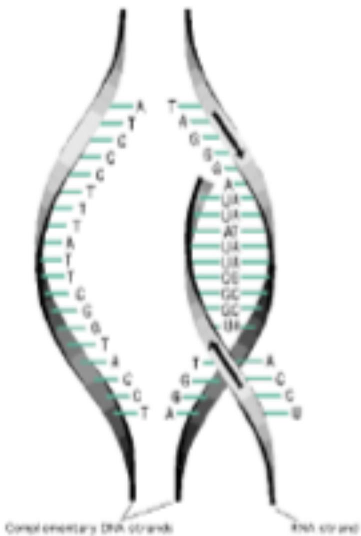
Sense vs. Antisense strands

- **Sense strand** - the “other” strand, not transcribed.
- **Antisense strand** - the one mRNA attaches to, and is complimentary to.
- mRNA is similar to the sense strand, except T→U.



Antisense DNA from the left: GTAGGT…
mRNA: CAUCCA…

mRNA



DNA	Coding Strand (Codons)	5' > > > - - - - - - - T T C - - - - - - - > > > 3'
	Template Strand (Anti-codons)	3' < < < - - - - - - - A A G - - - - - - - < < < 5'
mRNA	Message (Codons)	5' > > > - - - - - - - U U C - - - - - - - > > > 3'
tRNA	Tranfer (Anti-codons)	3' < < < A A G < < < 5'
Protein	Amino Acid	**Amino** > > > Phenylalanine > > > **Carboxy**

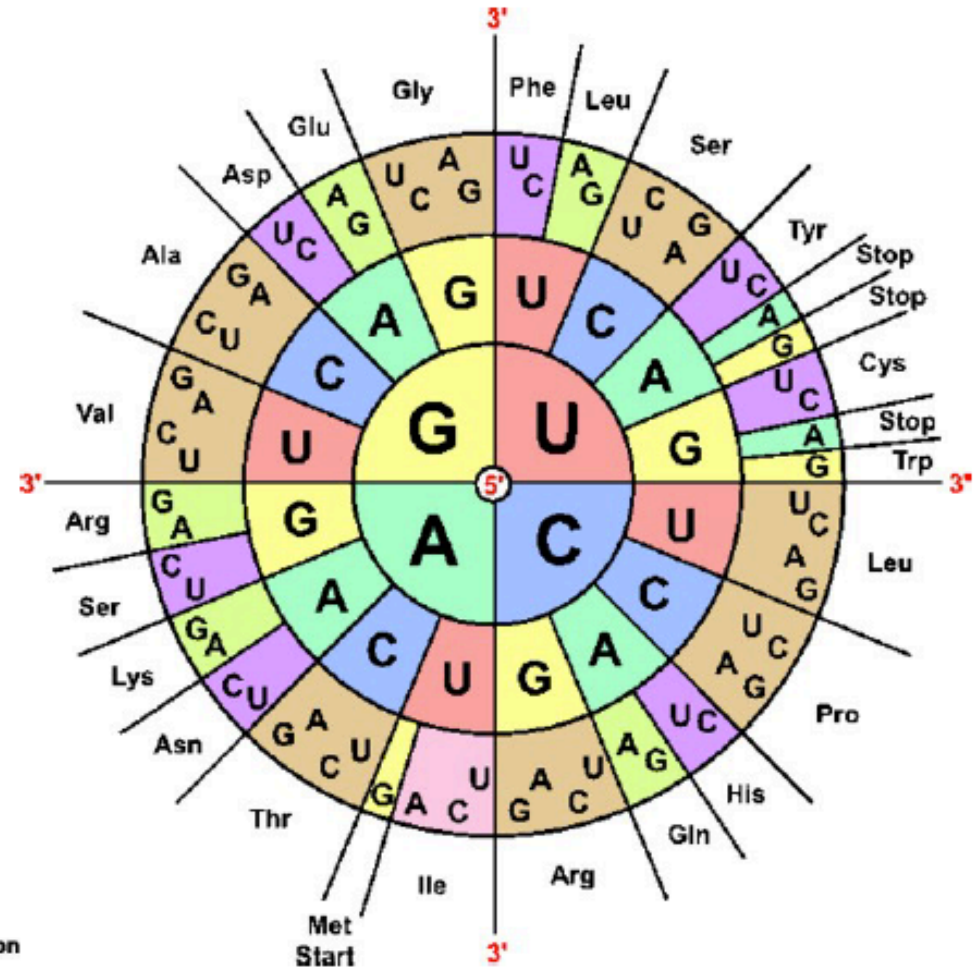
Coding Strand = Antisense strand: TTC
Anti-coding = Sense strand
mRNA: UUC

Protein Biosynthesis

Codons

- mRNA is translated in "chunks" of three, called **codons**
- The starting nucleotide is determined using bioinformatics to find the **reading frame**
- The genetic code is **degenerate**

(similar, but not identical)



5' AUG CAA CCC GAC UCC AGC 3' ← Codon

3' UAC GUU GGG CUG AGG UAG 5' ← AntiCodon

Met--Gln---Pro---Asp--Phe--Ser ← Amino Acids

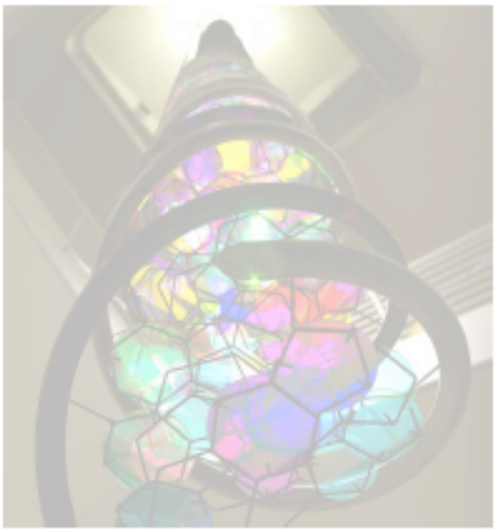
Protein Biosynthesis

Codon Chart

Second Letter

1st letter	U		C		A		G		3rd letter
U	UUU	Phe	UCU		UAU	Tyr	UGU	Cys	U
	UUC		UCC	Ser	UAC		UGC		C
	UUA	Leu	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp	G
C	CUU		CCU		CAU	His	CGU		U
	CUC	Leu	CCC	Pro	CAC		CGC	Arg	C
	CUA		CCA		CAA	Gln	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU		ACU		AAU	Asn	AGU	Ser	U
	AUC	Ile	ACC	Thr	AAC		AGC		C
	AUA		ACA		AAA	Lys	AGA	Arg	A
	AUG	Met	ACG		AAG		AGG		G
G	GUU		GCU		GAU	Asp	GGU		U
	GUC	Val	GCC	Ala	GAC		GGC	Gly	C
	GUA		GCA		GAA	Glu	GGA		A
	GUG		GCG		GAG		GGG		G

Central Dogma



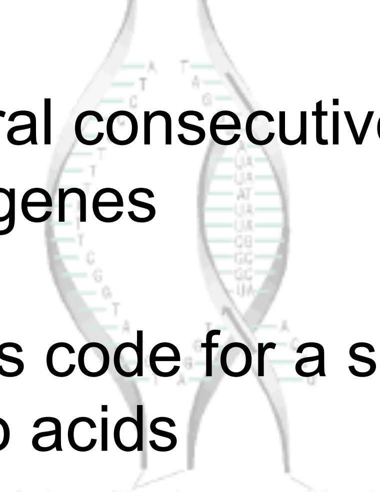
Several nucleic acids linked together form DNA

Three nucleic acids in a row form a codon, which codes for different amino acids

Several consecutive codons form genes

Genes code for a sequence of amino acids

Several amino acids linked together form proteins

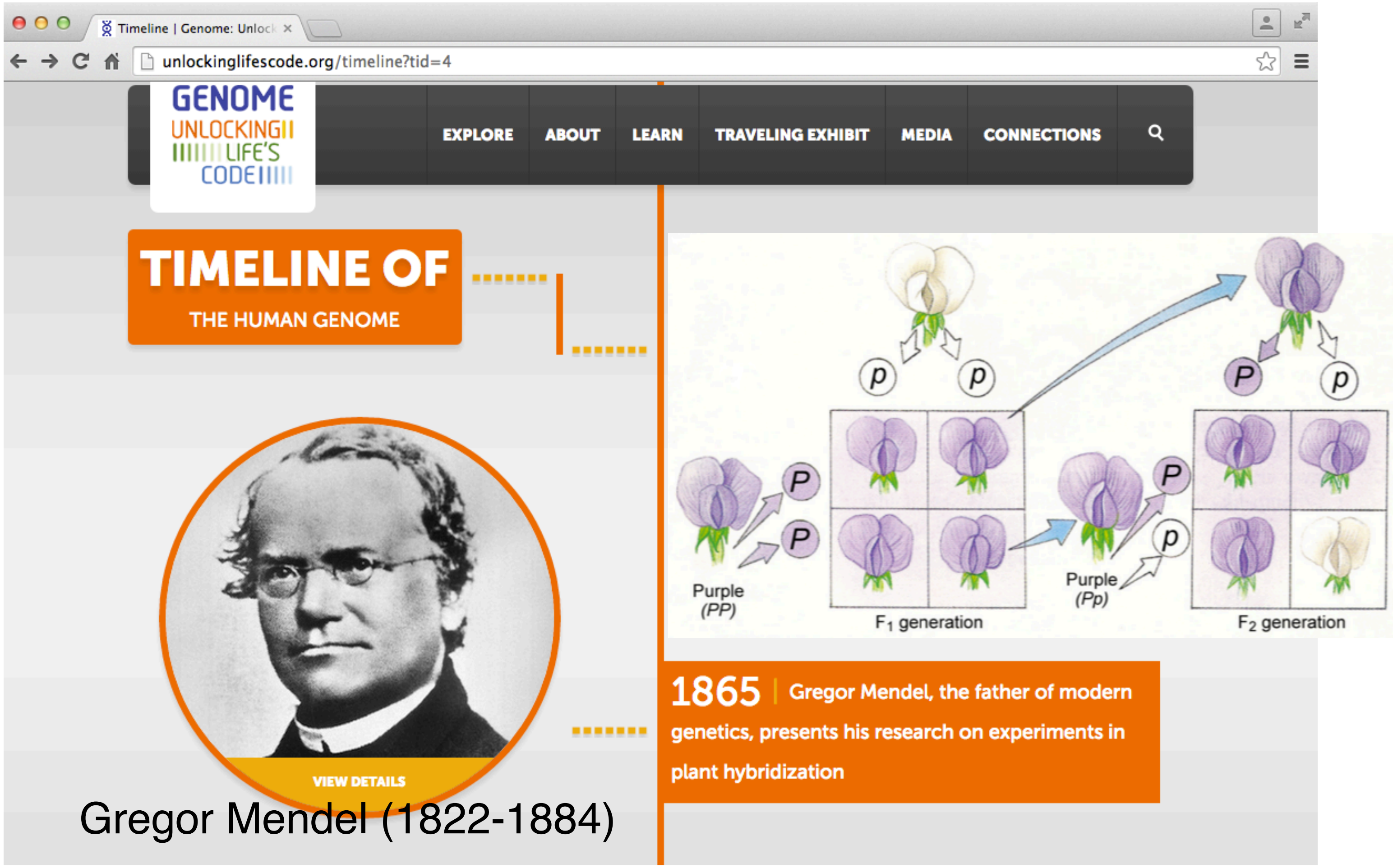


~22,000 define a human

1865

DNA: Genetics & Genomics

Timelines



Gregor Mendel (1822-1884)

https://www2.edc.org/weblabs/Mendel/MendelMenu.html

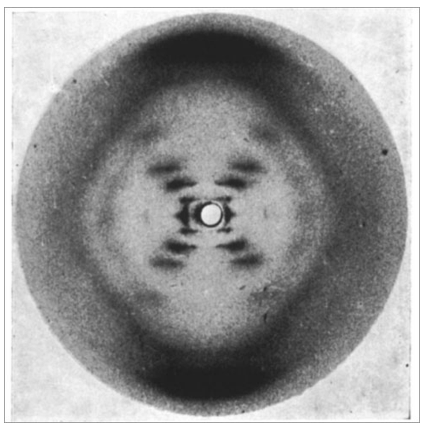
1953

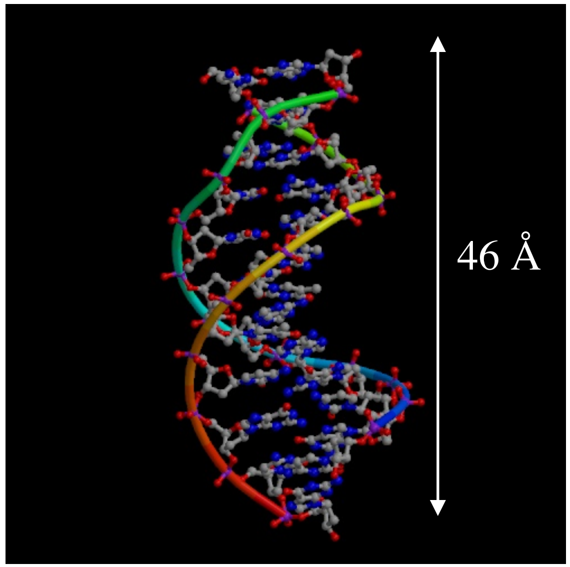
DNA: Molecular Discovery

X-Ray Crystal Structure

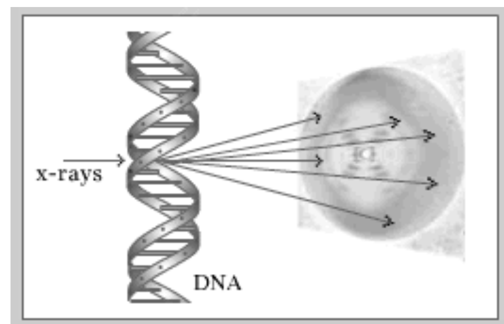
http://info.bio.cmu.edu/courses/03231/ProtStruc/ProtStruc.htm

β-DNA: Rosalind Franklin





12 base sequence



http://molvis.sdsc.edu/pdb/dna_b_form.pdb equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

[2] Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1920).
[3] Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 285 (1949).
[4] Von Arx, W. S., Woods Hole Papers in Phys. Oceanog. Meteor., **11** (3) (1950).
[5] Ekman, V. W., *Arkiv. Mat. Astron. Fysik.* (Stockholm), **2** (11) (1905).

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

We wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three inter-twined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

This figure is purely diagrammatic. The two ribbons symbolize the two phosphate—sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3′,5′ linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There is a residue on each chain every 3·4 A. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 A. The distance of a phosphorus atom from the fibre axis is 10 A. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data[5,6] on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereo-chemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

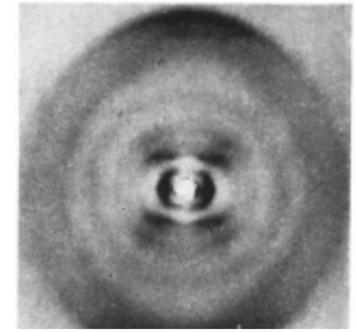
We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on inter-atomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at

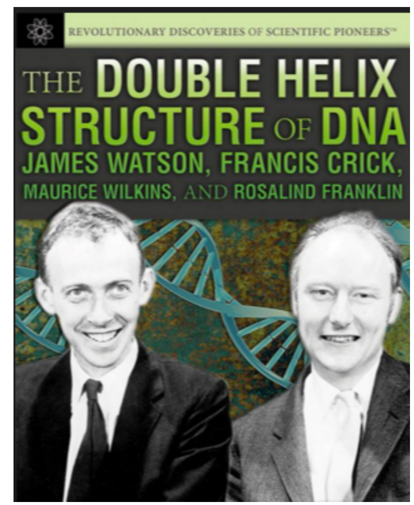
King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. Watson
F. H. C. Crick

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.

[1] Pauling, L., and Corey, R. B., *Nature*, **171**, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, **39**, 84 (1953).
[2] Furberg, S., *Acta Chem. Scand.*, **6**, 634 (1952).
[3] Chargaff, E., for references see Zamenhof, S., Brawerman, G., and Chargaff, E., *Biochim. et Biophys. Acta*, **9**, 402 (1952).
[4] Wyatt, G. R., *J. Gen. Physiol.*, **36**, 201 (1952).
[5] Astbury, W. T., Symp. Soc. Exp. Biol. 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).
[6] Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, **10**, 192 (1953).



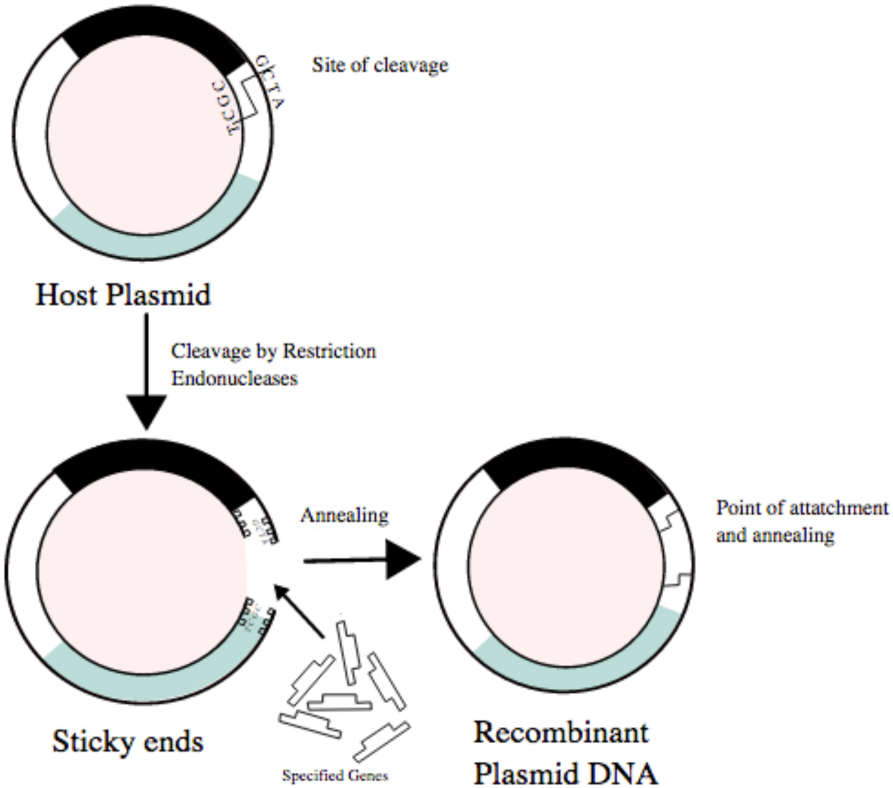


1975

Restriction Enzymes / Recombinant DNA

Berg, Boyer, Cohen, and many others

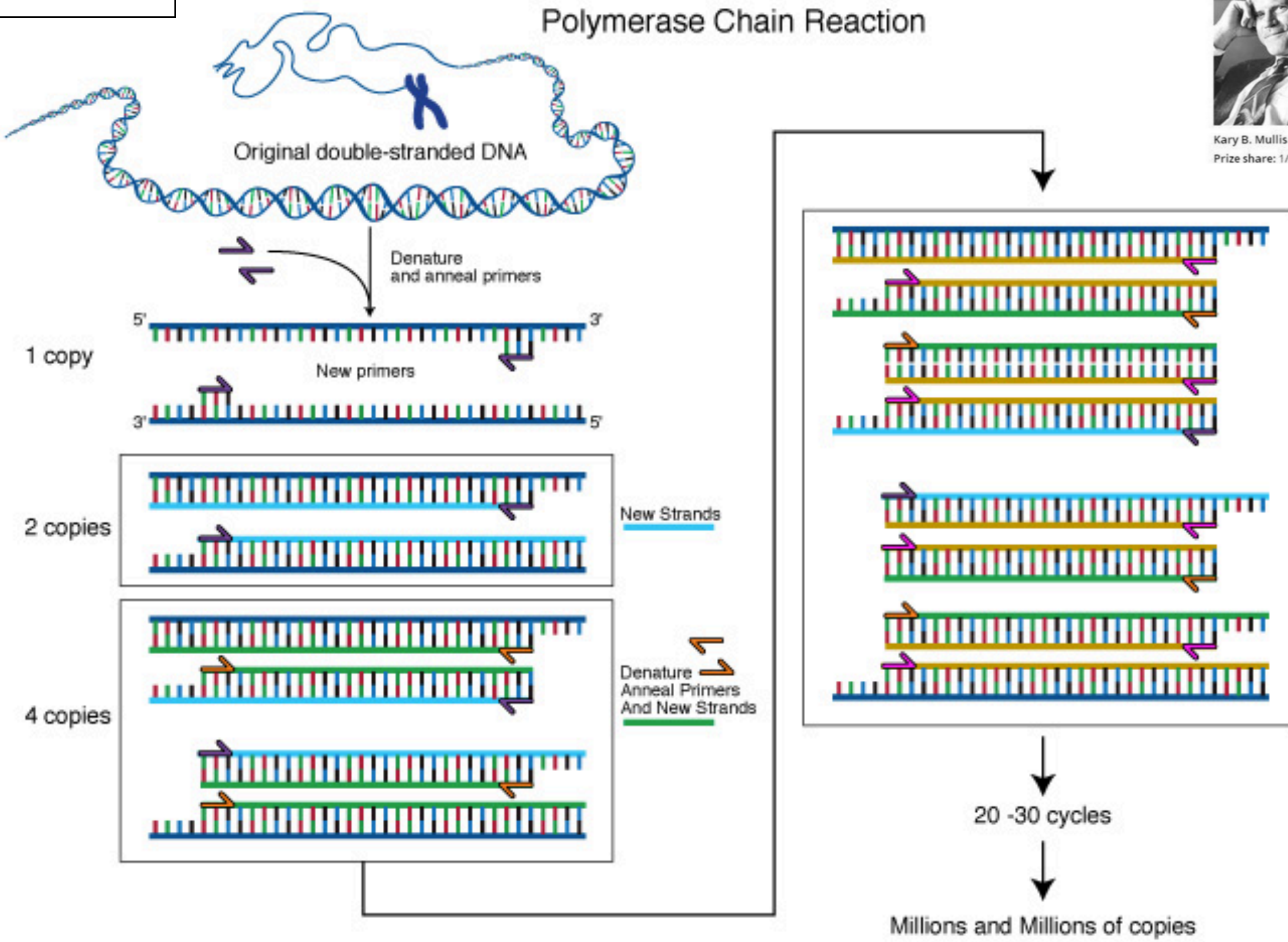
http://nar.oxfordjournals.org/content/early/2013/10/18/nar.gkt990.full



1989

PCR: Polymerase Chain Reaction

Kary Mullis, Cetus-Chiron-Roche, Emeryville



The Nobel Prize in Chemistry 1993

Kary B. Mullis
Prize share: 1/2

Michael Smith
Prize share: 1/2

https://www.dnalc.org/resources/3d/19-polymerase-chain-reaction.html

Start

The Human Genome Project:
Exploring our Molecular Selves.

3D Animation

DYNAMIC TIMELINE | QUICK SEARCH

EXIT

BACK | MORE INFORMATION | MORE ON THIS YEAR

Roger Salquist Chairman CEO Calgene

1994 FLAVR SAVR tomato

The FDA approved the sale of the first genetically modified food — the FLAVR SAVR tomato, deeming it as safe as conventionally-bred tomatoes.

The FDA's decision on the FLAVR SAVR tomato — marketed by Calgene, Inc. of Davis, California — marked the first time the agency evaluated a food that was genetically engineered. FLAVR SAVR tomatoes are modified to stay firm after harvest, so they can be left on the vine longer before shipping. The FDA decided the change in the tomatoes was not great enough to warrant mandated labeling describing the alteration.

Genes, Variation & Human History | The Future of Research & Medicine | How to Sequence a Genome | ELSI | Glossary

1995

Genetic Fingerprinting

Blood on glove found on Simpson's property appeared to contain genetic markers of Simpson and both victims.

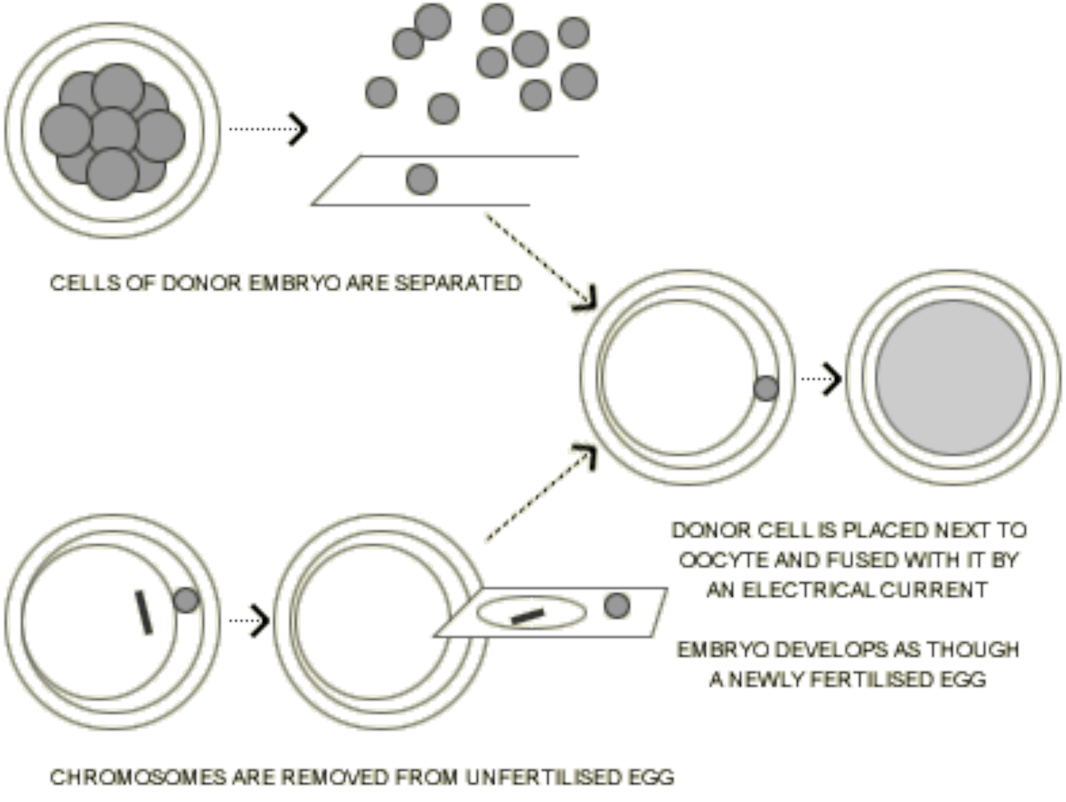
OJ Simpson and the bloody glove.

http://www.genome.gov/25019879
http://unlockinglifescode.org/timeline?tid=4

1996

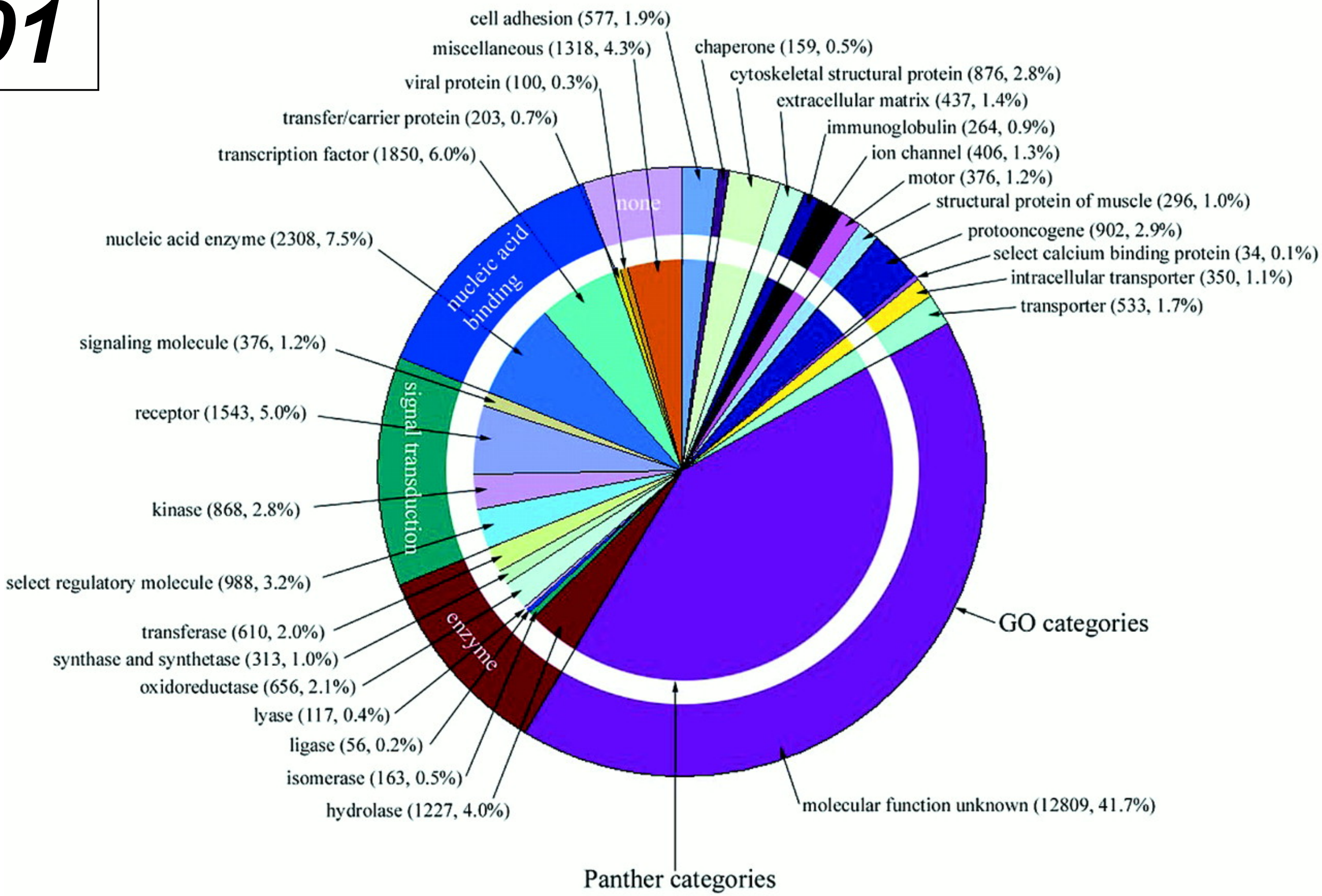
CLONING

Hello
Dolly!



Human Genome: Distribution of the molecular functions of 26,383 human genes.

2001

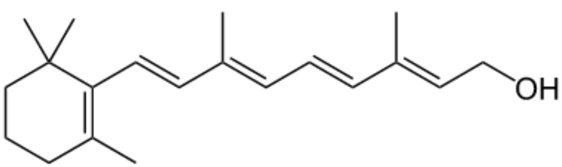


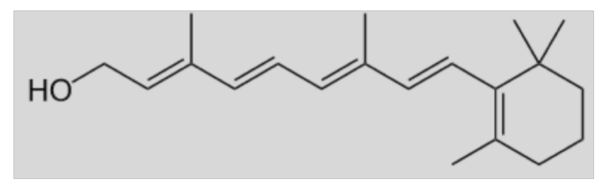
J. Craig Venter et al. Science 2001;291:1304-1351

2001

Golden Rice

http://www.goldenrice.org/





Hunan Study 2008

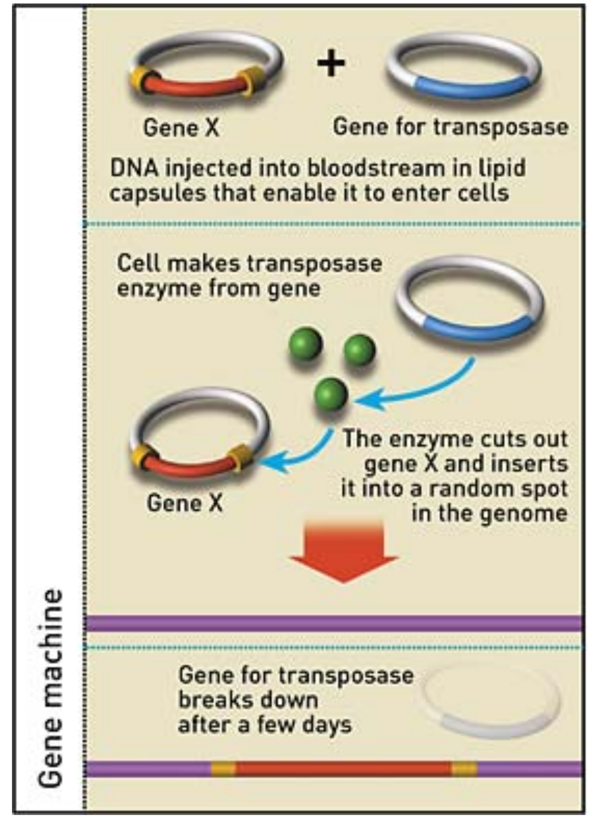
Golden Rice Paper 2012

Patents for Humanity Awards 2015

http://news.sciencemag.org/asiapacific/2013/09/golden-rice-not-so-golden-tufts

Transgenic Crops

Genetically Modified Organisms (GMOs)



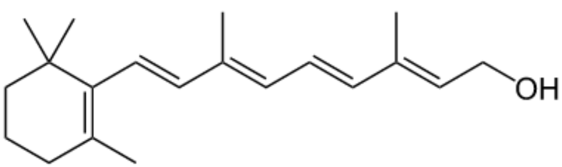
http://www.greenpeace.org/international/Global/international/publications/agriculture/2013/458%20-%20Golden%20Illusion-GE-goldenrice.pdf

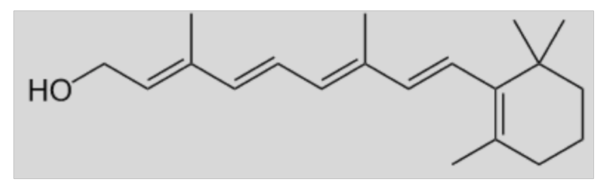
http://www.i-sis.org.uk/rice.php

2015

Golden Rice

http://www.goldenrice.org/





Hunan Study 2008

WITHDRAWN July 2015

Patents for Humanity Awards 2015

http://news.sciencemag.org/asiapacific/2013/09/golden-rice-not-so-golden-tufts

The American Journal of CLINICAL NUTRITION

« Previous | Next Article »
Table of Contents

β-Carotene in Golden Rice is as good as β-carotene in oil at providing vitamin A to children[1,2,3,4]

This Article
First published August 1, 2012, doi: 10.3945/ajcn.111.030775

WITHDRAWN:

For lack of evidence that all human participants provided full consent

supported

by Massachusettes Court (August 3, 2015)

(0.3 mg), GR β-carotene (0.6 mg), and spinach β-carotene (1.4 mg) to retinol were 2.0, 2.3, and 7.5 to 1 by weight, respectively.

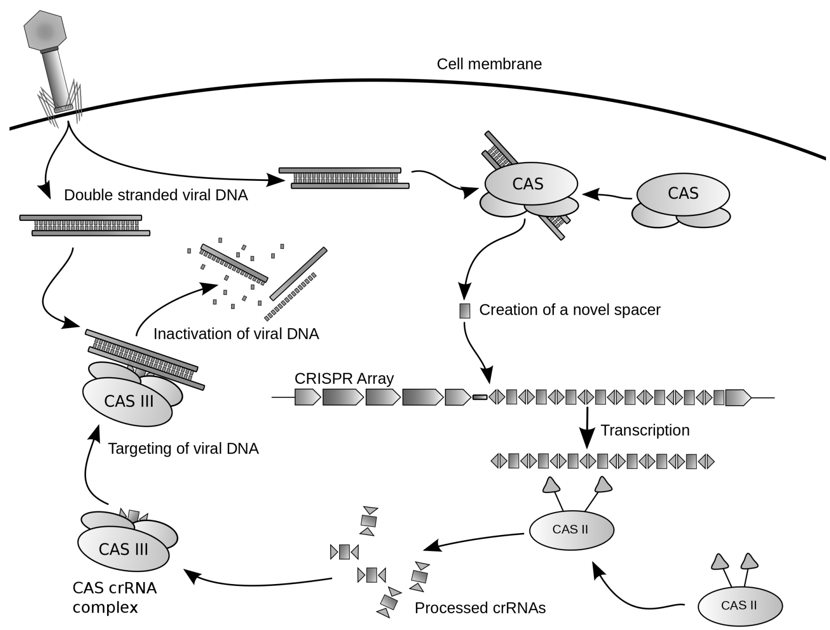
Conclusions: The β-carotene in GR is as effective as pure β-carotene in oil and better than that in spinach at providing vitamin A to children. A bowl of ~100 to 150 g cooked GR (50 g dry weight) can provide ~60% of the Chinese Recommended Nutrient Intake of vitamin A for 6-8-y-old children. This trial was registered at www.clinicaltrials.gov as NCT00680212.

+ Google Scholar
+ PubMed
+ Agricola
− Social Bookmarking

2012

Genome Editing / CRISPR-Cas9

https://www.youtube.com/watch?v=2pp17E4E-O8
https://www.youtube.com/watch?v=SuAxDVBt7kQ

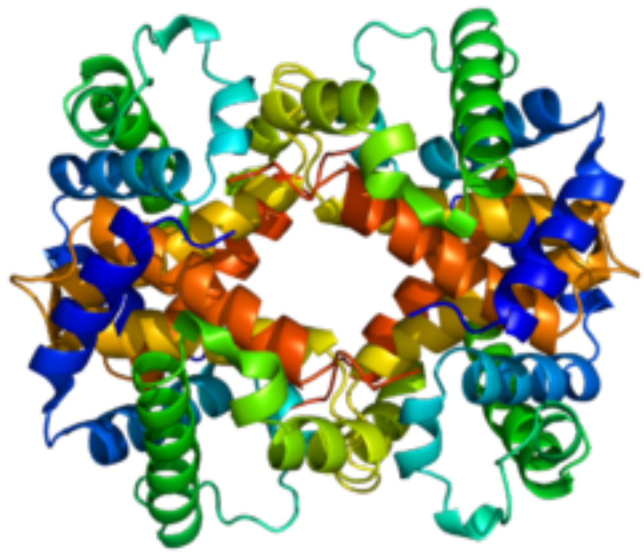


2016

Genome Editing / CRISPR-Cas9

Target

β-Thalassemia: Shortage of β-globin Protein



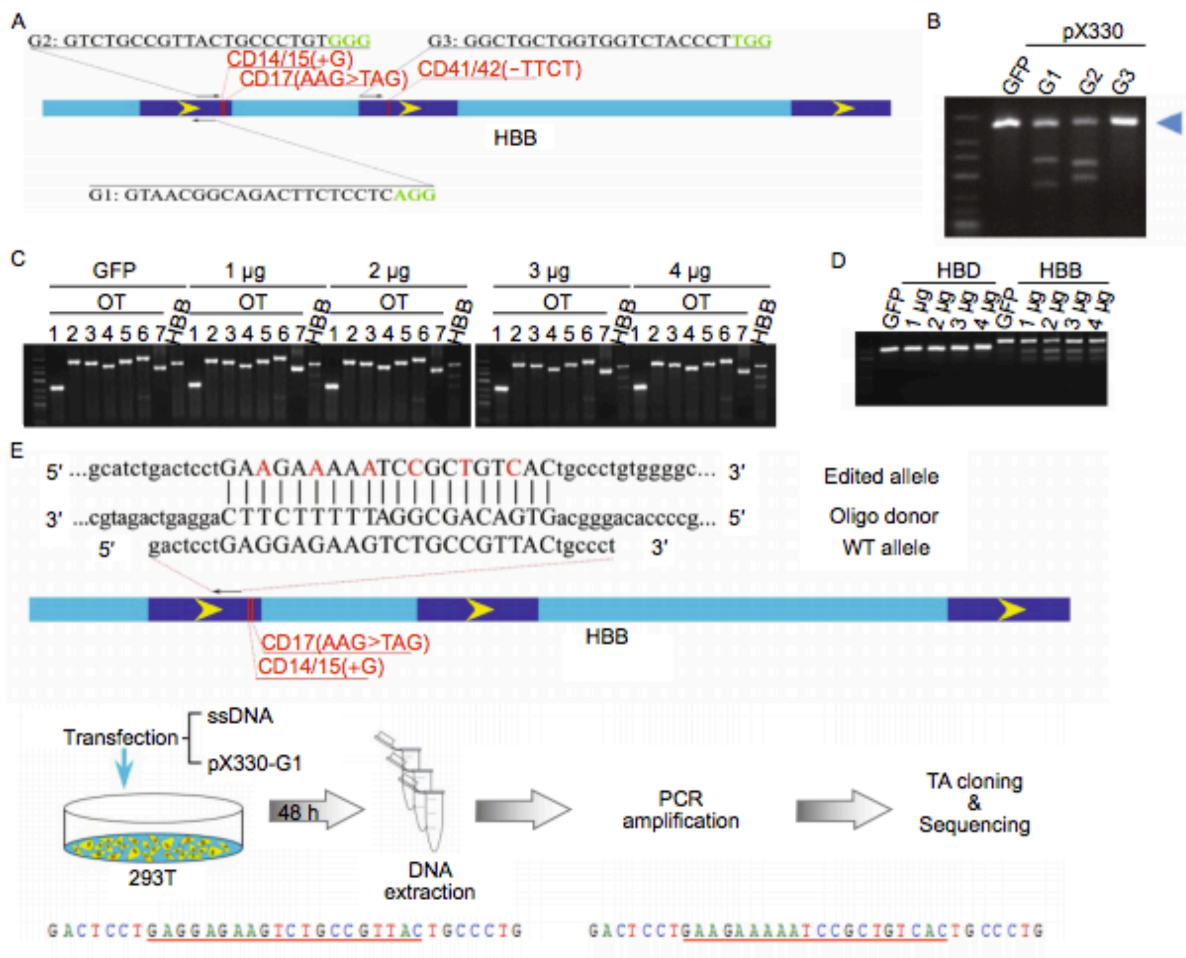
Normal β-globin

https://www.dnalc.org/resources/3d/17-sickle-cell.html

2016

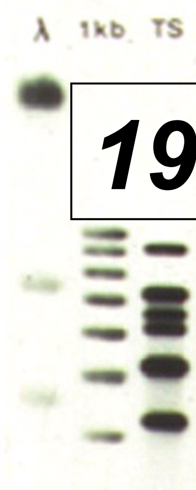
Genome Editing / CRISPR-Cas9
β-Thalassemia / Human Embryo Research

http://chemconnections.org/general/chem121/Gene%20Editing/Gene%20Editing%202015-0153.pdf



Protein & Cell

Genetic Fingerprinting

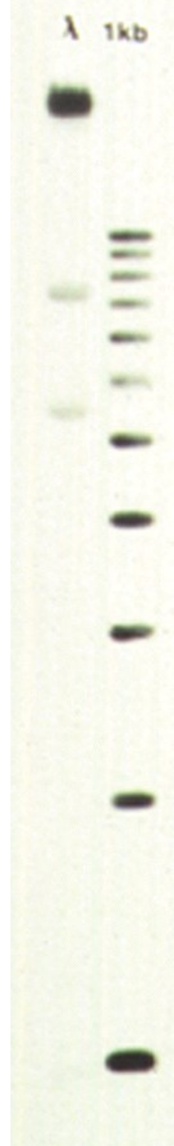


1985

500
nanograms
Amount of DNA needed for fingerprinting when the technique was first published in 1985. It corresponds to about one drop of blood or 100,000 cells.

WHEN DNA IS LYING

0.1
nanogram
The amount that, in some cases, suffices today. It corresponds to about 20 cells, a number that could be found in a fingerprint.

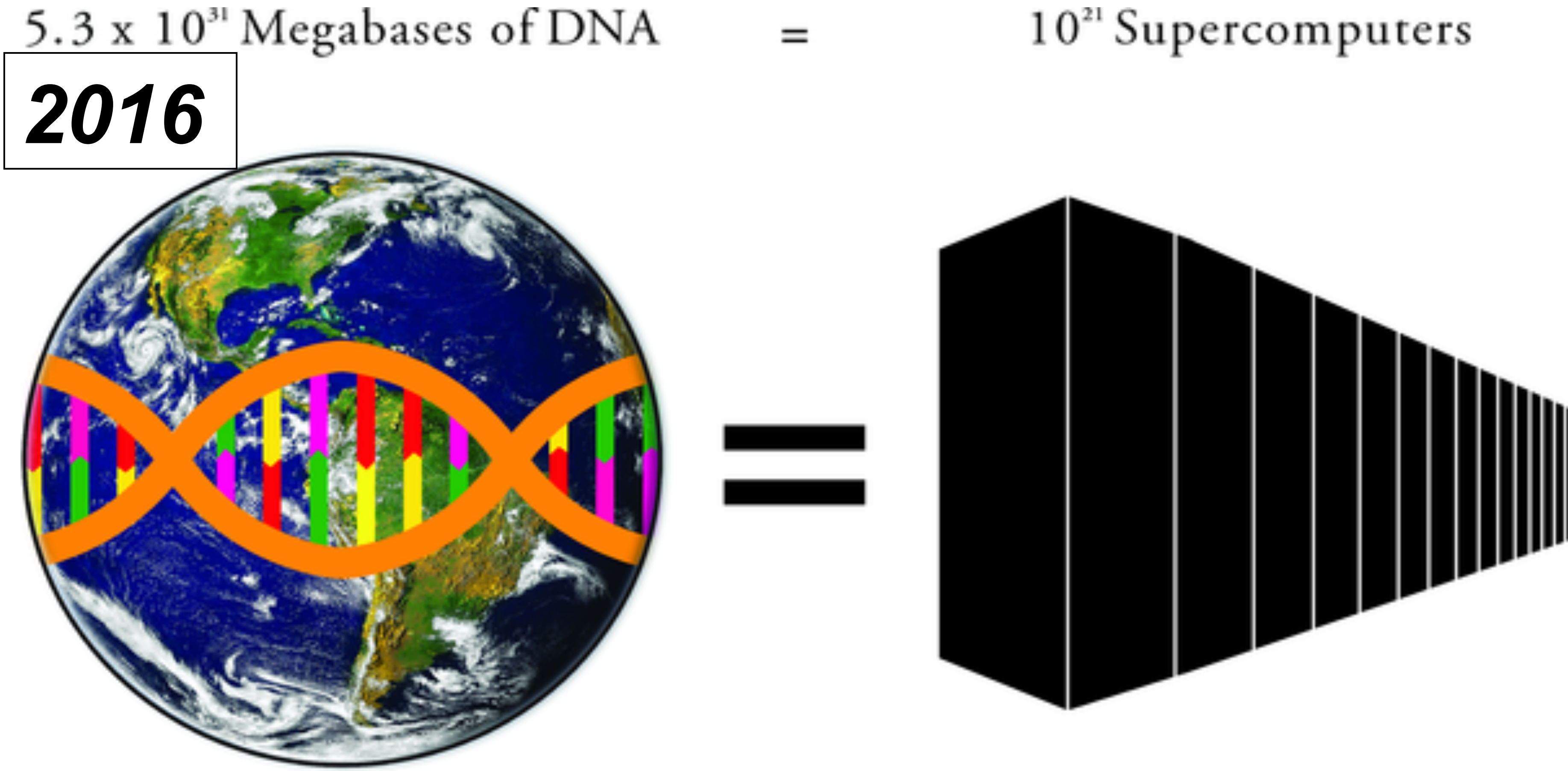


2016

- Forensics
- Paternity
- Military-ID
- Food
- Wine
- Anthropology
- Medical Diagnosis

http://science.sciencemag.org/content/sci/351/6278/1133.full.pdf

Fig 1. Storing the total amount of information encoded in DNA in the biosphere, 5.3 × 1031 megabases (Mb), would require approximately 1021 supercomputers with the average storage capacity of the world's four most powerful supercomputers.



http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1002168#pbio-1002168-g001

Landenmark HKE, Forgan DH, Cockell CS (2015) An Estimate of the Total DNA in the Biosphere. PLoS Biol 13(6): e1002168. doi:10.1371/journal.pbio.1002168
http://127.0.0.1:8081/plosbiology/article?id=info:doi/10.1371/journal.pbio.1002168

PLOS | BIOLOGY

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Table 1. The total DNA content in the biosphere

	DNA amount (Mb)
Prokaryotes	$1.6 (1.1) \times 10^{31}$
Unicellular eukaryotes	$1.3 (0.9) \times 10^{29}$
Fungi	$1.7 (3.4) \times 10^{27}$
Animals	$4.2 (1.5) \times 10^{29}$
Plants	$3.6 (3.4) \times 10^{31}$
Viruses	$4.0 (3.4) \times 10^{29}$
Total	$\mathbf{5.3 (3.6) \times 10^{31}}$

doi:10.1371/journal.pbio.1002168.t001

Landenmark HKE, Forgan DH, Cockell CS (2015) An Estimate of the Total DNA in the Biosphere. PLoS Biol 13(6): e1002168. doi:10.1371/journal.pbio.1002168
http://127.0.0.1:8081/plosbiology/article?id=info:doi/10.1371/journal.pbio.1002168

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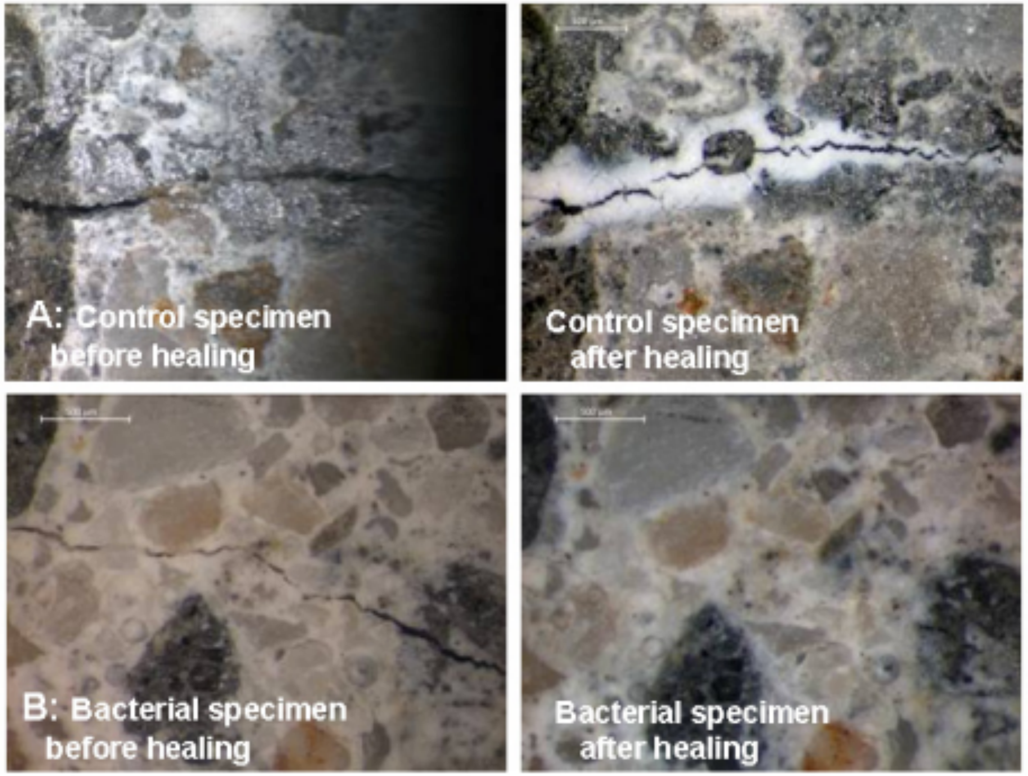
2016

Bioengineering: Structural Materials & Molecules

Bacteria & Yeast

Healing Concrete

http://heronjournal.nl/56-12/1.pdf



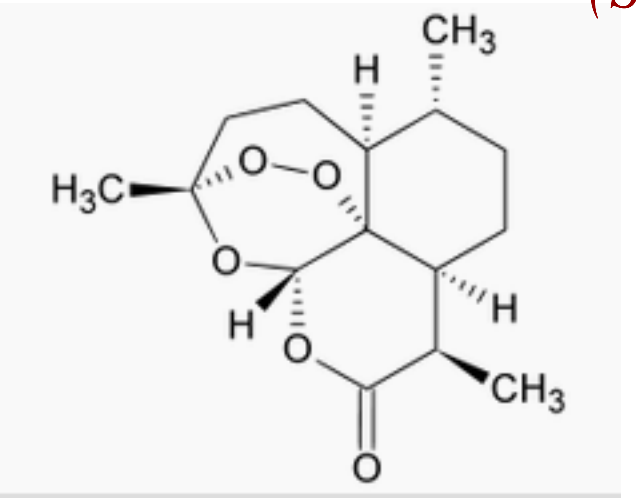
2017-2019

Bioengineering:

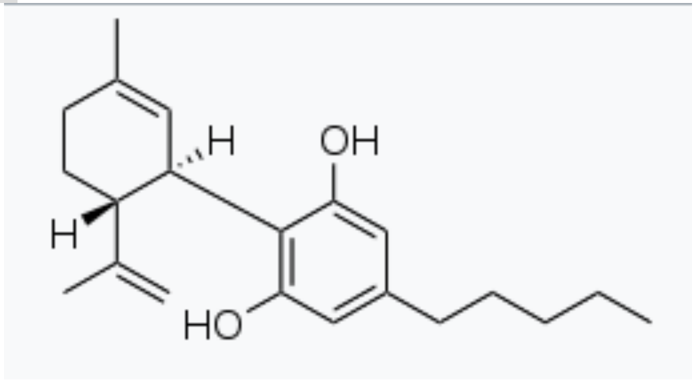
Bacteria, Yeast & Chemical Synthesis

Brewer's Yeast (Saccharomyces cerevisiae)

Chinese Wormwood (Artemisia annua)



anti-malarial



cannabadiol (CBD)