BIG IDEAS FORUM

The Singularity of Genetics

Being philosophical . . .

The future is not just something that will happen tomorrow;

it is something that is already happening . . .

we just haven't notice it yet!

Disposition

Genetics

- Cell tissue
- Genetics
- Gene editing
- Applied Genetics
- Importance of Genetics
- Future of Genetics/Medicine
- and
- Epigenetics

Cell Tissue

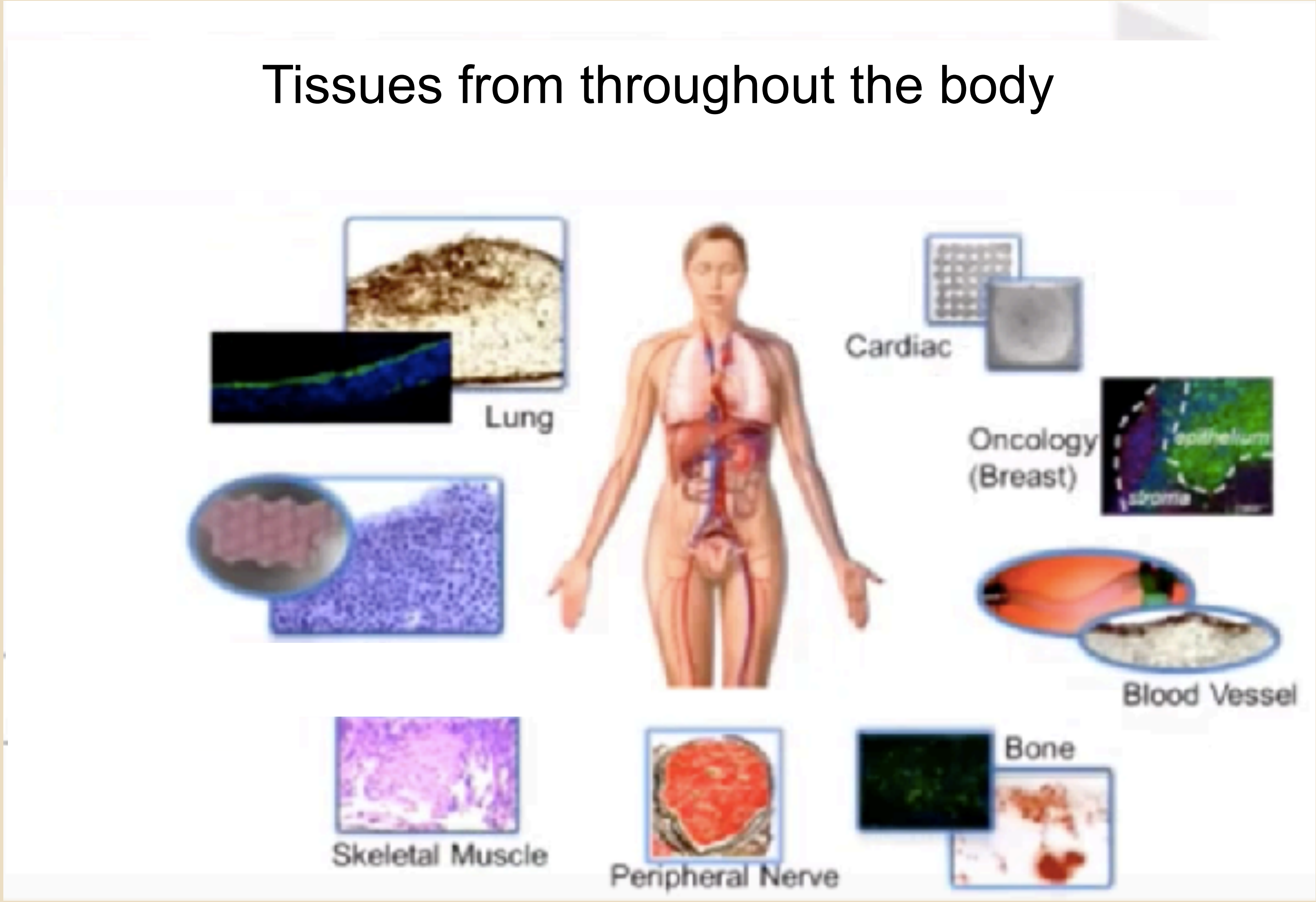
- Goal: Growing new organs
- Purpose:
    - Biological replication
    - Synthetic cell tissue

to deal with shortage of organs

Cell Tissue

- Growing new organs - 3D-bioprinting - in 3 steps
- - build a scaffold
- - add nutrients (growth media)
- - infuse with stem cells (patient specific) - iPPS cells

Cell Tissue



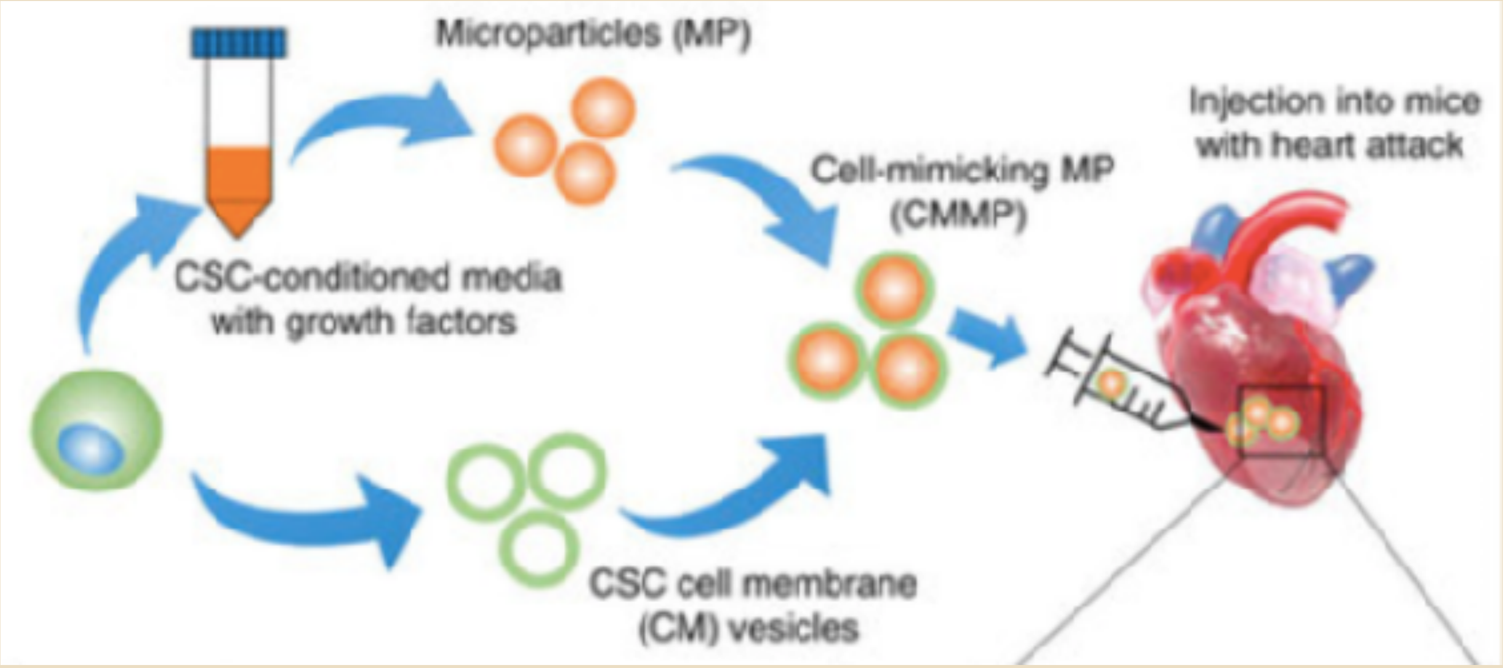
Tissues from throughout the body
Lung
Cardiac
Oncology
(Breast)
epithelium
stroma
Blood Vessel
Bone
Skeletal Muscle
Peripheral Nerve

Cell Tissue

- Making semi-synthetic tissue (organs)
- Why (semi)synthetic?
  - - ethical questions related to (embryonic) stem cells
  - - shortage of donor material

Cell Tissue

The making of a mouse heart (myocardial infarction)



1: glycolic acid micro particle (MP)
2: infused w cargo (nutrients) from cardiac stem cells (CSC);
3: they become cell mimicking MP (CMMP) covered in the CSC membrane
4: injected into heart.

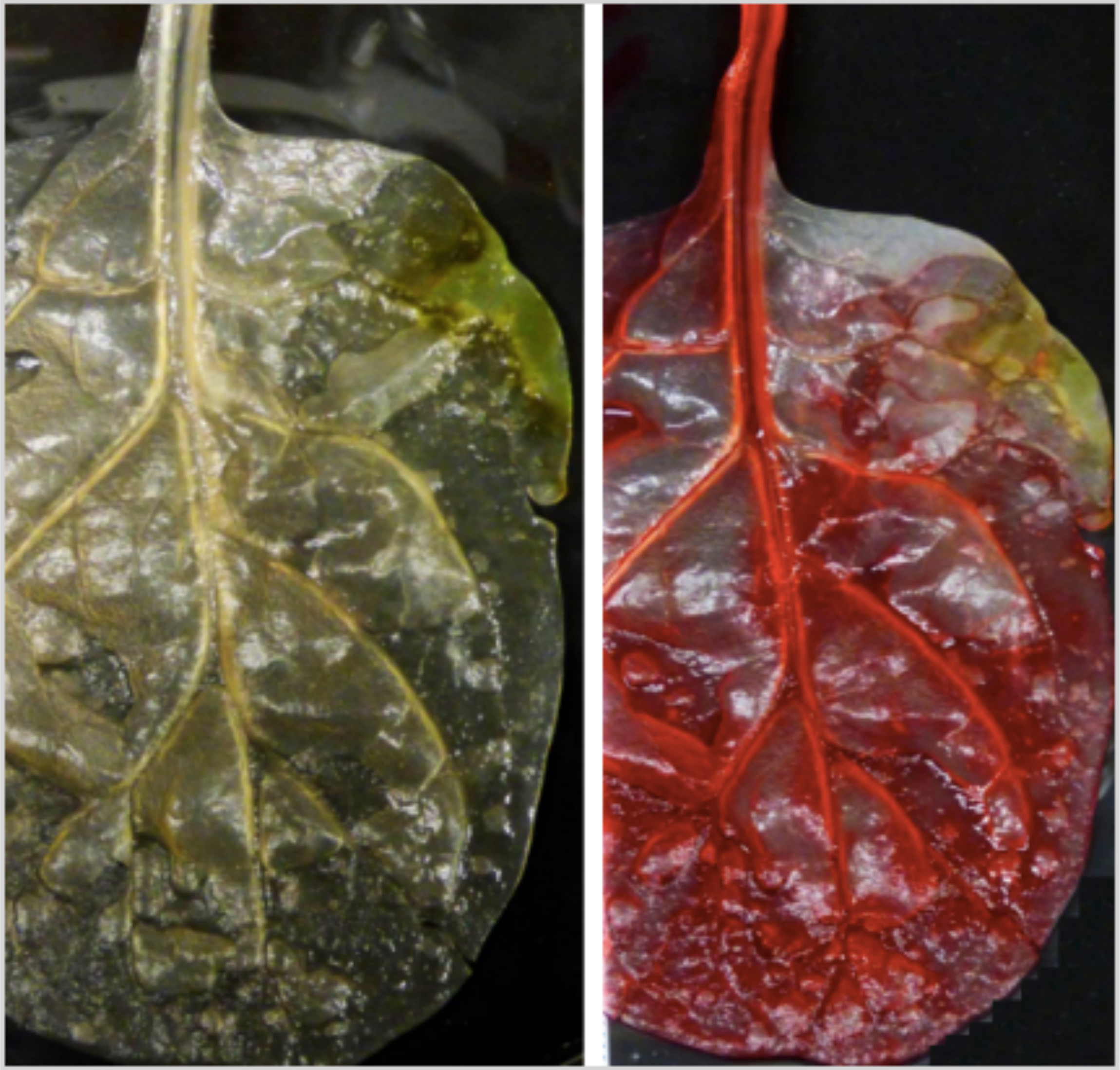
Cell Tissue

LEFT:
Spinach leaf - decellularized 7 days- leaving a scaffold

Cell Tissue

RIGHT:
(1) Red water flows through the veins; then (2) coated with HUVEC to form endothelial blood vessel cells; then (3) (cardiac muscle cells) (hPS-CM) were then seeded to the outer surfaces of the scaffold

Cell Tissue

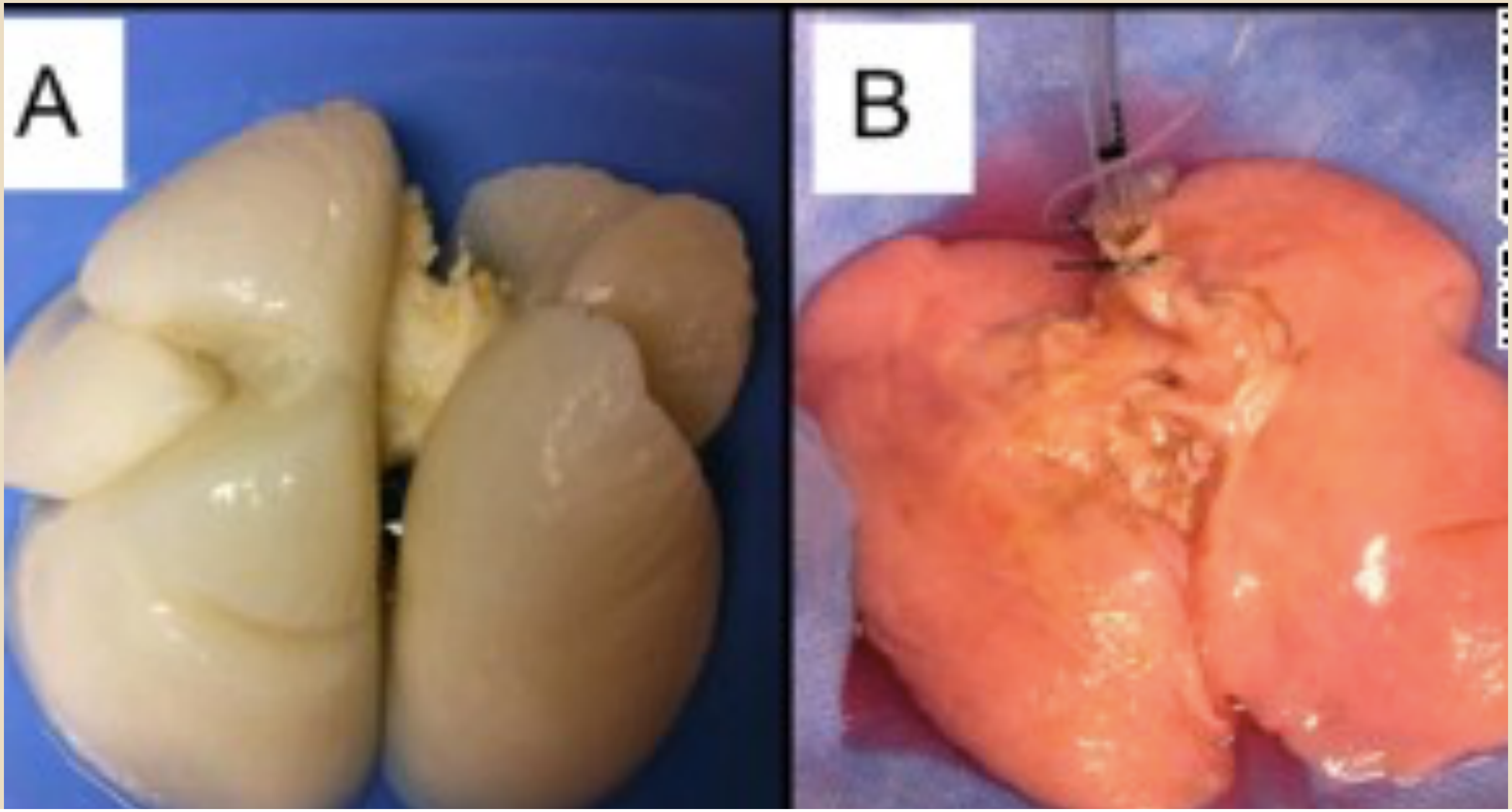


LEFT:
Spinach leaf - decellularized 7 days- leaving a scaffold

RIGHT:
(1) Red water flows through the veins; then (2) the inside is coated with HUVEC to form endothelial blood vessel cells; then (3) cardiac muscle cells (hPS-CM) were then seeded to the outer surfaces of the scaffold

RESULT: Spinach leaf was beating for 21 days!

Cell Tissue



1. Lung A is stripped of nearly everything, leaving a scaffolding of collagen and elastin.
2. Cells from another lung added to the scaffolding.
3. Structure immersed in chamber filled with a liquid nutrients for the cells to grow.
4. After about four weeks, an engineered human lung (B) emerged.

Cell Tissue

Embryos that are less than 0.001% human - and the rest pig - have been made and analysed by scientists.

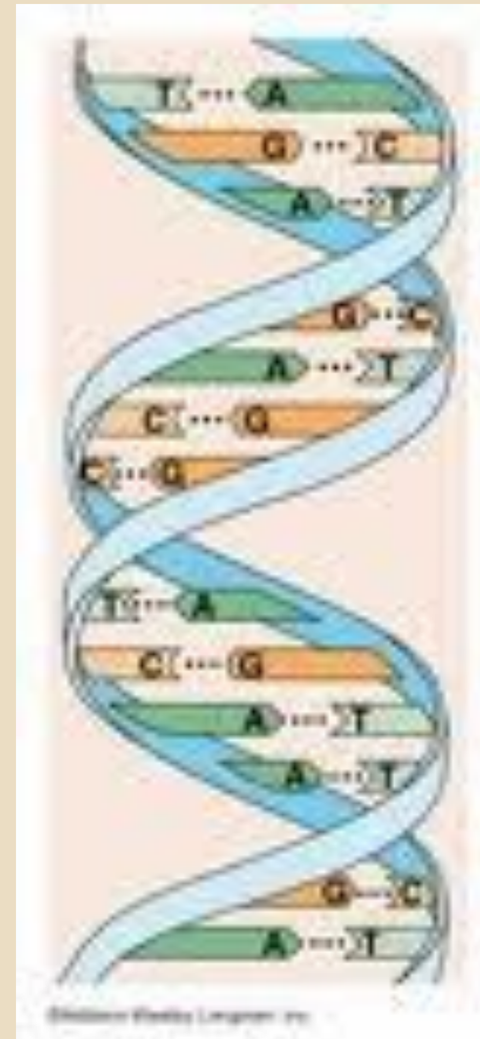
Genetics

“Historically” * we have been . . .

Identifying (cataloging) the human genome

Understanding the genes, how the work

* James Watson and
  Francis Crick, 1953



Genetics

Knowledge is one thing . . .

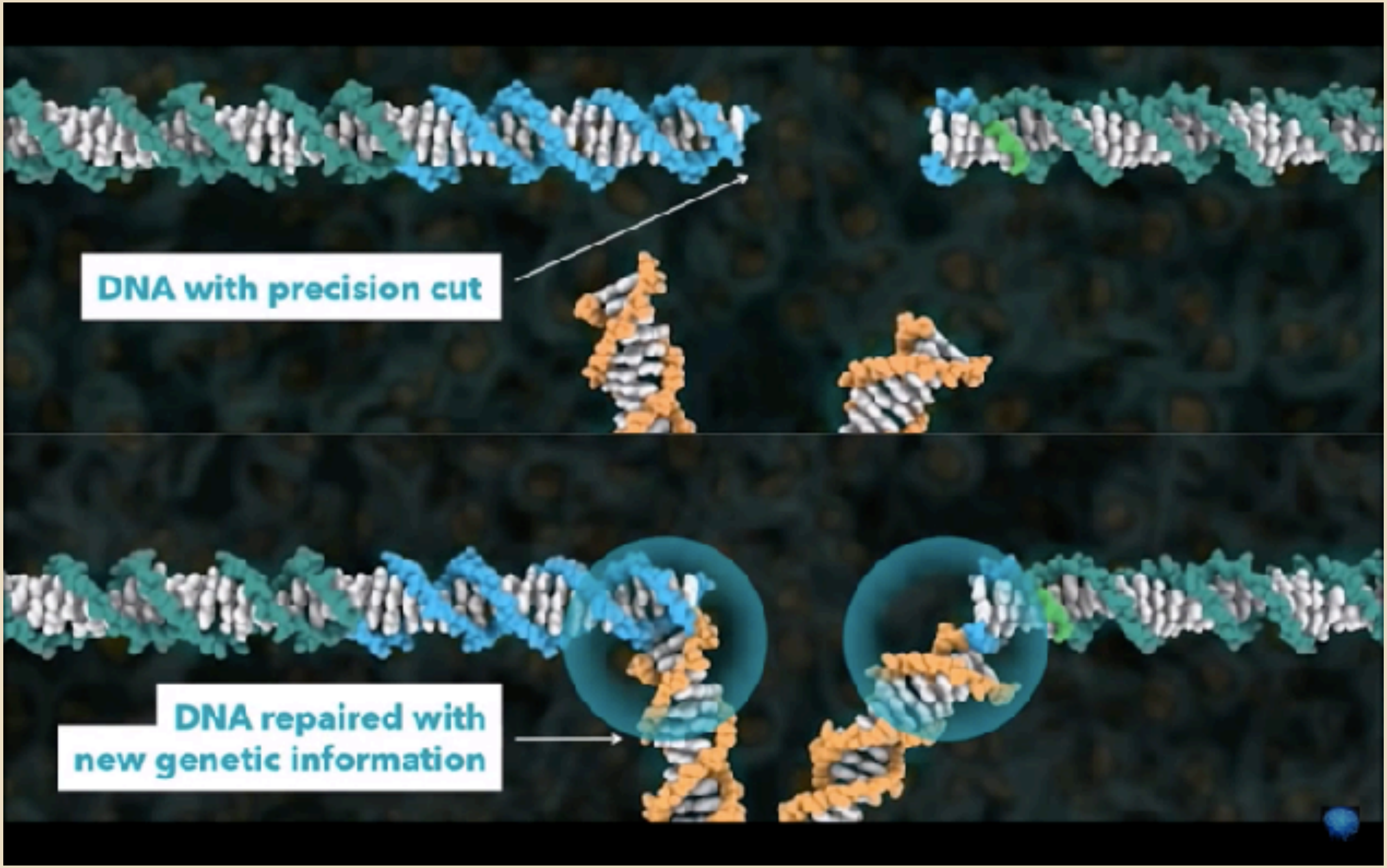
but what do we use it for?

- generating useful organisms (bacteria) and GMO
- human disease repair
- human enhancement

Genetics

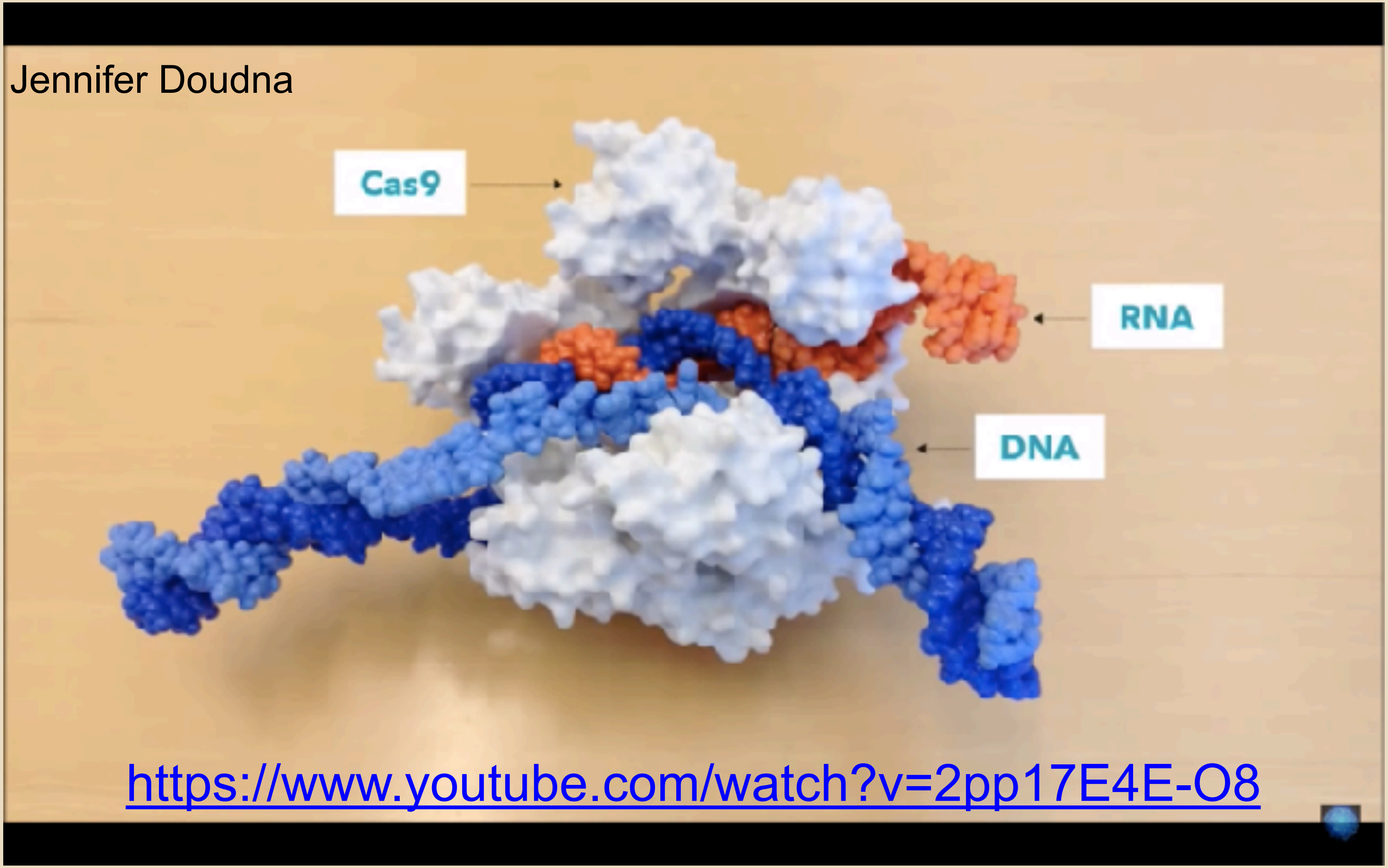
1. Use cells as they are
2. Modify cells and use them for their original purpose
3. Change cells and use them for something completely new

But first: Gene editing



Genetics CRISPR-cas9 (cas13a)

Genetics CRISPR-cas9 (cas13a)



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

Applied Genetics

1. Use cells as they are

- Isolate stem cells from e.g. an injured animals' hearts and infuse them back into the heart of the same animal

- The stem cells form new heart muscle and blood vessel cells. In fact, the new cells have a pre-determined cardiac 'fate.' Even in the culture dish, they beat!

Animals → Humans

Applied Genetics

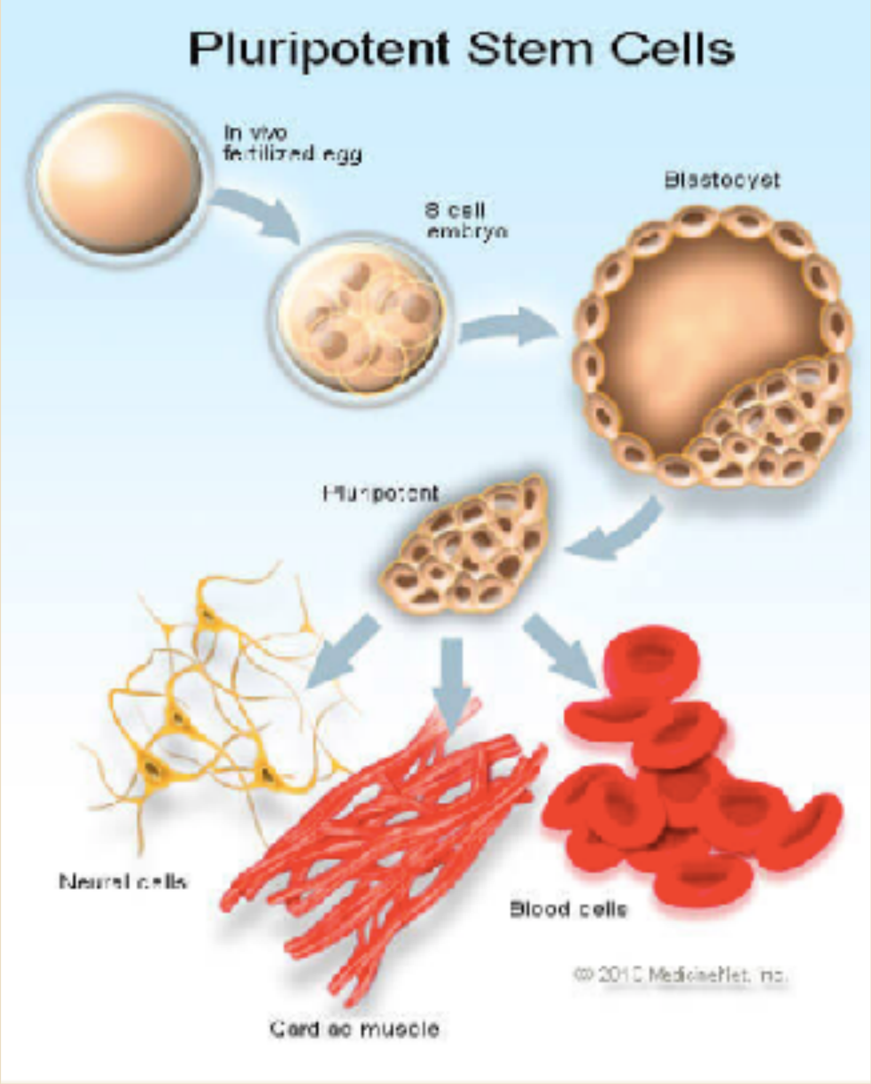
2a. Modify cells - and use them for their original purpose

- (a) Stem cells (embryonic stem cells)
- (b) Pluripotent stem cells - PSC (or PPSC)
- (c) Induced pluripotent stem cells

(a) Self-replicating cells derived from human embryos or human fetal tissue, that develop into any cells and tissues of the body

(b) Although human pluripotent stem cells may be derived from embryos or fetal tissue, such stem cells are not themselves *embryos*

Applied Genetics



Applied Genetics

2b. Modify cells - and use them for their original purpose

- (a) Stem cells -
- (b) Pluripotent stem cells - PSC (or PPSC)
- (c) Induced pluripotent stem cells - iPCS or iPPCS

(c) ***Mature***/adult (specialized) cells, often skin cells, that are induced (reprogramed*) to become PPSC

* introducing 4 specific transcription factors

Applied Genetics

3. Change cells and use them for something completely new

- bacteria to convert CO_2 into fuels in a single-step process
- M. miehei produces human insulin or rennet
- yeast to produce anti-malaria compound
- microbes reprogrammed to produce industrial ingredients, e.g. synthetic rubber, or eliminate oil
- strawberries that glow in the dark (no kidding!)

Applied Genetics

3. Change cells and use them for something completely new

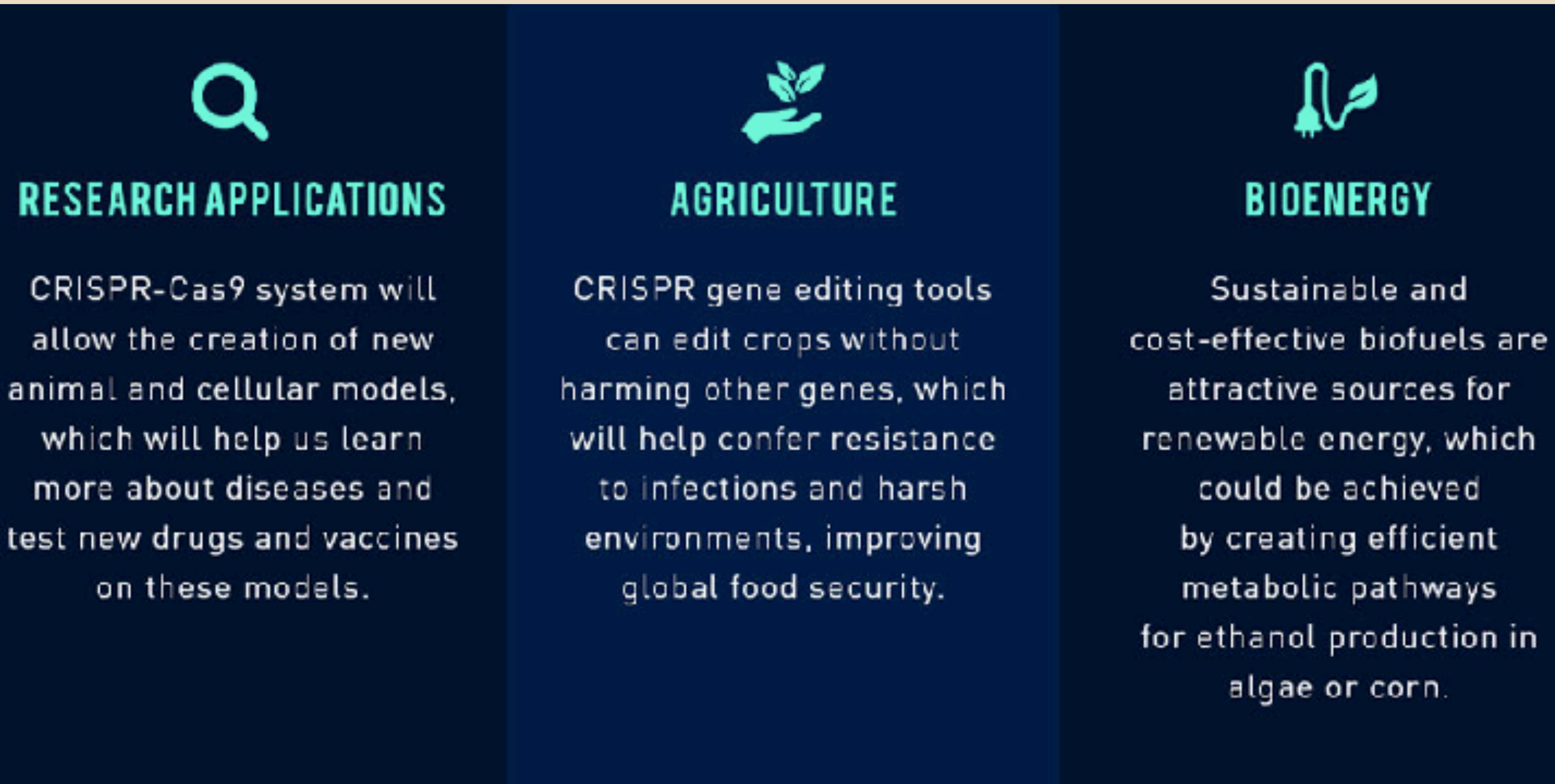
- bacteria to convert CO_2 into fuels in a single-step process
- M. miehei produces human insulin or rennet
- yeast to produce anti-malarial compound
- microbes reprogrammed to produce industrial ingredients, e.g. synthetic rubber, or eliminate oil
- strawberries that glow in the dark (no kidding!)

But what about humans?

Applied Genetics

What is it that we want to accomplish?

Genetics - Why is CRISPR-Cas9 so important



Genetics - Why is CRISPR-Cas9 so important

HUMAN HEALTH

CRISPR-Cas9 system will revolutionize gene therapy and make it possible to treat large number of diseases that would be impossible to treat without this technique. This includes diabetes, cancer, cystic fibrosis and sickle-cell anemia.

NEW MATERIALS

Manipulating biological circuits using CRISPR-Cas9 will facilitate the generation of useful synthetic materials that could useful in various applications such as oral drug delivery and the production of biosensors

DRUG DEVELOPMENT

Engineering cells to optimize high yield generation of drug precursors in bacterial factories could significantly reduce the cost and accessibility of useful therapeutics

Future of genetics

The Optimists View

Synthetic biology will surely usher in a fantastic world of

- abundance.
- longer, healthier lives enabled by intelligent systems that diagnose our diseases before symptoms appear
- truly personalized medicine (CRISPR-enabled cures for genetic diseases, cancer and beyond)

The optimists see synthetic biology as a burgeoning field with **unmatched potential for human good** — potential that's only comparable to that of artificial intelligence.

Epigenetics

Same genes – different people

Single-cell twins are born with identical genes but can become surprisingly different as they grow up.

Epigenetics is: Anything other than DNA that determines the development of an organism -

Specifically:

Factors that cause this divergence by changing how individual genes behave. They *tag on* to the DNA as early as in utero or anytime later in life

‘ ‘

Future of genetics

The Pessimists Views

- humans identify very strongly with biology and consider 'engineering life' to be unnatural, unethical and arrogant
- worry about how synthetic biology will affect our jobs and our ecosystems
- bio-terrorists can fabricate synthetic pathogens that can survive, multiply and cause harm

The pessimists are concerned about **unintended consequences** and misuse/abuse (chimera genes) is so great that the risks of synthetic biology (synbio) outweigh the benefits.

Future of genetics

The Realists Views

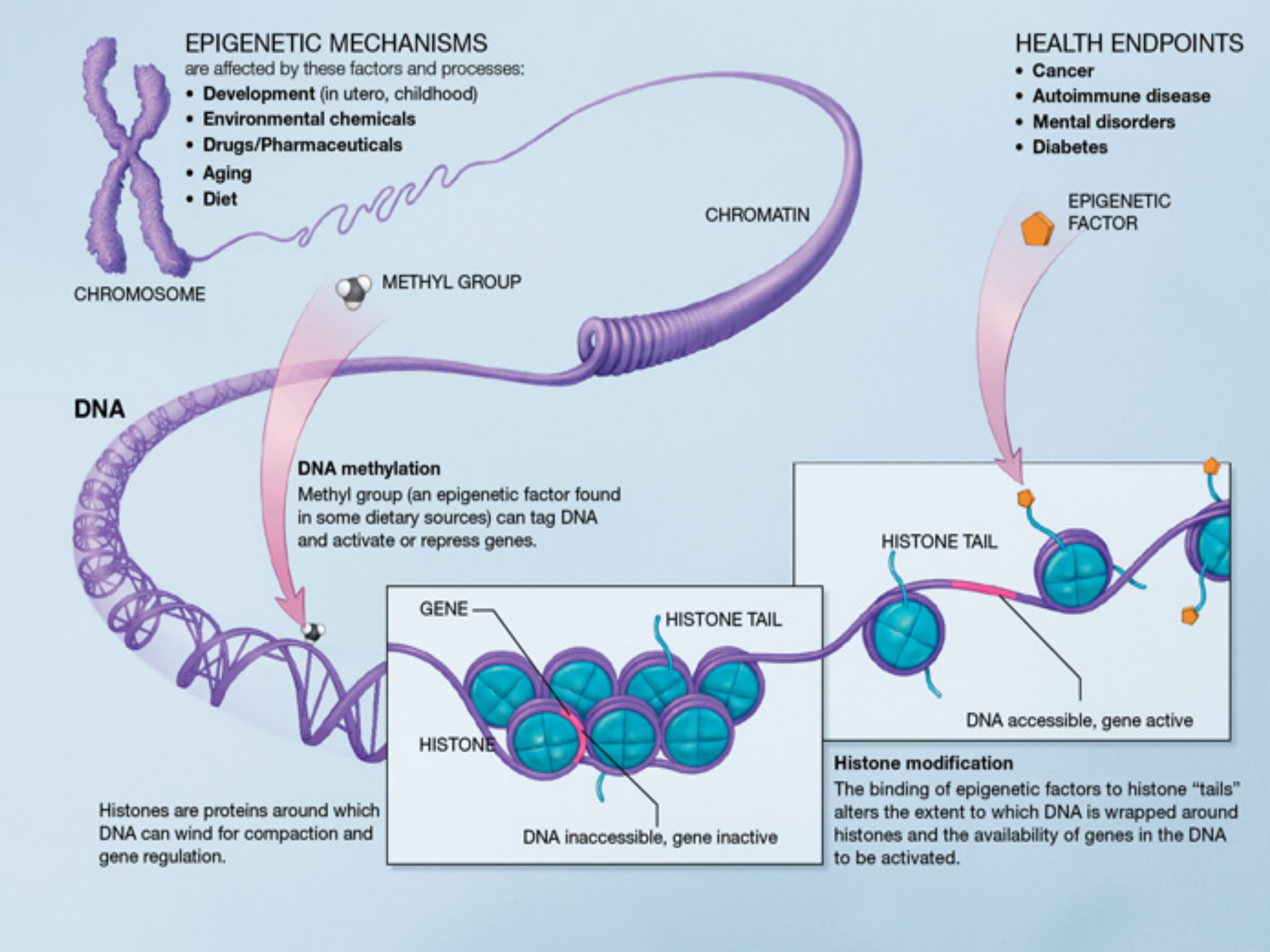
- hurdles must be overcome before the good stuff starts happening
- first, we need to develop standards for engineering life, abstractions for biological code and better ways of sharing experimental procedures

Future of genetics

The Realists Views

- hurdles must be overcome before the good stuff starts happening
- first, we need to develop standards for engineering life, abstractions for biological code and better ways of sharing experimental procedures

All agree on one thing—
we are moving fast into the synbio era.


EPIGENETIC MECHANISMS
are affected by these factors and processes:
• Development (in utero, childhood)
• Environmental chemicals
• Drugs/Pharmaceuticals
• Aging
• Diet
HEALTH ENDPOINTS
• Cancer
• Autoimmune disease
• Mental disorders
• Diabetes
CHROMOSOME
CHROMATIN
EPIGENETIC FACTOR
METHYL GROUP
DNA
DNA methylation
Methyl group (an epigenetic factor found in some dietary sources) can tag DNA and activate or repress genes.
HISTONE TAIL
GENE
HISTONE TAIL
HISTONE
DNA accessible, gene active
DNA inaccessible, gene inactive
Histone modification
The binding of epigenetic factors to histone "tails" alters the extent to which DNA is wrapped around histones and the availability of genes in the DNA to be activated.
Histones are proteins around which DNA can wind for compaction and gene regulation.

Epigenetics

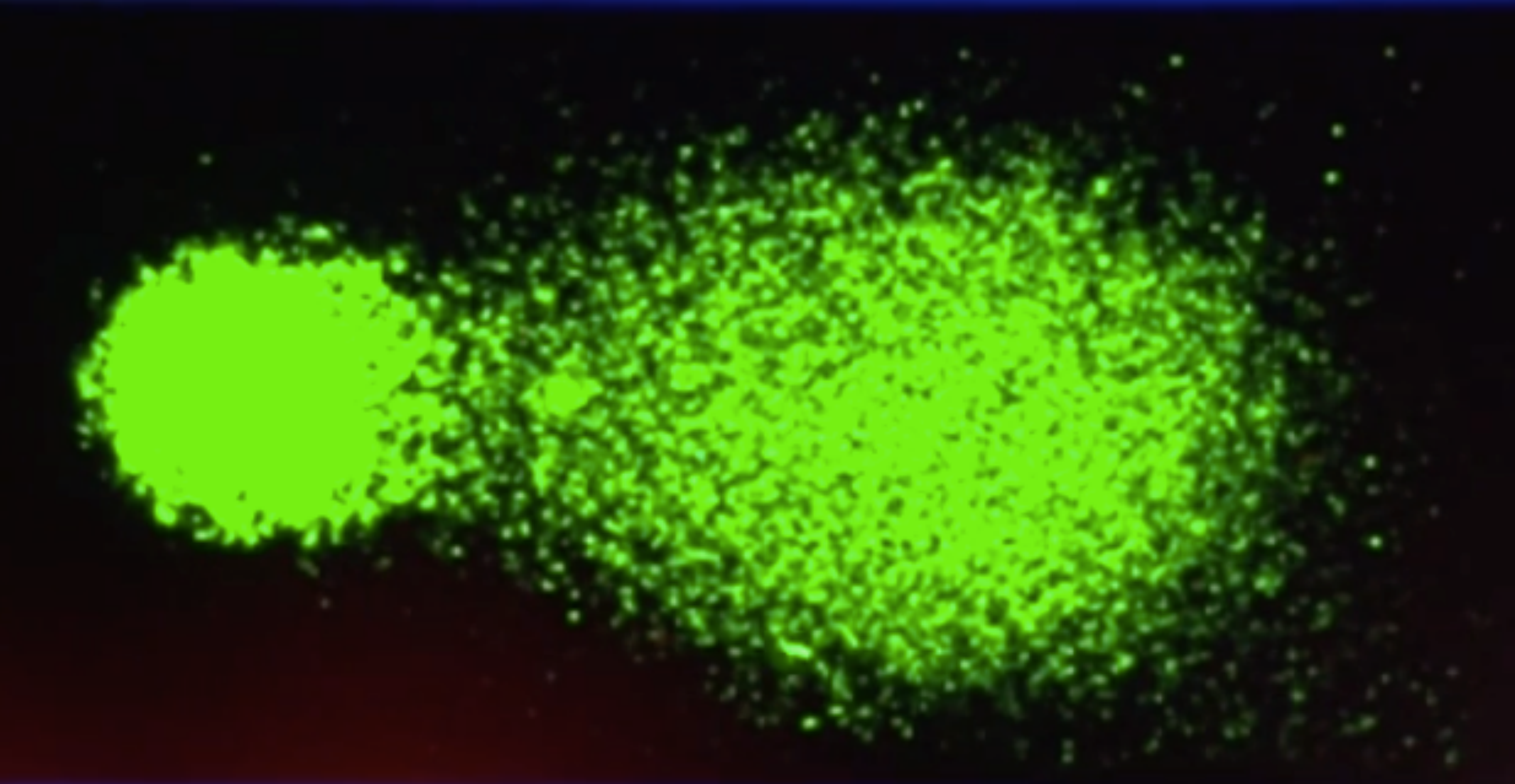
These *factors* (methyl groups) come from the

- nutrition
- environmental chemicals
- pharmaceutical drugs
- pollutants, etc.
- even aging and stress!

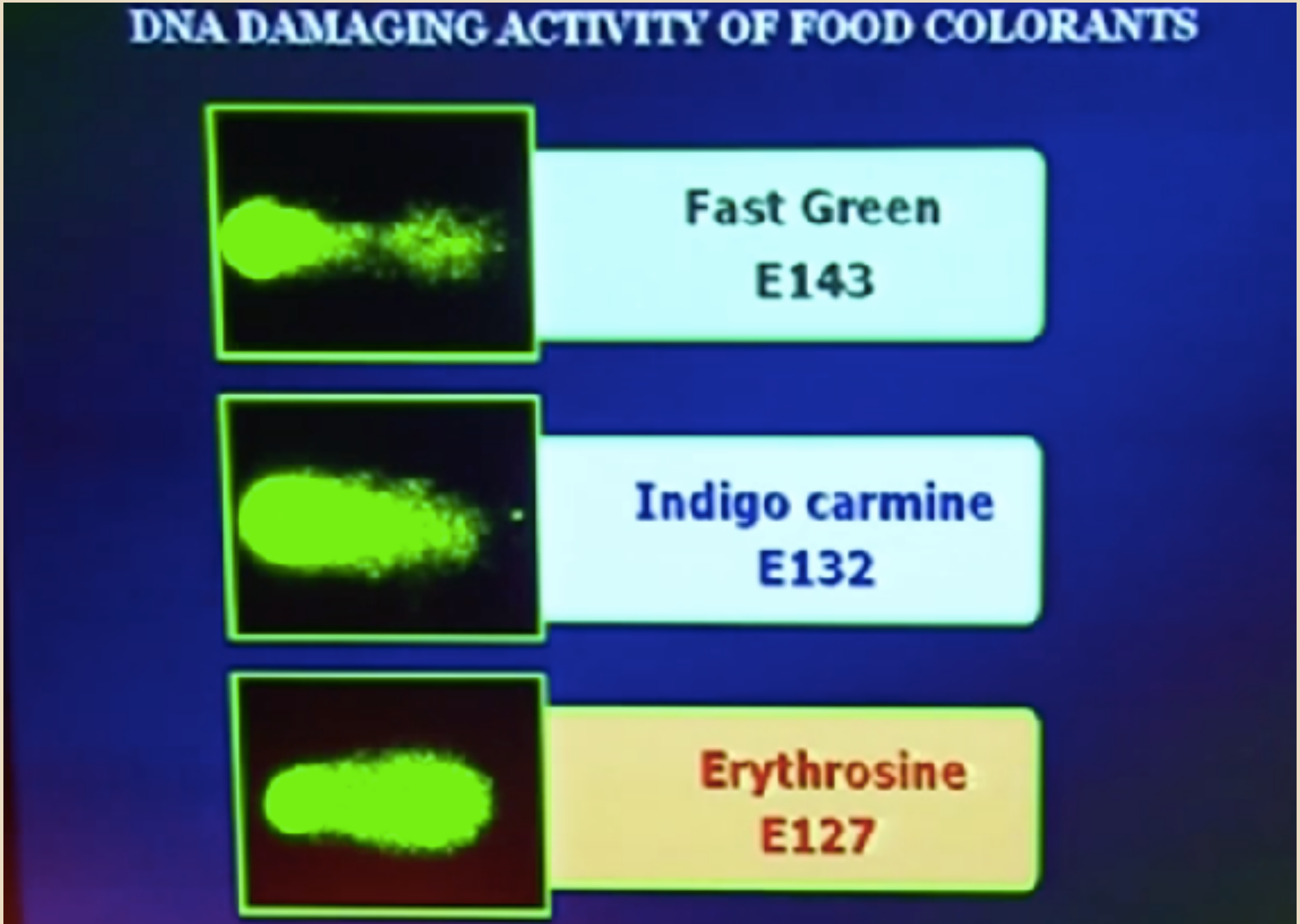
. . . and they are inheritable!

‘ ‘

DNA IS EXPOSED TO EXTENSIVE STRESS



Epigenetics and environment



The Singularity of Genetics

See you in the future!

Thank You!

torben.riise@gmail.com

SOURCES: Nest slide!

The Singularity of Genetics

Sources:

Future diagnostic device: 1:19
https://futurism.com/videos/a-noninvasive-device-that-can-diagnose-13-medical-conditions/

Artificial womb 1:07
https://www.youtube.com/watch?v=dxn6msihFjc

Ten medical innovations: 10:07
https://www.youtube.com/watch?v=tQR12rebKrg

Outlook 2020: 6:57
https://www.youtube.com/watch?v=totMfYaq8O8

CRISPR Cas9:
https://www.youtube.com/watch?v=2pp17E4E-O8

HOW DOES IT WORK?

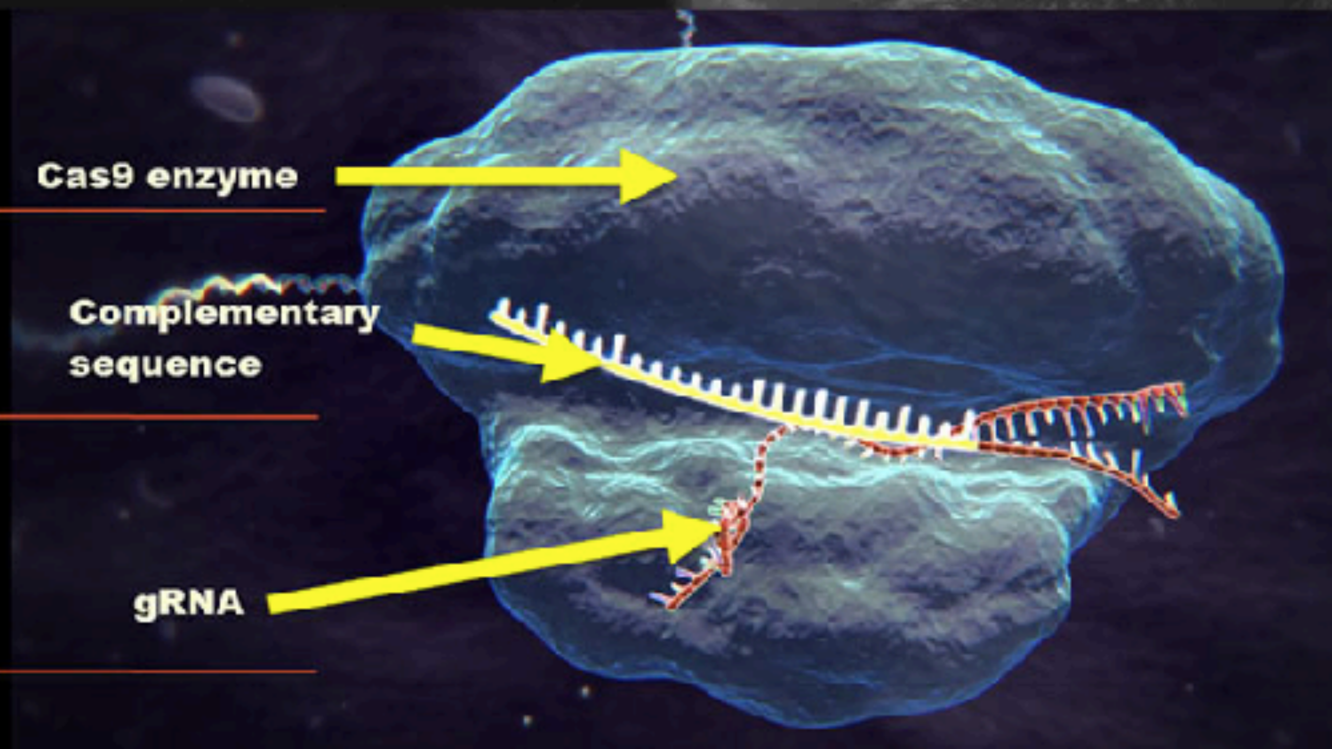
STEP 1: FORMATION OF THE EDITING COMPLEX

Cas9 enzyme pairs with guide RNA, which carries a sequence matching that of the target gene.

An RNA-guided nuclease enzyme that can cut DNA

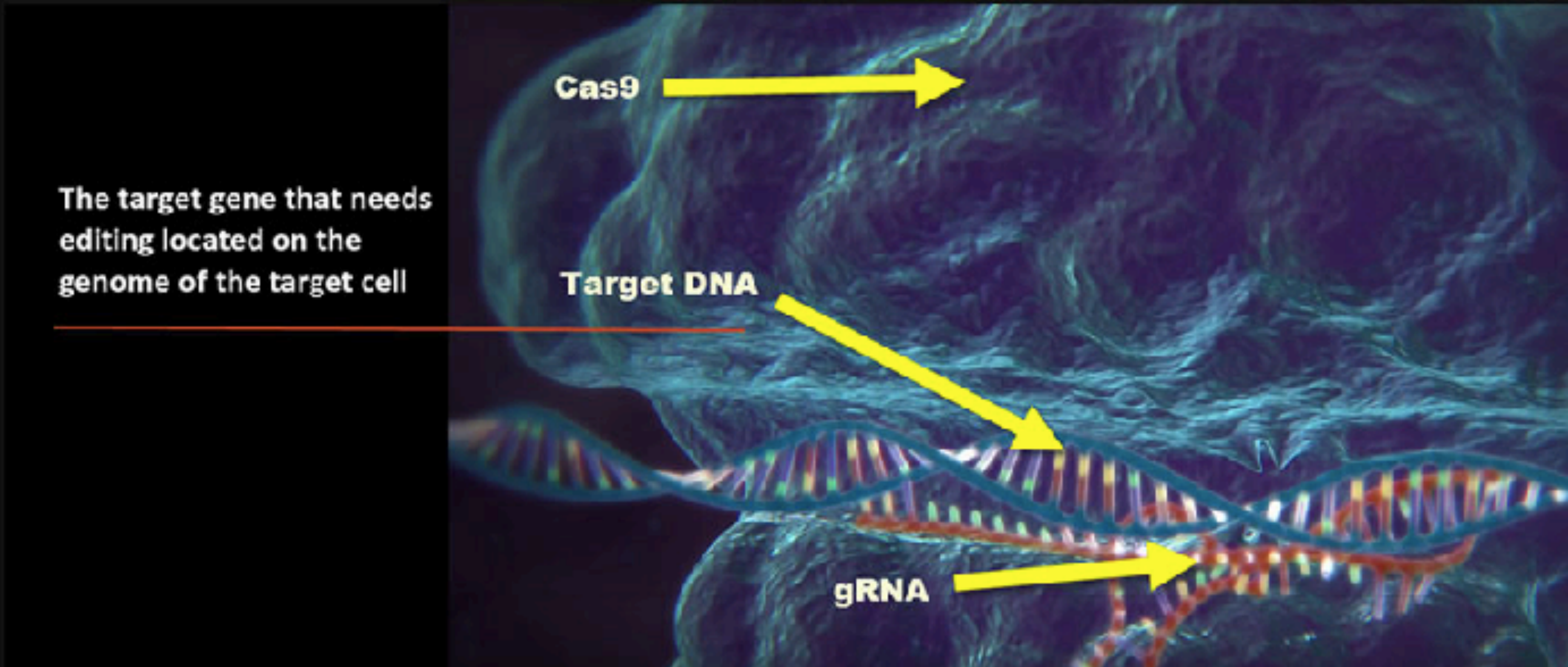
Gene sequence matching the target gene that needs editing

Guide RNA to carry the complementary sequence and deliver Cas9 to the genome



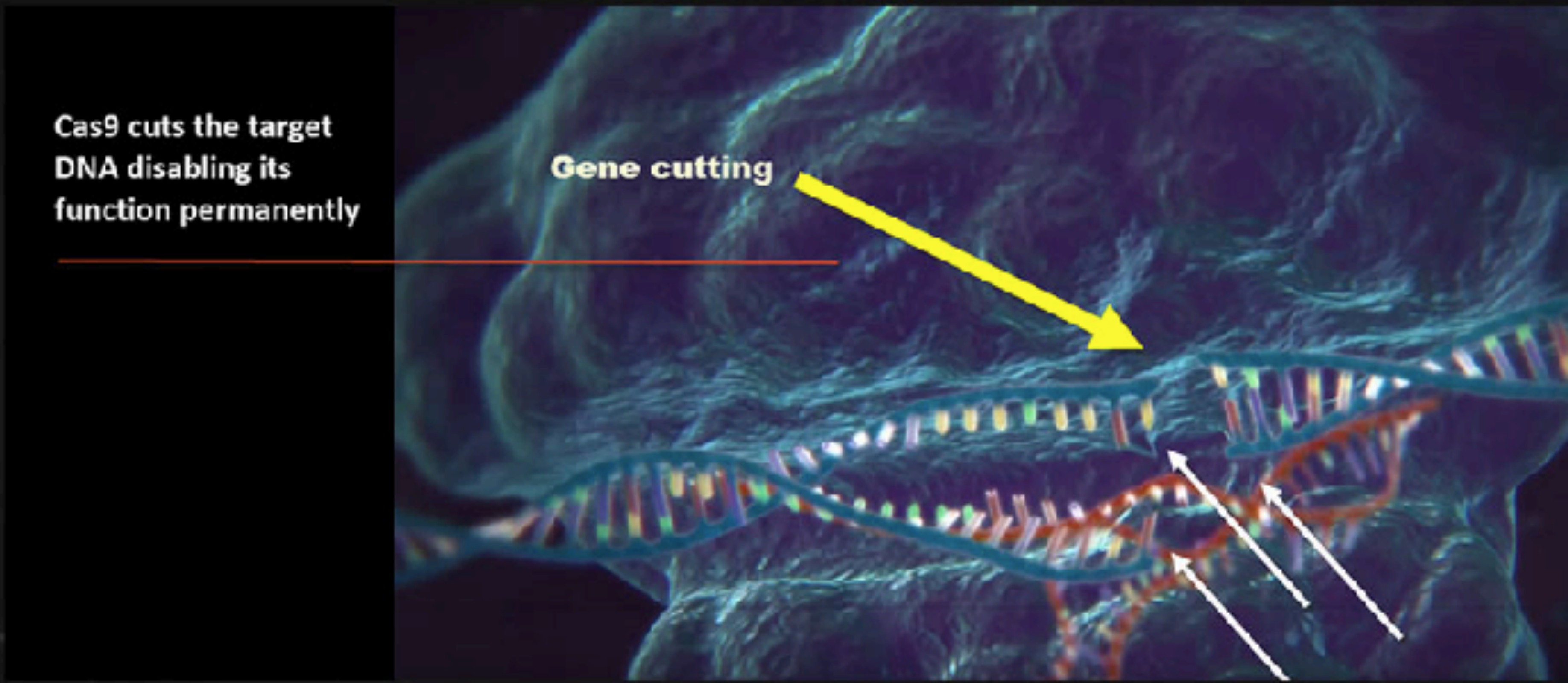
STEP 2: PAIRING WITH THE TARGET GENE

The complex (Cas9, gRNA and the complementary sequence) binds precisely to the target gene in the genome.



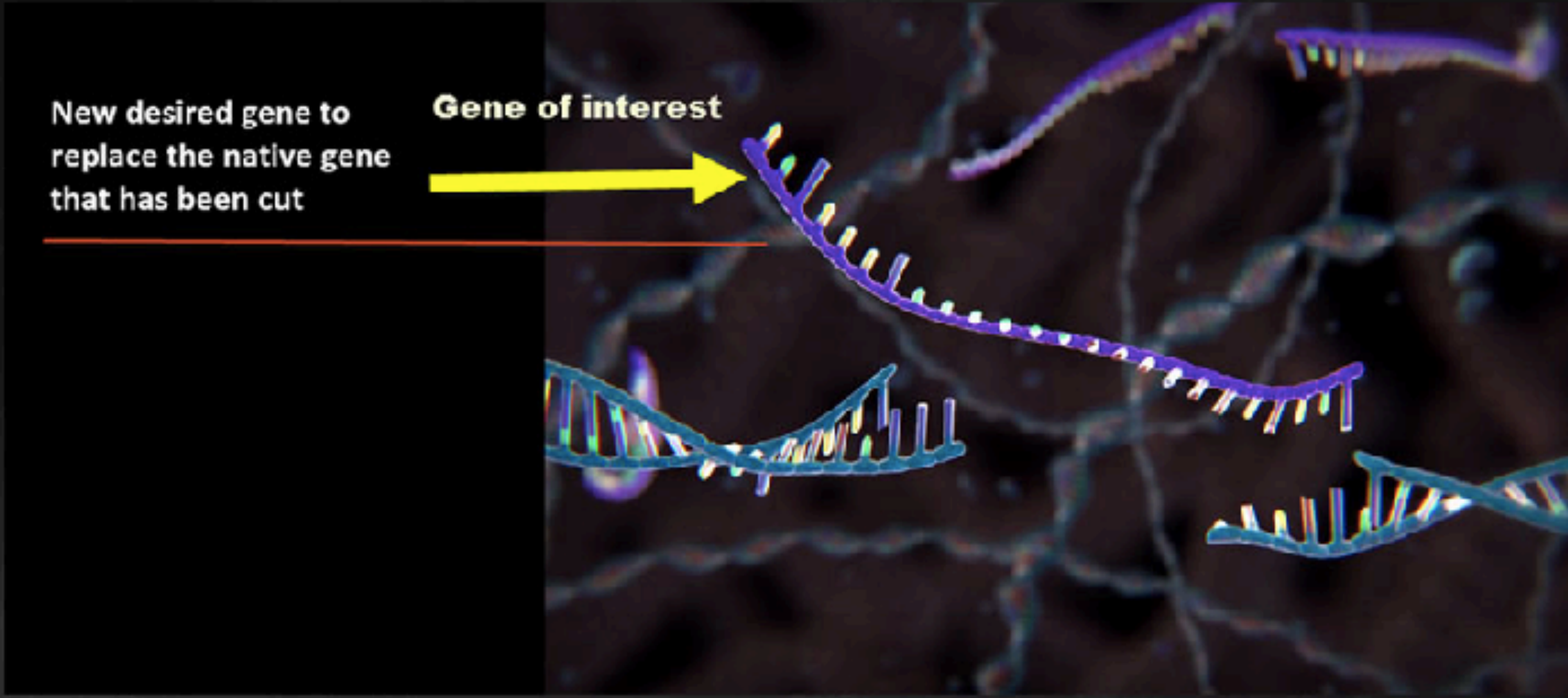
STEP 3: CUTTING THE TARGET DNA

Cas9 enzyme cuts the target gene on the genome. The cell attempts to repair the DNA but that creates a mutation that disables its function permanently.



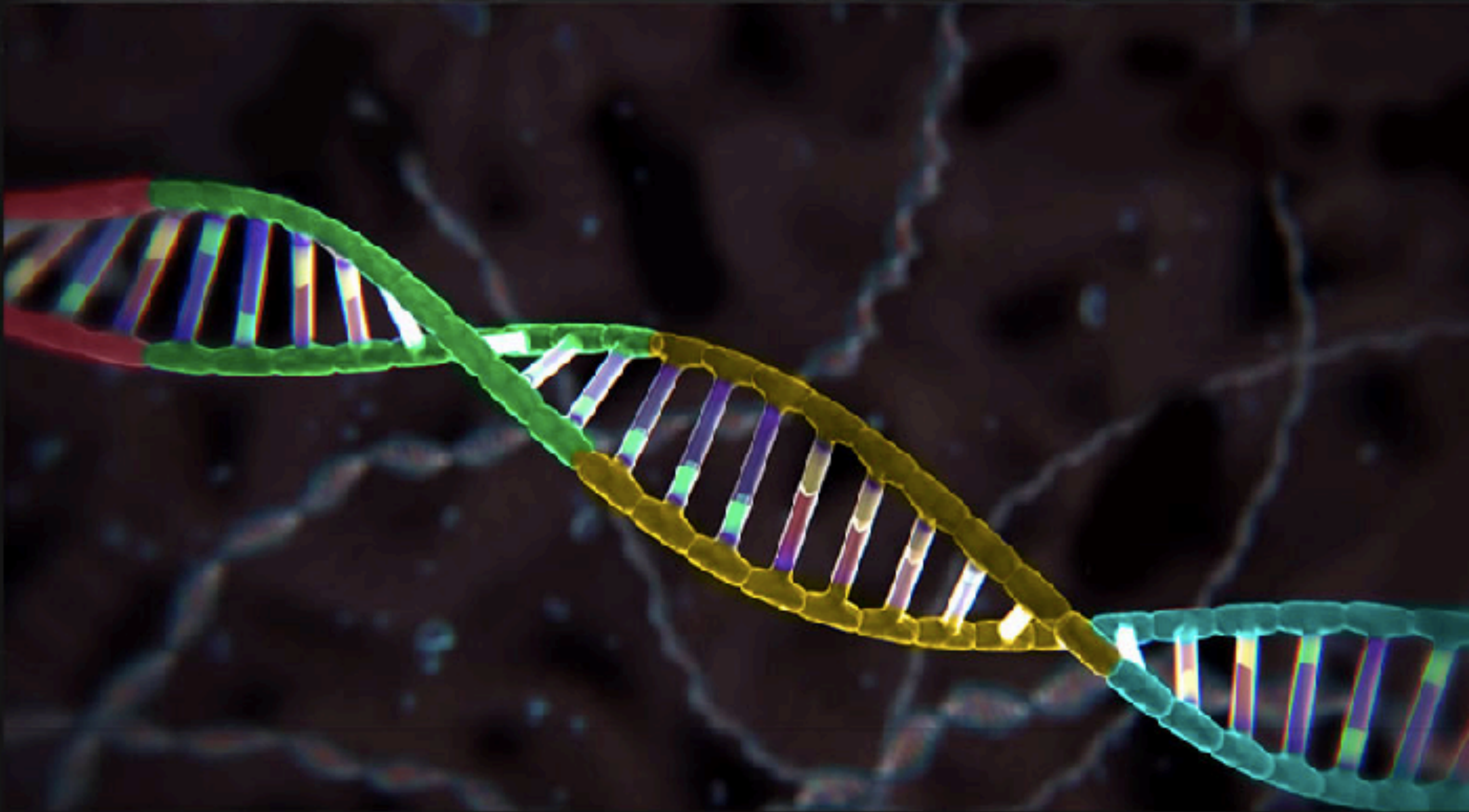
STEP 4: INSERTING A NEW GENE

A short fragment of DNA or the desired gene with a specific function is then inserted to fill the gap and replace the original gene.



STEP 5: PRODUCTION OF THE DESIRED PROTEIN

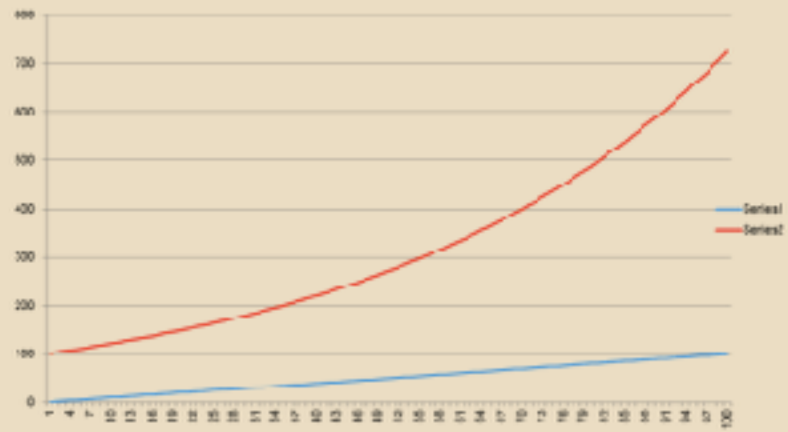
The new gene is now ready to produce the desired protein in the cell or in a test tube



A few words about the singularity

Money in the bank . . .

$1	10%	25%
1	1.10	1.25
2	1.21	1.56
3	1.33	1.95
4	1.46	2.44
5	1.61	3.05
6	1.77	3.81
7	1.95	4.77
8	2.14	5.96
9	2.36	7.45
10	2.59	9.31



A few words about the singularity

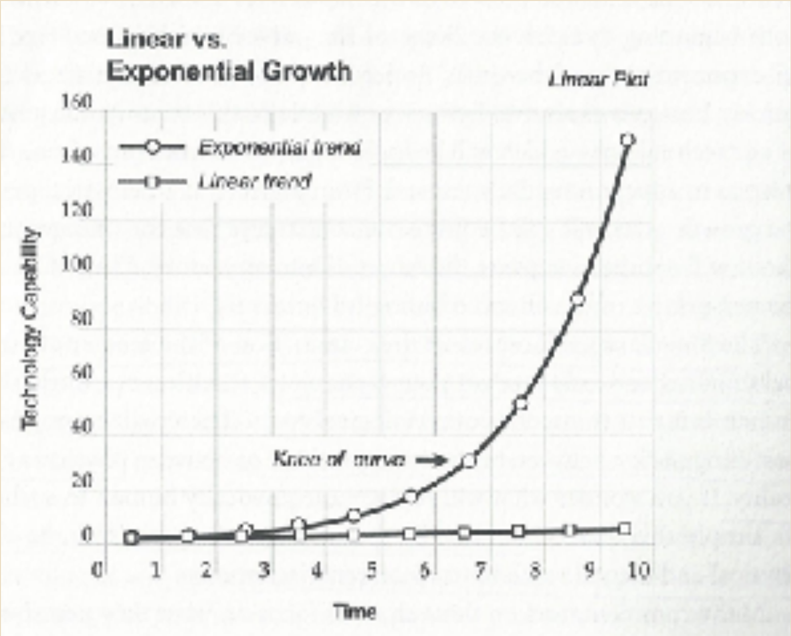
Money in the bank . . .

$1	50%	100%
Period 1	1.5	2
2	2.25	4
3	3.38	8
4	5.06	16
5	7.59	32
6	11.39	64
7	17.09	128
8	25.63	256
9	38.44	512
10	56.77	1024

A few words about the singularity

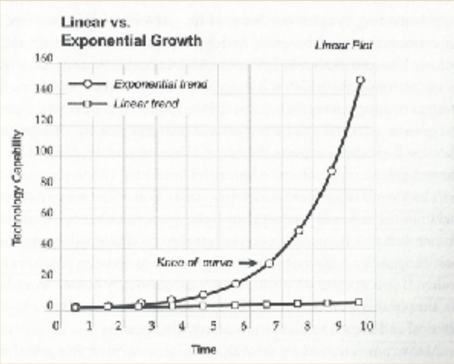
Money in the bank . . .

$1	50%	100%
Period 1	1.5	2
2	2.25	4
3	3.38	8
4	5.06	16
5	7.59	32
6	11.39	64
7	17.09	128
8	25.63	256
9	38.44	512
10	56.77	1024
20		1.05 million

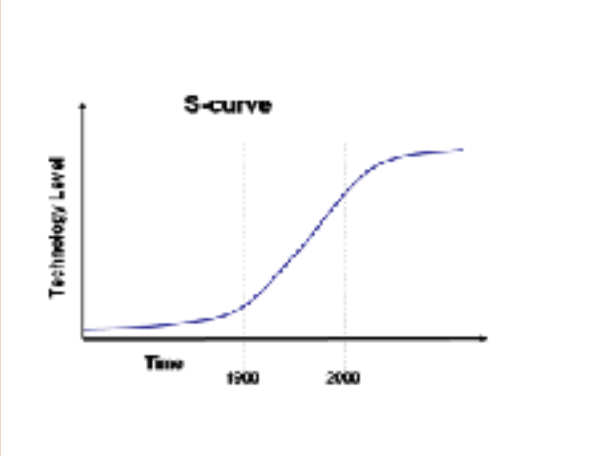


A few words about the singularity

Why do we *misjudge* the future?
– because over a short period of time, the curve looks flat



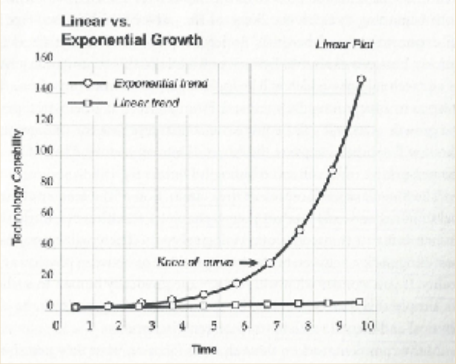
–There must be limits to how fast and far we can go



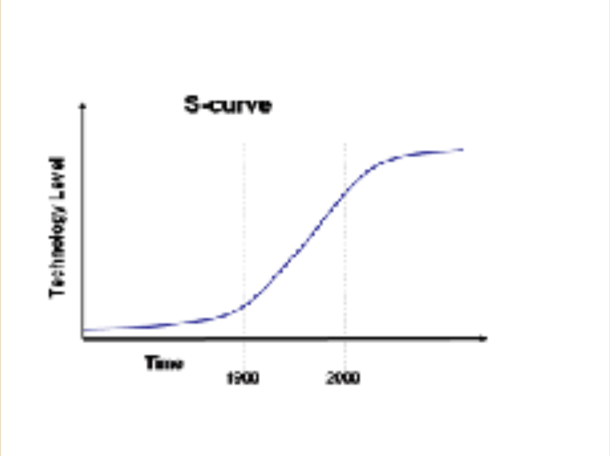
A few words about the singularity

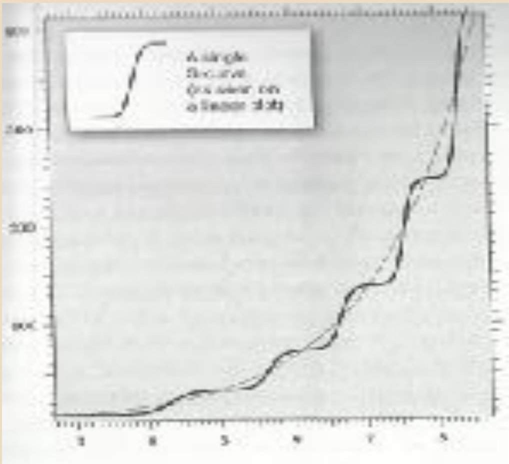
Why do we *misjudge* the future?

– because over a short period of time, the curve looks flat



–There must be limits to how fast and far we can go

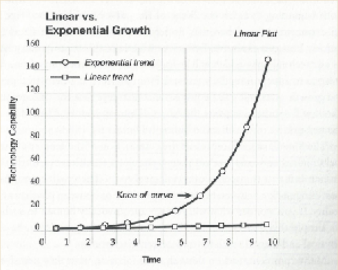


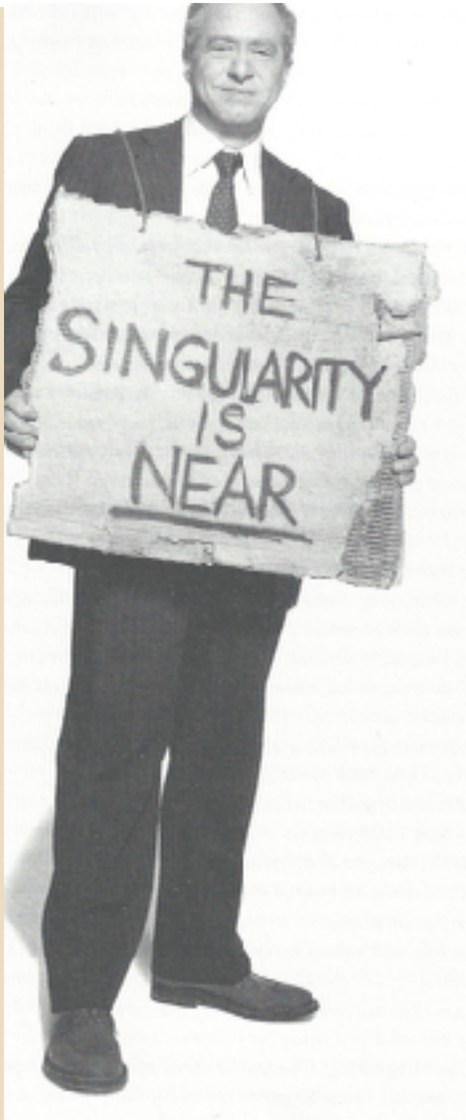


A few words about the singularity

Ray Kurzweil:

A future period in which . . . technological changes will be so *rapid and their impact so deep*, that human life will be *irreversibly* transformed!





A few words about the singularity