

# Welkom

bij HOVO Utrecht

Levenswetenschappen  
2025-2026



# leergang levenswetenschappen



Celbiologie (introductiecursus, najaar 2025)  
=> Hoe werkt leven?

Biotechnologie (voorjaar 2026)  
=> Het manipuleren van leven

Afweer (najaar 2026)  
=> hoe blijven we in leven

Ontwikkelingen (voorjaar 2027)  
Alles wat relevant is voor de levenswetenschappen



=> Wat is leven?

## Vervolgcurcus

## Biotechnologie.



DNA/RNA-technologie

=> Gentherapie/mRNA therapie

Afweersysteem

=> Immunotherapie

Stamcellen

=> Stamceltherapie

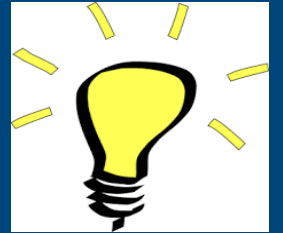
Cybernetica

=> Verbeteren (integratie technologie en biologie)

Synthetic biology

=> Wat is leven?

# Introductie: Dr. Ruud Licht



- Medisch-Bioloog (Universiteit van Amsterdam)
- Doctor in de Celbiologie (Radboud Universiteit Nijmegen)
- Meer dan 20 jaar onderzoek gedaan, bij verschillende universitaire centra
- Waaronder **UMC Utrecht**

⇒ **Stamcellen en gen-techniek** (Biotechnologie)

⇒ **Vaccins, auto-immuniteit** (Immunologie)

- Nu >10 jaar HOVO-docent (Brabant / Utrecht)

⇒ **Laborant** Covid / Long Covid Biobank (NMCB)

⇒ mantelzorger



<https://sciencelight.nl/>



## Science Light

Wetenschap, eenvoudig uitgelegd door Dr. R. Licht

[Celbiologie](#) [Biotechnologie](#) [Afweer](#) [Ontwikkelingen](#) [Video's](#) [Lichtpuntjes](#) [English](#)

## Hoi,

mei 10, 2020

17 reacties

Ik ben Dr. Ruud Licht, HOVO-docent

Klik op een menu hier boven voor links naar dia's van de praatjes voor het HOVO, en nog wat extra zaken.

U kunt mij ook een berichtje te sturen (hiernaast).

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### BERICHTEN

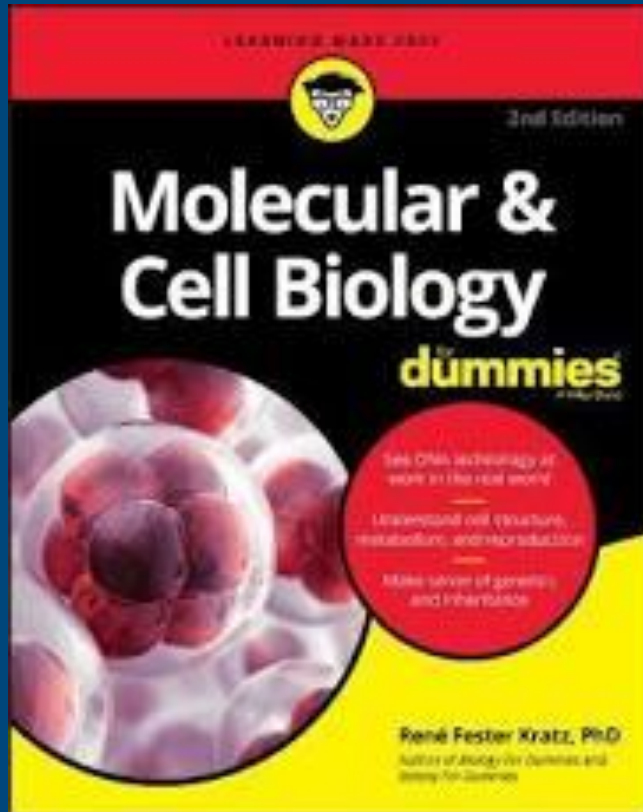
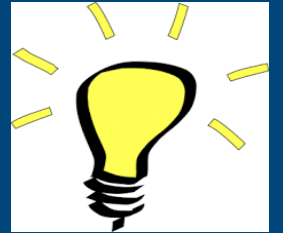
- [Hoi,](#)  
mei 10, 2020

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### REACTIES

- Cees Onderwater, Dordrecht op [Hoi,](#)
- Wim Iding op [Hoi,](#)

# Boek Celbio/**Biotech**



(Engels)

H.7 Informatie

(DNA/RNA)

H.11 Energie

(mitochondriën, quantumbiologie)

H.6 Biochemie

(atomen, lading, eiwitten, medicijnen)

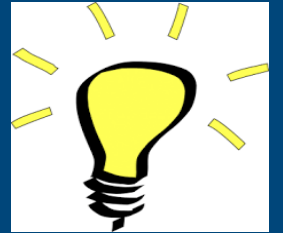
H.9 Communicatie

(samenwerking, ziekte)

**H.20 Genome editing**

## Vervolgcurcus

## Biotechnologie.



DNA/RNA-technologie

=> gentherapie/mRNA therapie

Afweersysteem

=> Immunotherapie

Stamcellen

=> stamceltherapie

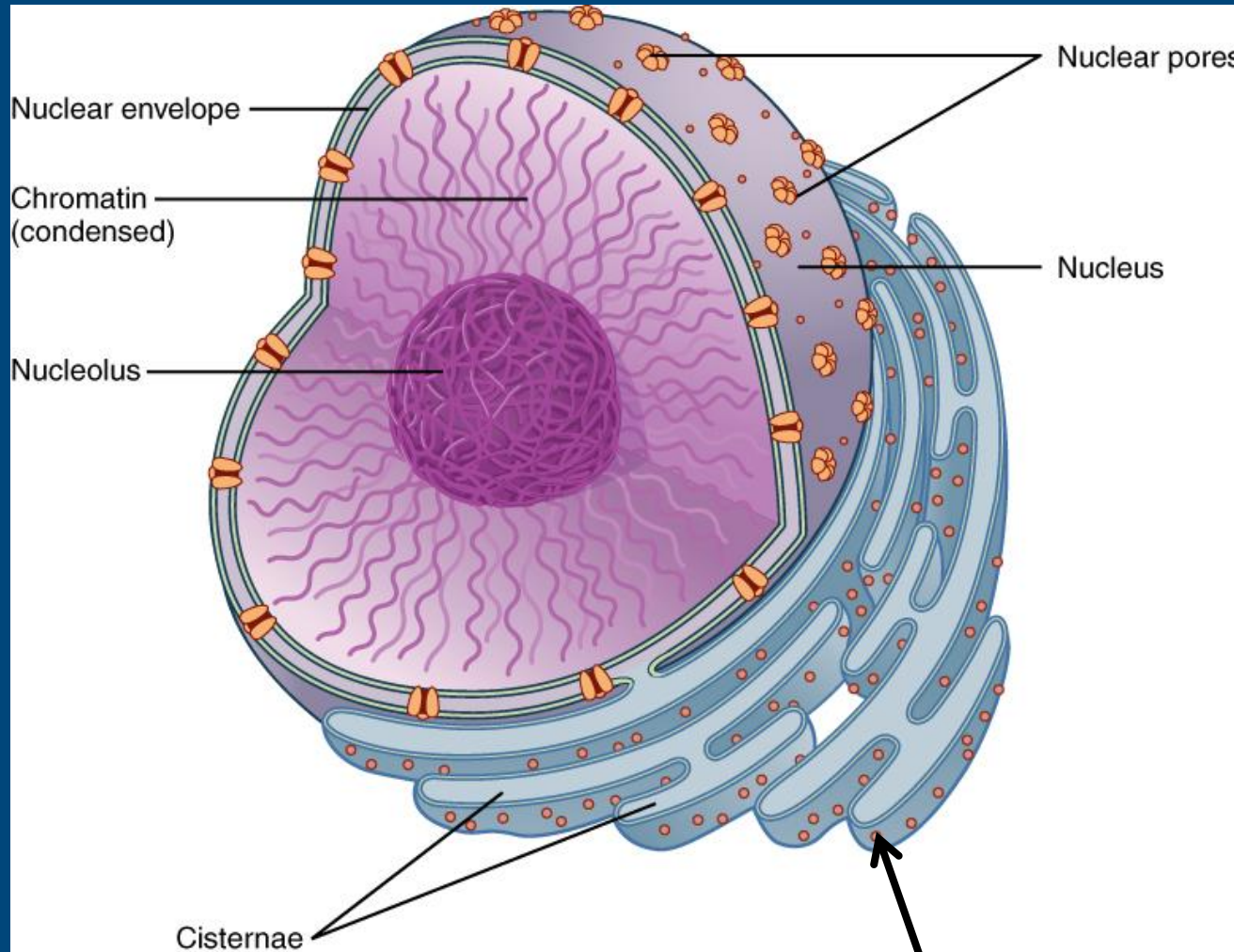
Cybernetica

=> verbeteren (integratie technologie en biologie)

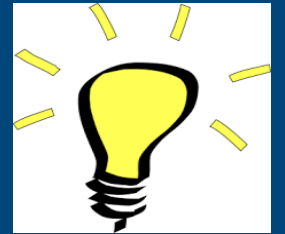
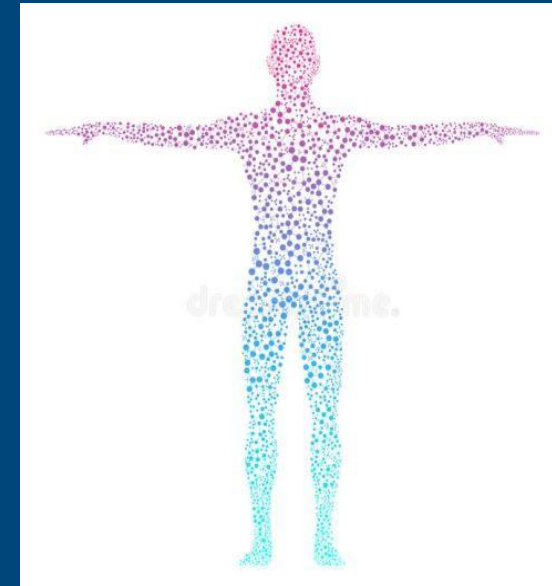
Synthetic biology

=> wat is leven?

# De celkern, met daarin DNA

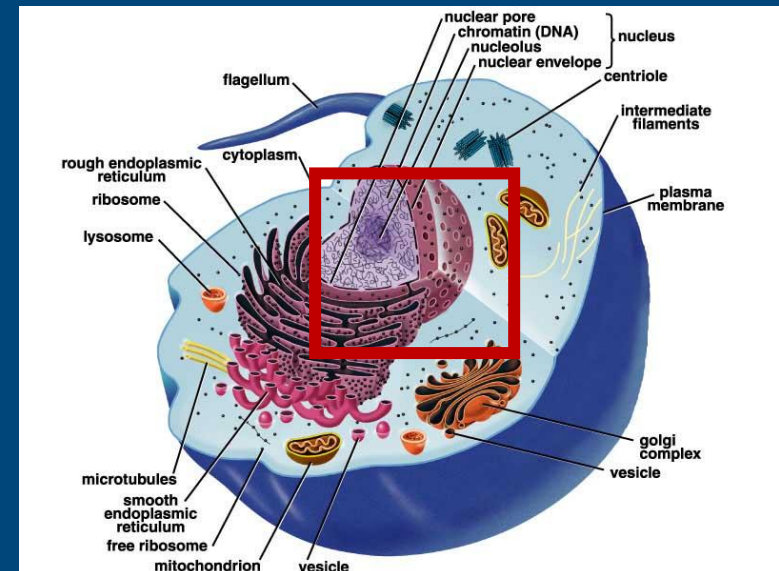


Ruw Endoplasmatisch Reticulum met ribosomen (mRNA => eiwit)

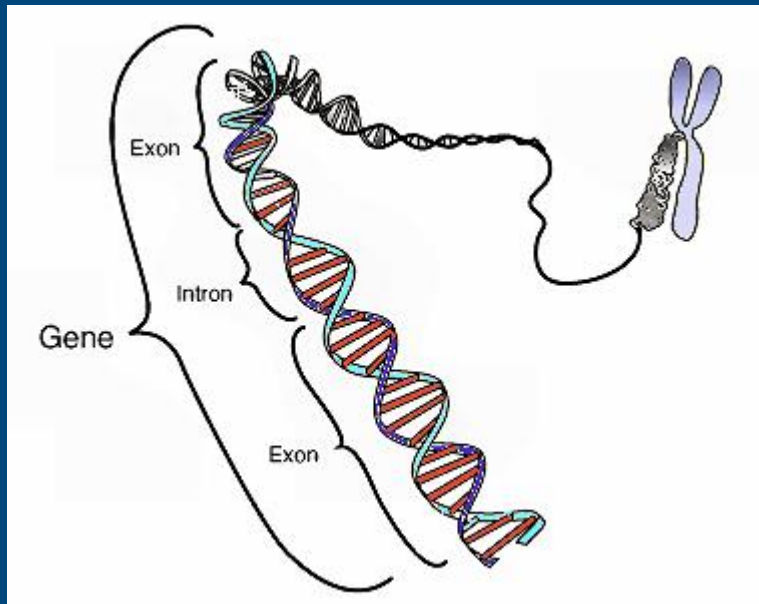
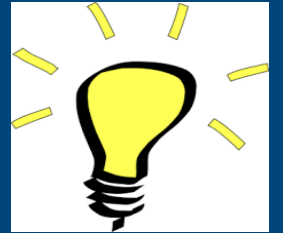


Leven bestaat uit cellen  
<https://youtu.be/SEejivHRIbE>

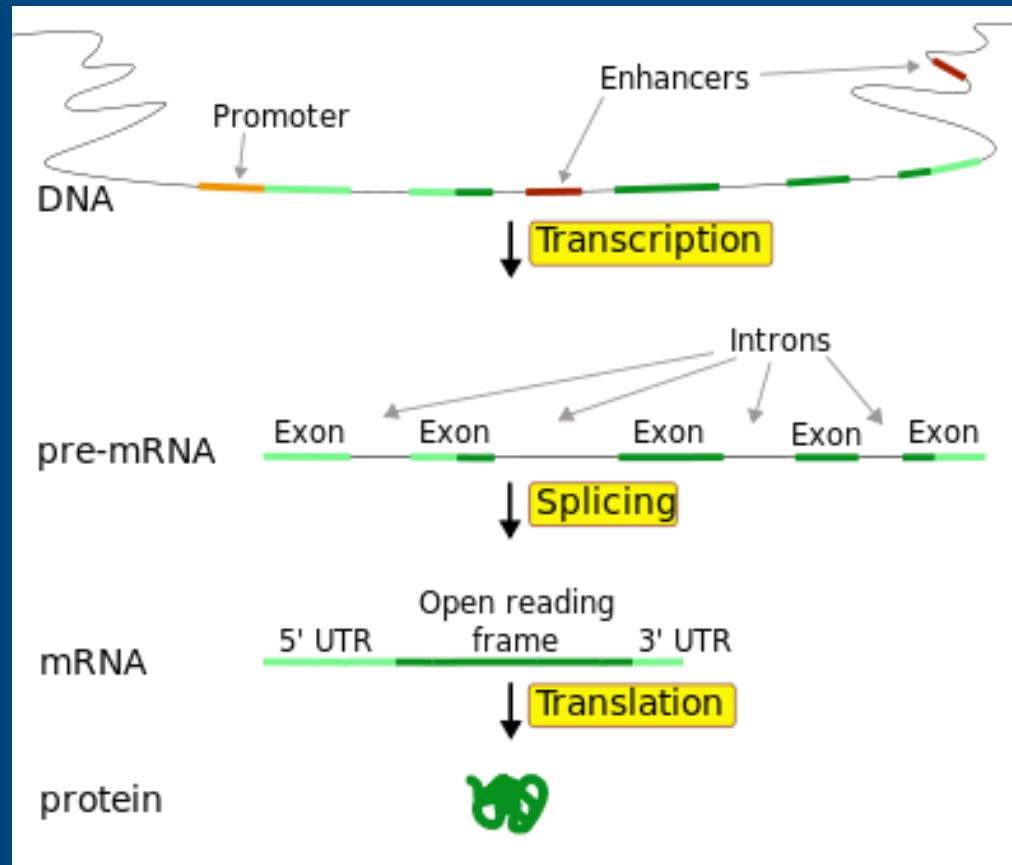
## Een (eukaryote) cel met celkern



Gen => RNA => Eiwit



Een gen produceert 2-30 mRNAs/uur



Gen

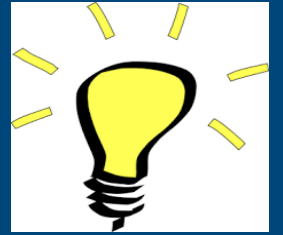
RNA

Eiwit

Watson, Crick, Franklin, Wilkins.

Central dogma of molecular biology

Gen => RNA => Eiwit  
filmpjes, **biologische nanotech**



<https://www.youtube.com/watch?v=nHM4UUVHPQM>

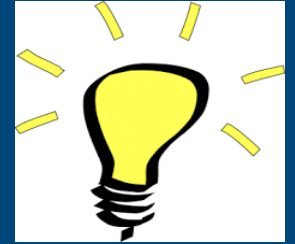
<https://www.youtube.com/watch?v=gG7uCskUOrA>

IKEA vergelijking:

DNA is de gebruiksaanwijzing (informatie),

Eiwitten vormen de kast (deze bouwen iets)

# DNA/RNA, de taal (**informatie**) van het leven



## DNA

Erfelijke eigenschappen

Toepassingen:

- Gentherapie
- Synthetische biologie

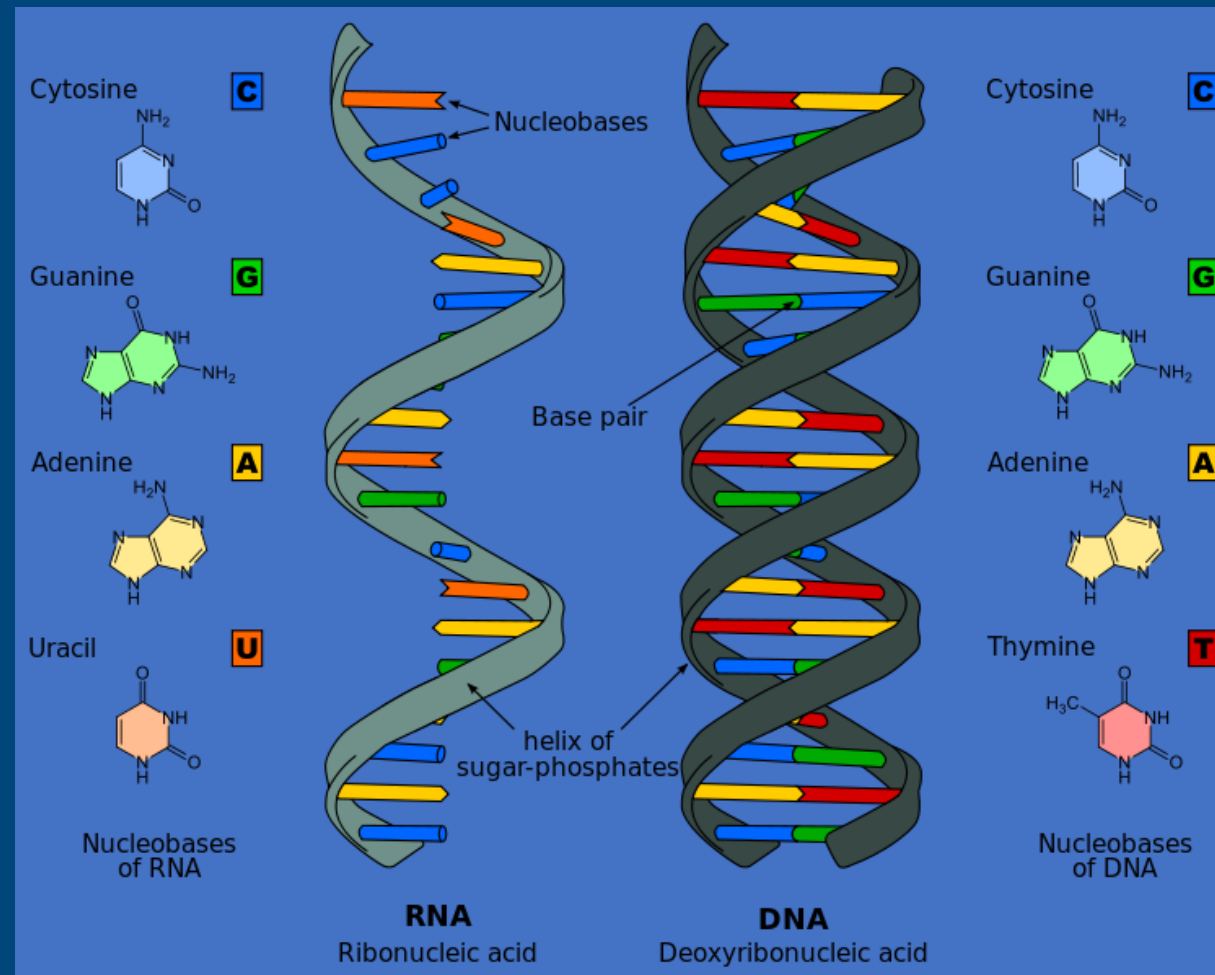
## RNA

Belangrijk regelsysteem

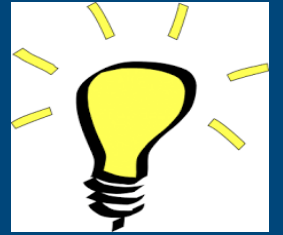
Epigenetica

Toepassingen:

- RNAi
- Stamcellen (iPS)
- mRNA vaccins



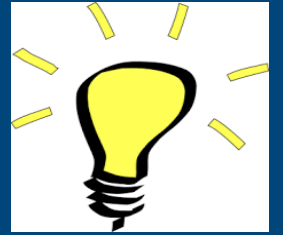
DNA is een code = informatie  
=> biologie wordt **informatie technologie**



- A/T/C/G
  - 20 aminozuren
  - 26 letters
  - 0/1
- DNA  
eiwit  
Nederlands  
binair (computer)

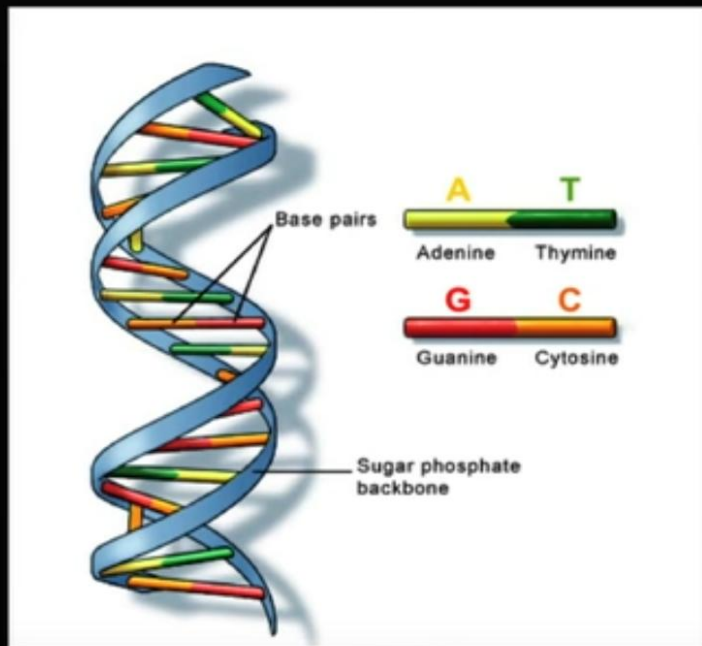
=> uitwisselbaar!

# Biologie wordt informatietechnologie !



TEDxCaltech - J. Craig Venter - Future Biology

## CONVERTING THE ANALOG GENETIC CODE INTO DIGITAL CODE



GENETIC CODE

**ATGAATTGACTTACCGTAGG**

COMPUTER BINARY CODE

```
01000001 01010100 01000111
01000001 01000001 01010100
01010100 01000011 01000111
01000001 01000011 01010100
01010100 01000001 01000011
01000011 01000111 01010100
01000001 01000111 01000111
```

U.S. National Library of Medicine

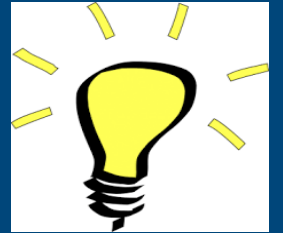
0:58 / 16:15

independently organized TED event

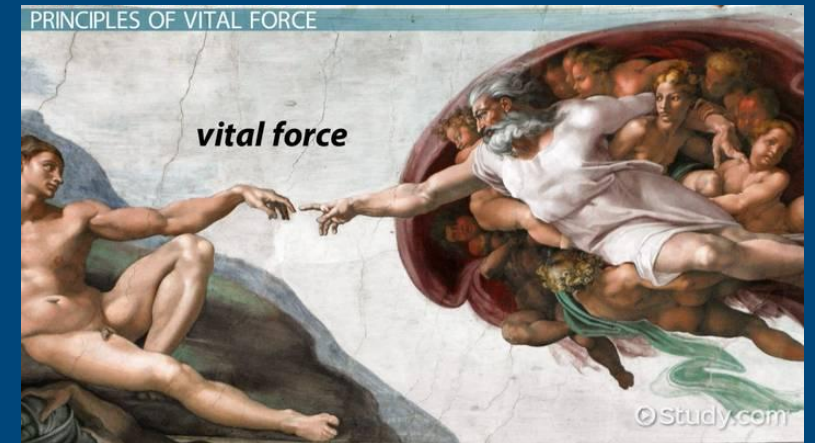
TEDxCaltech



# Vis Vitalis



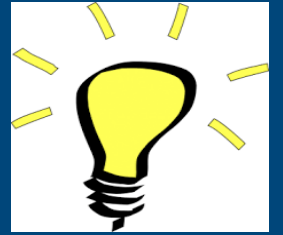
- **Vitalism** is an idea that living organisms are differentiated from the non-living by the presence of forces, properties or powers including those which may not be physical or chemical. Varied forms of vitalist theories were held in former times and they are now considered pseudoscientific concepts.<sup>[1][a]</sup> Where vitalism explicitly invokes a vital principle, that element is often referred to as the "vital spark", "energy", "élan vital" (coined by vitalist Henri Bergson), "vital force", or "***vis vitalis***", which some equate with the soul. In the 18th and 19th centuries, vitalism was discussed among biologists, between those belonging to the mechanistic school who felt that the known mechanics of physics would eventually explain the difference between life and non-life and vitalists who argued that the processes of life could not be reduced to a mechanistic process. Vitalist biologists such as Johannes Reinke proposed testable hypotheses meant to show inadequacies with mechanistic explanations, but their experiments failed to provide support for vitalism. Biologists now consider vitalism in this sense to have been refuted by empirical evidence, and hence regard it either as a superseded scientific theory,<sup>[4]</sup> or as a pseudoscience since the mid-20th century
- <https://en.wikipedia.org/wiki/Vitalism>



## Leven is..

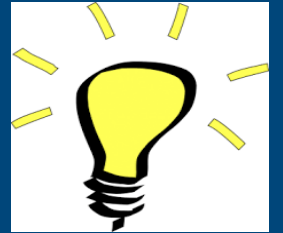
- Een informatie systeem

=> Manipuleerbaar met informatietechnologie (IT)



NB wordt lang lijstje..

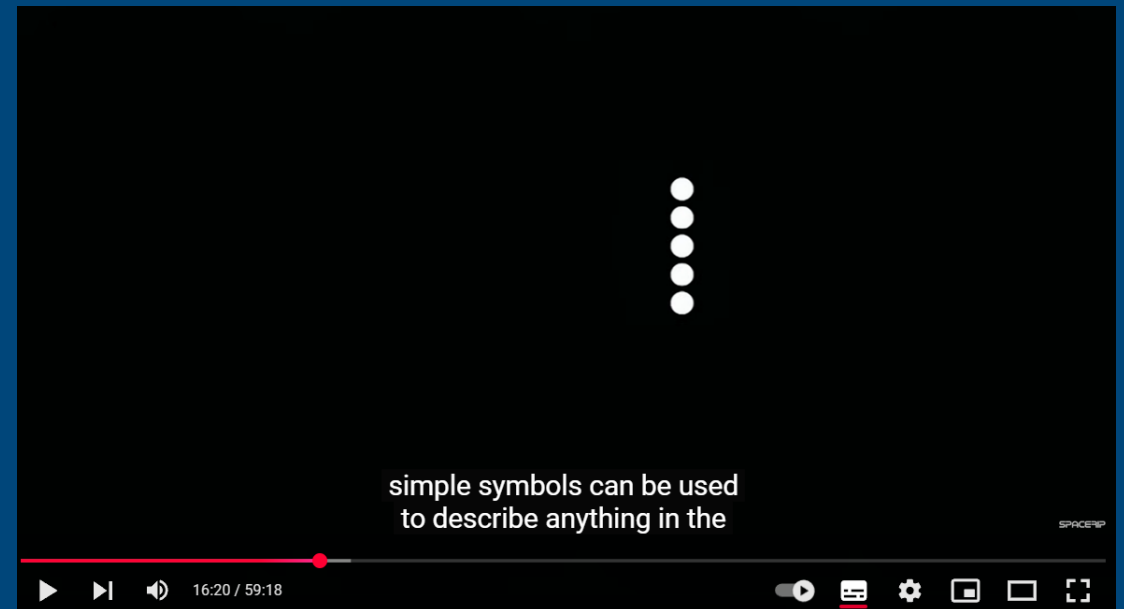
# Information



- <https://youtu.be/ryOpnel0ci0>
- [https://youtu.be/1afrzErFy\\_k](https://youtu.be/1afrzErFy_k)

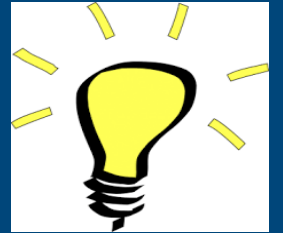


Claude Shannon (information theory, inventor of the bit)



# AlphaFold

## Kunstmatige intelligentie

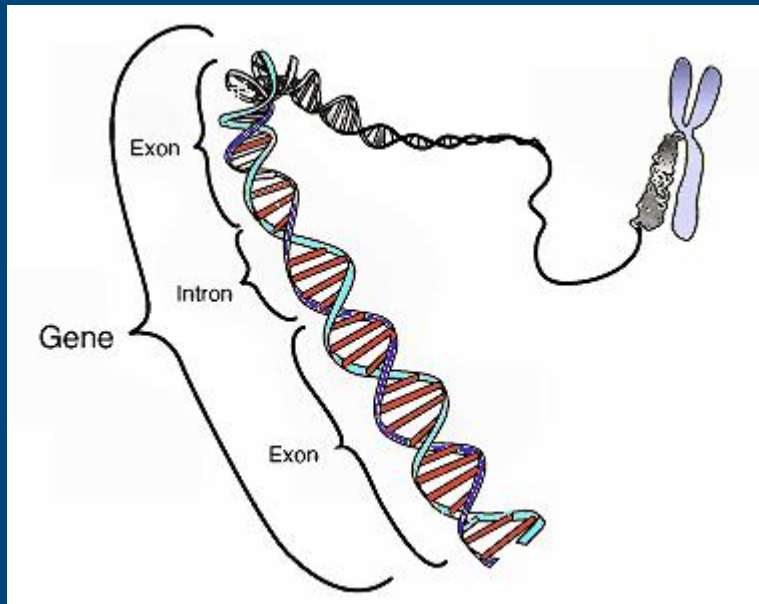
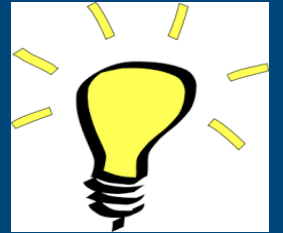


- Nobel 2025
- the number of ways a protein could theoretically fold before settling into its final 3D structure is astronomical. In 1969 Cyrus Levinthal noted that it would take longer than the age of the known universe to enumerate all possible configurations of a typical protein by brute force calculation – Levinthal estimated 10<sup>300</sup> possible conformations for a typical protein. Yet in nature, proteins fold spontaneously, some within milliseconds – a dichotomy sometimes referred to as Levinthal's paradox

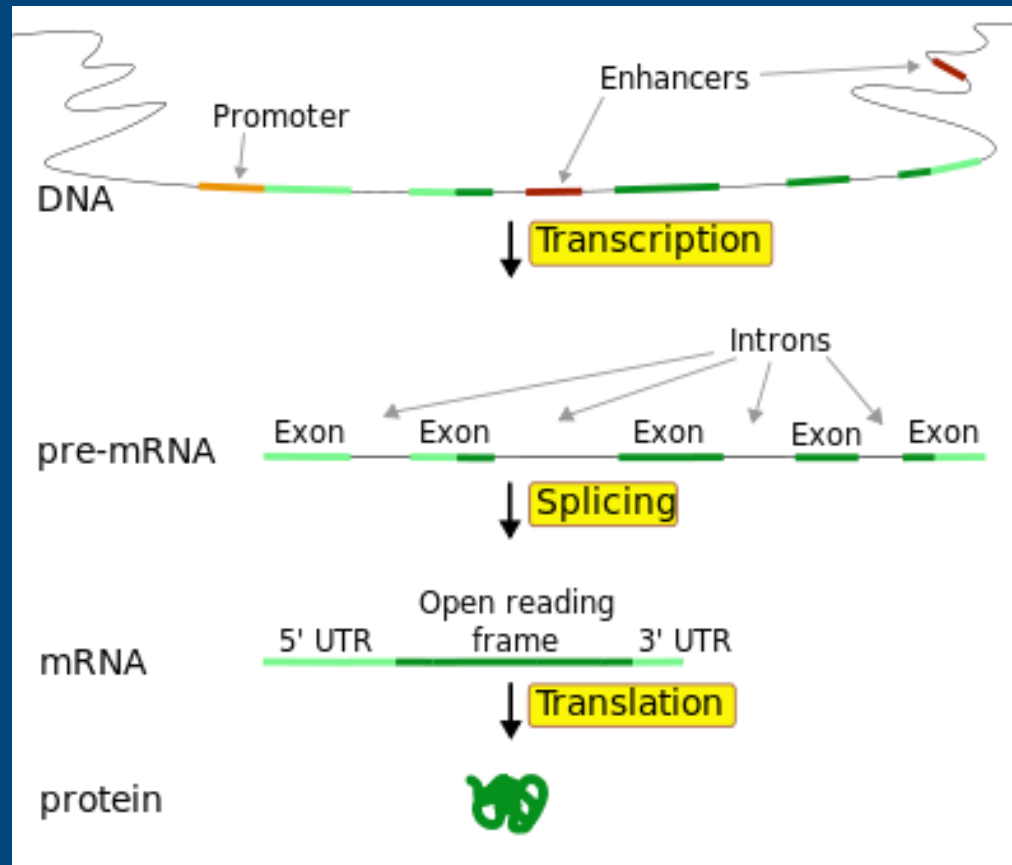
<https://deepmind.com/blog/article/alphafold-a-solution-to-a-50-year-old-grand-challenge-in-biology>

[https://youtu.be/P\\_fHJIYENDI](https://youtu.be/P_fHJIYENDI)

Gen => RNA => Eiwit



Een gen produceert 2-30 mRNAs/uur



Gen

RNA

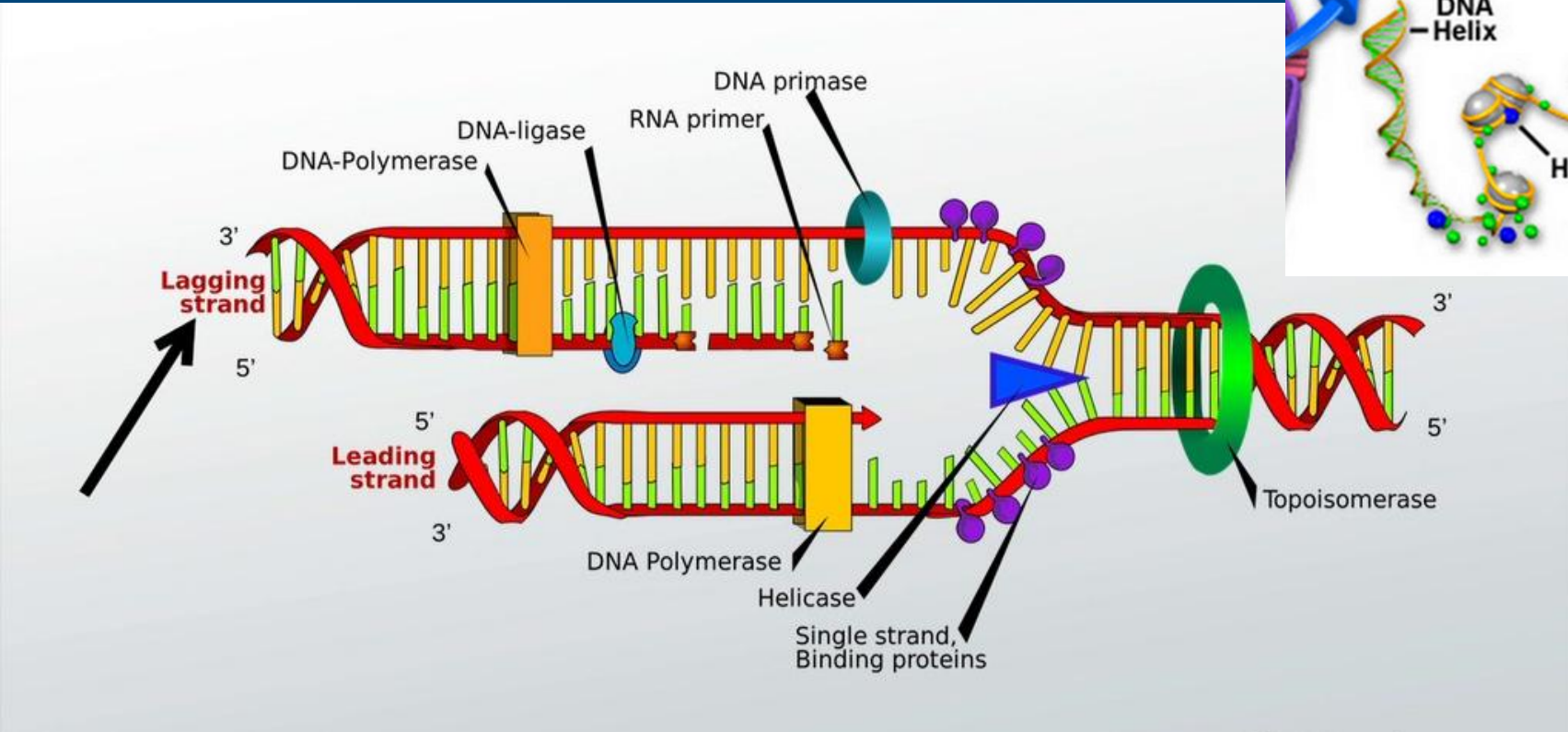
Eiwit

Watson, Crick, Franklin, Wilkins.

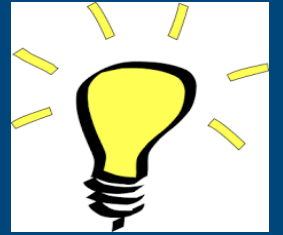
Central dogma of molecular biology

# Eiwitten in de celkern

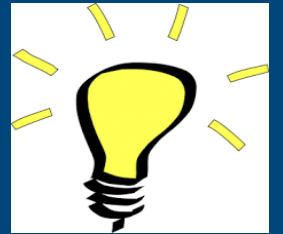
=> DNA machinerie



=> Vouwen, kopiëren, knippen, plakken



# Biotechnologie: Enzymen opzuiveren => Gebruiken voor **gentechnologie**.



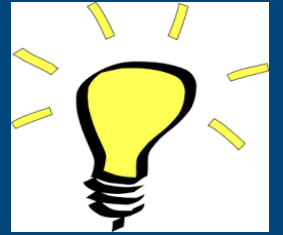
DNA (Taq) polymerase,  
maakt kopie van DNA  
in reageerbuis!

Voor veel mol.biol.  
is geen cel nodig!

<https://youtu.be/fkUDu042xic>  
<https://youtu.be/iQsu3Kz9NYo>

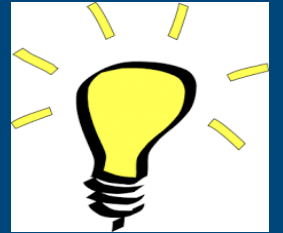
## Leven is..

- Een informatie systeem
- Manipuleerbaar met informatietechnologie
- **Individuele processen kunnen ook buiten een levend systeem plaatsvinden**



# DNA technieken (engels)

=> **in silico**



- <https://youtu.be/8cYvyYOjzOc>
- <https://youtu.be/xlrwef2Y3f0>
- <https://youtu.be/iYaxOwZLIAk>
- <https://youtu.be/y7kny3Xy4k4>
- <https://youtu.be/buzWMKIHbB>
- <https://youtu.be/fzB7tOwv4xk>
- <https://www.youtube.com/watch?v=FvHRio1yyhQI>
- <https://www.youtube.com/watch?v=jFCD8Q6qSTM>
- <https://www.youtube.com/watch?v=mMIRBNUuX6I>
- [https://www.youtube.com/watch?v=LmdH9u\\_WTqI](https://www.youtube.com/watch?v=LmdH9u_WTqI)
- <https://www.youtube.com/watch?v=1S0x3aRCviM>
- <https://www.youtube.com/watch?v=avM1Yg5oEu0>
- <https://youtu.be/8cYvyYOjzOc>
- [https://youtu.be/tcPgdR9\\_t64](https://youtu.be/tcPgdR9_t64)



**epje**  
(ependorf tube, plastic)

# Werken met de taal van het leven



Lezen = Sequencing

Knippen = Restrictie-enzymen (klonen van GFP gen)

Schrijven = Synthese

Plakken = Insertie => vaak nog virus (vector) voor nodig (=> CRISPR)

=> **Molecular Biology** Toolkit

=> DNA is een taal, en moleculaire biologie = taalkunde

<https://youtu.be/fzB7tOwv4xk>

# DNA synthese (schrijven)

<https://youtu.be/Dwrte-CBomw>

=> synthetische biologie

<https://youtu.be/DxoLoOtyIU>

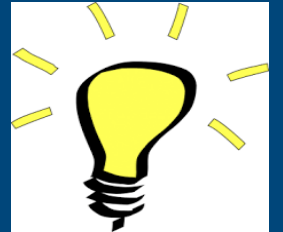
## iteratie:

De 1<sup>e</sup> stap is het moeilijkst

Daarna gaat het steeds sneller (exponentieel)

Zeker als na verloop van tijd bedrijven gaan meedoen

=> Kurzweil



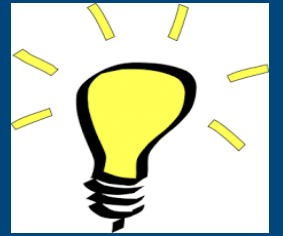
**DNA in 2 days.  
It's actually  
a thing now.**

Twist DNA. Easier, faster, higher quality.

Try 2 day DNA

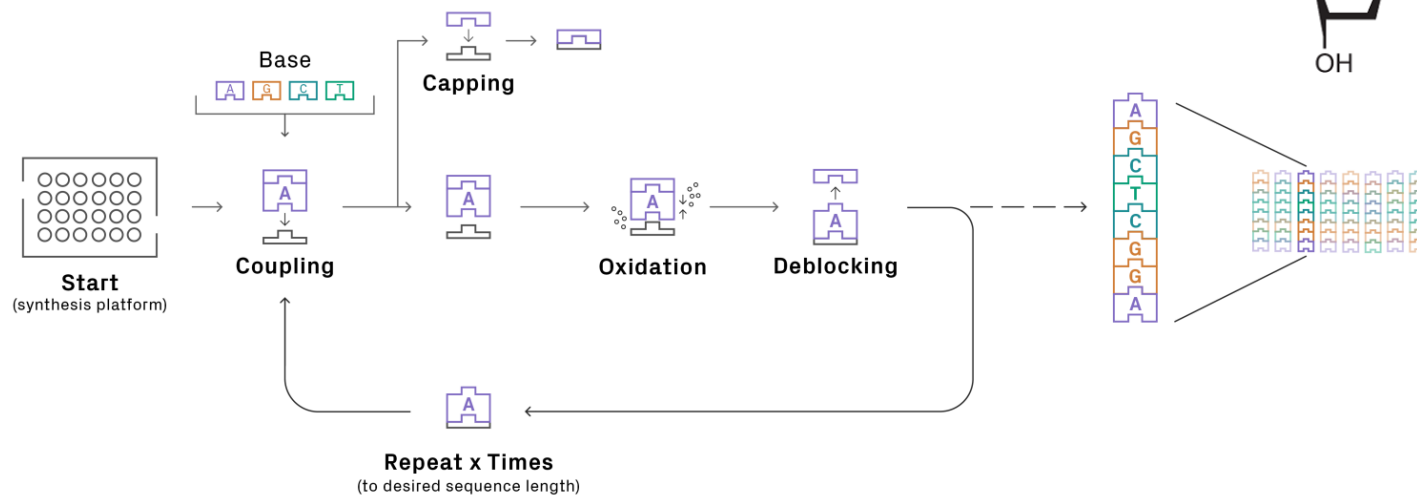


# DNA/RNA synthese (schrijven)

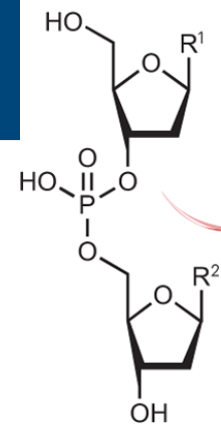


- Oligonucleotide synthesis cycle

## Oligonucleotide Synthesis



2 Base dinucleotide



**1963**  
Solid-phase synthesis

**2000s**  
Enzymatic synthesis using protected nucleotides

>10 kb DNA

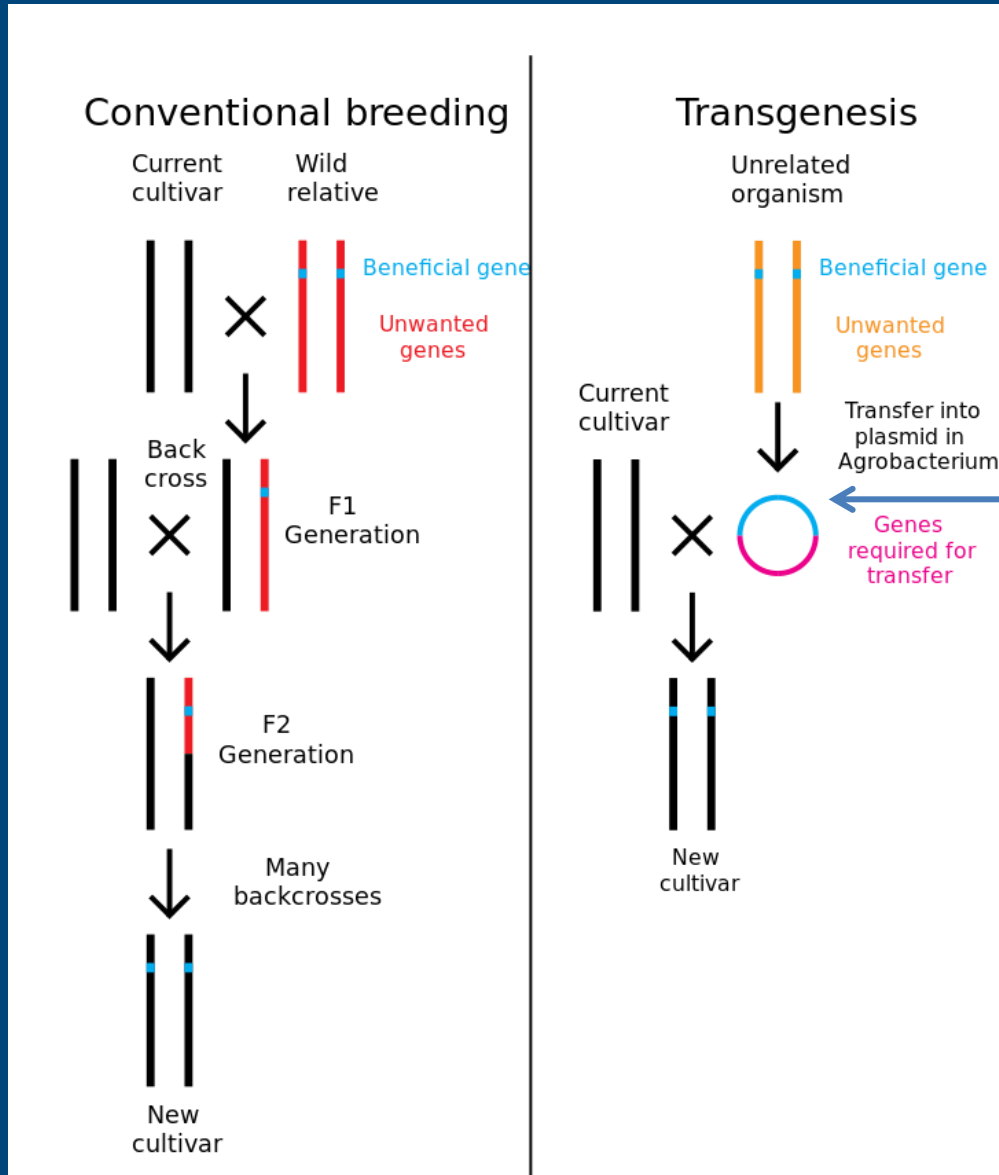
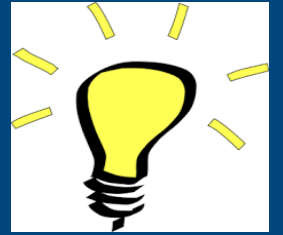
**2021**  
First synthesis of >10 kb DNA

**1981**  
Phosphoramidite chemistry

**2009**  
Nature Methods Gibson

10kb = 10.000 nucleotiden  
= 1 gen

# 1<sup>e</sup> stappen mol biol waren nog kruisingen

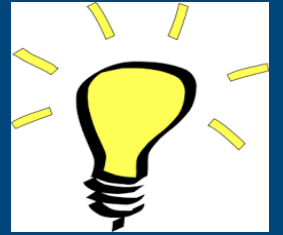


Zelfde, alleen sneller en gericht.  
Met vector (klonen).

NB CRISPR vervangt nog veel  
specifieker

Directed evolution

# Vragen



- 12 deelnemers/excursie => mail hovo
- Quantumbiologie
- Stamp collecting => Emergentie
- Chaperones
- Symbiose
- Synth.biol.
- Dna extractie
- Singularity
- OpenClaw
- Hybride aap/mens
- Epigenetica
- Eiwit vouwing
- Biotech doen we al heel lang

**VRAAGEN:**

- 12 deeln.
- excursie
- Quantumbiologie
- stamp-collectie
- emergegentie
- chaperones
- symbiose
- synthet. biol.
- DNA expressie

epi-Genetische modificatie

singularity

17A

17B

17C

17D

17E

17F

17G

17H

17I

17J

17K

17L

17M

17N

17O

17P

17Q

17R

17S

17T

17U

17V

17W

17X

17Y

17Z

17AA

17AB

17AC

17AD

17AE

17AF

17AG

17AH

17AI

17AJ

17AK

17AL

17AM

17AN

17AO

17AP

17AQ

17AR

17AS

17AT

17AU

17AV

17AW

17AX

17AY

17AZ

17BA

17BB

17BC

17BD

17BE

17BF

17BG

17BH

17BI

17BJ

17BK

17BL

17BM

17BN

17BO

17BP

17BQ

17BR

17BS

17BT

17BU

17BV

17BW

17BX

17BY

17BZ

17CA

17CB

17CC

17CD

17CE

17CF

17CG

17CH

17CI

17CJ

17CK

17CL

17CM

17CN

17CO

17CP

17CQ

17CR

17CS

17CT

17CU

17CV

17CW

17CX

17CY

17CZ

17DA

17DB

17DC

17DD

17DE

17DF

17DG

17DH

17DI

17DJ

17DK

17DL

17DM

17DN

17DO

17DP

17DQ

17DR

17DS

17DT

17DU

17DV

17DW

17DX

17DY

17DZ

17EA

17EB

17EC

17ED

17EE

17EF

17EG

17EH

17EI

17EJ

17EK

17EL

17EM

17EN

17EO

17EP

17EQ

17ER

17ES

17ET

17EU

17EV

17EW

17EX

17EY

17EZ

17FA

17FB

17FC

17FD

17FE

17FF

17FG

17FH

17FI

17FJ

17FK

17FL

17FM

17FN

17FO

17FP

17FQ

17FR

17FS

17FT

17FU

17FV

17FW

17FX

17FY

17FZ

17GA

17GB

17GC

17GD

17GE

17GF

17GG

17GH

17GI

17GJ

17GK

17GL

17GM

17GN

17GO

17GP

17GQ

17GR

17GS

17GT

17GU

17GV

17GW

17GX

17GY

17GZ

17HA

17HB

17HC

17HD

17HE

17HF

17HG

17HH

17HI

17HJ

17HK

17HL

17HM

17HN

17HO

17HP

17HQ

17HR

17HS

17HT

17HU

17HV

17HW

17HX

17HY

17HZ

17IA

17IB

17IC

17ID

17IE

17IF

17IG

17IH

17II

17IJ

17IK

17IL

17IM

17IN

17IO

17IP

17IQ

17IR

17IS

17IT

17IU

17IV

17IW

17IX

17IY

17IZ

17JA

17JB

17JC

17JD

17JE

17JF

17JG

17JH

17JI

17JJ

17JK

17JL

17JM

17JN

17JO

17JP

17JQ

17JR

17JS

17JT

17JU

17JV

17JW

17JX

17JY

17JZ

17KA

17KB

17KC

17KD

17KE

17KF

17KG

17KH

17KI

17KJ

17KK

17KL

17KM

17KN

17KO

17KP

17KQ

17KR

17KS

17KT

17KU

17KV

17KW

17KX

17KY

17KZ

17LA

17LB

17LC

17LD

17LE

17LF

17LG

17LH

17LI

17LJ

17LK

17LL

17LM

17LN

17LO

17LP

17LQ

17LR

17LS

17LT

17LU

17LV

17LW

17LX

17LY

17LZ

17MA

17MB

17MC

17MD

17ME

17MF

17MG

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17MI

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17MU

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17MW

17MX

17MY

17MZ

17NA

17NB

17NC

17ND

17NE

17NF

17NG

17NH

17NI

17NJ

17NK

17NL

17NM

17NN

17NO

17NP

17NQ

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17NT

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17PN

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17PP

17PQ

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17PS

17PT

17PU

17PV

17PW

17PX

17PY

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17QB

17QC

17QD

17QE

17QF

17QG

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17QI

17QJ

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17QL

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17RJ

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17UA

17UB

17UC

17UD

17UE

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17UI

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17YR

17YS

17YT

17YU

17YV

17YW

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17ZH

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17ZS

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17ZV

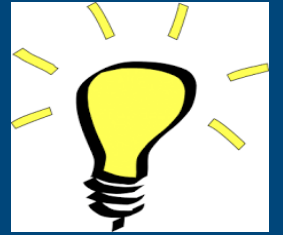
17ZW

17ZX

17ZY

17ZZ

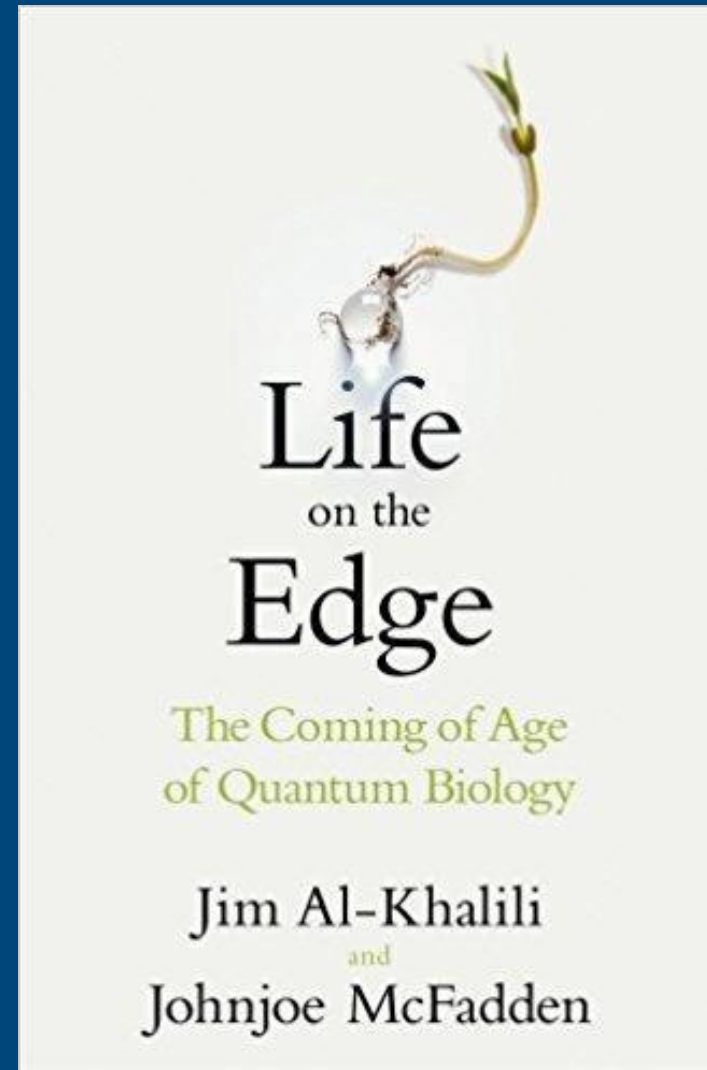
Jim al-khalili: Entropy, energy,  
information and quantum biology



Jim Al-Khalili, Johnjoe McFadden

2015

ISBN100552778079



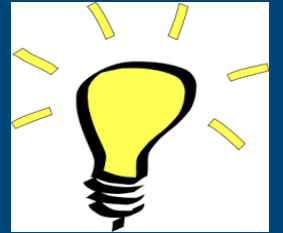
# stamp collecting



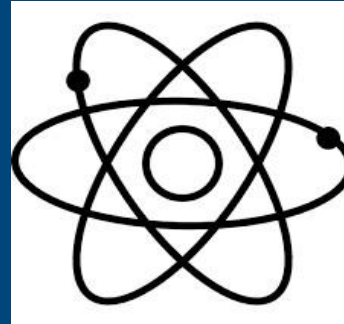
- The famous quote attributed to Nobel laureate Ernest Rutherford is: "**All science is either physics or stamp collecting**". Often used to argue that physics is the only fundamental science, this phrase highlights a distinction between, on one hand, studying basic principles, and on the other, classifying data, such as in biology or chemistry

# Klein naar groot

quantumfysica

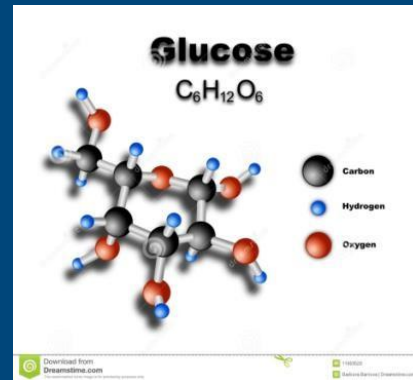


- Atoom ( $10^{-12}$ )

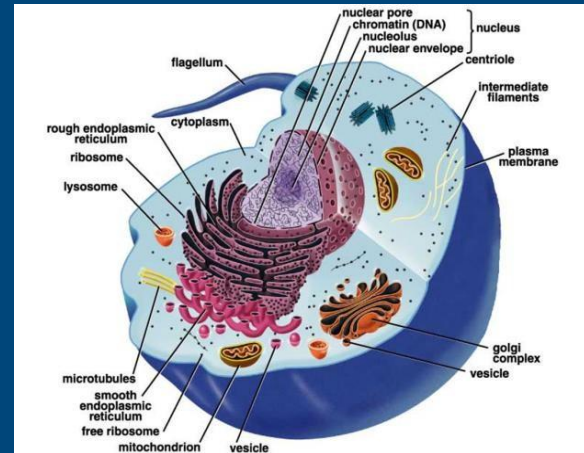


Natuurkunde

- Molecuul ( $10^{-9}$ )



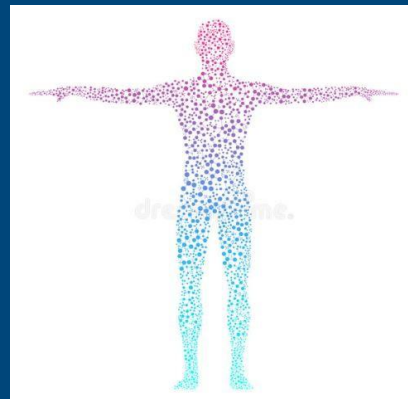
- Cel ( $10^{-6}$ )



scheikunde

Elk niveau heeft  
emergente  
verschijnselen  
die niet perse  
deterministisch  
volgen uit  
onderliggende  
niveau's

- Mens ( $10^0$ )



biologie

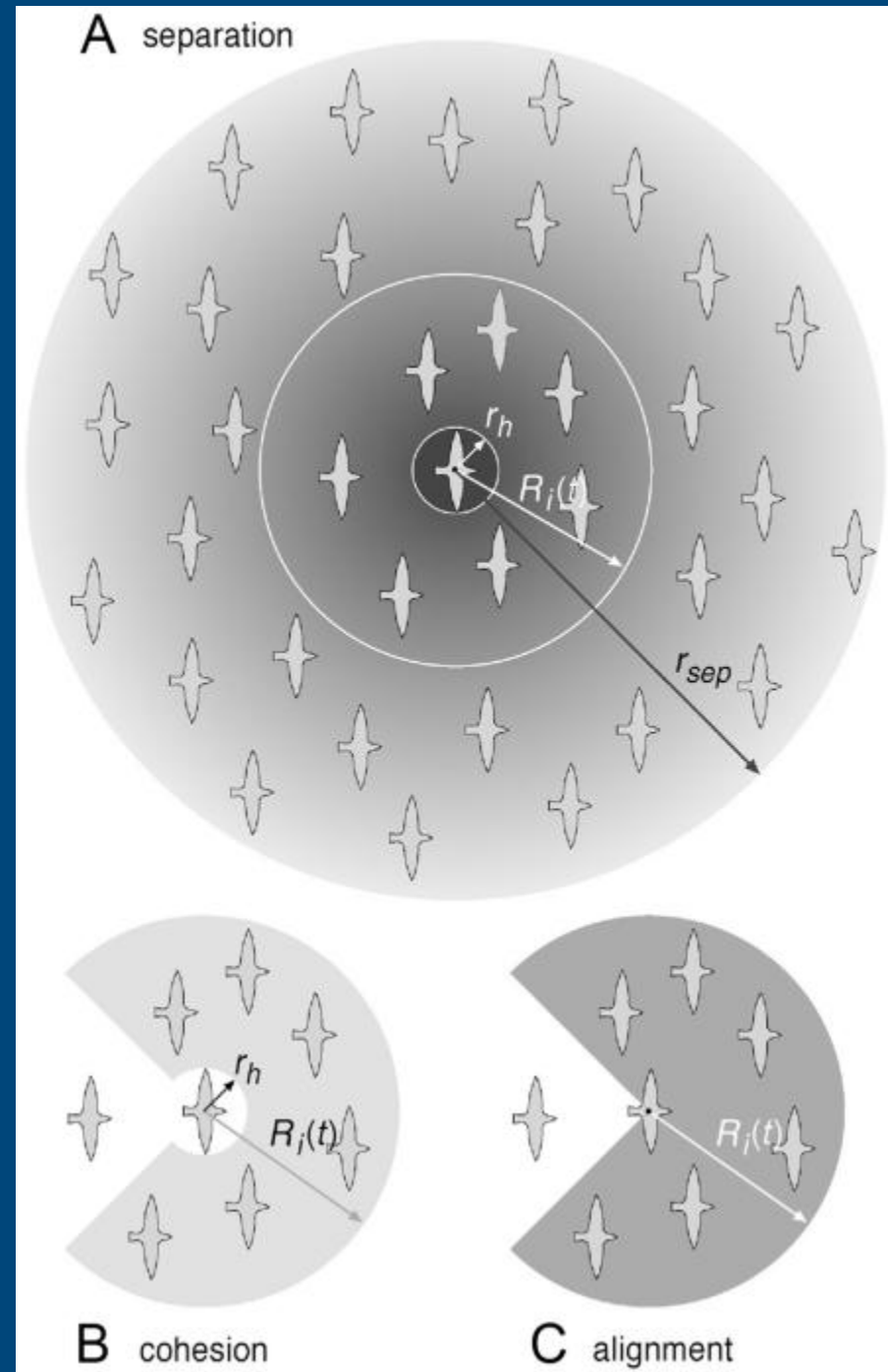
sociologie

# Emergentie

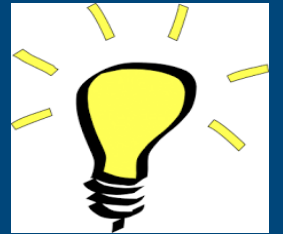
- Geen leider in een zwerm
- Alleen een paar simpele (sociale) regels

=> complex gedrag

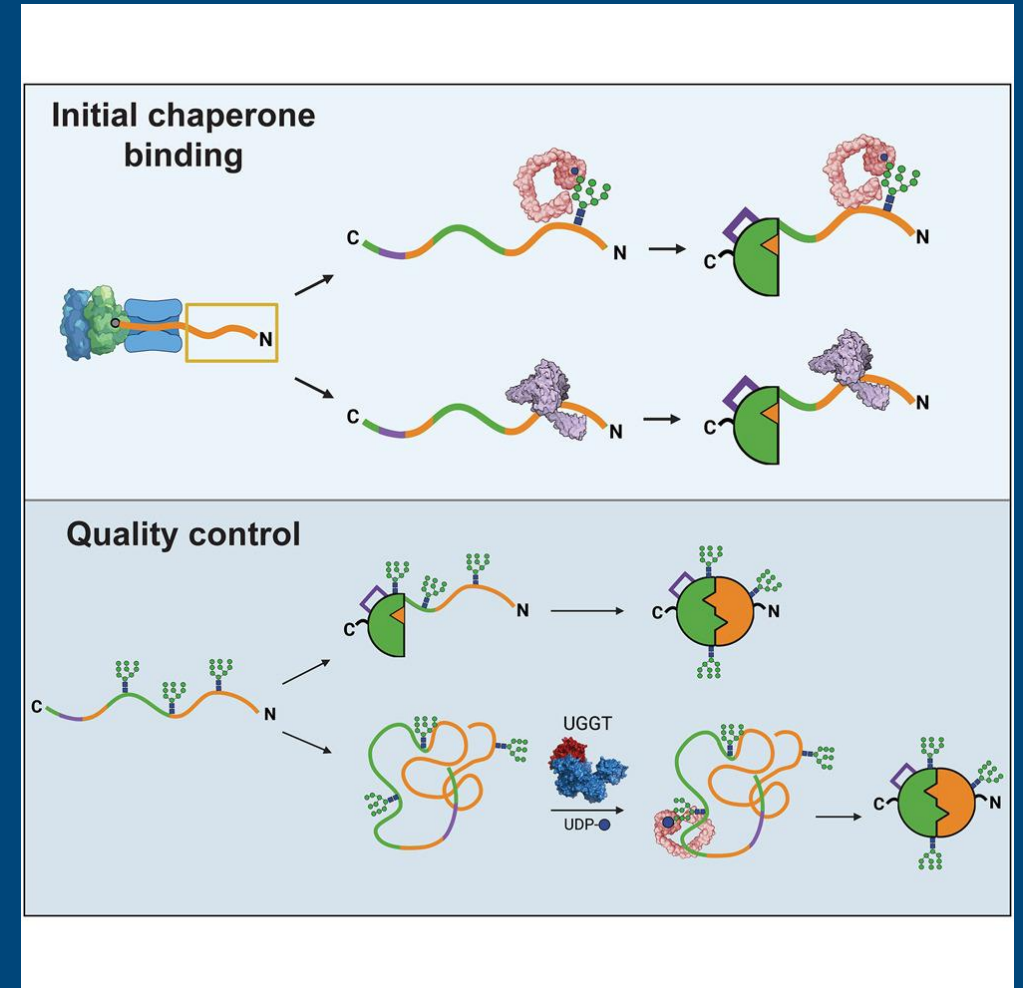
<https://pubmed.ncbi.nlm.nih.gov/21829627/>



# Chaperones

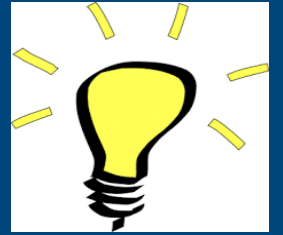


- In molecular biology, **molecular chaperones** are proteins that assist the conformational folding or unfolding of proteins or macromolecular protein complexes. There are a number of classes of molecular chaperones, all of which function to assist large proteins in proper protein folding during or after synthesis, and after partial denaturation.
- The majority of molecular chaperones do not convey any steric information for protein folding, and instead assist in protein folding by binding to and stabilizing folding intermediates until the polypeptide chain is fully translated.
- [https://en.wikipedia.org/wiki/Chaperone\\_\(protein\)](https://en.wikipedia.org/wiki/Chaperone_(protein))
- <https://www.cell.com/molecular-cell/fulltext/S1097-2765%2823%2900922-X>



# AlphaFold

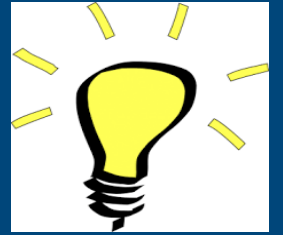
## Kunstmatige intelligentie



- Nobel 2025
- the number of ways a protein could theoretically fold before settling into its final 3D structure is astronomical. In 1969 Cyrus Levinthal noted that it would take longer than the age of the known universe to enumerate all possible configurations of a typical protein by brute force calculation – Levinthal estimated 10<sup>300</sup> possible conformations for a typical protein. Yet in nature, proteins fold spontaneously, some within milliseconds – a dichotomy sometimes referred to as Levinthal's paradox

<https://deepmind.com/blog/article/alphafold-a-solution-to-a-50-year-old-grand-challenge-in-biology>  
[https://youtu.be/P\\_fHJIYENDI](https://youtu.be/P_fHJIYENDI)

# Life is symbiotic, up to the genome.

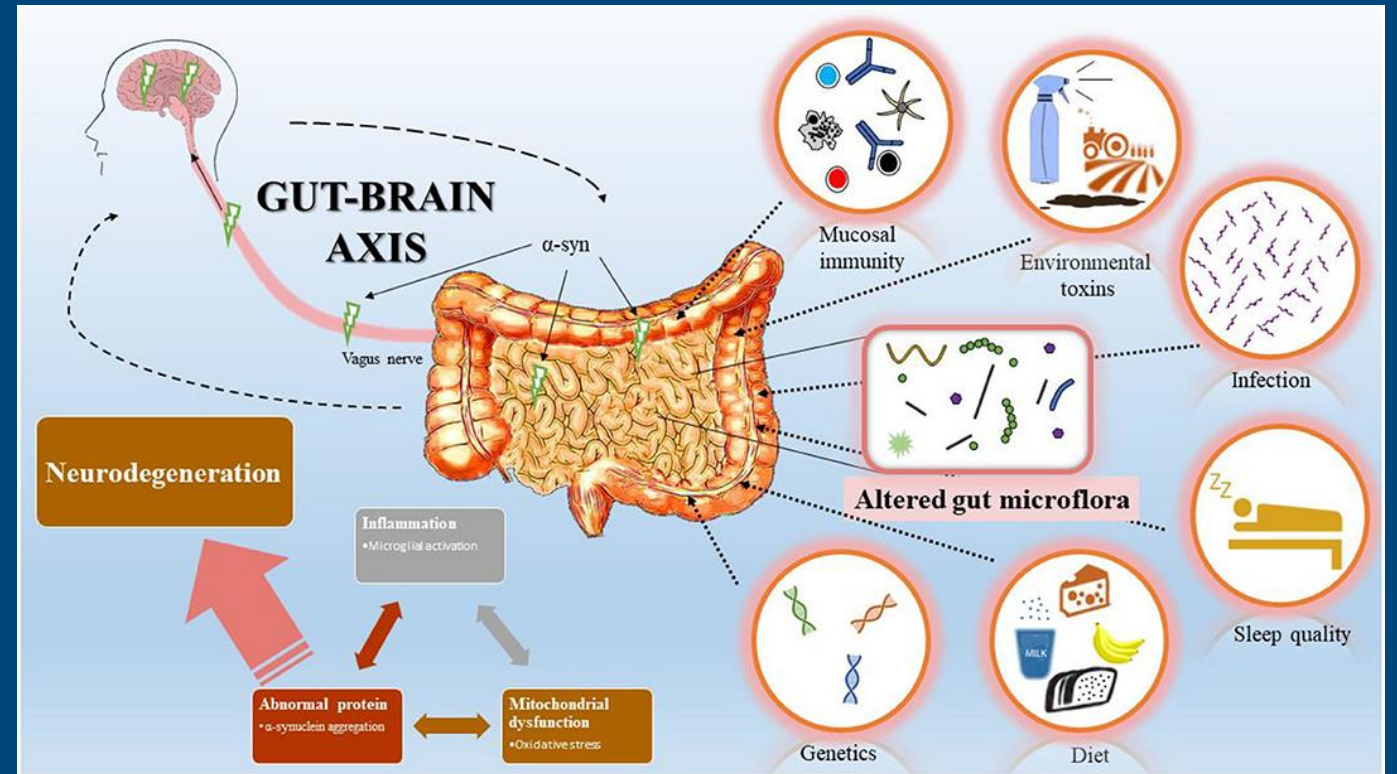


- Bacteria in gut and on skin
- Viral sequences in DNA (maybe even 10%)

⇒ “Half of you is not actually you”.

And it is impossible, for any lifeform, to live in isolation for a long time.

You need bacteria, trees and other people to live in “deep time”



<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC138943/>

<https://nl.wikipedia.org/wiki/Retrotransposon>

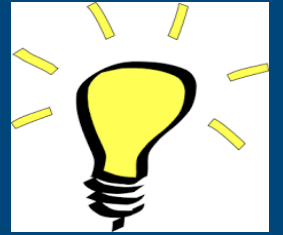
<https://www.the-scientist.com/?articles.view/articleNo/45503/title/Viral-Remnants-Help-Regulate-Human-Immunity/>

## Leven is..

- Een informatie systeem
- Manipuleerbaar met informatietechnologie

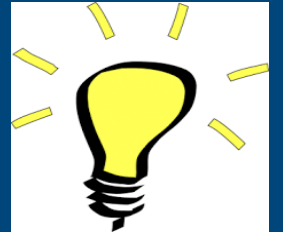
- Symbiotisch

=> Meer hierover in college 5



# Synthetic biology

## Minimal Life

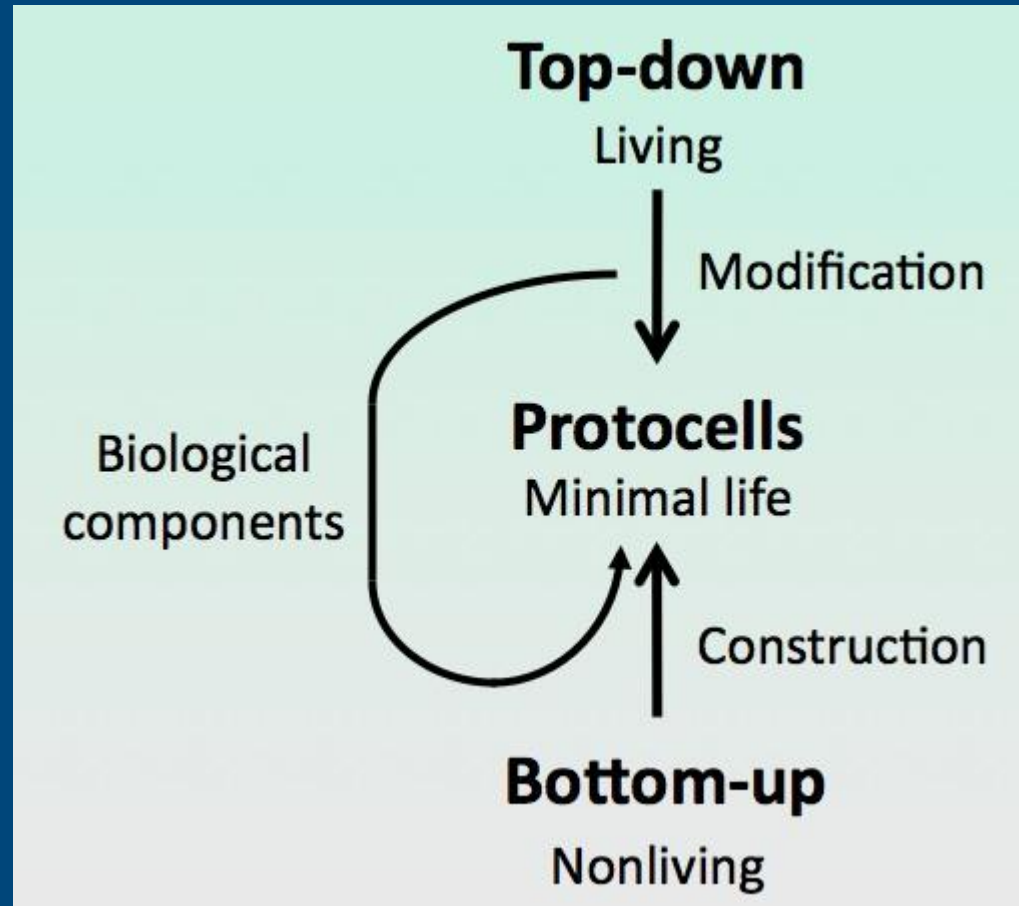


### What is life?

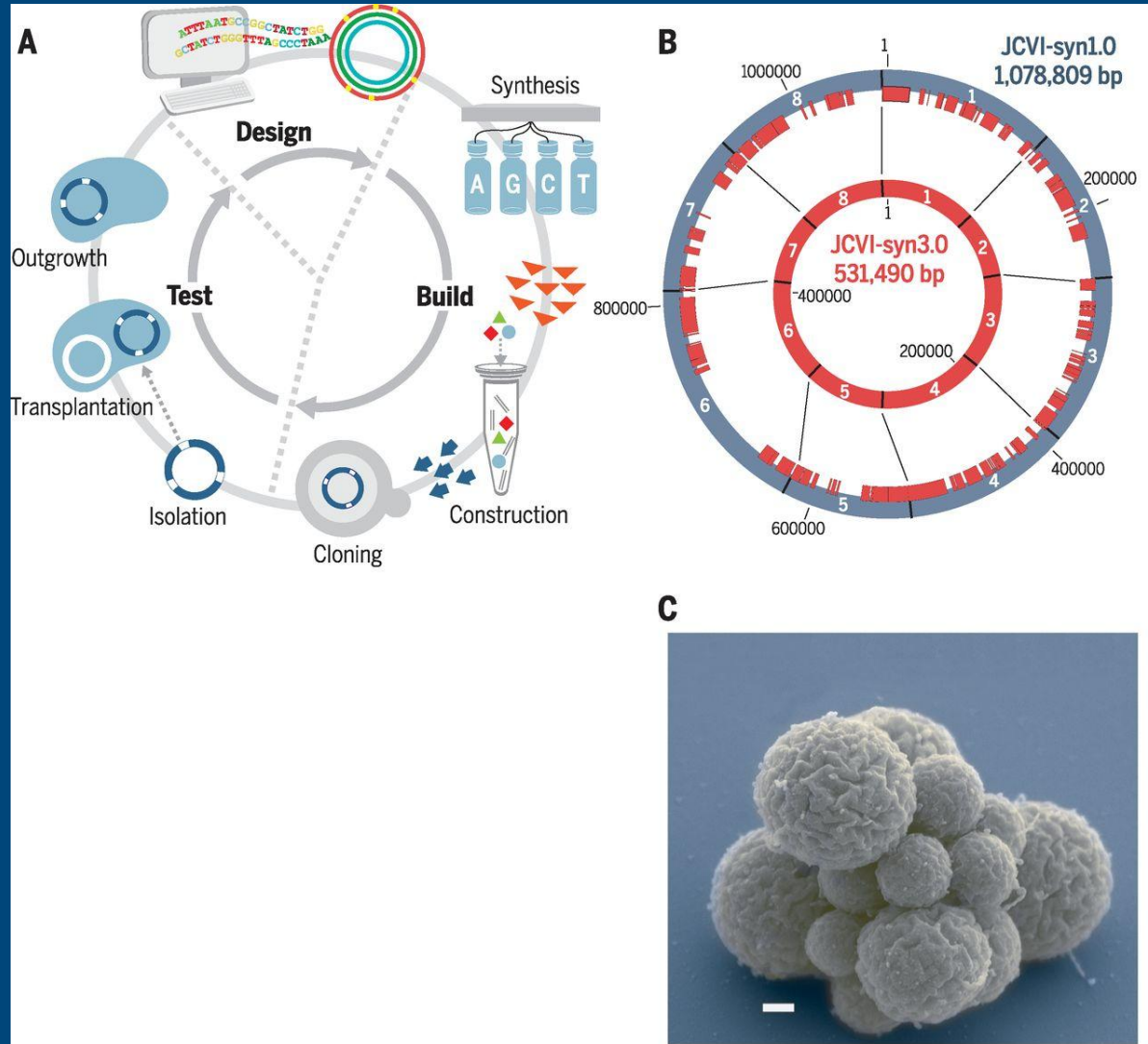
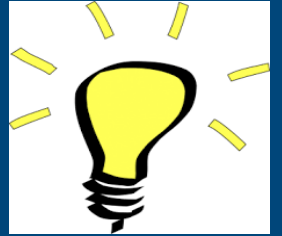
Take away genes until cells are no longer living

Or, plugging in various sets of genes until a cell is alive

Mycoplasma  
“laboratorium”



# Design and synthesis of a minimal bacterial genome => G. Venter



473 genes!

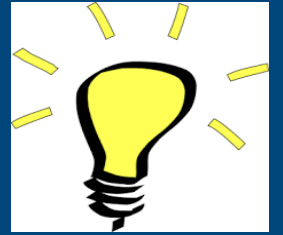
A conserved core of about 250 essential genes, +149 genes with unknown biological functions.

=> Building complexity?

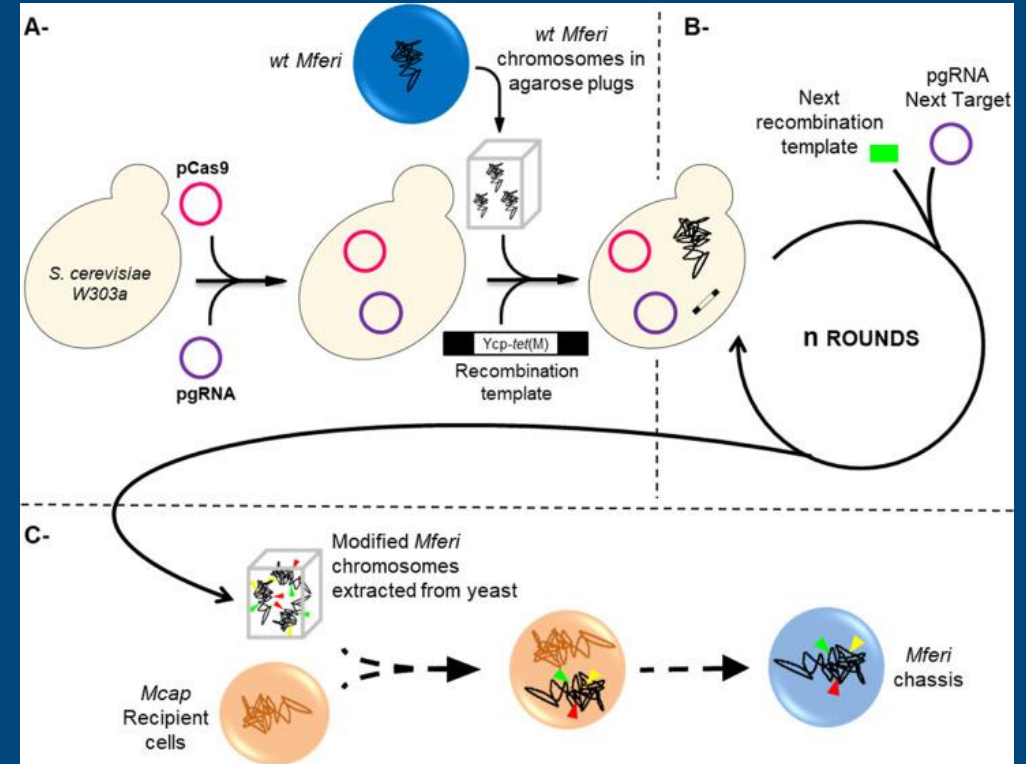
<http://science.sciencemag.org/content/351/6280/aad6253>



# Genome transplantation in mycoplasma



- Genome Engineering of the Fast-Growing *Mycoplasma feriruminatoris* toward a Live Vaccine Chassis
- the *M. feriruminatoris* genome was cloned in yeast, modified by iterative cycles of Cas9-mediated deletion of loci encoding virulence factors, and transplanted back in *Mycoplasma capricolum* subsp. *capricolum* recipient cells to produce the designed *M. feriruminatoris* chassis.
- <https://pmc.ncbi.nlm.nih.gov/articles/PMC9128628/>



# 1 The accelerating pace of change ...



# 2 ... and exponential growth in computing power ...

Computer technology, shown here climbing dramatically by powers of 10, is now progressing more each hour than it did in its entire first 90 years

## COMPUTER RANKINGS

By calculations per second per \$1,000



**Analytical engine**  
Never fully built, Charles Babbage's invention was designed to solve computational and logical problems



**Colossus**  
The electronic computer, with 1,500 vacuum tubes, helped the British crack German codes during WW II



**UNIVAC I**  
The first commercially marketed computer, used to tabulate the U.S. Census, occupied 943 cu. ft.

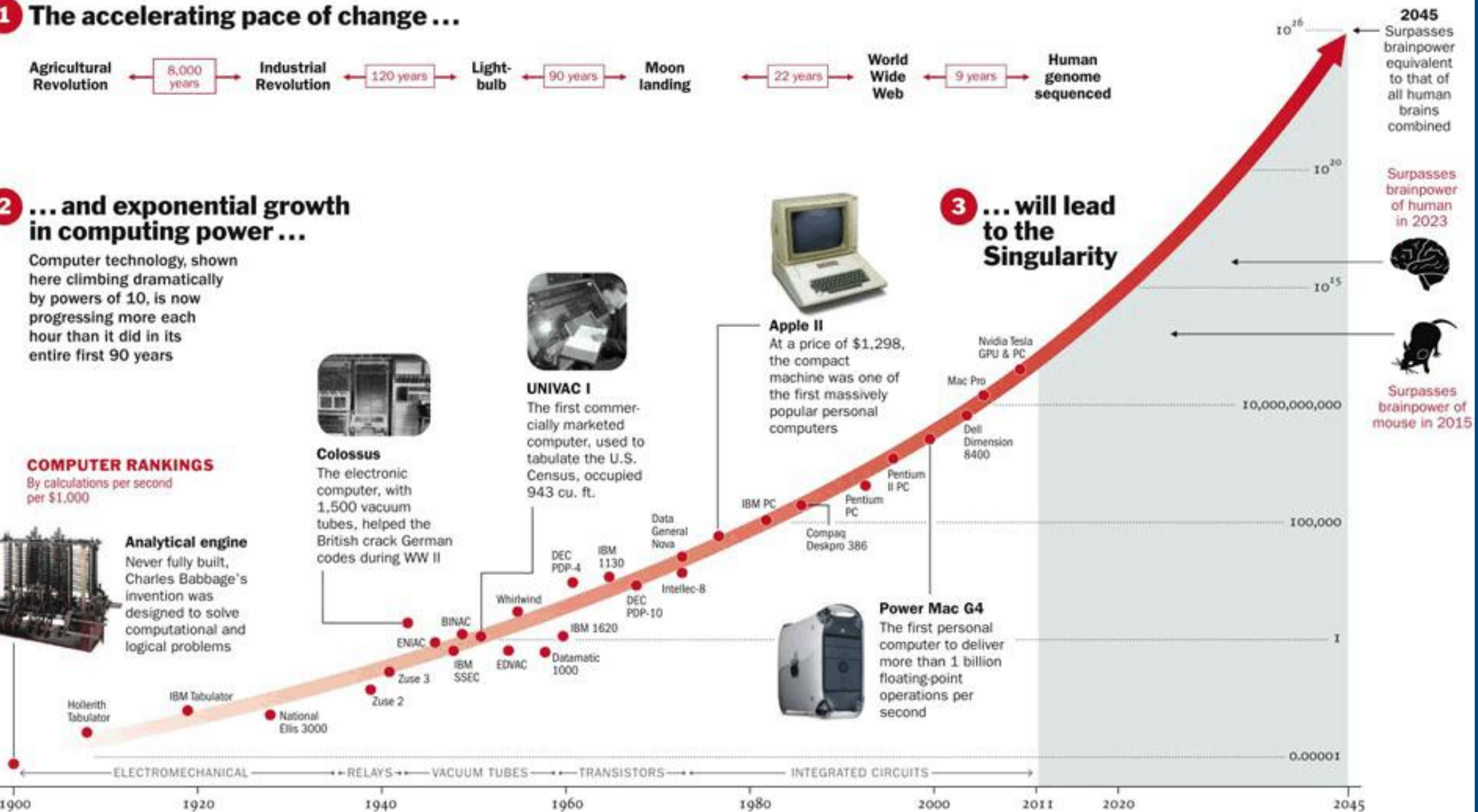


**Apple II**  
At a price of \$1,298, the compact machine was one of the first massively popular personal computers



**Power Mac G4**  
The first personal computer to deliver more than 1 billion floating-point operations per second

# 3 ... will lead to the Singularity



ELECTROMECHANICAL → RELAYS → VACUUM TUBES → TRANSISTORS → INTEGRATED CIRCUITS

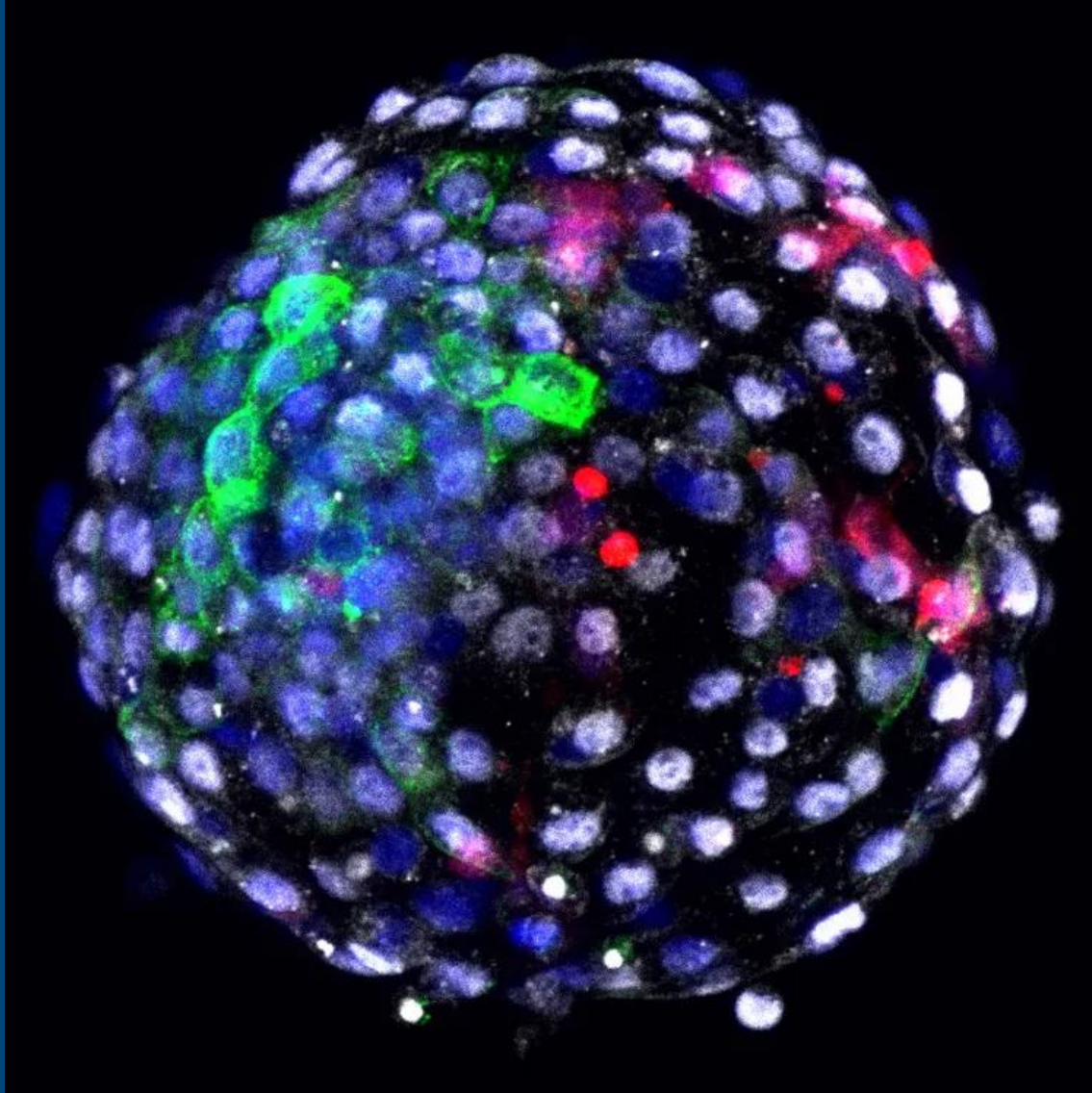
# OpenClaw

Code modifying AI bot

<https://youtu.be/YFjfBk8HI5o>

## Hybrid embryo.

First monkey embryos containing human cells.



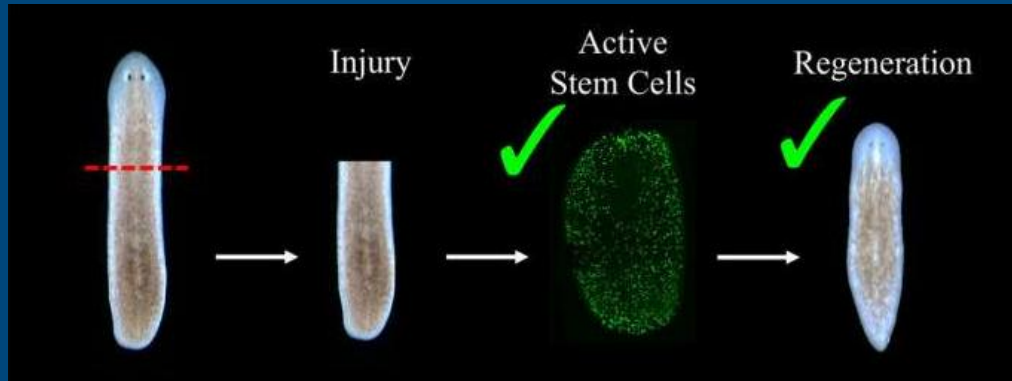
Toepassingen om onderzoek te verbeteren leiden tot methoden die **ethische grenzen** raken.

En ethiek veranderen?

=> **College 3**

# Planaria: Kampioen regeneratie.

## Waarom kunnen wij dit niet? => college 3



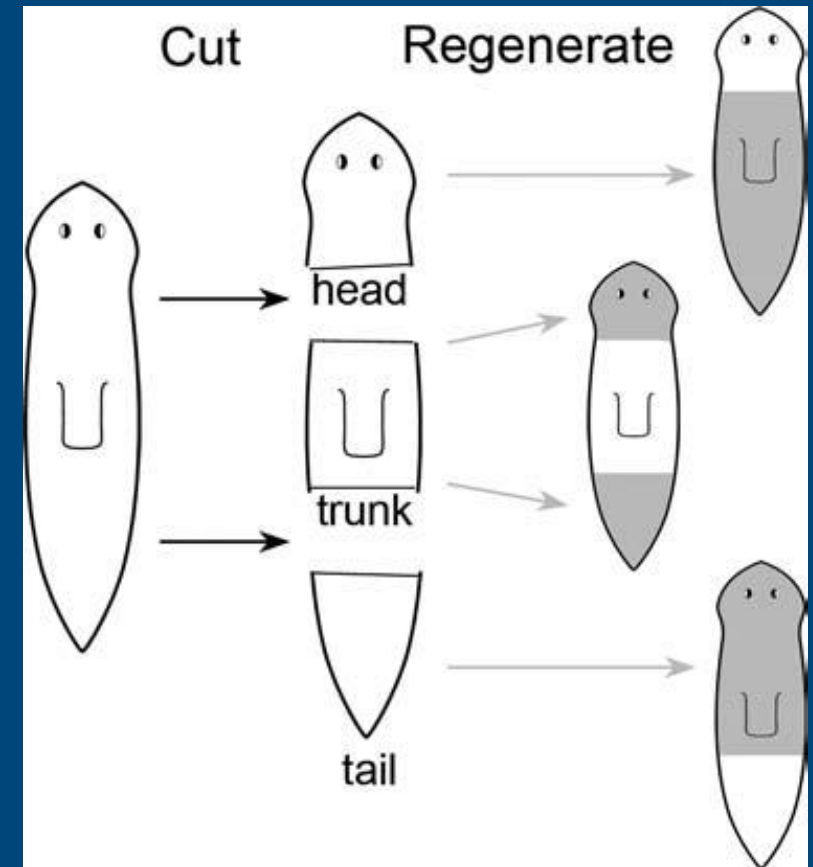
Platwormen (Planaria) zijn relatief eenvoudig.

Een **ingewikkelder** organisme zoals de mens is moeilijker te regenereren. En is **warmbloedig**.

⇒ Kan maar kort inactief zijn. We moeten door..

⇒ Scarring = **litteken**weefsel (**fibrose**) als methode om de rest van het weefsel weer snel te laten functioneren.

⇒ Gebeurt ook na beschadiging stamcelcompartiment



<https://en.wikipedia.org/wiki/Planarian>

<https://onlinelibrary.wiley.com/doi/full/10.1111/trf.14836>

# Stamcel Nobel 2012

John B. Gurdon and **Shinya Yamanaka**  
(Nobel al binnen 10 jaar na ontdekking!)

Mature cells can be reprogrammed (iPS)  
to become pluripotent

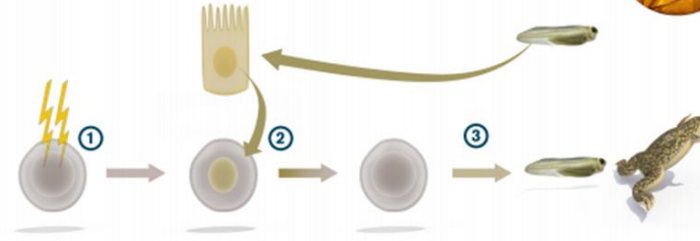
Elke cel heeft nog al het DNA

Patient levert eigen materiaal voor  
therapie !

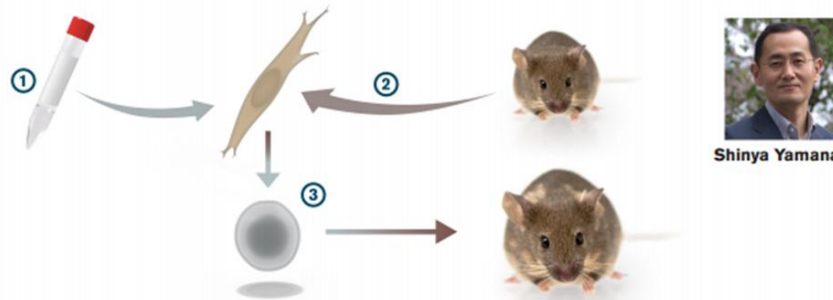
## The Nobel Prize in Physiology or Medicine 2012



John B. Gurdon

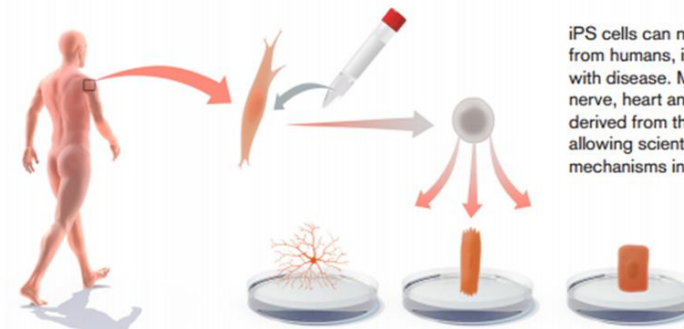


John B. Gurdon eliminated the nucleus of a frog egg cell (1) and replaced it with the nucleus from a specialised cell taken from a tadpole (2). The modified egg developed into a normal tadpole (3). Subsequent nuclear transfer experiments have generated cloned mammals (4).

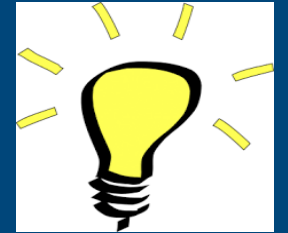


Shinya Yamanaka

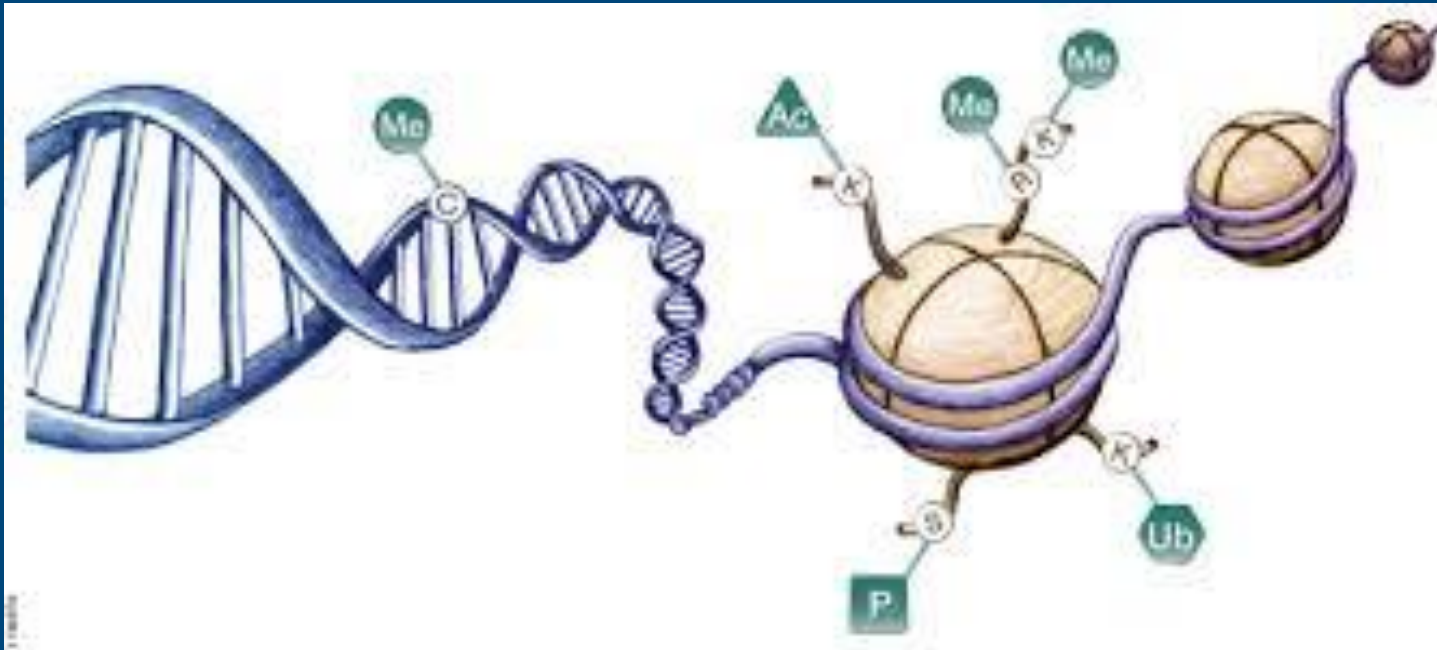
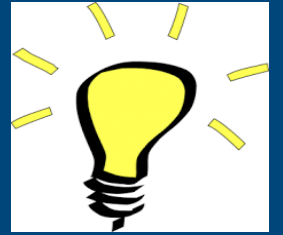
Shinya Yamanaka studied genes that are important for stem cell function. When he transferred four such genes (1) into cells taken from the skin (2), they were reprogrammed into pluripotent stem cells (3) that could develop into all cell types of an adult mouse. He named these cells induced pluripotent stem (iPS) cells.



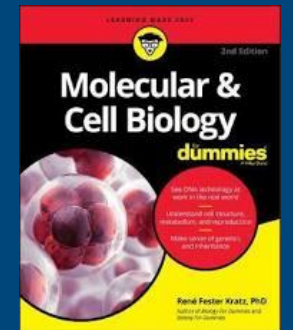
iPS cells can now be generated from humans, including patients with disease. Mature cells including nerve, heart and liver cells can be derived from these iPS cells, thereby allowing scientists to study disease mechanisms in new ways.



# Epigenetische modificatie



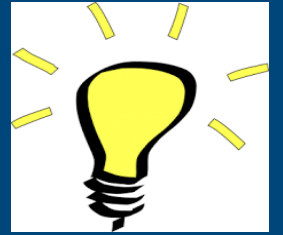
<https://www.youtube.com/watch?v=mHak9EZjySs&list=PL761BC3F8B2447983>



- Aan/uit zetten van genen  
=> Differentiatie van cellen (huidcel v levercel)  
=> Van stamcel tot organisme  
=> Kanker, Veroudering  
=> X-chromosomale inactivatie (video)

MCB H.18, p.309

# Biotechnologie, **traditioneel** en modern.



- Gebruik maken van gisten en schimmels, veredeling gewassen, fokken dieren
- Medische therapie
- Gentechnologie



Biotech doen we al heel lang,  
en wordt alleen maar  
belangrijker  
=> **Niets nieuws!**

The cell programming revolution – with Mark Kotter

## History of programming biology



**10,000**  
years ago



**1700s**



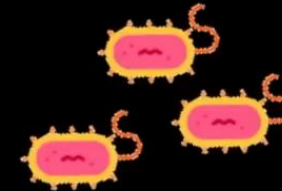
**1800s**



**1950s**



**1970s**



**1980s**



Afspelen (k)

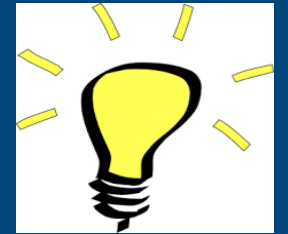
**1990s**



**2000s**



**2010s**

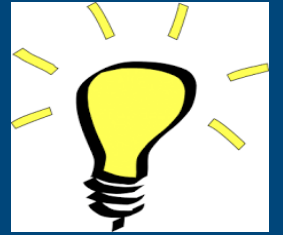


<https://youtu.be/jrVQXHmxH7Y>

▶ ⏪ 🔊 6:13 / 29:22 • Programming biology >



# GM semantiek



- Veredeling
- Fokken
- Manipulatie
- Modificatie
- Frankenstein food



⇒ Gaat allemaal over hetzelfde fenomeen.

Alleen de specifieke uitkomst zou waarde moeten bepalen

Hoort een aubergine er zo uit te zien? En een hond? Producten behaald via **veredeling**

=> ethiek/waarde

Volgende week

Biotechnologie.



DNA/RNA-technologie

=> Gentherapie/mRNA therapie

Afweersysteem

=> Immunotherapie

Stamcellen

=> Stamceltherapie

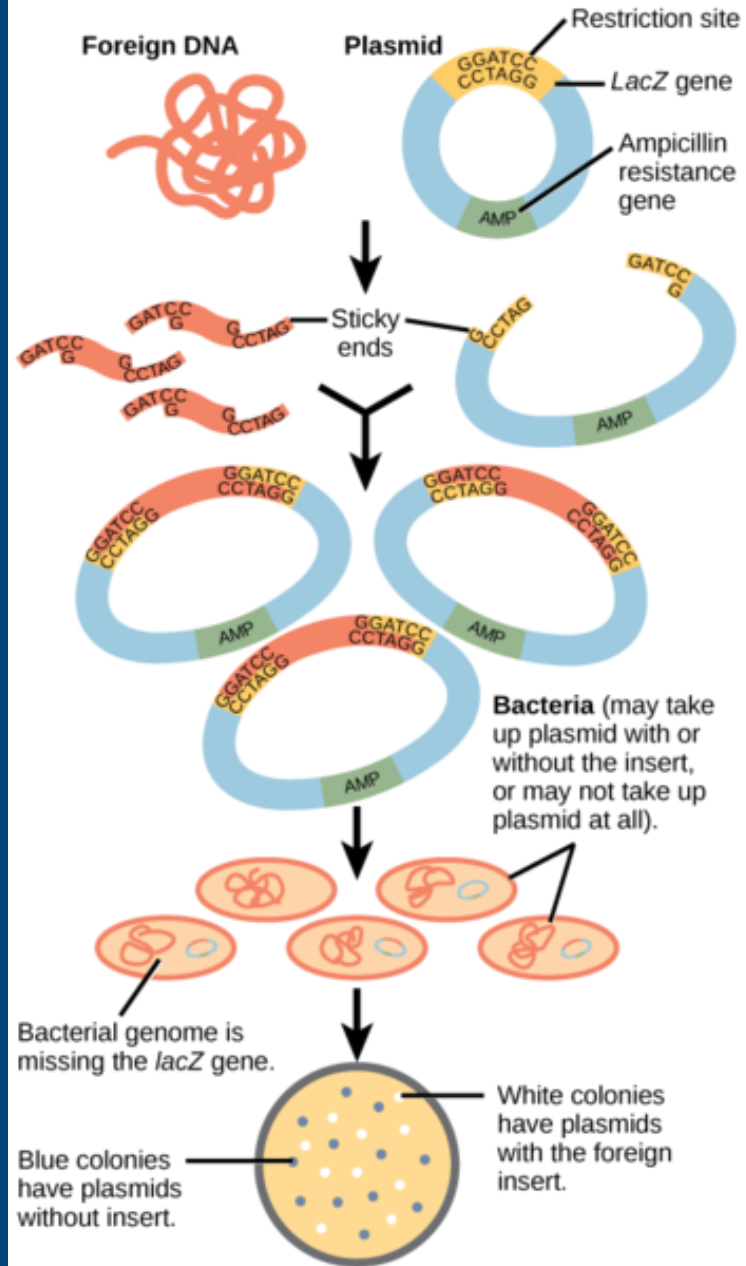
Cybernetica

=> Verbeteren (integratie technologie en biologie)

Synthetic biology

=> Wat is leven?

## Molecular Cloning



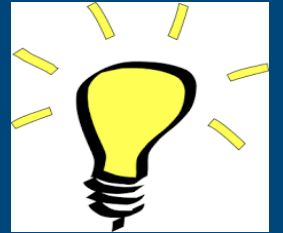
The foreign DNA and plasmid are cut with the same **restriction enzyme**, which recognizes a particular sequence of DNA called a *restriction site*. The restriction site occurs only once in the plasmid, and is located within the *lacZ* gene, a gene necessary for metabolizing lactose.

The restriction enzyme creates sticky ends that allow the foreign DNA and cloning vector to anneal. An enzyme called ligase glues the annealed fragments together.

The ligated cloning vector is transformed into a bacterial host strain that is ampicillin sensitive and is missing the *lacZ* gene from its genome.

Bacteria are grown on media containing ampicillin and X-gal, a chemical that is metabolized by the same pathway as lactose. The ampicillin kills bacteria without plasmid. Plasmids lacking the foreign insert have an intact *lacZ* gene and are able to metabolize X-gal, releasing a dye that turns the colony blue. Plasmids with an insert have a disrupted *lacZ* gene and produce white colonies.

# Klonen van een gen



- Restrictie enzymen knippen op specifieke plekken.

**NB Plasmiden en restrictie enzymen komen uit bacterien**

⇒boek mol.biol, H.20 (p.332)

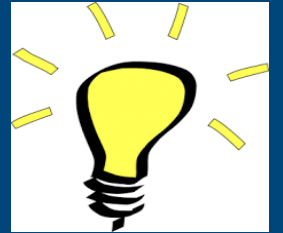
⇒Recombinant DNA tech

- Wordt nu aangevuld met CRISPR
- Resistentie gen vergemakkelijkt selectie

<https://bio.libretexts.org/>  
[https://bio.libretexts.org/Bookshelves/Introductory and General Biology/Biology \(Kimball\)/11%3A Genomics/11.01%3A Recombinant DNA and Gene Cloning](https://bio.libretexts.org/Bookshelves/Introductory_and_General_Biology/Biology_(Kimball)/11%3A_Genomics/11.01%3A_Recombinant_DNA_and_Gene_Cloning)

Uitwisselen van DNA is  
natuurlijk, zelfs bij de mens

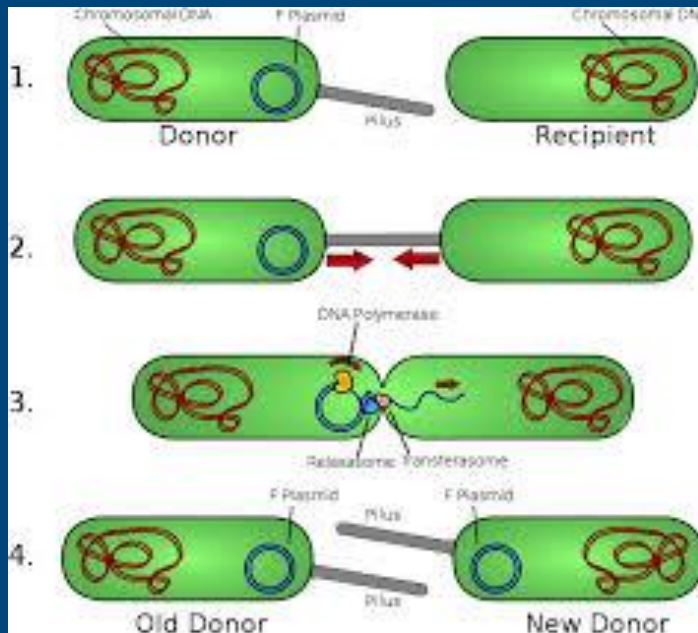
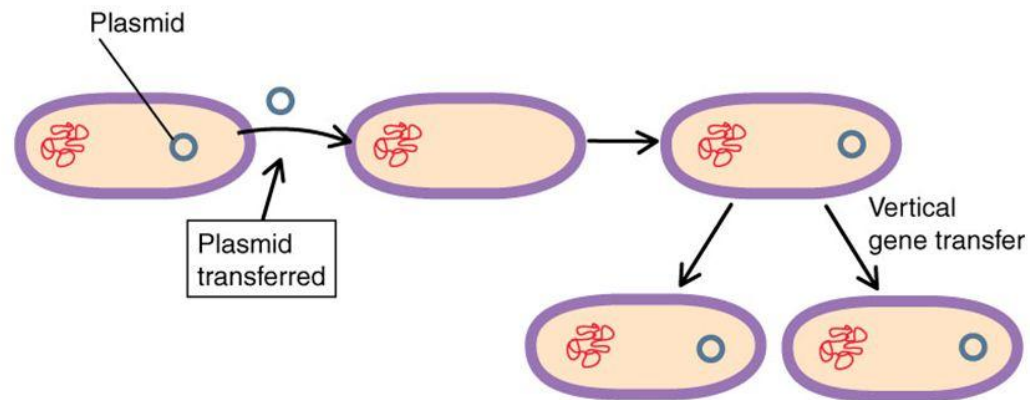
(10% DNA in humane genoom is  
afkomstig van virussen)



# Horizontal gene transfer

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## (b) Horizontal gene transfer



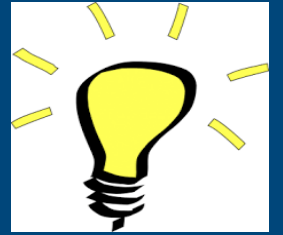
- <https://www.bioplek.org/animaties/celtotaal/bacterie.html>



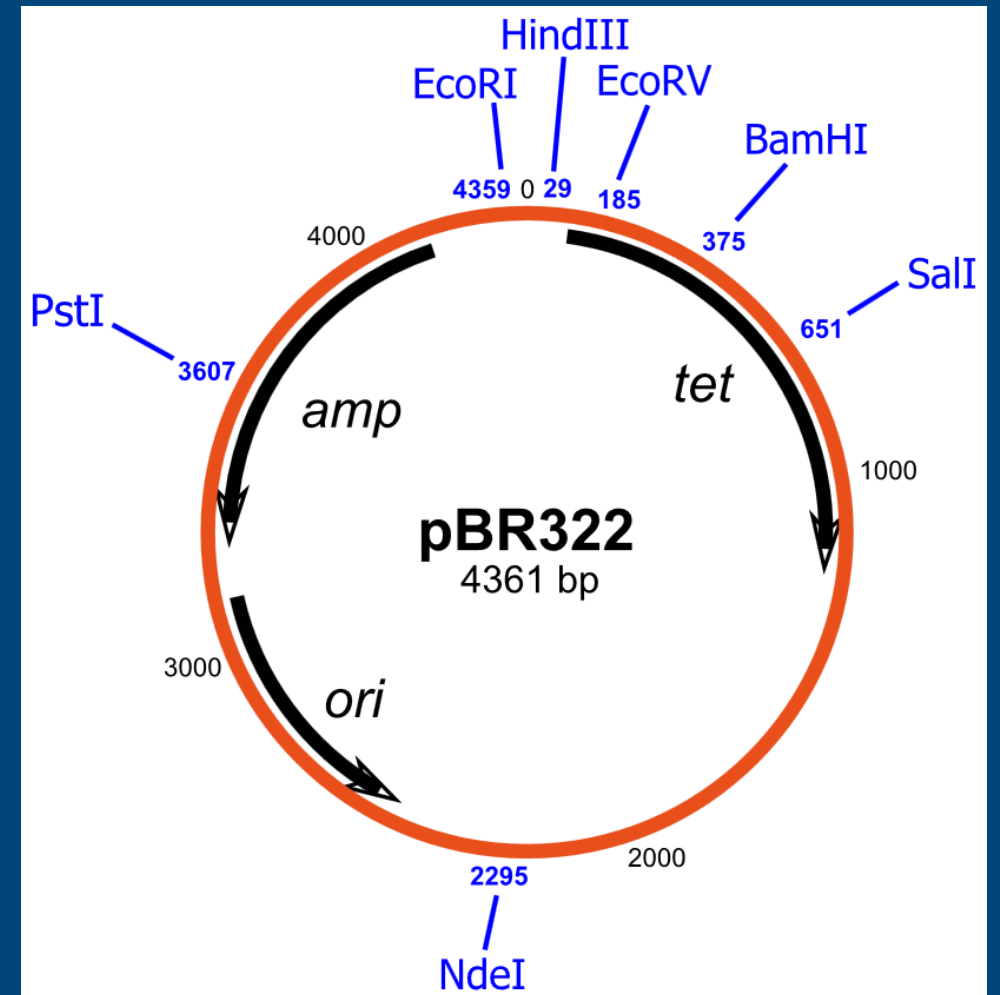
## Leven is..

- Een informatie systeem
- Manipuleerbaar met informatietechnologie
- Individuele processen kunnen ook buiten een levend systeem plaatsvinden
- **Uitwisseling van informatie is natuurlijk**

# Vector (Plasmide)



- **Relatief** eenvoudig
- Groot potentieel



# Sugar Synthesis from CO<sub>2</sub> in *Escherichia coli*

⇒ Quick fix for the climate !?



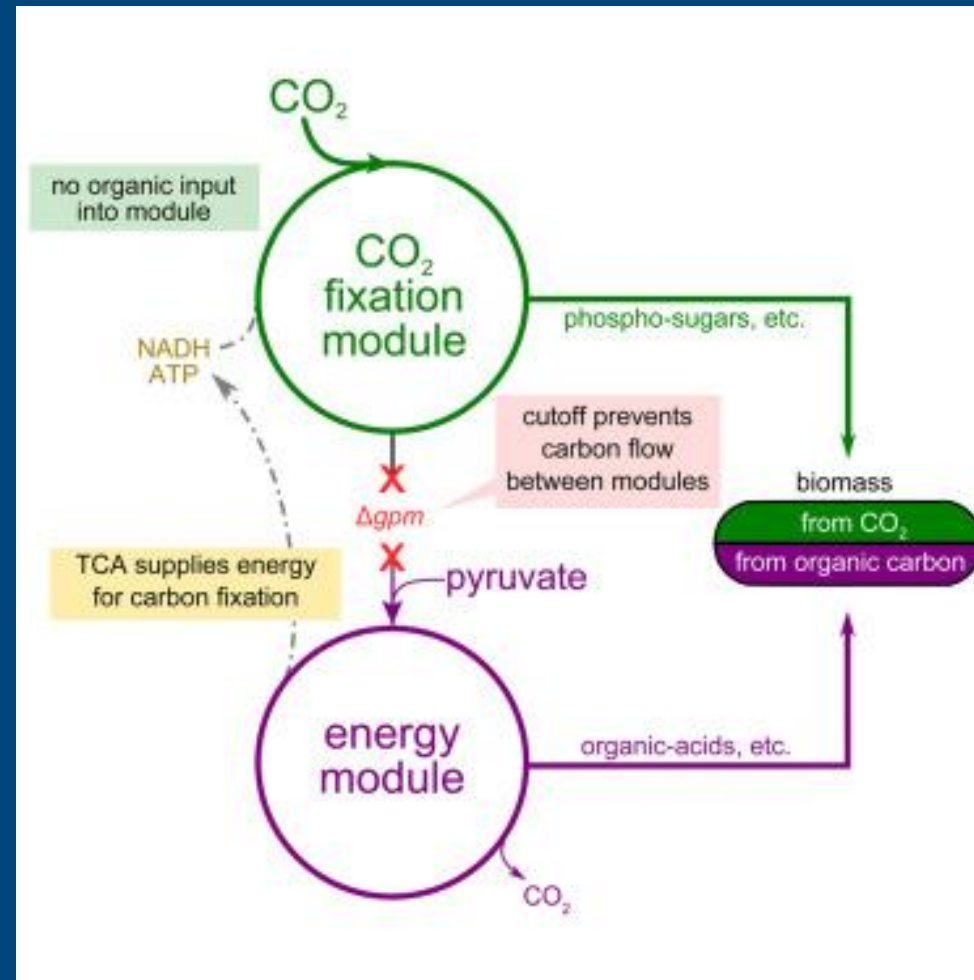
Biomass from CO<sub>2</sub> directly by E.coli.

⇒ Toepassing bij CO<sub>2</sub> productie

⇒ Of zelfs uit atmosfeer halen

Here, we demonstrate how a combination of rational metabolic rewiring, recombinant expression, and laboratory evolution has led to the biosynthesis of sugars and other major biomass constituents in *E. coli*. But no net. negative CO<sub>2</sub>

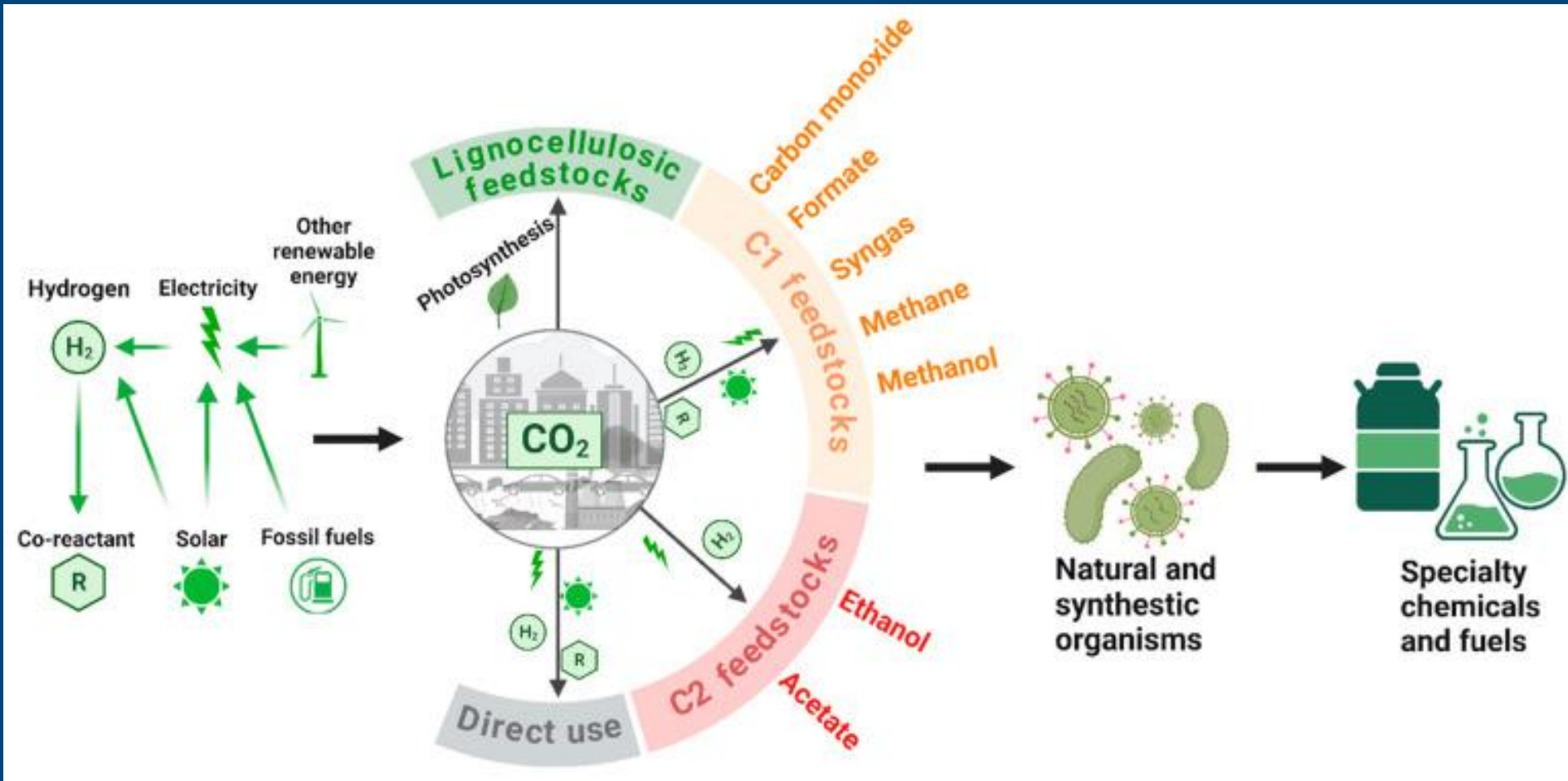
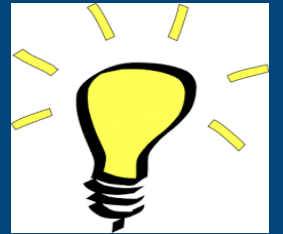
⇒ Biotech kan de wereldproblemen helpen oplossen



<https://www.nature.com/articles/d41586-019-03679-x>

<https://pubmed.ncbi.nlm.nih.gov/articles/PMC11446362/>

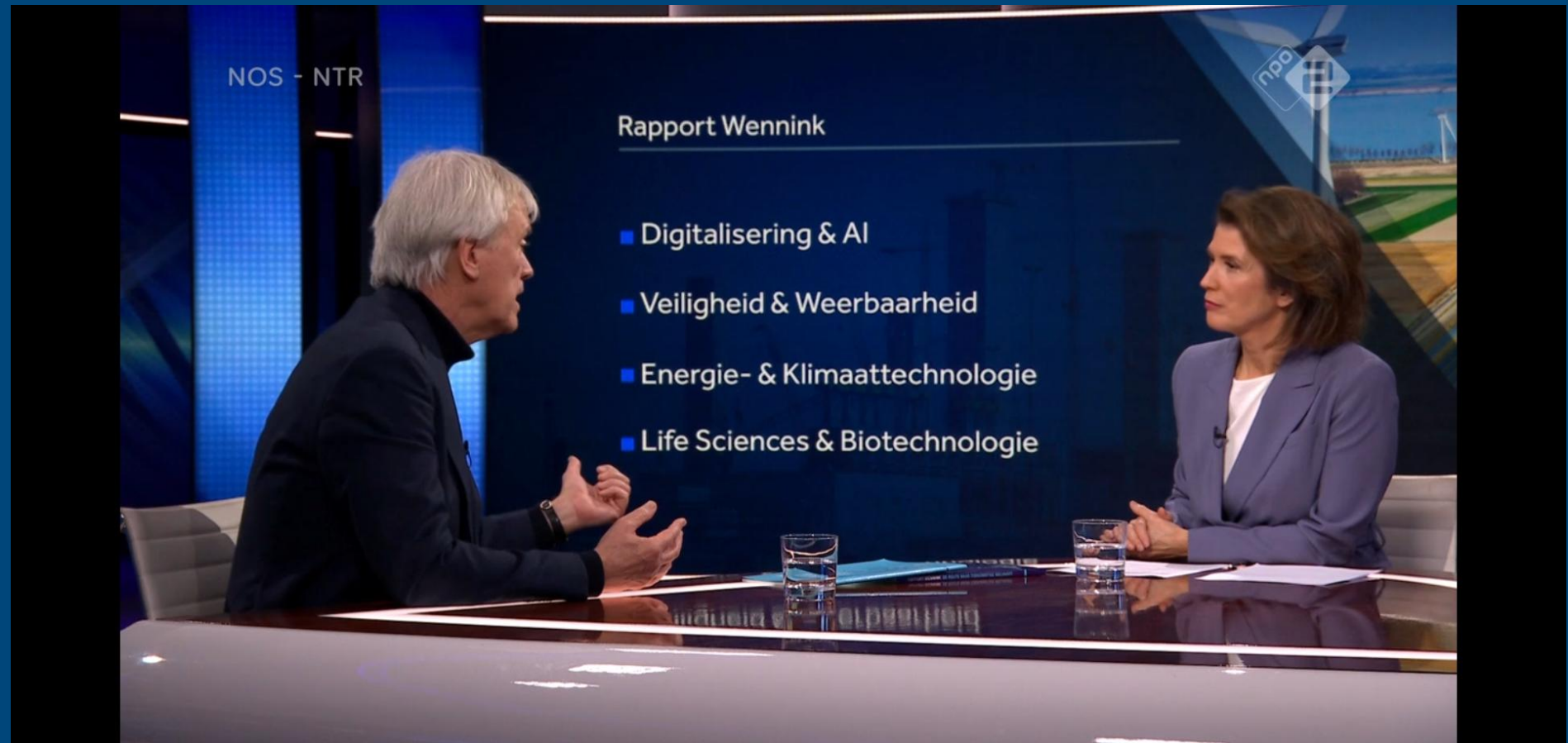
# Perspectives for Using CO<sub>2</sub> as a Feedstock for Biomanufacturing of Fuels and Chemicals



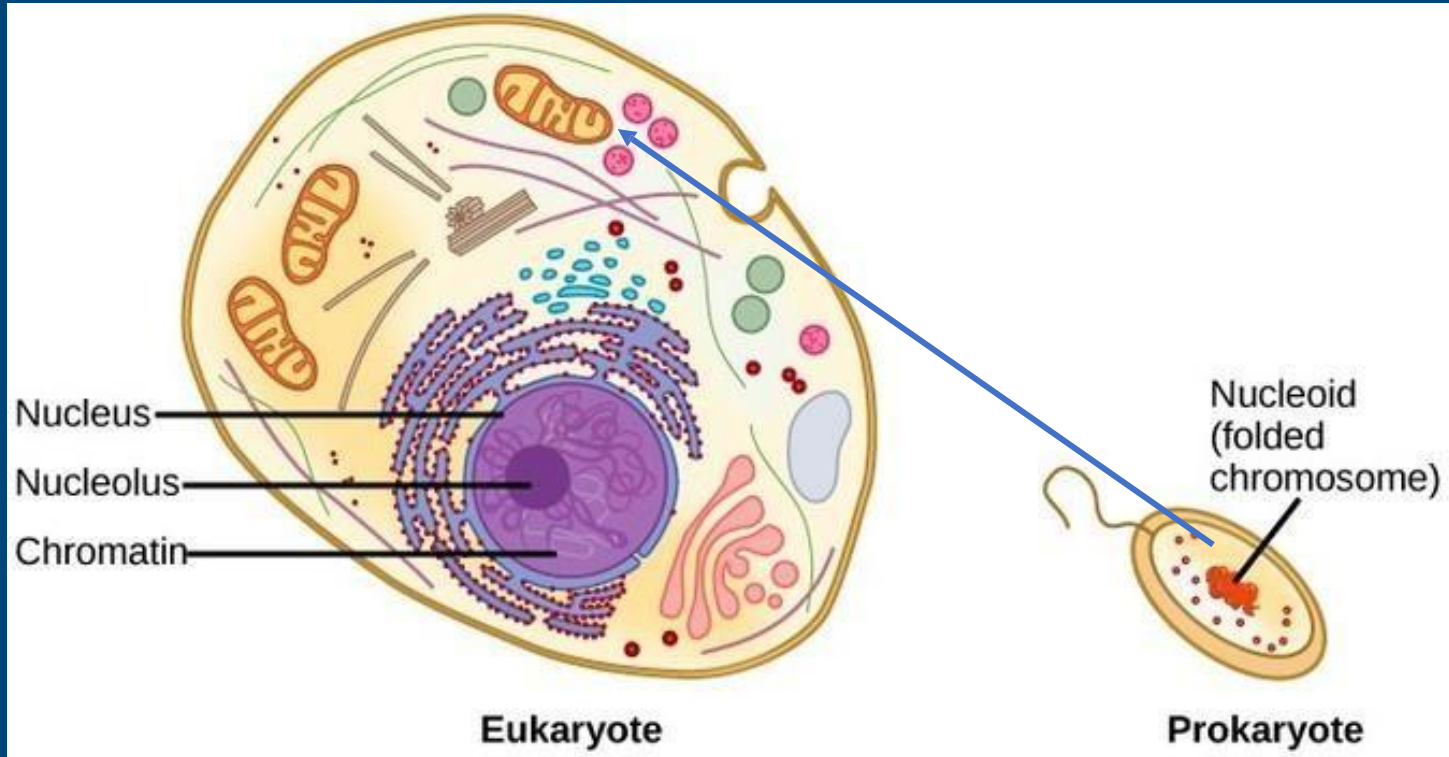
<https://pubmed.ncbi.nlm.nih.gov/articles/PMC10740661/>

# Biotech als groeimotor

Wennink (ASML)



# Eukaryoot v Prokaryoot



Prokaryoot is eigenlijk nog kleiner dan op plaatje

<https://www.youtube.com/watch?v=kGd-5HSDo6g>

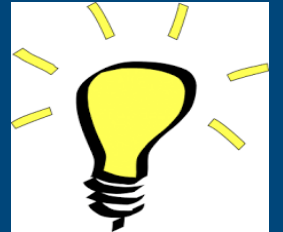
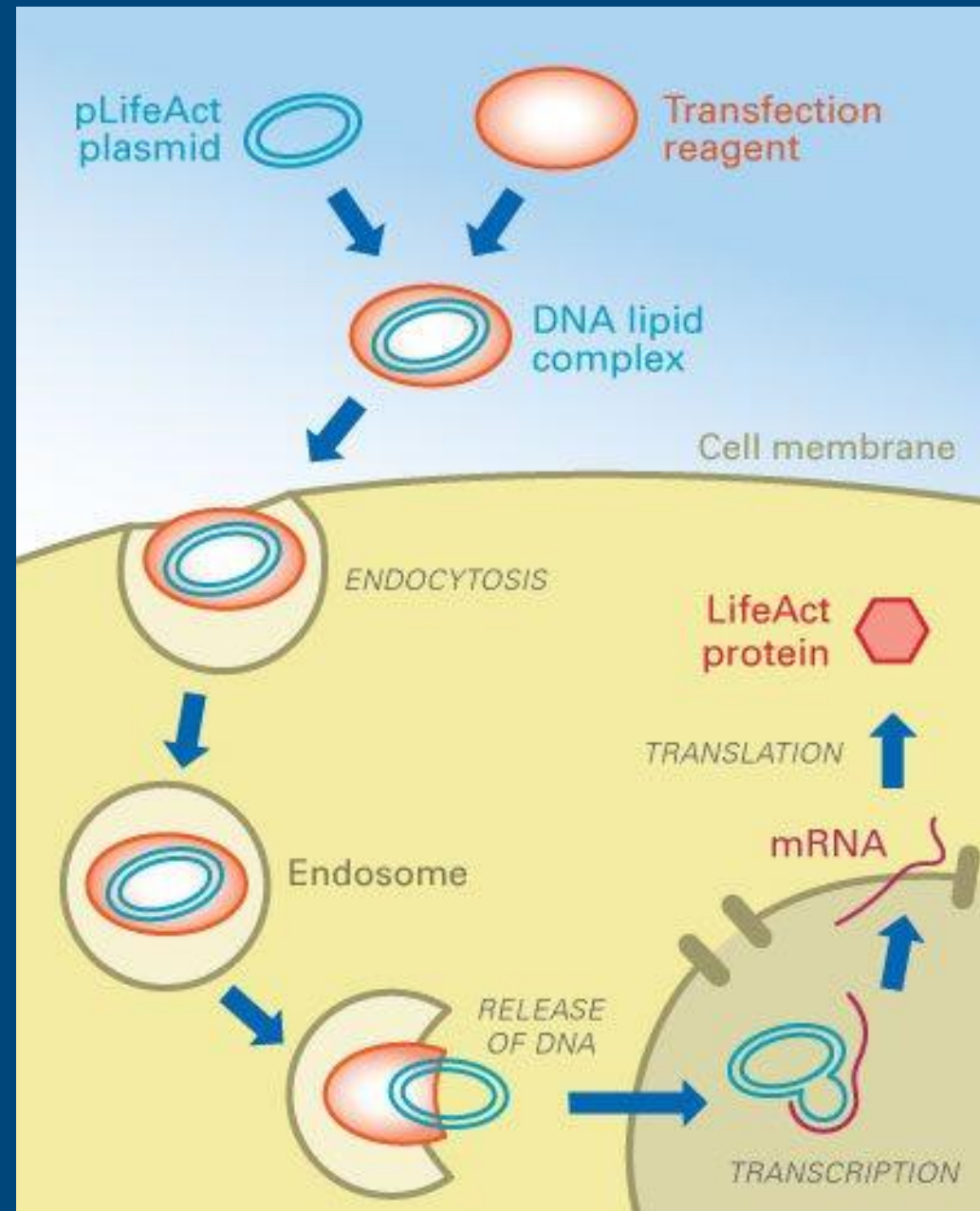
<http://www.bioplek.org/animaties/celtotaal/celstart.html>

# Transfectie

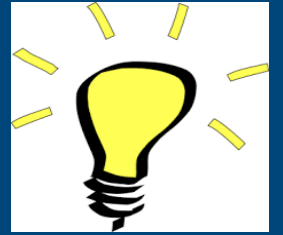
- **Transfection** is the process of deliberately introducing naked or purified nucleic acids into eukaryotic cells
- <https://en.wikipedia.org/wiki/Transfection>

⇒Bacterie maakt zo bijv. menselijk eiwit

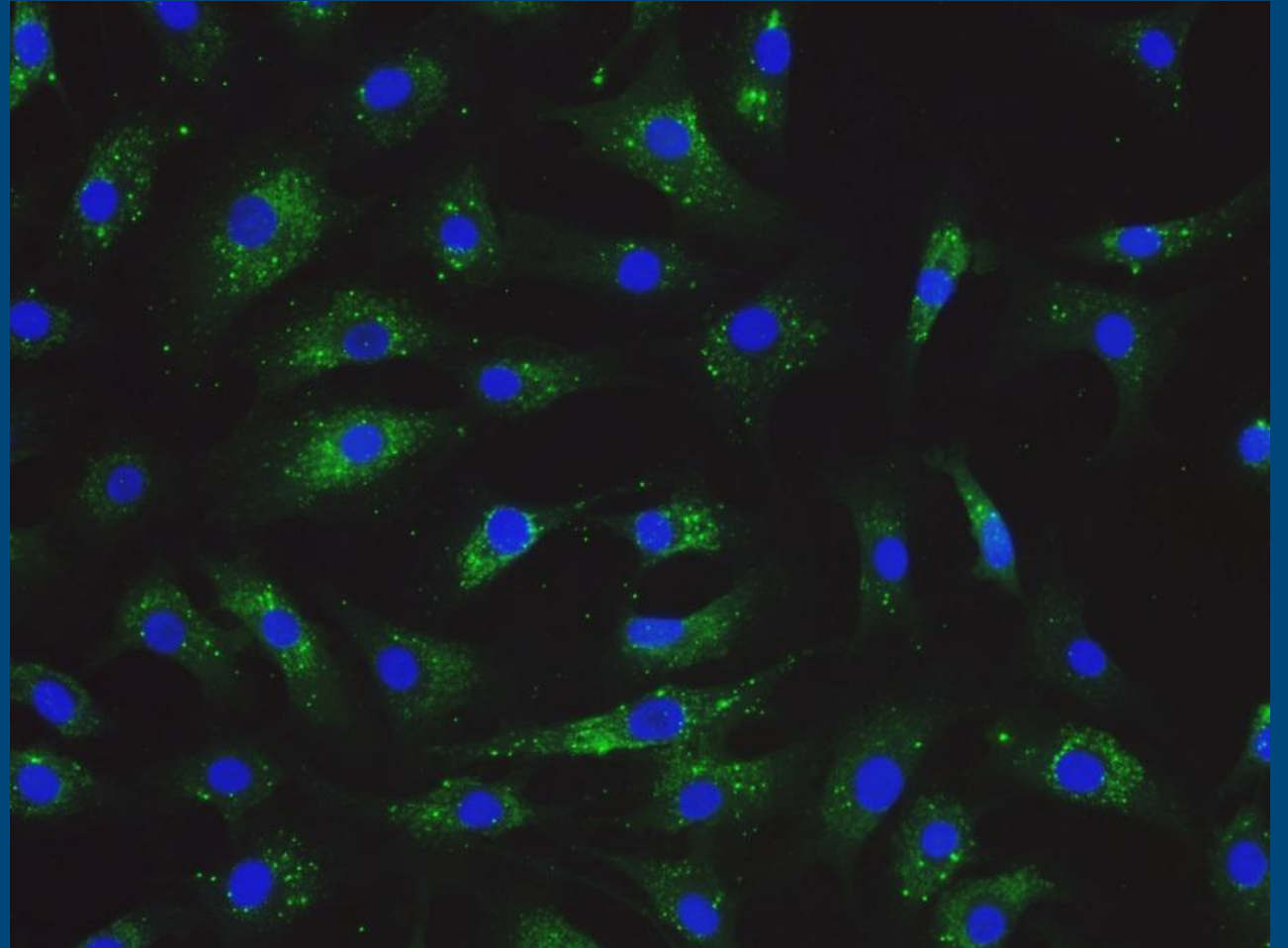
- Transduction is often used to describe virus-mediated gene transfer into prokaryotic cells.



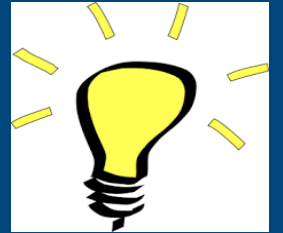
# Genetische manipulatie



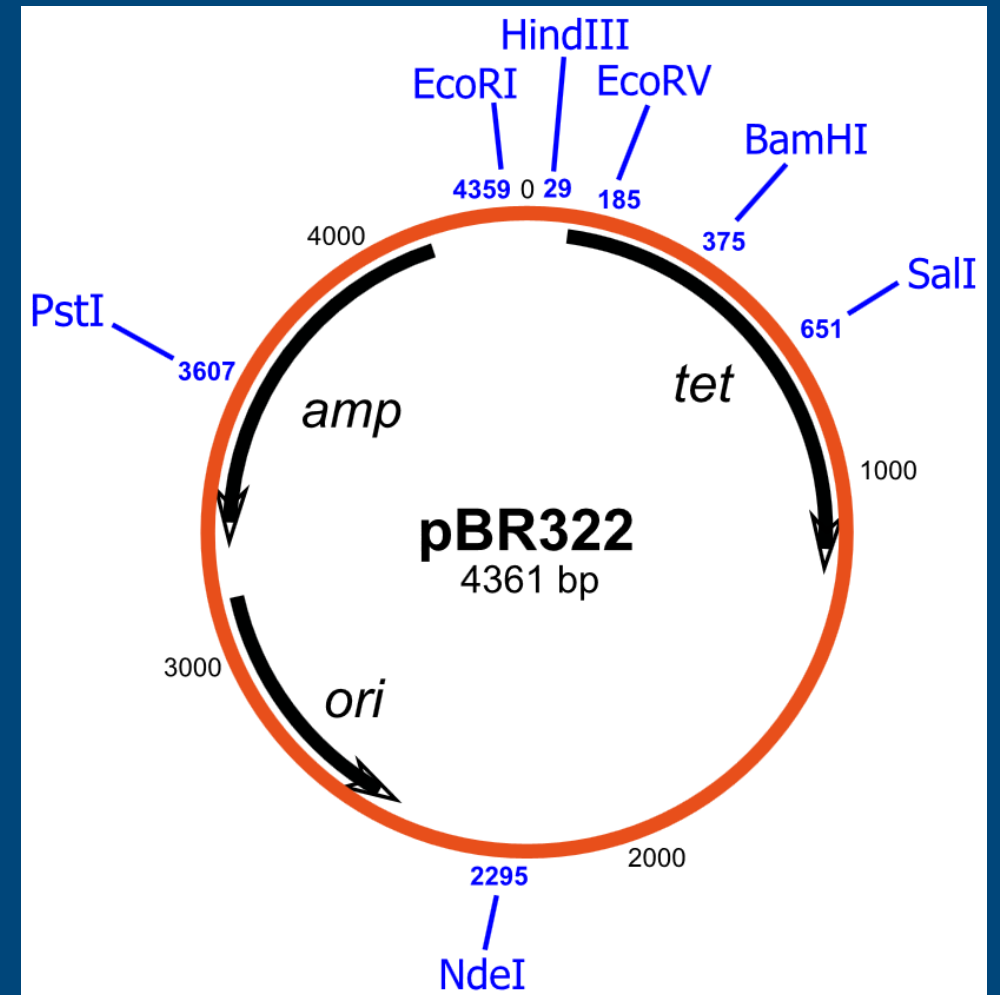
- Synthese of klonen van gen
- Maken vector
- **Transfectie => disruptie van celmembraan**  
(alleen *nodig bij non-virale vectoren*)
- Selectie en quality control
- Verspreiding
- Eten
- Doel
- Noodzakelijkheid



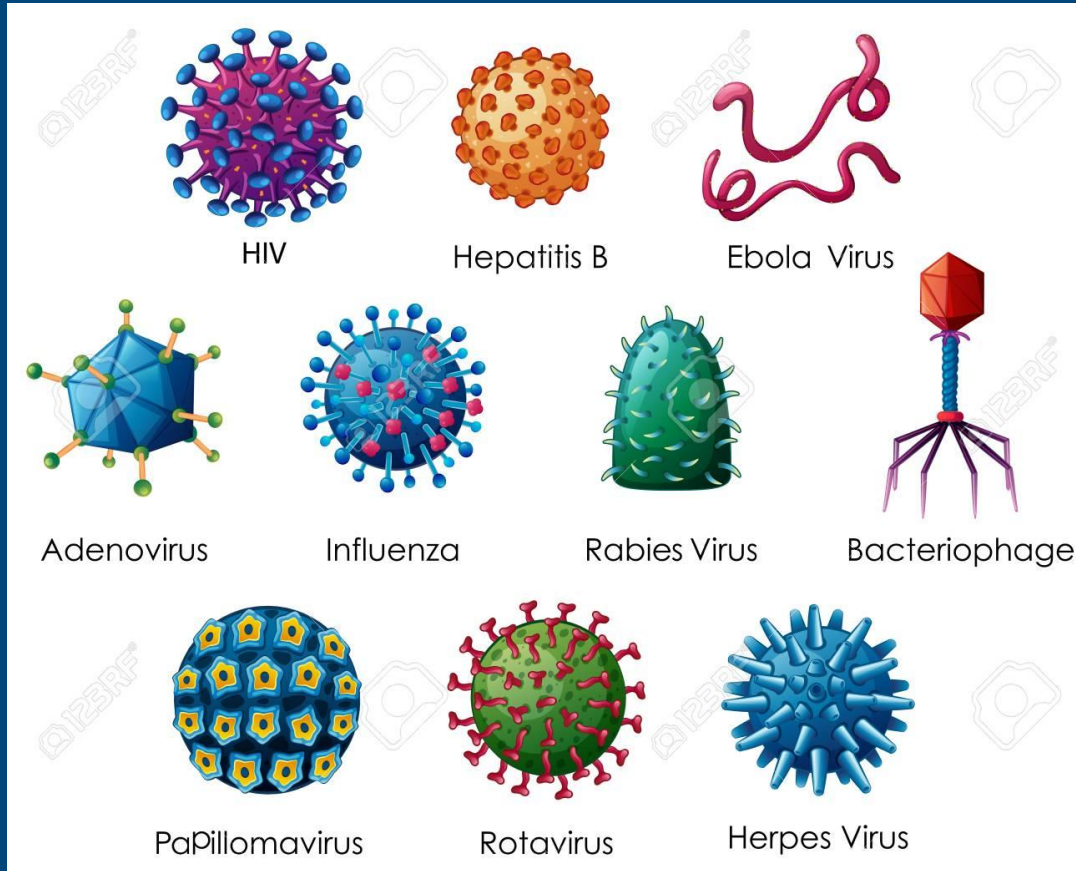
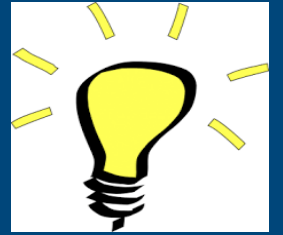
# Vector (Plasmide)



- Meer dan 1 kopie  
=> overexpressie  
=> **Genomische instabiliteit**
- Kans op problemen in bacterie of plant is klein en niet erg.
- Maar mens en dier wel
- NB Worden wel steeds beter/veiliger

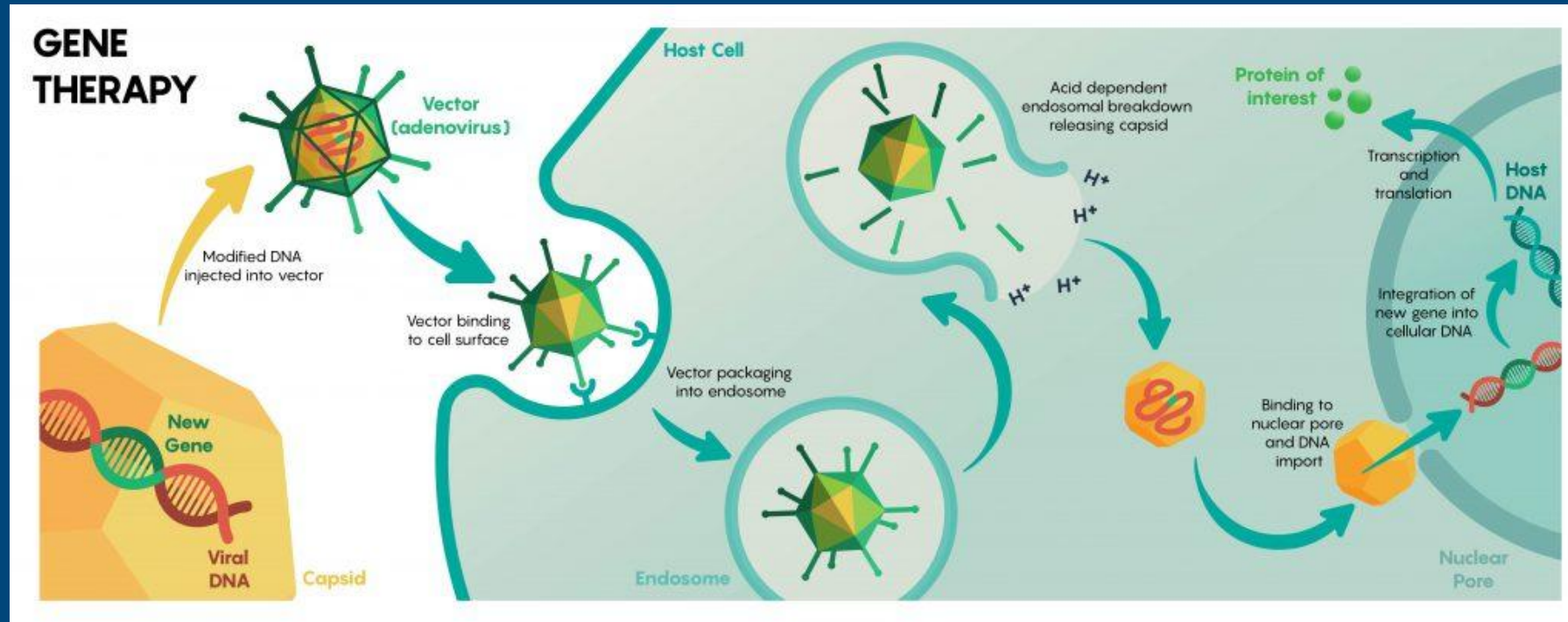
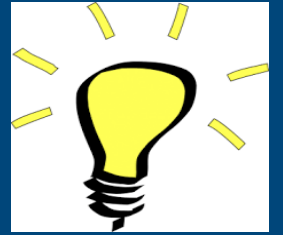


# Virus als **vector** => delivery



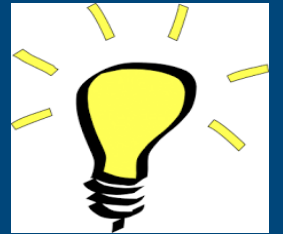
- Vector = vehikel voor aflevering (delivery)
- Zijn bij uitstek geschikt om genetisch materiaal in menselijke cellen te krijgen (doen ze van nature).
- 10% van ons genoom is oud virus materiaal
- Bij vaccins gebruiken we getemde virussen om virussen te bestrijden
- Maar is ingewikkeld om te maken en te testen (=> recombinatie, waarbij het virus weer helemaal actief wordt uitsluiten)
- Er is vaak al bestaande afweer tegen deze virussen

# Delivery: 2 traps raket



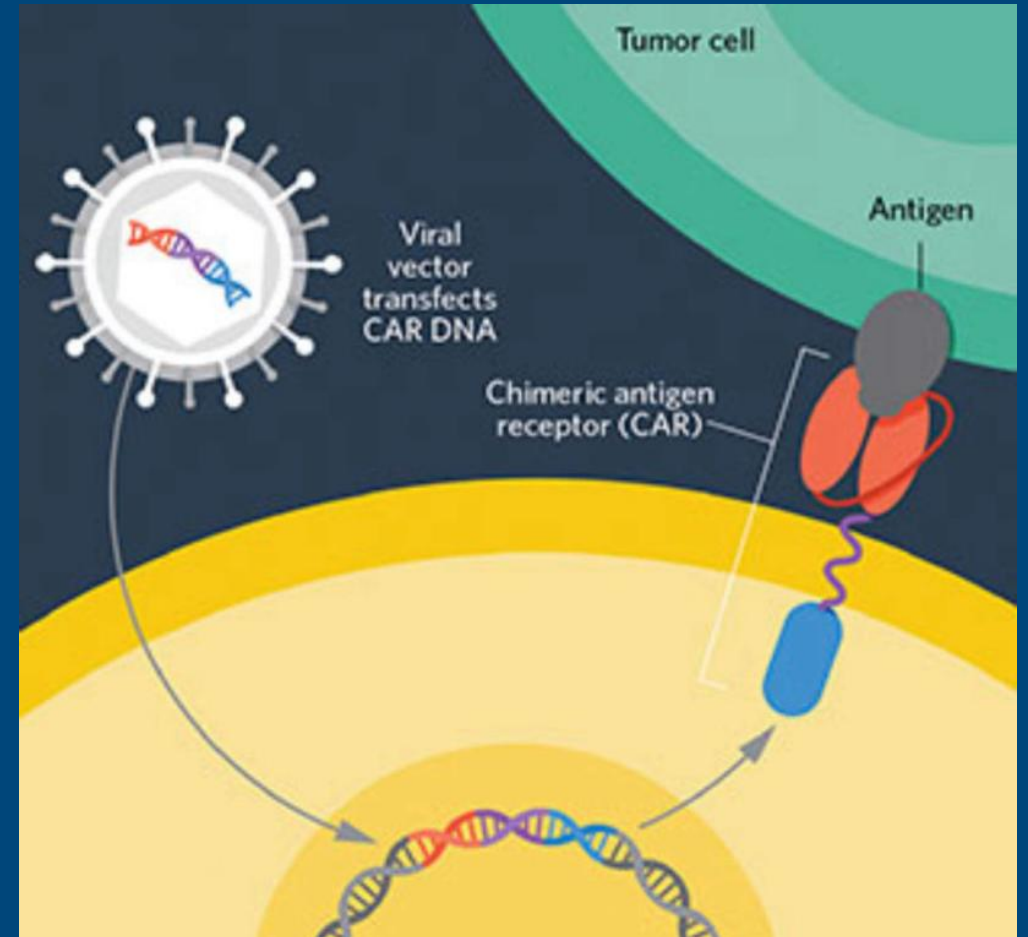
- ⇒ Homing naar de cel
- ⇒ Integratie van DNA

# Introductie: CAR-T

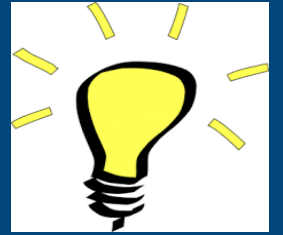


- Opvoeden van de afweer om kanker te herkennen
- Levend medicijn
- **Biologische robot**
- If there isn't a cure for their cancer today, there's a reasonable chance that around the corner, there's going to be one.

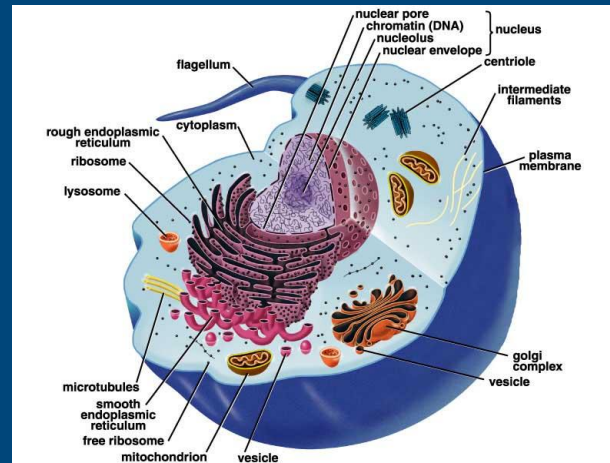
<https://www.nature.com/articles/d41586-022-00241-0>



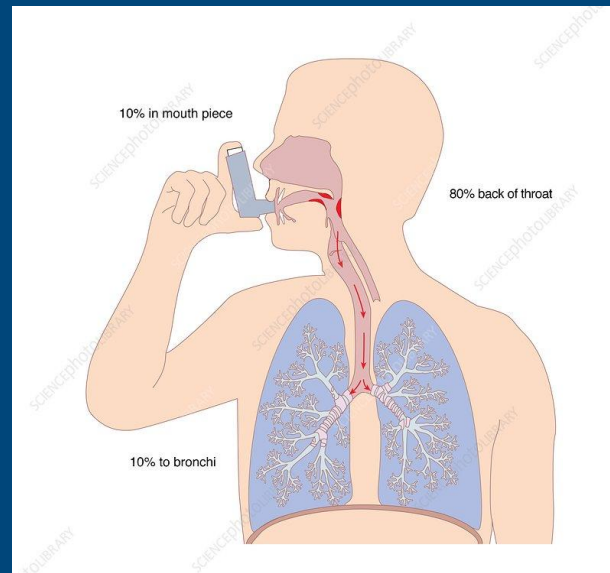
# The delivery problem



- 1 cel => OK
- Elke cel in kweekbak => al lastig



- Taaislijmziekte => heel lastig
- Heel mens => onmogelijk?

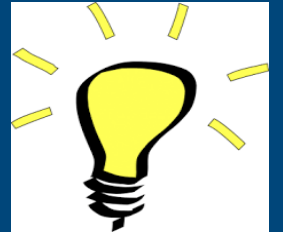
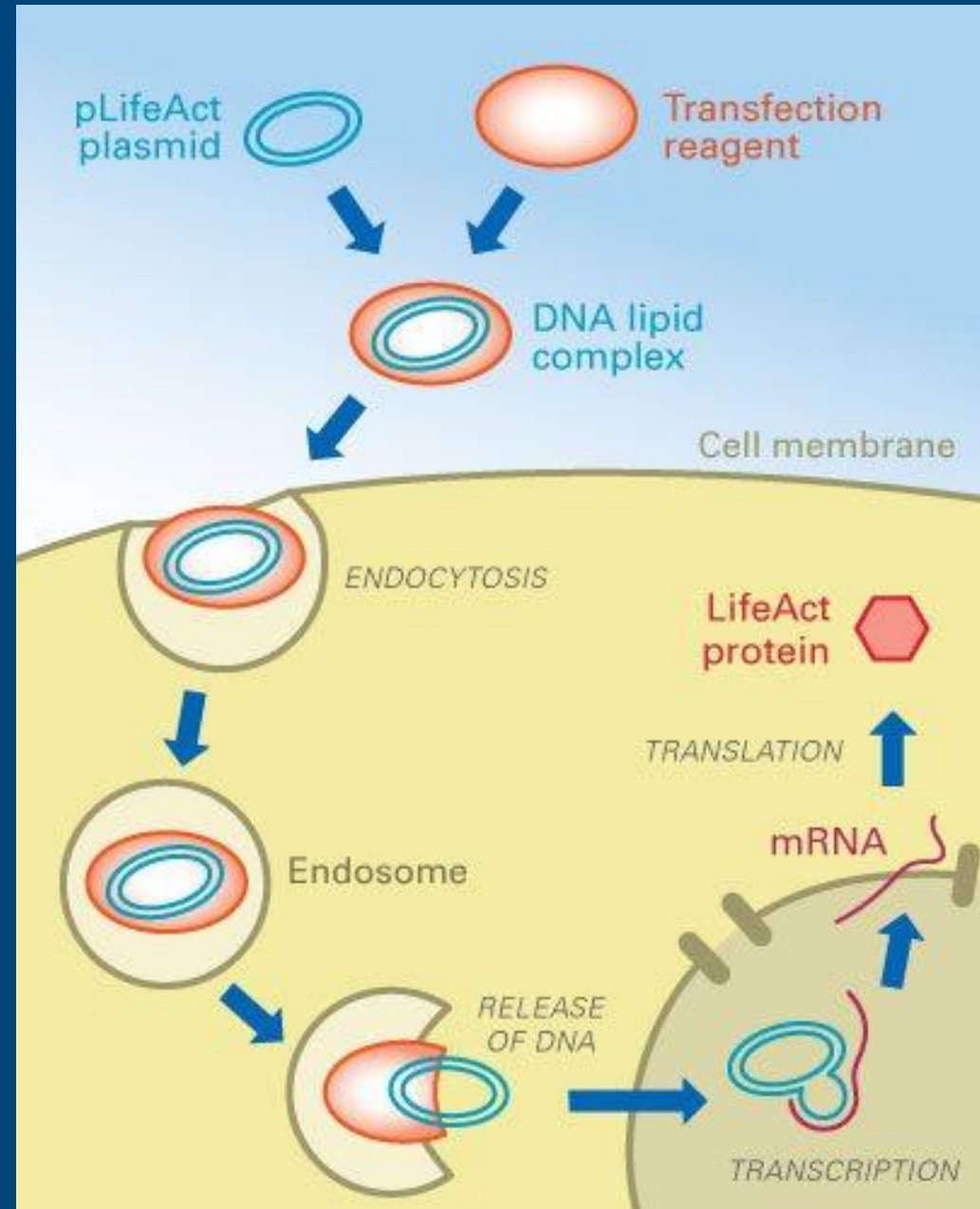


# Transfectie

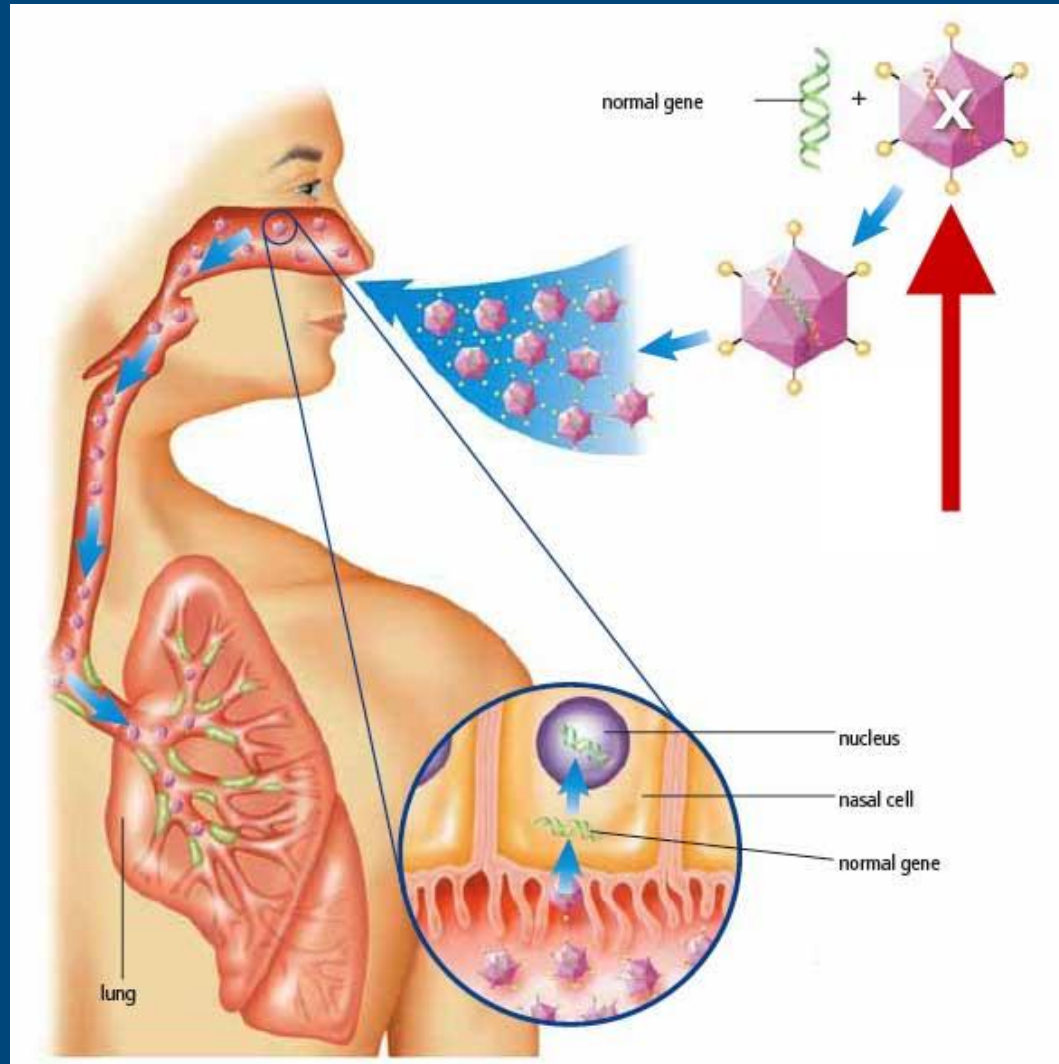
- **Transfection** is the process of deliberately introducing naked or purified nucleic acids into eukaryotic cells
- <https://en.wikipedia.org/wiki/Transfection>

⇒ Bacterie maakt zo bijv. menselijk eiwit

- Transduction is often used to describe virus-mediated gene transfer into prokaryotic cells.



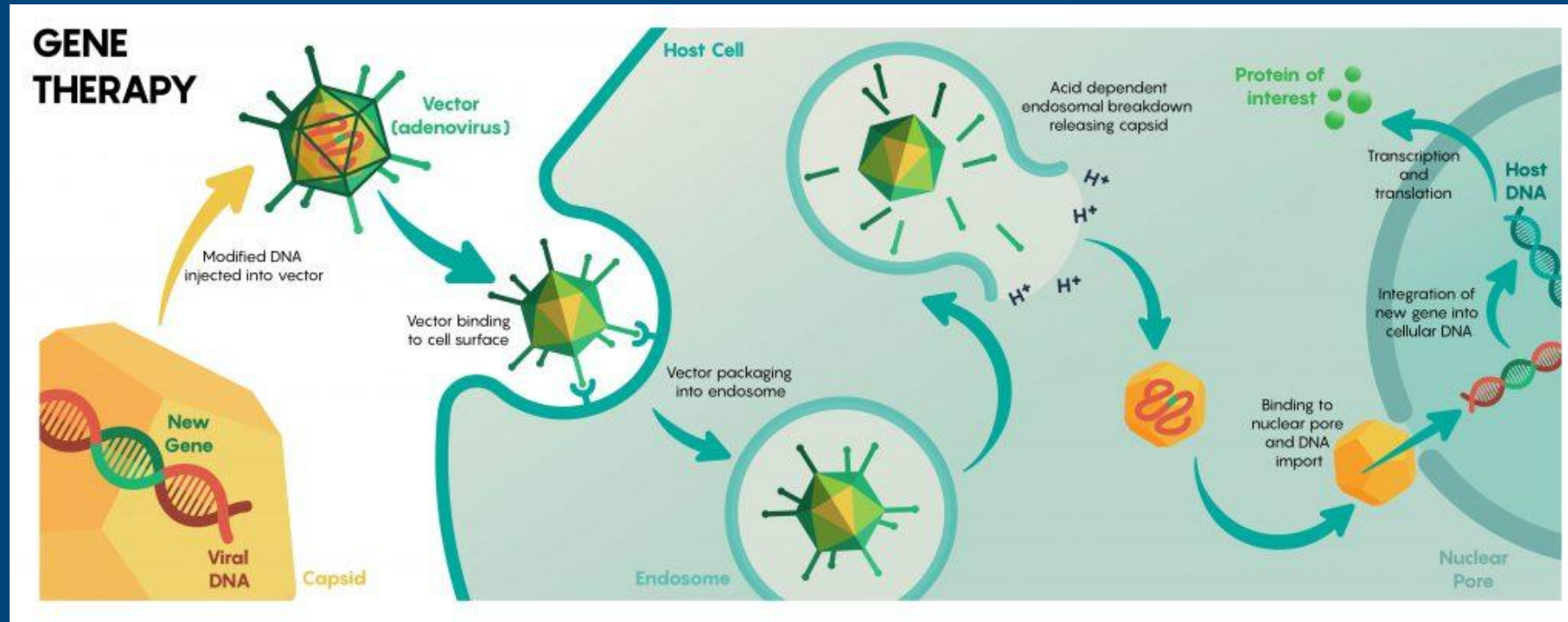
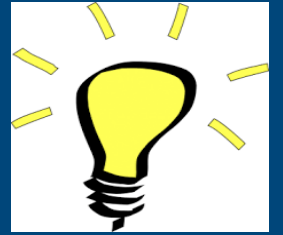
# Delivery: Gene therapy treatment for cystic fibrosis



<http://learn.genetics.utah.edu/content/genetherapy/casestudy/>

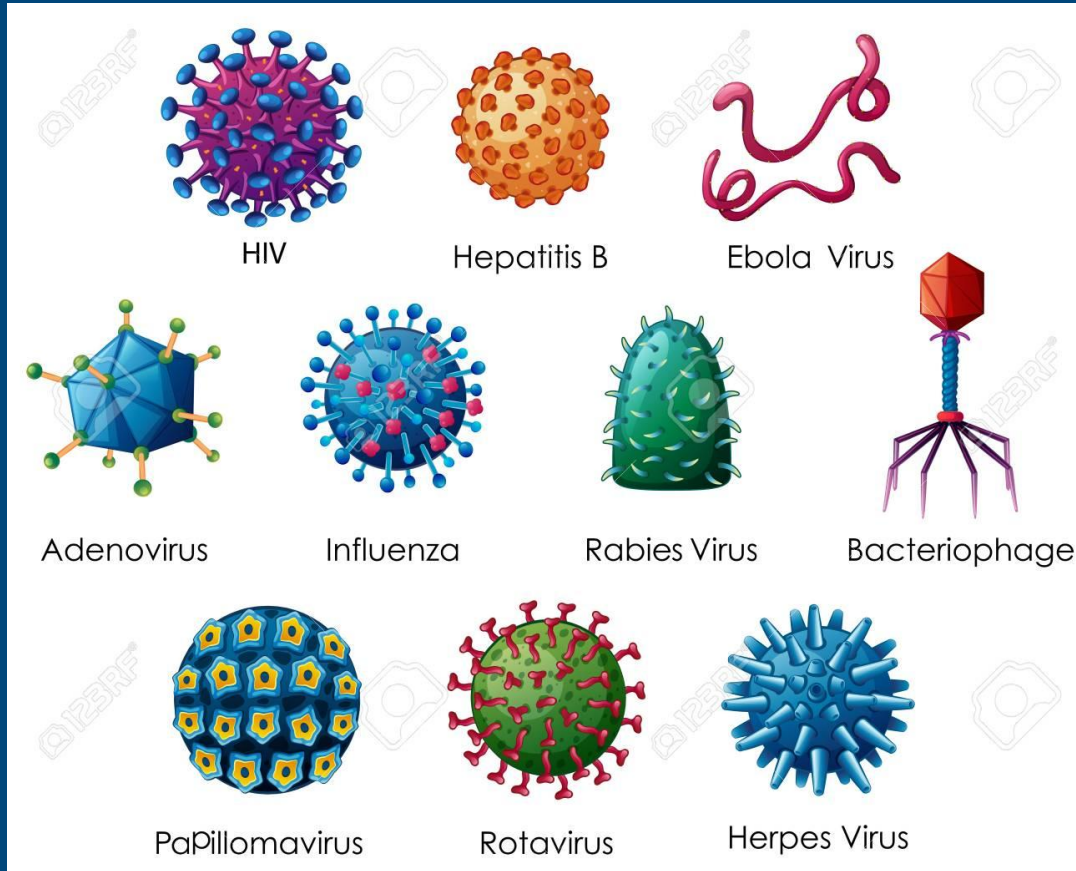
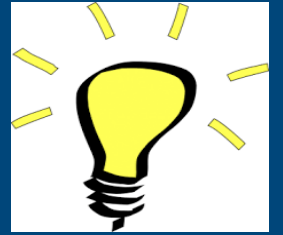
<http://perspectivesinmedicine.cshlp.org/content/3/2/a009472.full>

# Delivery: 2 traps raket



- ⇒ Homing naar de cel
- ⇒ Integratie van DNA

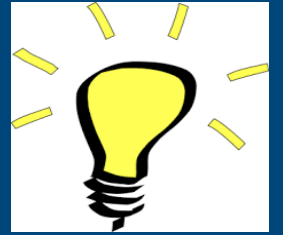
# Virus als **vector** => delivery



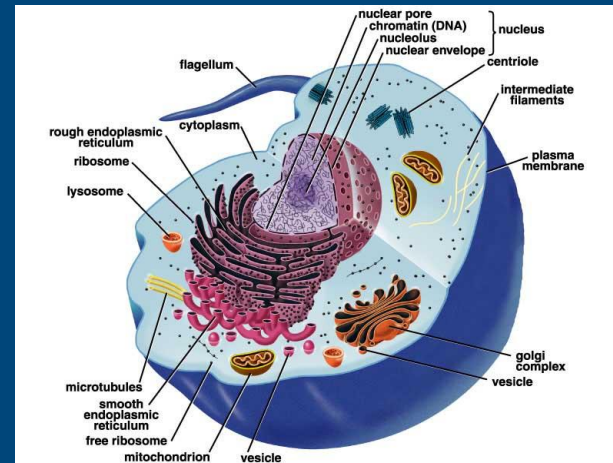
- Vector = vehikel voor aflevering (delivery)
- Zijn bij uitstek geschikt om genetisch materiaal in menselijke cellen te krijgen (doen ze van nature).
- 10% van ons genoom is oud virus materiaal
- Bij vaccins gebruiken we getemde virussen om virussen te bestrijden
- Maar is ingewikkeld om te maken en te testen (=> recombinatie, waarbij het virus weer helemaal actief wordt uitsluiten)
- **Insertie op meerdere locaties, en in oncogenen**



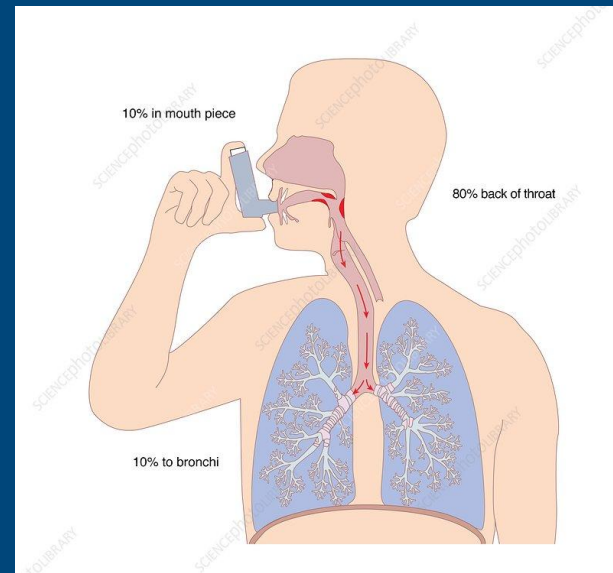
# The delivery problem



- 1 cel => OK
- Elke cel in kweekbak => al lastig

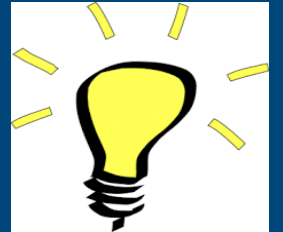
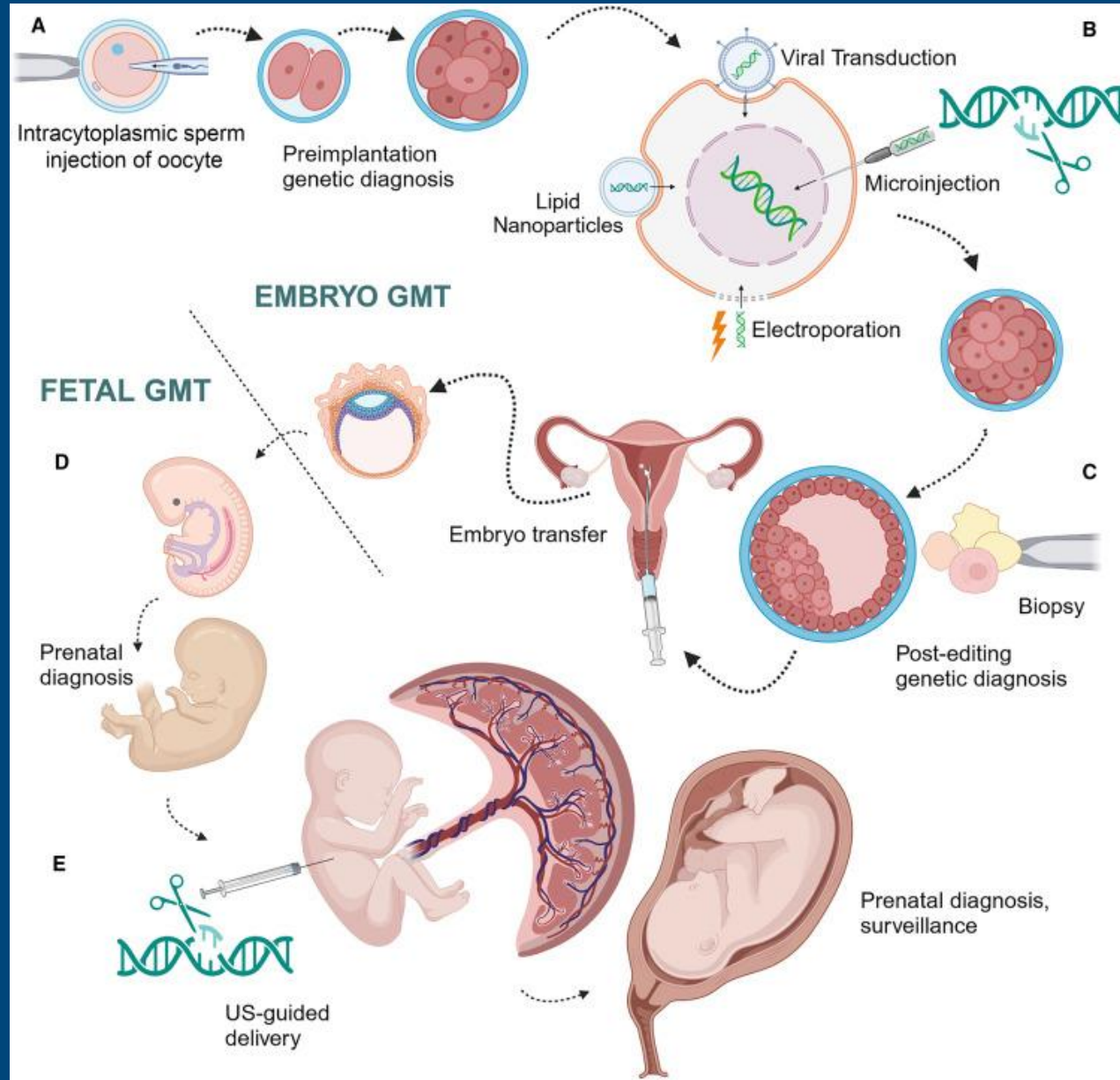


- Taaislijmziekte => heel lastig
- Heel mens => onmogelijk?

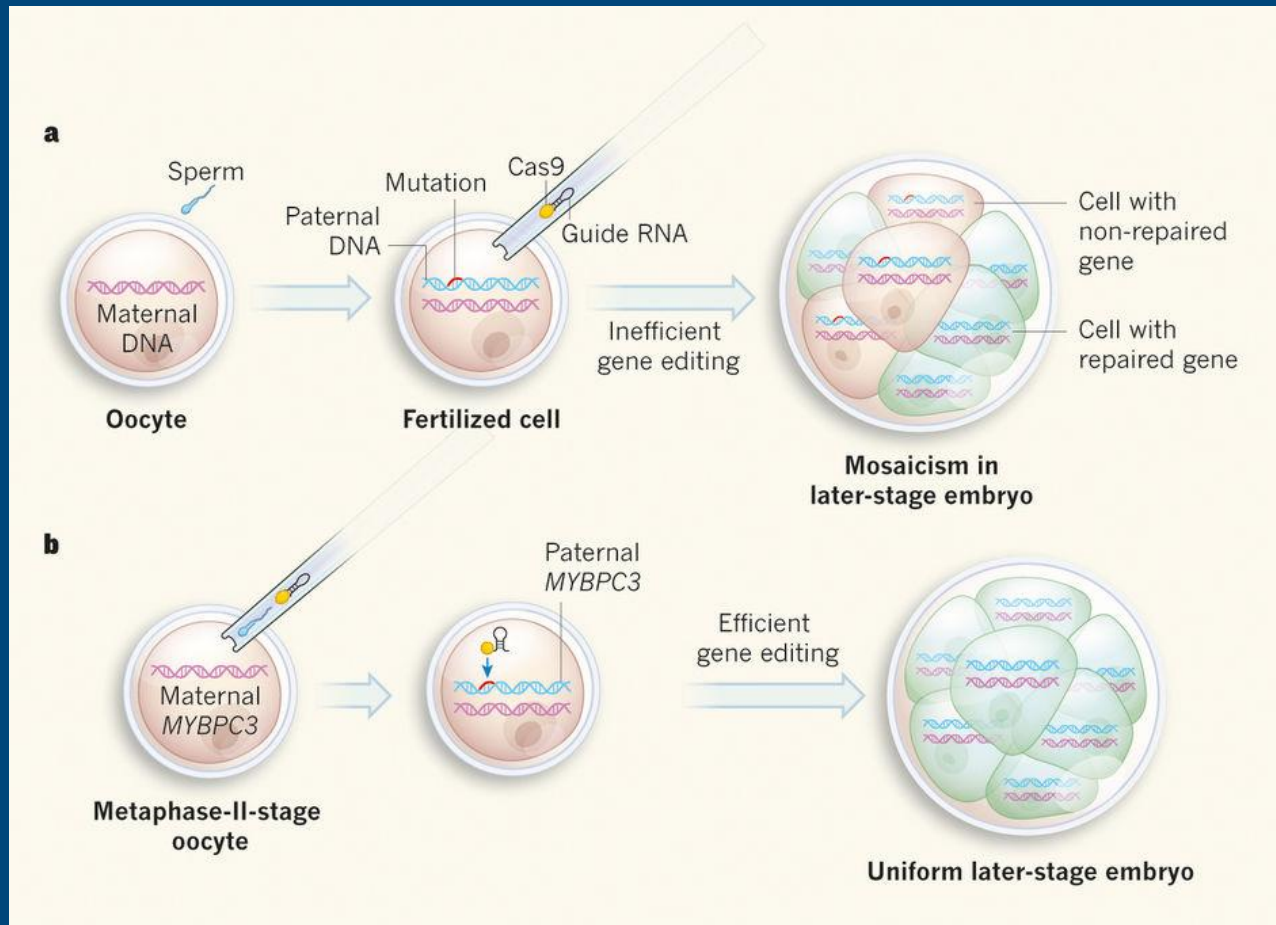


# Embryo editing

- <https://www.cell.com/molecular-therapy-family/advances/fulltext/S2329-0501%2824%2900045-7>



# Correction of a pathogenic gene mutation in **human** embryos using CRISPR

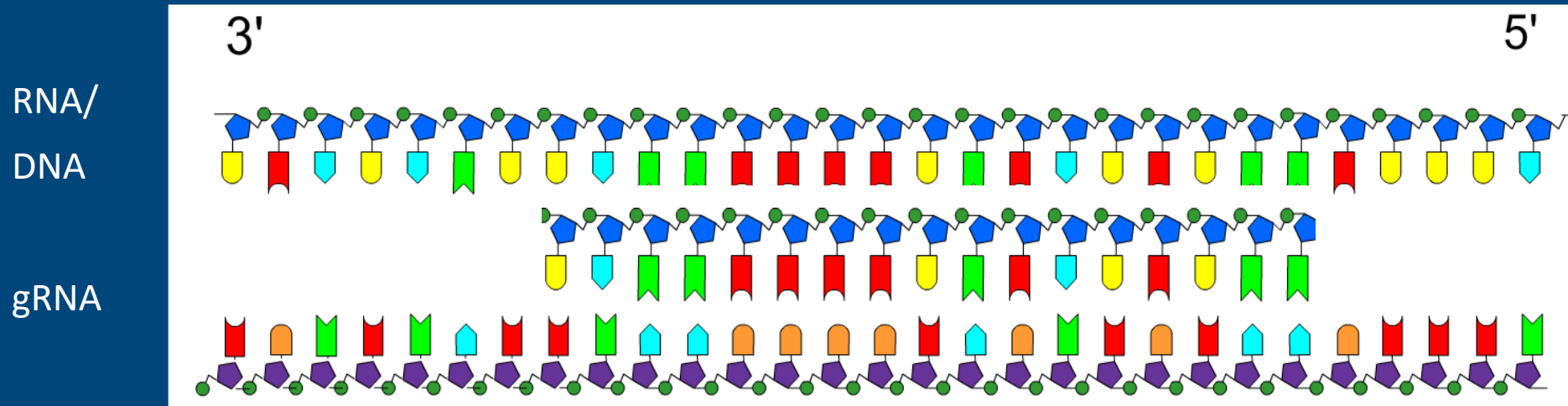
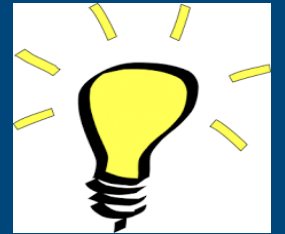
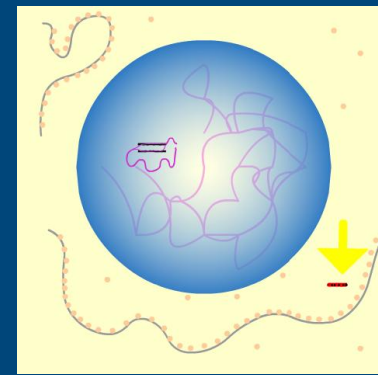


Insertie in elke cel,  
en op 1 locatie,  
in principe

[http://www.nature.com/nature/journal/v548/n7668/fig\\_tab/nature23533\\_F1.html](http://www.nature.com/nature/journal/v548/n7668/fig_tab/nature23533_F1.html)



# Biotech: guideRNA/primer actie



Kans =  $\frac{1}{4}$  voor 1<sup>e</sup> nucleotide, en  $\frac{1}{4}$  voor 2<sup>e</sup> nucleotide (er zijn 4 verschillende)

Kans =  $\frac{1}{4} \times \frac{1}{4} = \frac{1}{4^2} = 1$  op 16 voor 2 nucleotiden ( $\frac{1}{4^n}$  voor n nucleotiden)

Kans =  $\frac{1}{4^{20}}$  voor 20 nucleotiden =  $\frac{1}{1000.000.000.000}$

Aantal nucleotiden in het genoom = 3.000.000.000

Klein stukje GuideRNA/primer zorgt al voor specifieke herkenning

=> in principe geen off-target effects

=> Zelfde techniek is de basis van PCR (guide => primer)

# Orgaan v. systemisch (“germ-line”)



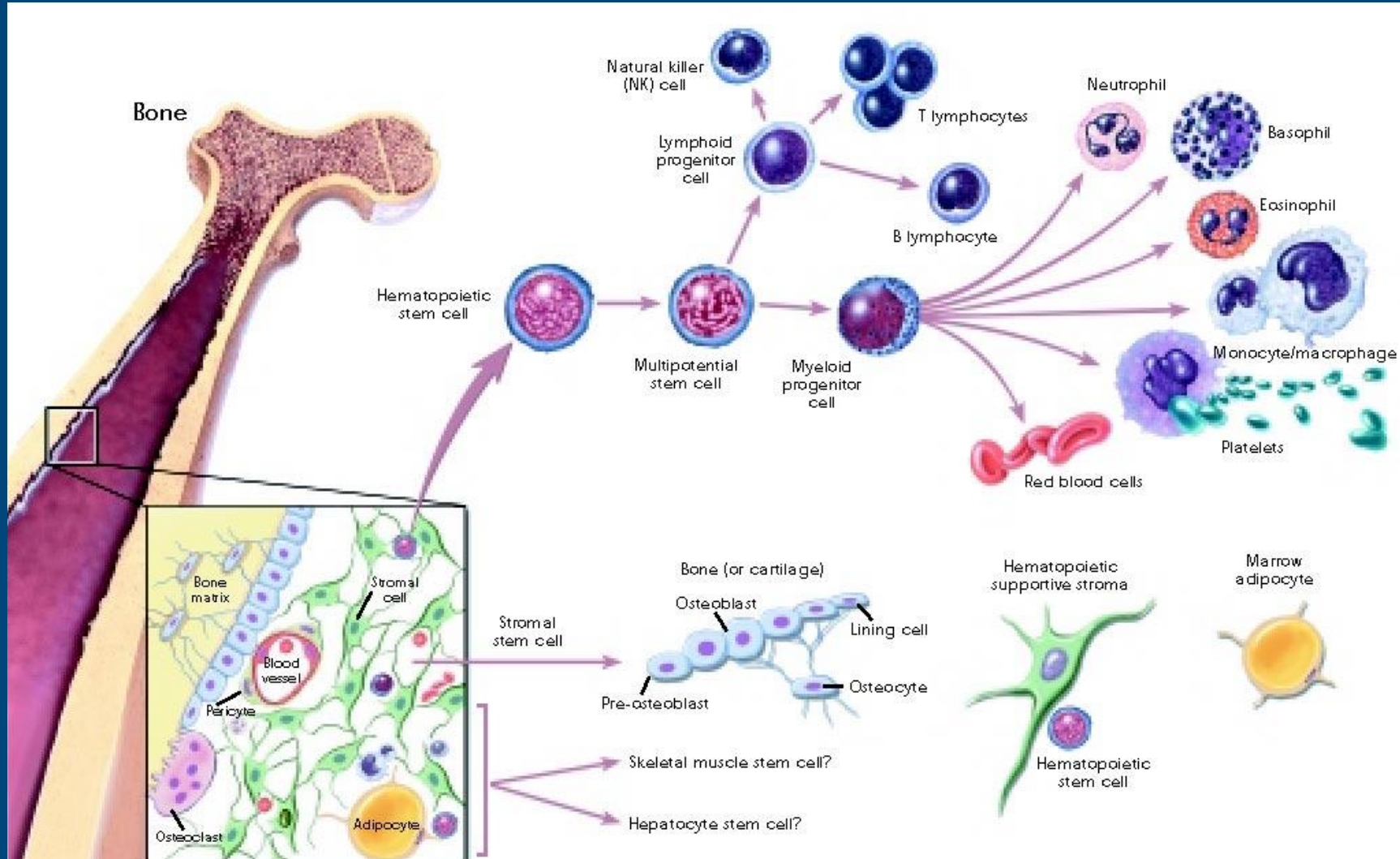
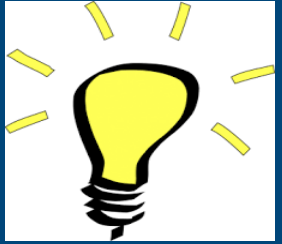
<http://www.bbc.com/news/magazine-28986843>



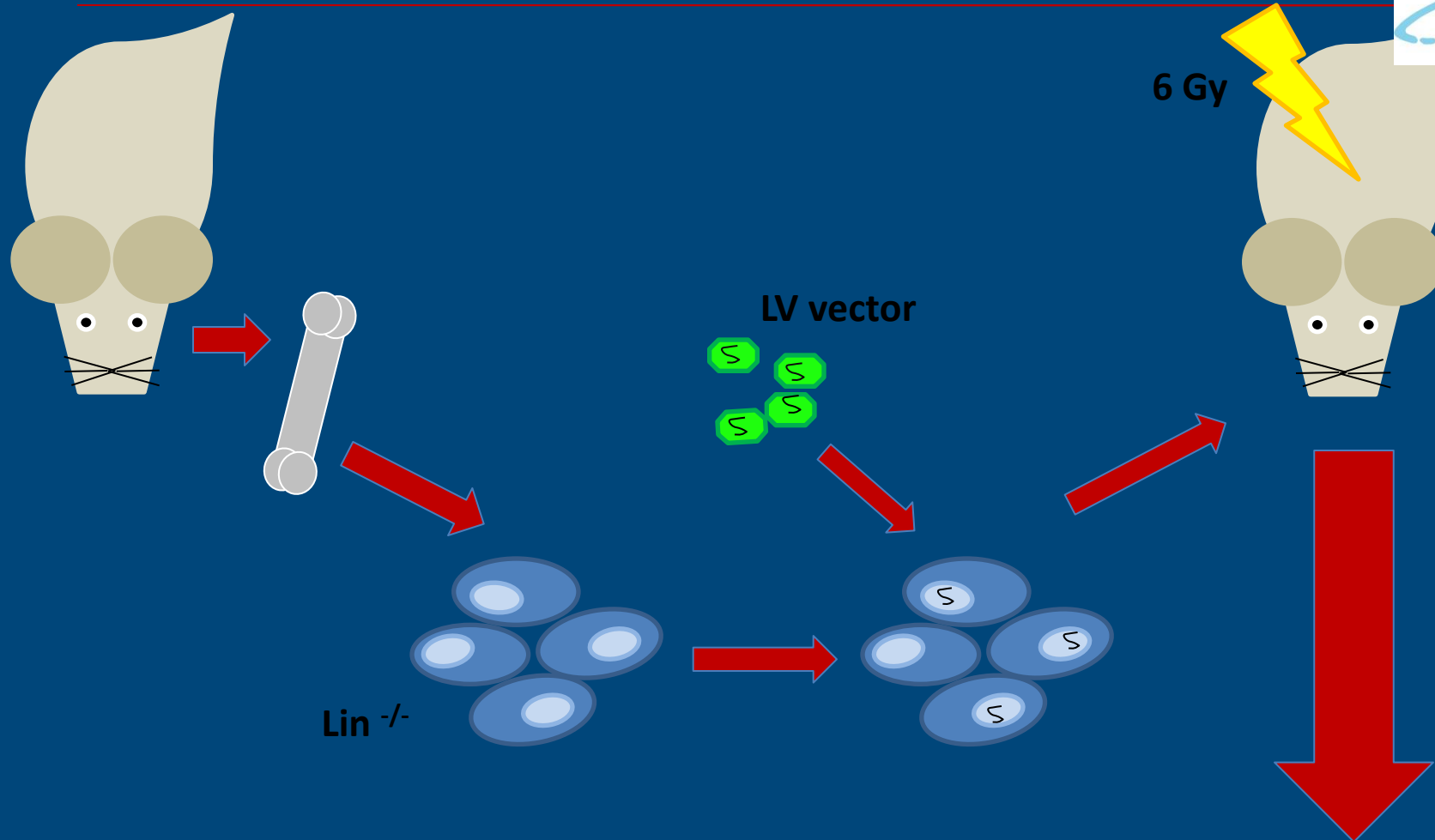
GFP-muis

Germ-line GM bij mensen:  
Kind van 3 ouders (3<sup>e</sup> nodig voor mitochondrien)  
En in China (HIV)  
Handig voor onderzoek, maar niet voor mensen  
Volgende generaties hebben de aanpassing ook  
=> **aanpassing van de soort**

# Celbio 2: Stamcellen in het beenmerg



# Experimental Approach (ex vivo)



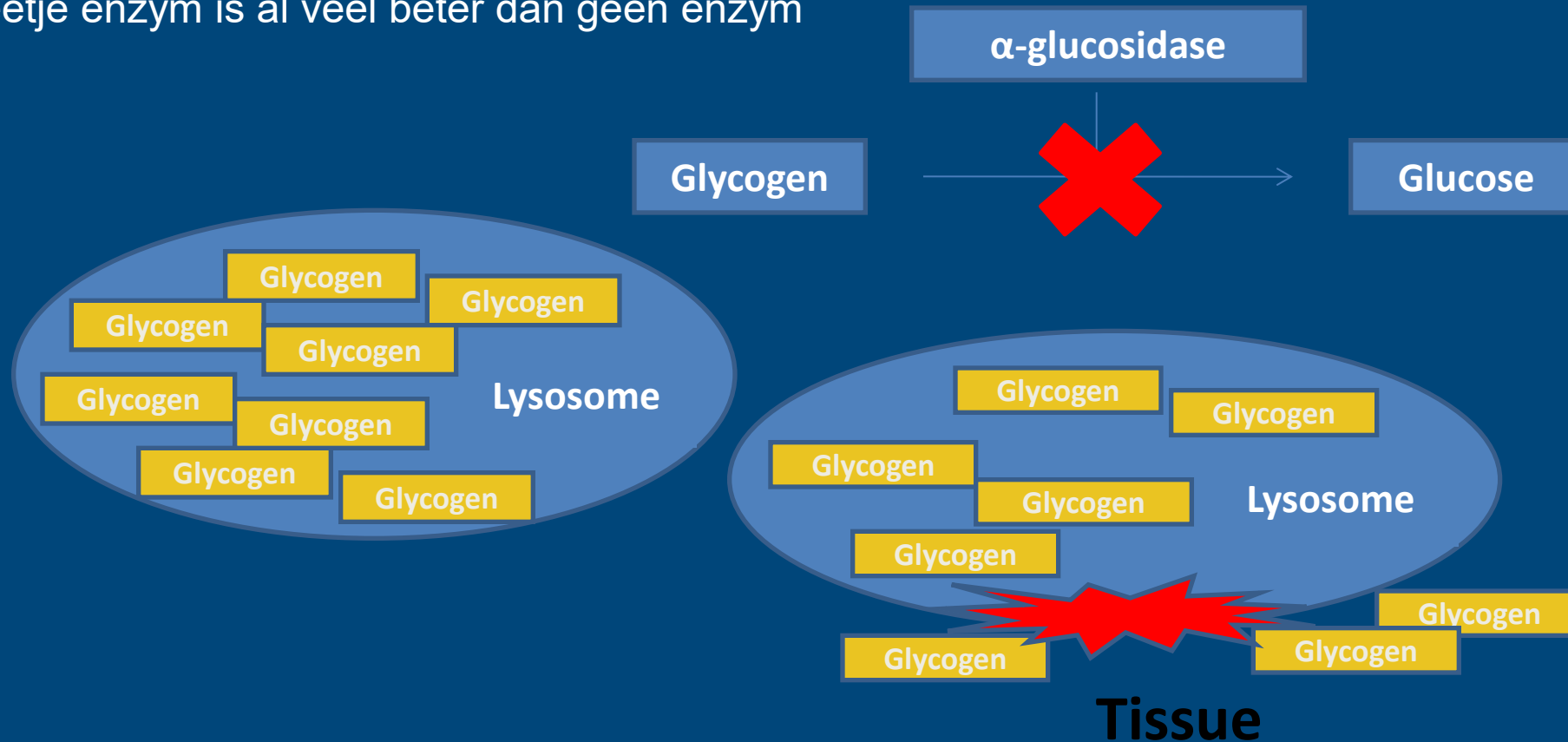
Expression of the transgene in all hematopoietic cells  
Ex vivo possible through use of stem cells (quality control)

stamcel => college 2

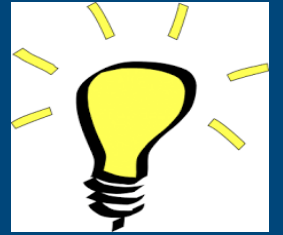
# Gen/stamceltherapie: Pompe Disease

Autosomal recessive lysosomal storage disorder  
Deficiency in  $\alpha$ -glucosidase (GAA)

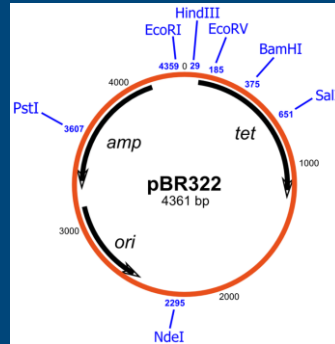
=> Klein beetje enzym is al veel beter dan geen enzym



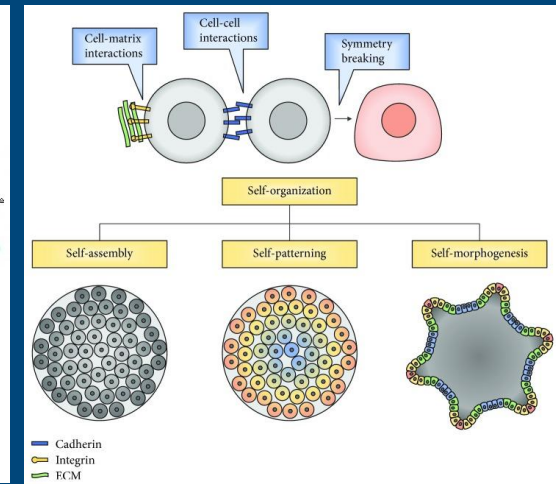
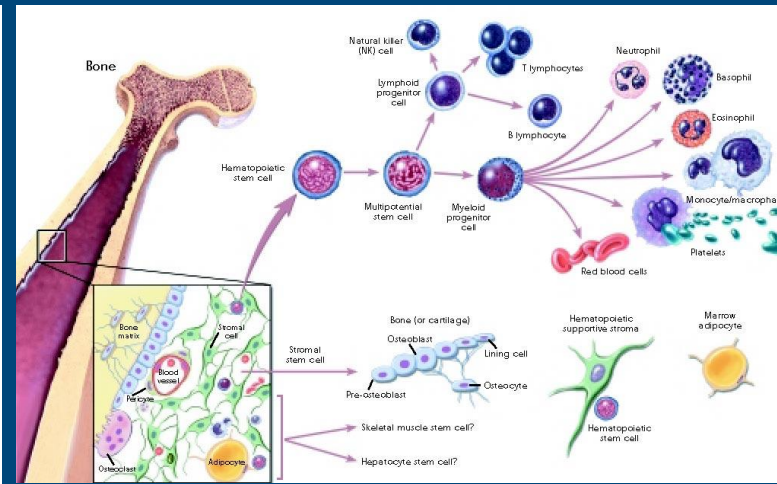
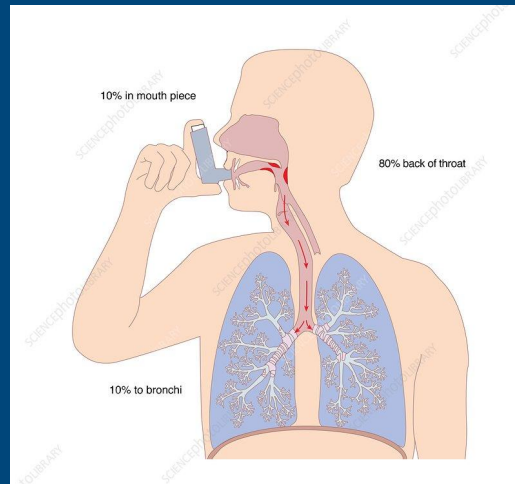
# The delivery problem



- Pflanzen, bacterien  
=> plasmide



- Mens  
=>Virus  
=>Stamcel  
=>Organoid (TE)



## Vervolgcurcus

## Biotechnologie.



DNA/RNA-technologie

=> gentherapie/mRNA therapie

Afweersysteem

=> Immunotherapie

Stamcellen

=> stamceltherapie

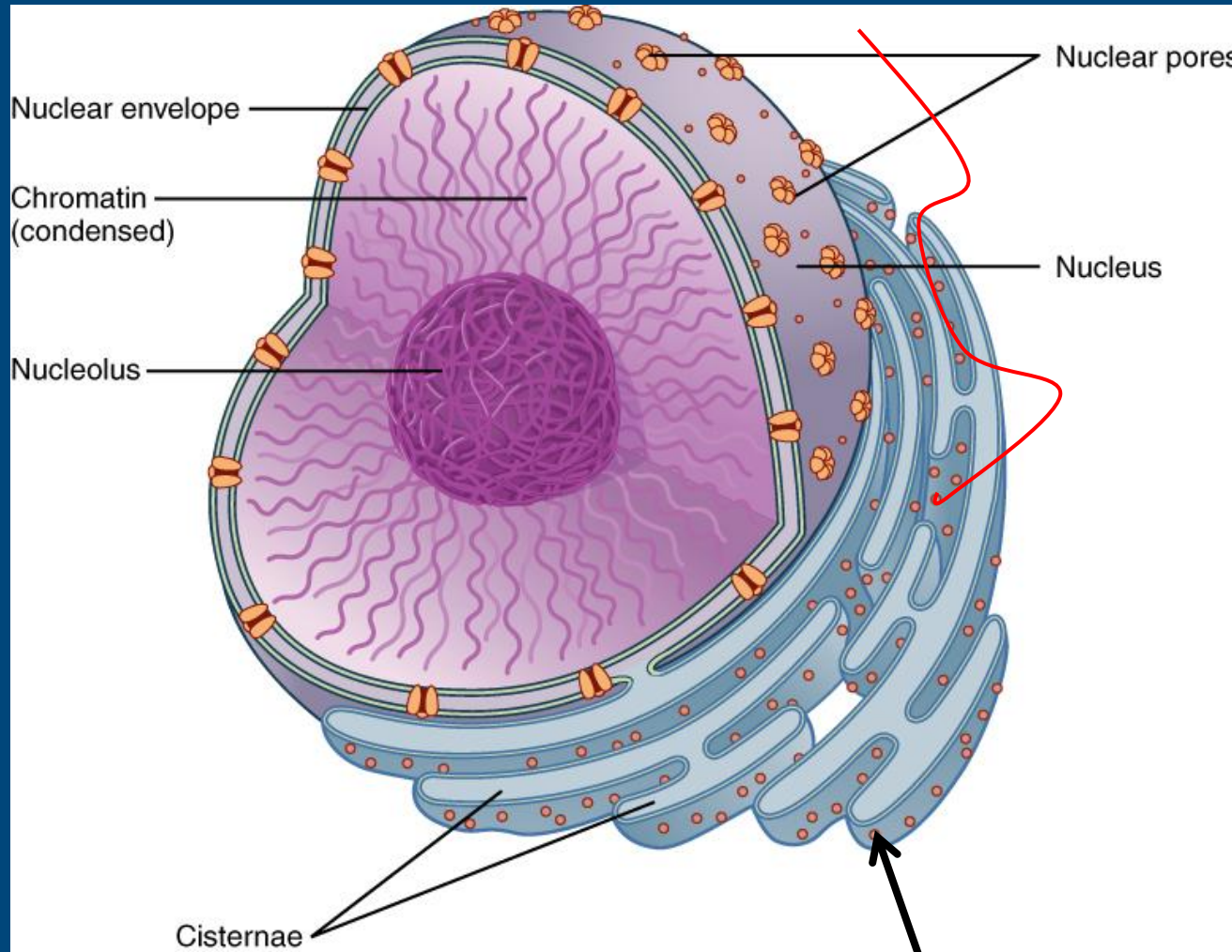
Cybernetica

=> verbeteren (integratie technologie en biologie)

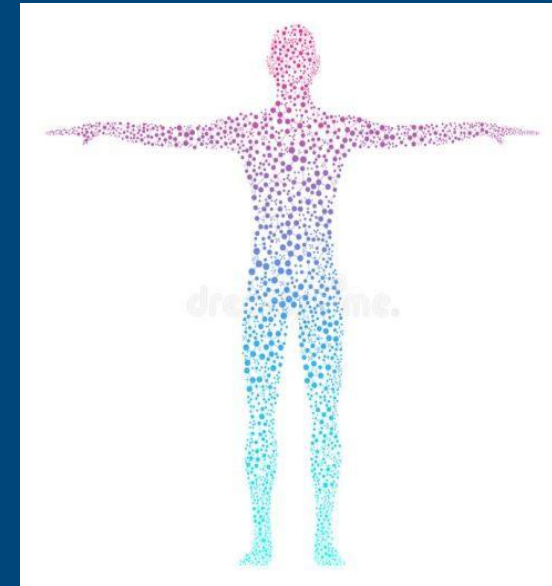
Synthetic biology

=> wat is leven?

# De celkern, met daarin DNA

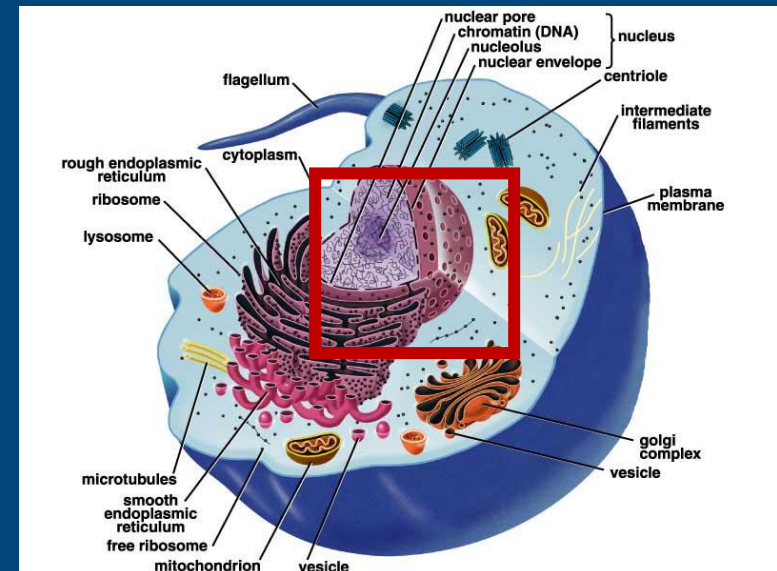


Ruw Endoplasmatisch Reticulum met ribosomen (mRNA => eiwit)



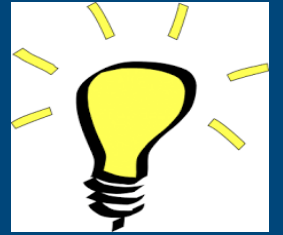
Leven bestaat uit cellen  
<https://youtu.be/SEejivHRIbE>

## Een (eukaryote) cel met celkern



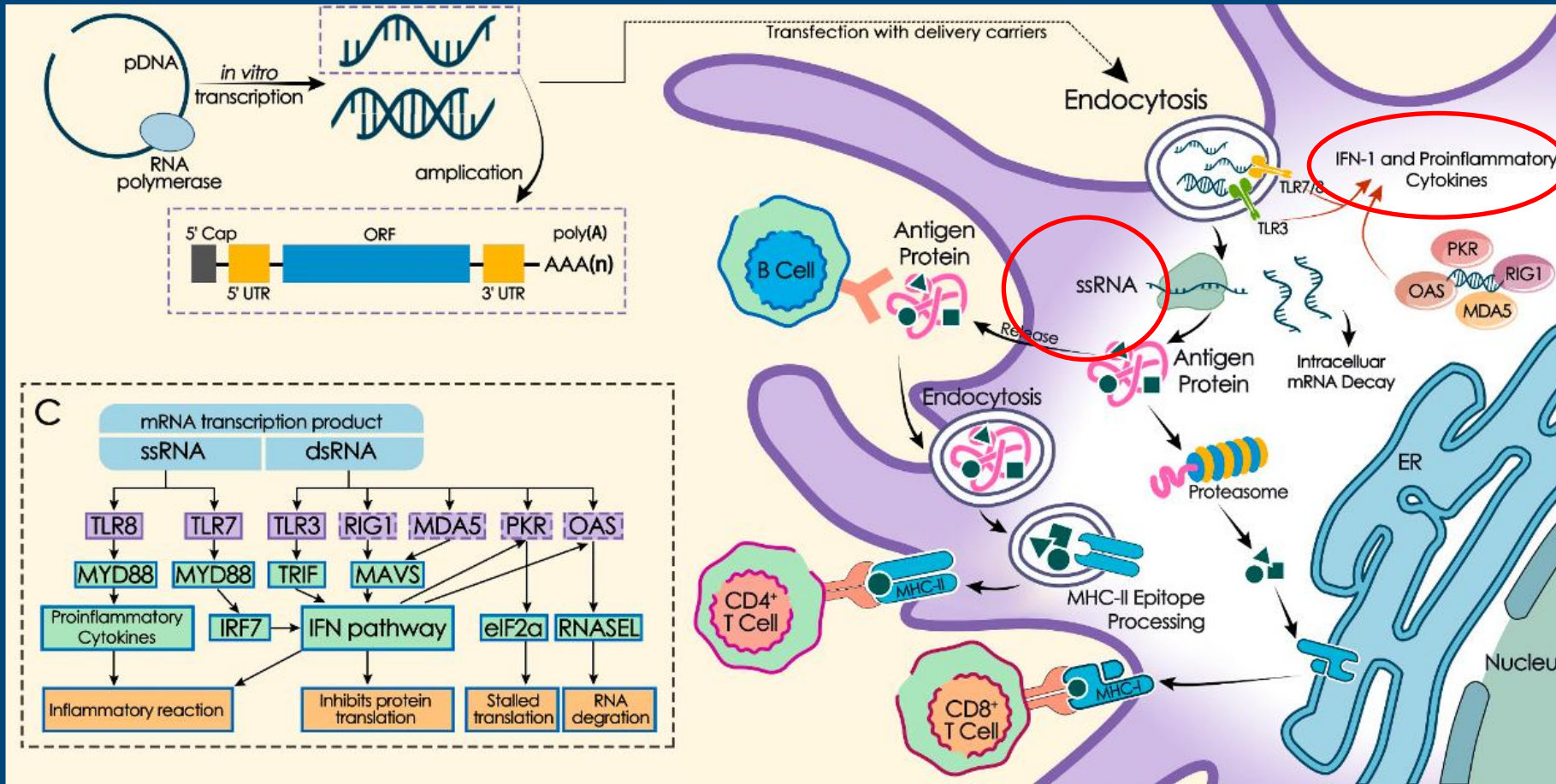
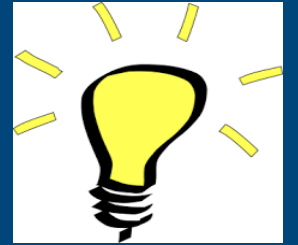
# mRNA is transient

- Eigenlijk dus geen gentherapie



# mRNA in Vaccin

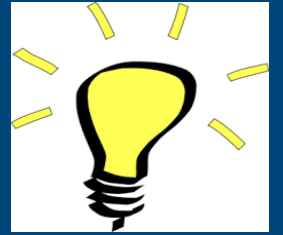
## Direct naar ribosoom, en meer



Werkingsmechanisme is niet helemaal duidelijk!

# Intracellulaire afweer (tegen virussen)

## De interferon respons



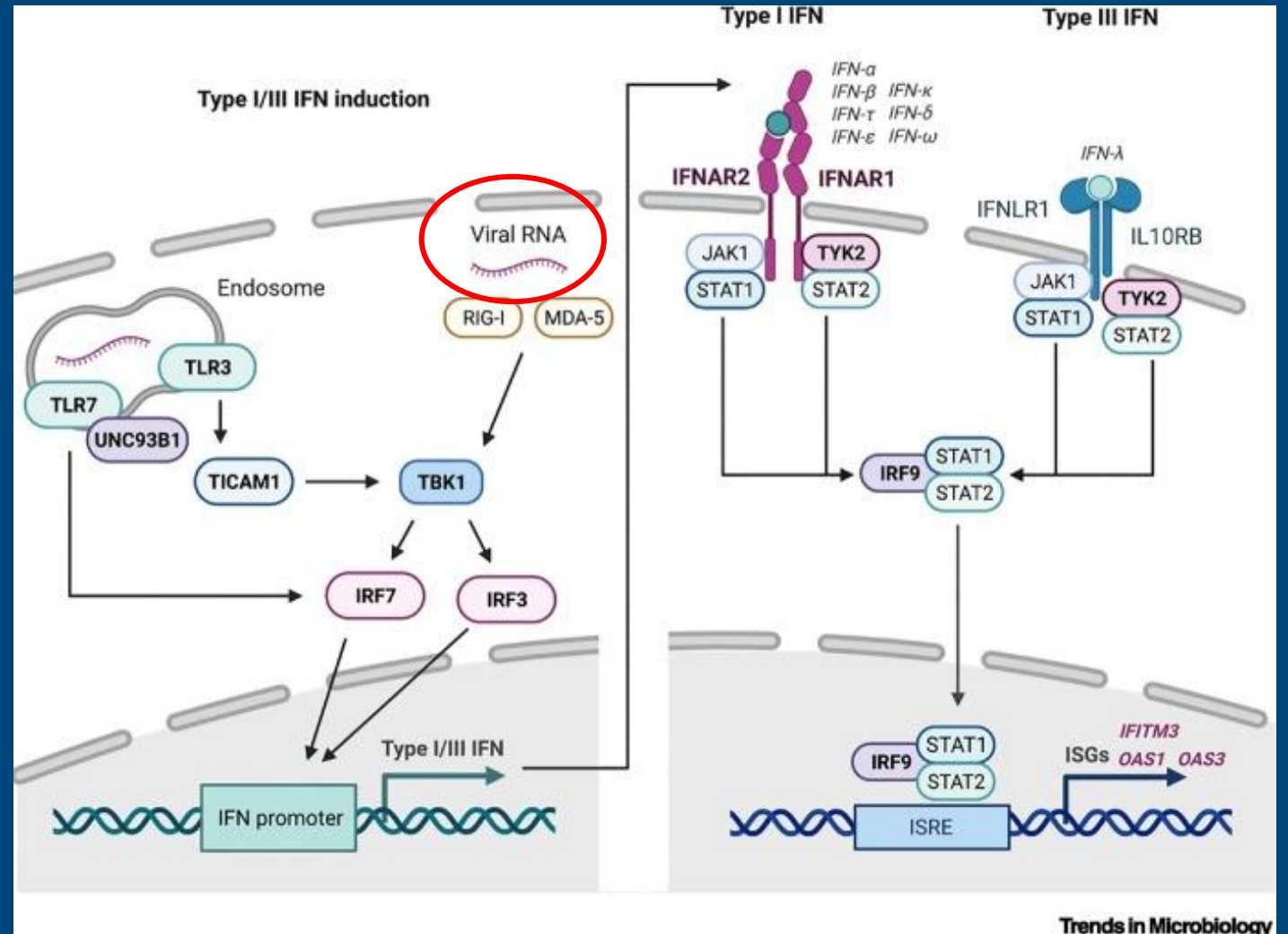
Simplified signaling cascades leading to transcription of type I/III interferon genes following infection with an **RNA virus** (*left panel*).

Simplified signaling cascades leading to transcription of interferon-stimulated genes (ISGs) following type I/III interferon stimulation (*right panel*).

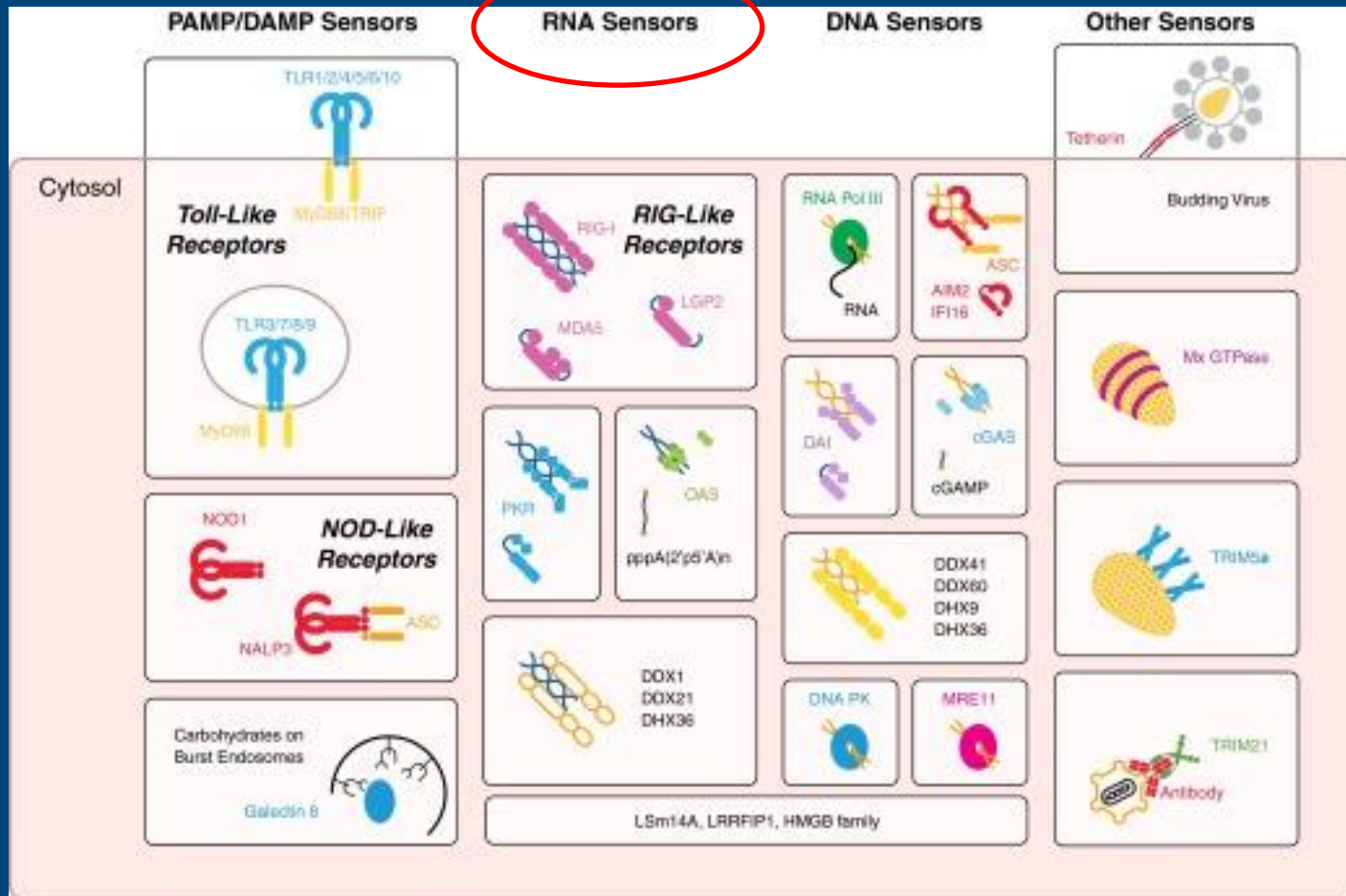
⇒ Meer MHC

⇒ Pro-inflammatoire cytokines

⇒ gevaar

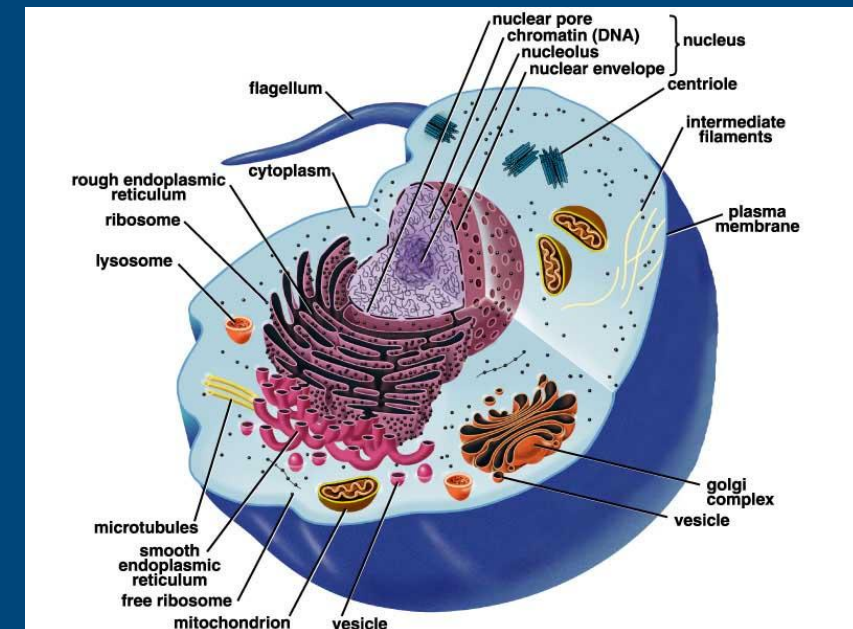


# Intracellulaire afweer: interferon => aspecifiek!



Intracellular pathogen sensors are soluble, cytoplasmic proteins. TLR, NLR, and galectin-8 sensing of burst endosomes detect **danger** associated with infection.

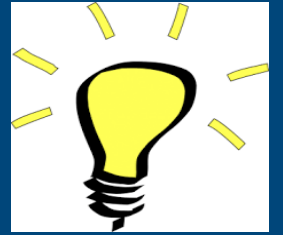
RNA komt in het cytoplasma normaal niet voor => virus!



[https://www.sciencemag.org/topic/crispr?r3f\\_986=http://science.sciencemag.org/content/327/5962/167.full](https://www.sciencemag.org/topic/crispr?r3f_986=http://science.sciencemag.org/content/327/5962/167.full)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4192899/>

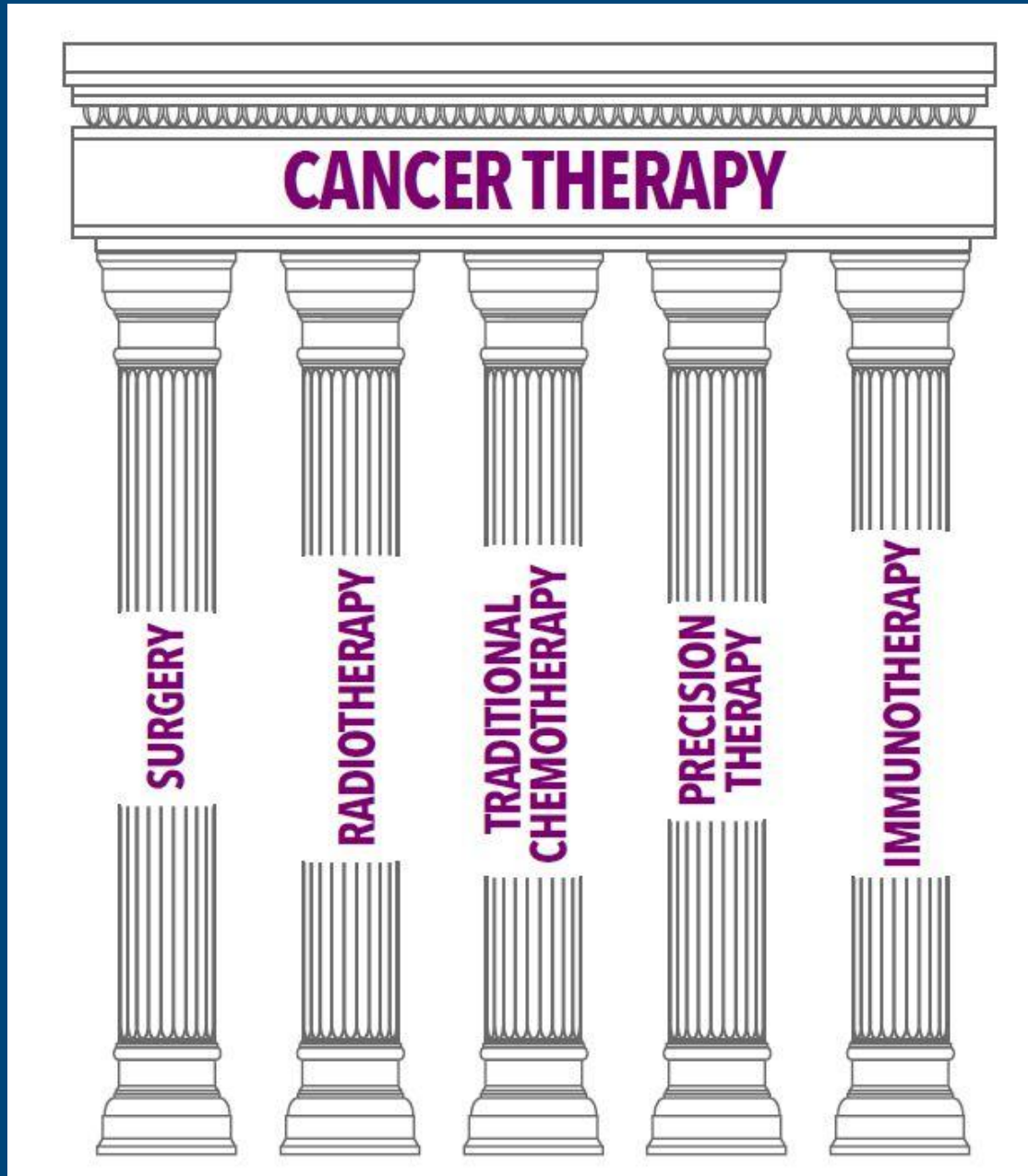
# mRNA tegen kanker



- <https://youtu.be/R83JCXSjvJo?t=2121>

Sunday with Laura Kuennsberg | 16th October 2022

Volgende week: Immunotherapy:



Surgery: wegsnijden

Radio: bestraling

Chemo: doden (alle) snel delende cellen

Precision: doden specifieke cellen (antilichamen)

**Immuuntherapie:**

Afweercellen opleiden tot tumor bestrijders

Verminderen supressie (antilichamen)

mRNA

mRNA/liposomes

Delivery problem solved