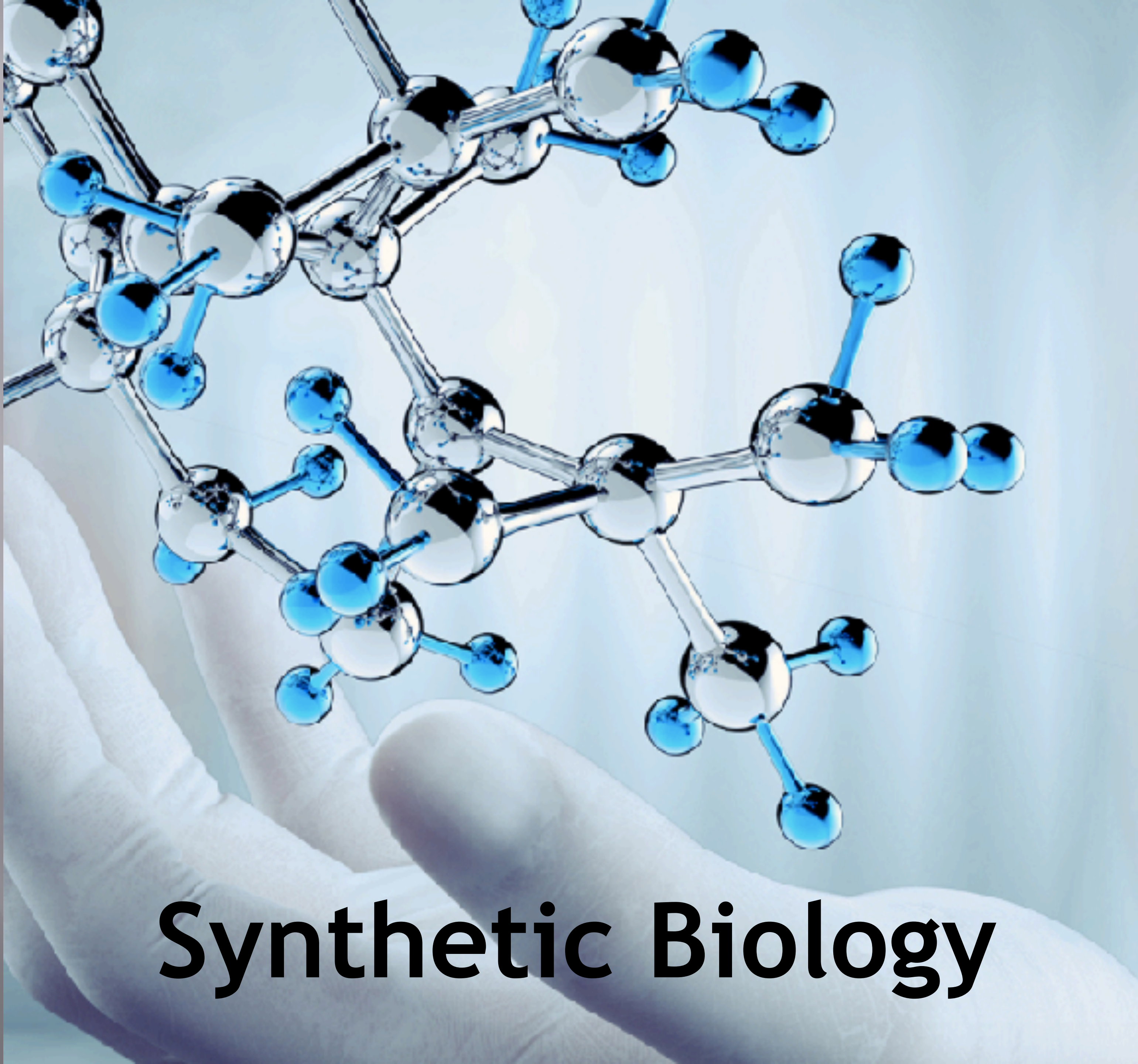


Synthetic Biology

SYNTHETIC BIOLOGY

- Tonight's perspective

  - HUMAN GENETICS 1-0-1

  - CURRENT

  - NEAR TERM DEVELOPMENTS

  - LONG TERM DEVELOPMENTS

  - PRO ET CON

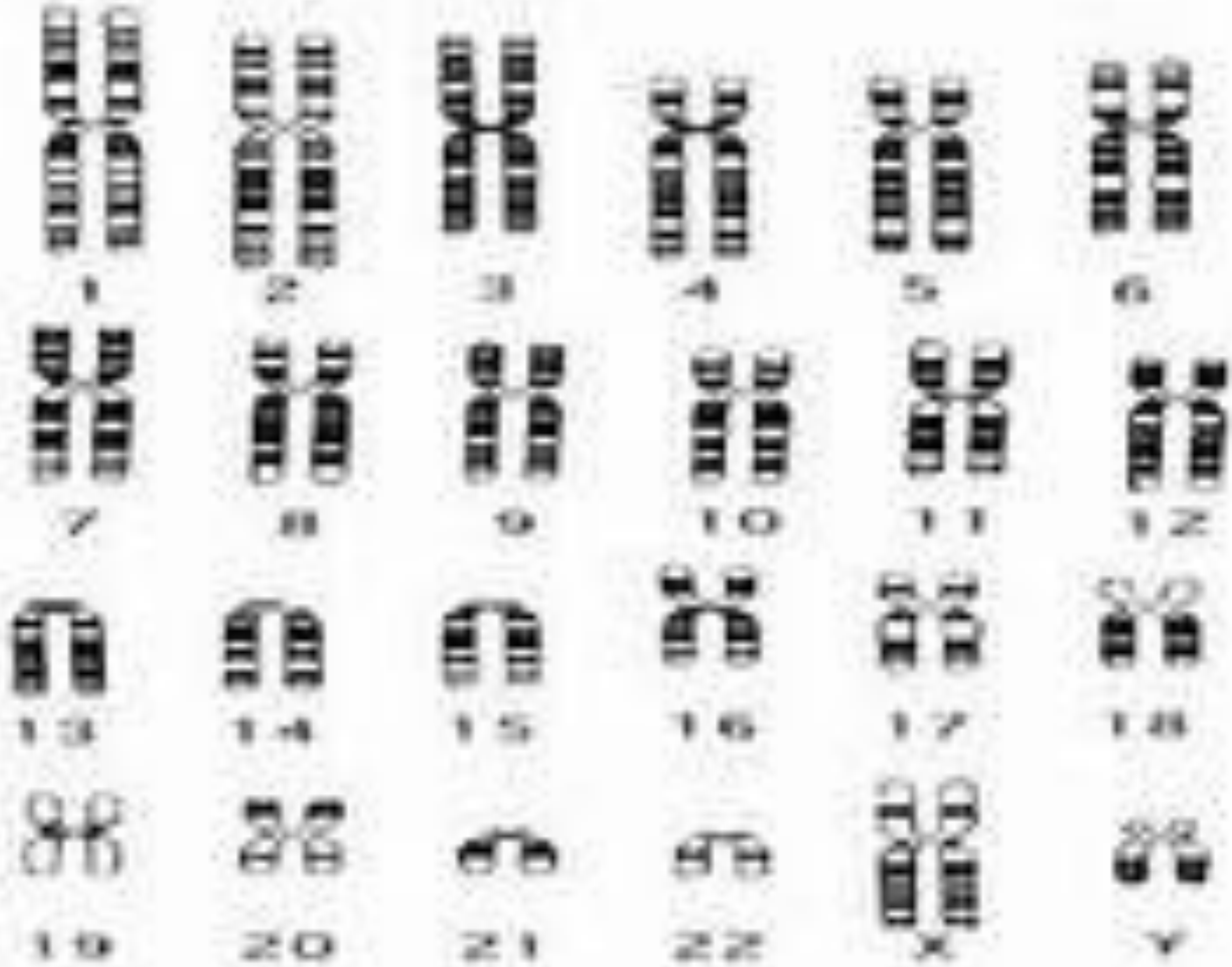
HUMAN GENETICS 1-0-1

- 23 chromosomes

- 20,000-25,000 pairs of genes

- 6,470 Mb (duploid)
- 3,235 Mb (haploid)

- 30-40 Trillion cells in the adult human body
  (50+ different types)
  (~80% are red blood cells)
- Mb = Million base pairs (A—T and C—G)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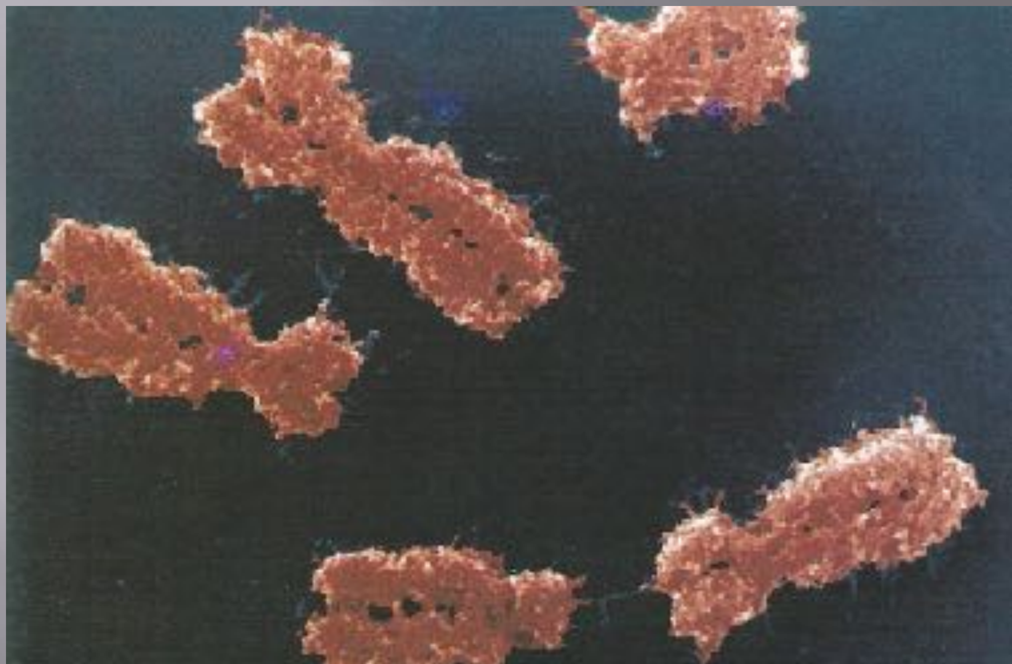
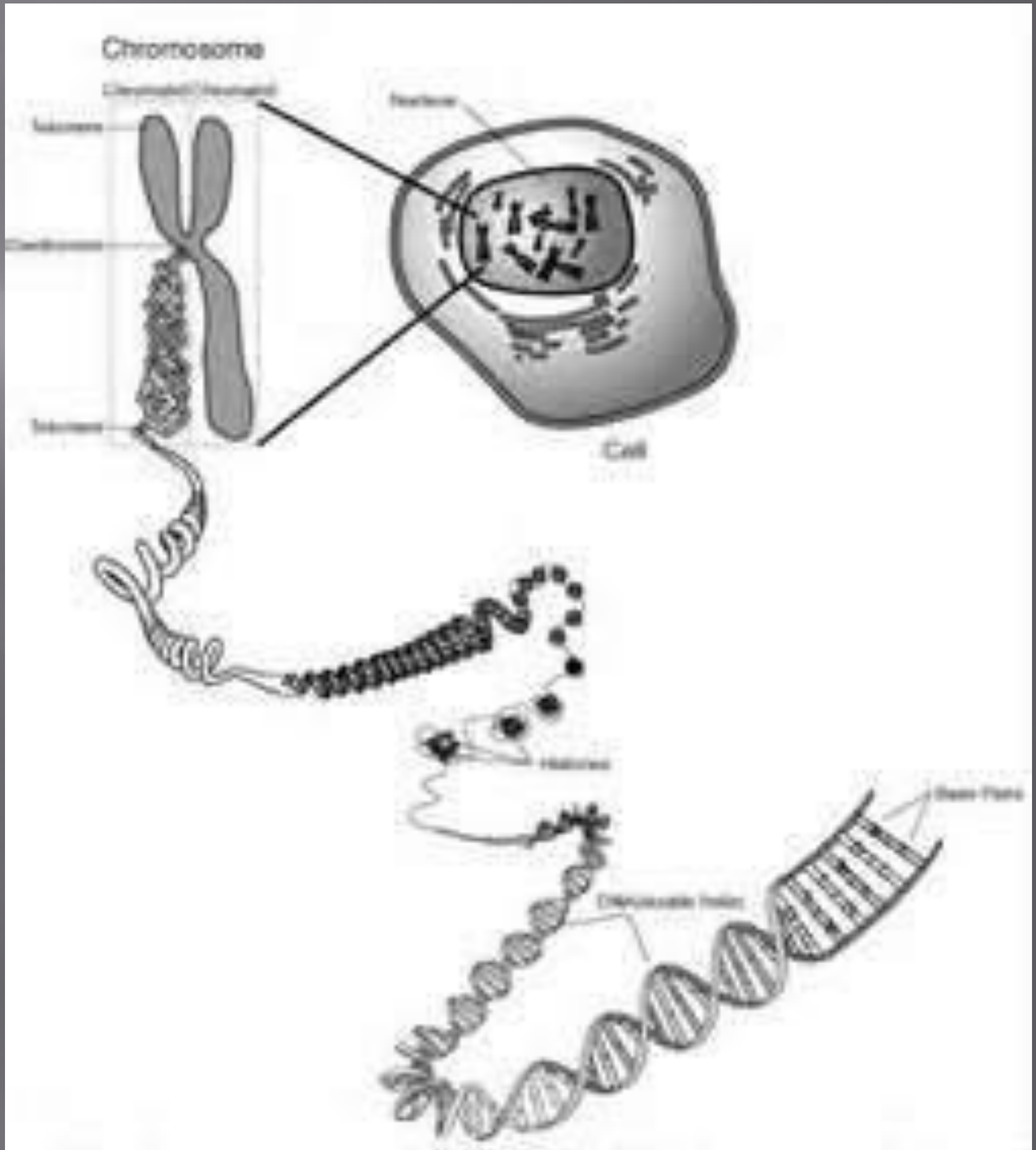
X
Y

HUMAN GENETICS 1-0-1

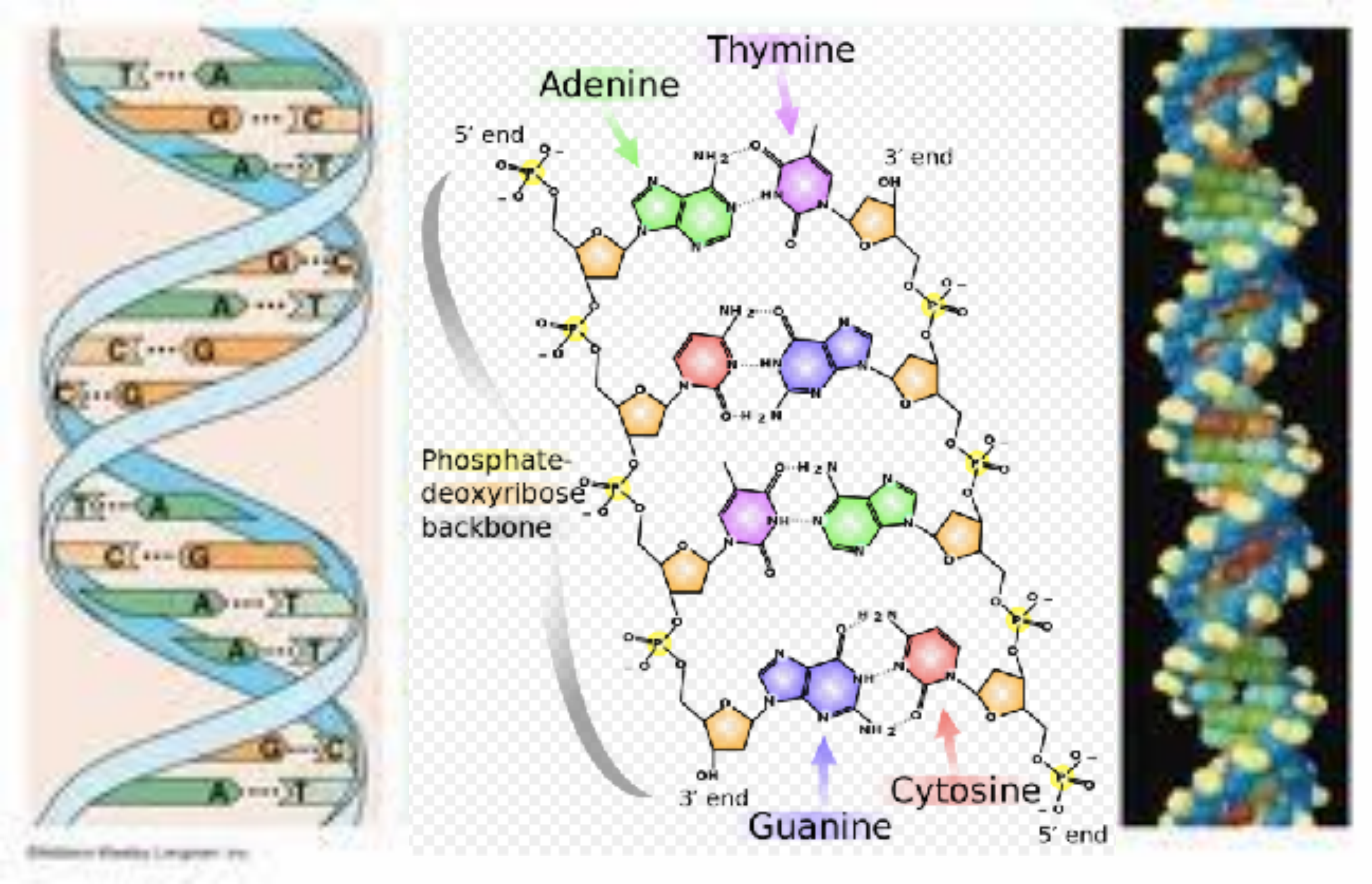


HUMAN GENETICS 1-0-1

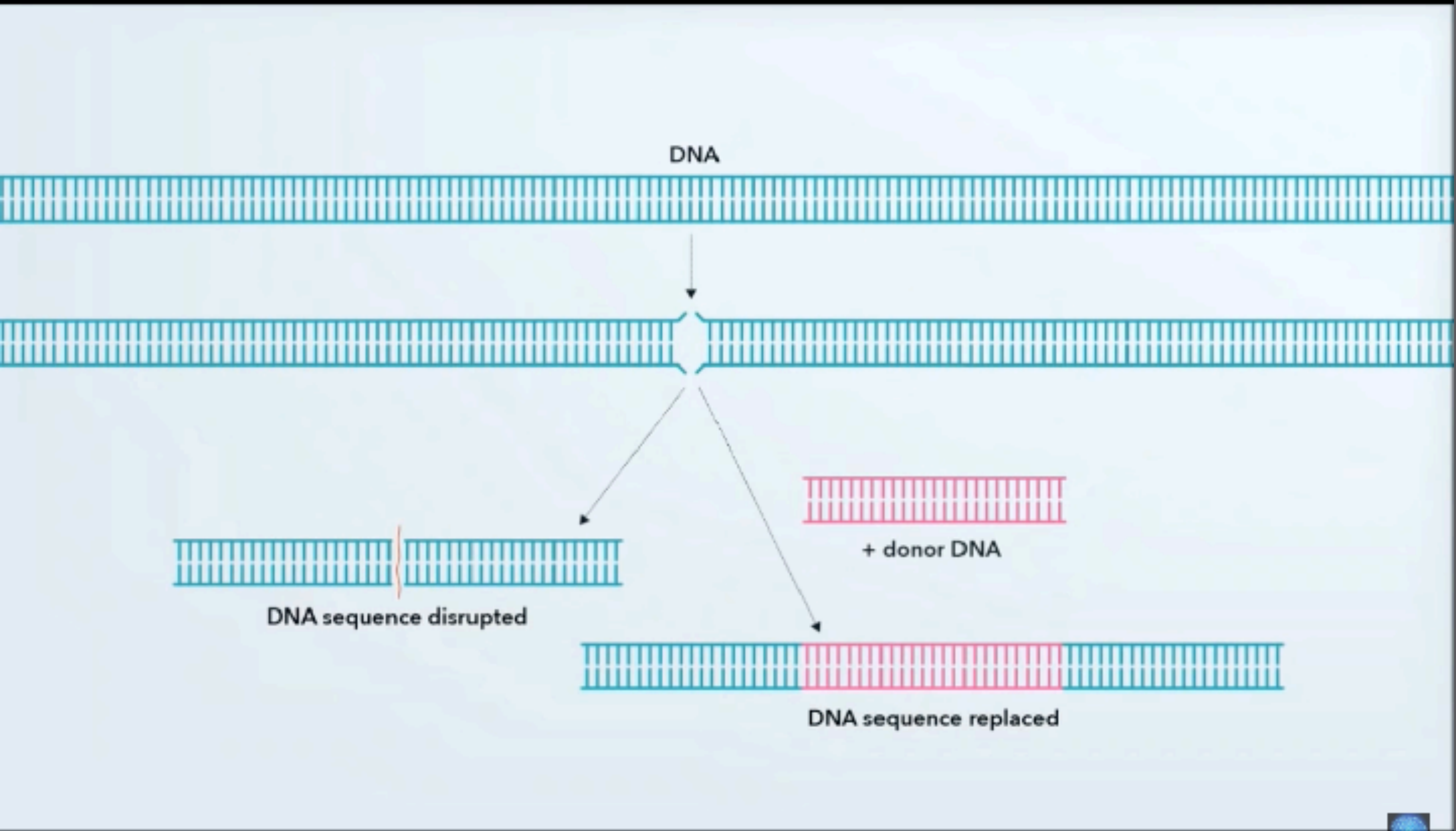
- DNA in a single cell is 6 ft long if fully stretched but is coiled up to fit into a cell only 1/2500 of an inch long



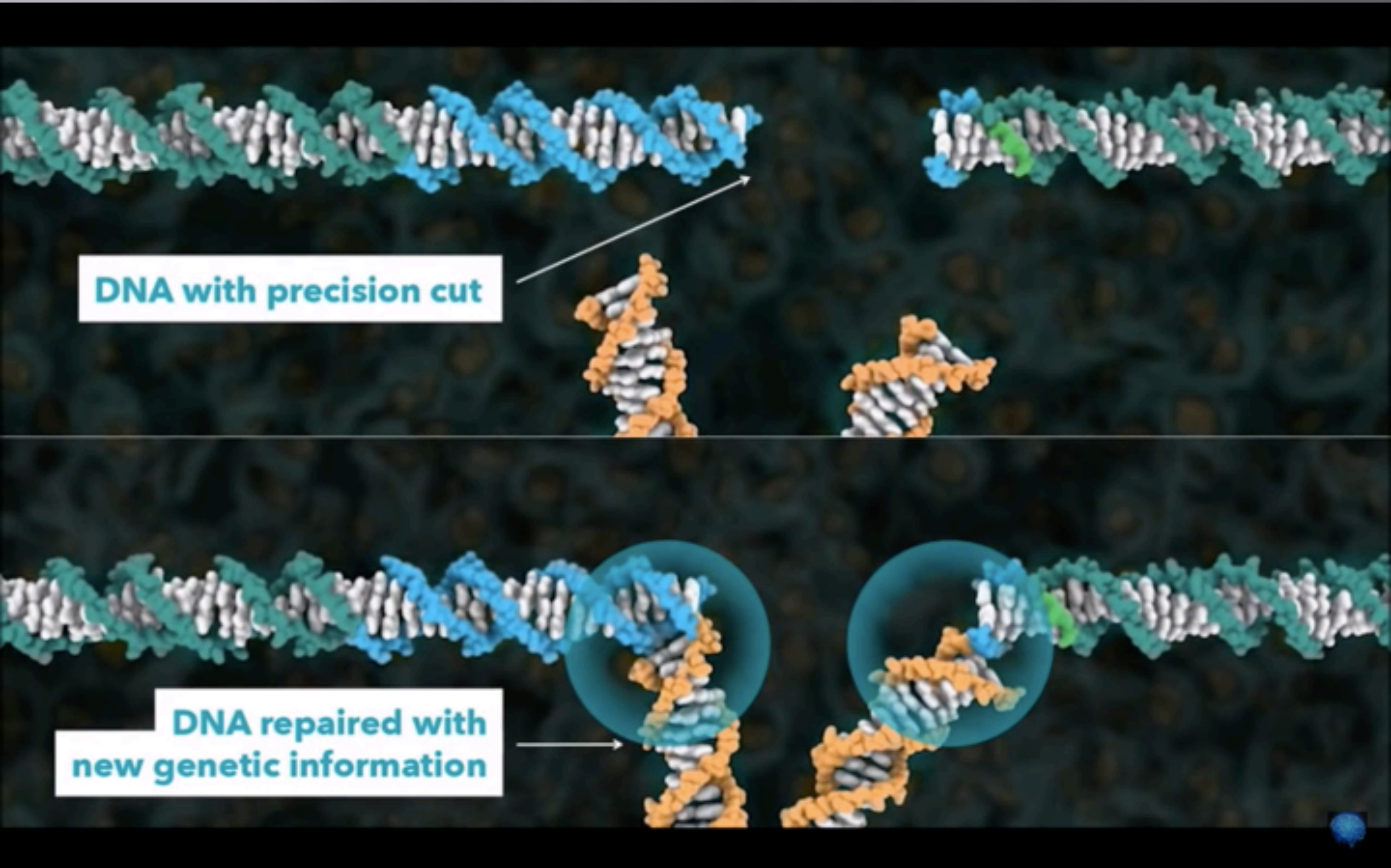
HUMAN GENETICS 1-0-1



HUMAN GENETICS 1-0-1



HUMAN GENETICS 1-0-1



SYNTHETIC BIOLOGY

- Tonight's perspective

  - HUMAN GENETICS 1-0-1

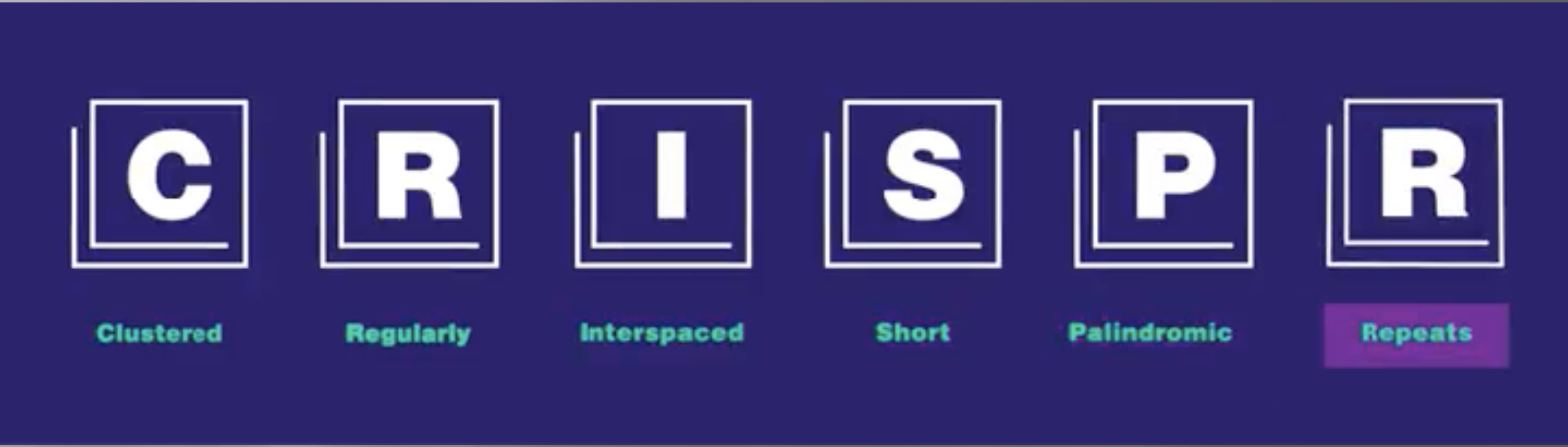
  - **CURRENT**

  - NEAR TERM DEVELOPMENTS
    tissue cultivation, stem cells, PPC

  - LONG TERM DEVELOPMENTS

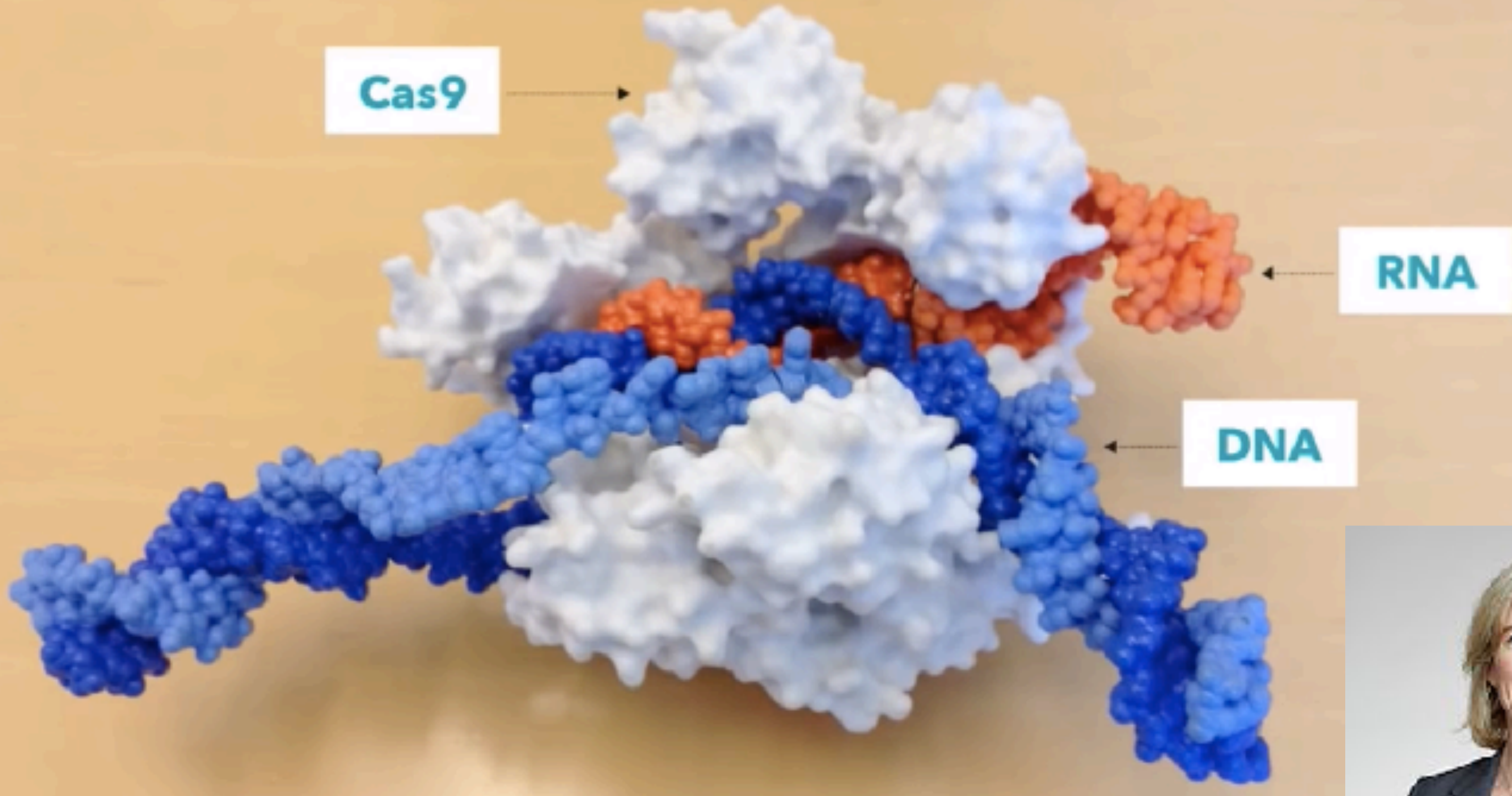
  - PRO ET CON

SYNTHETIC BIOLOGY 0-5 YEARS



SYNTHETIC BIOLOGY 0-5 YEARS

CRISPR-Cas9



SYNTHETIC BIOLOGY 0-5 YEARS

CRISPR-Cas9

SYNTHETIC BIOLOGY 0-5 YEARS

ADDING A NEW GENE

Desirable genes can be added into the genome allowing researchers to study their functions within the cells. These genes can also add new functions to the cell.

DELETING A GENE

Undesirable genes can be deleted from the genome allowing researchers to study their functions specific genes and learn about what happens to the cell when these genes are not in the genome

SYNTHETIC BIOLOGY 0-5 YEARS

ACTIVATING DEAD GENES

Genes that are essential for various functions but no longer function can be reactivated using CRISPR-Cas9 system.

CONTROLLING GENE ACTIVITY LEVEL

Genes are more active than normal can controlled to be produce just the right amount of proteins, which will help maintain the balance within the cell under desired conditions.

SYNTHETIC BIOLOGY

- Tonight’s perspective

  - HUMAN GENETICS 1-0-1

  - CURRENT

  - NEAR TERM DEVELOPMENTS
    tissue cultivation, stem cells, PPC

  - LONG TERM DEVELOPMENTS

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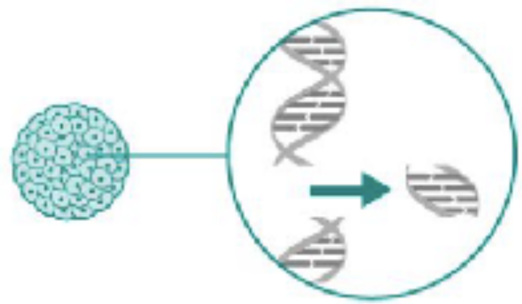
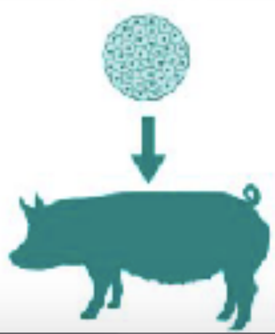
TISSUE CULTIVATION

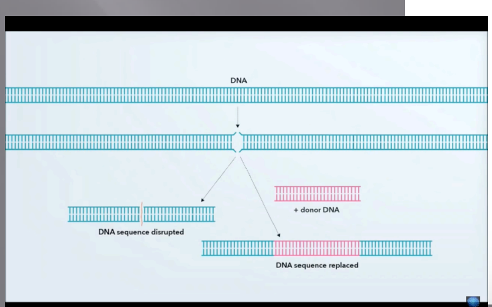
1 A day-old pig embryo is gene edited to delete the part of its DNA that would allow it to grow a pancreas.



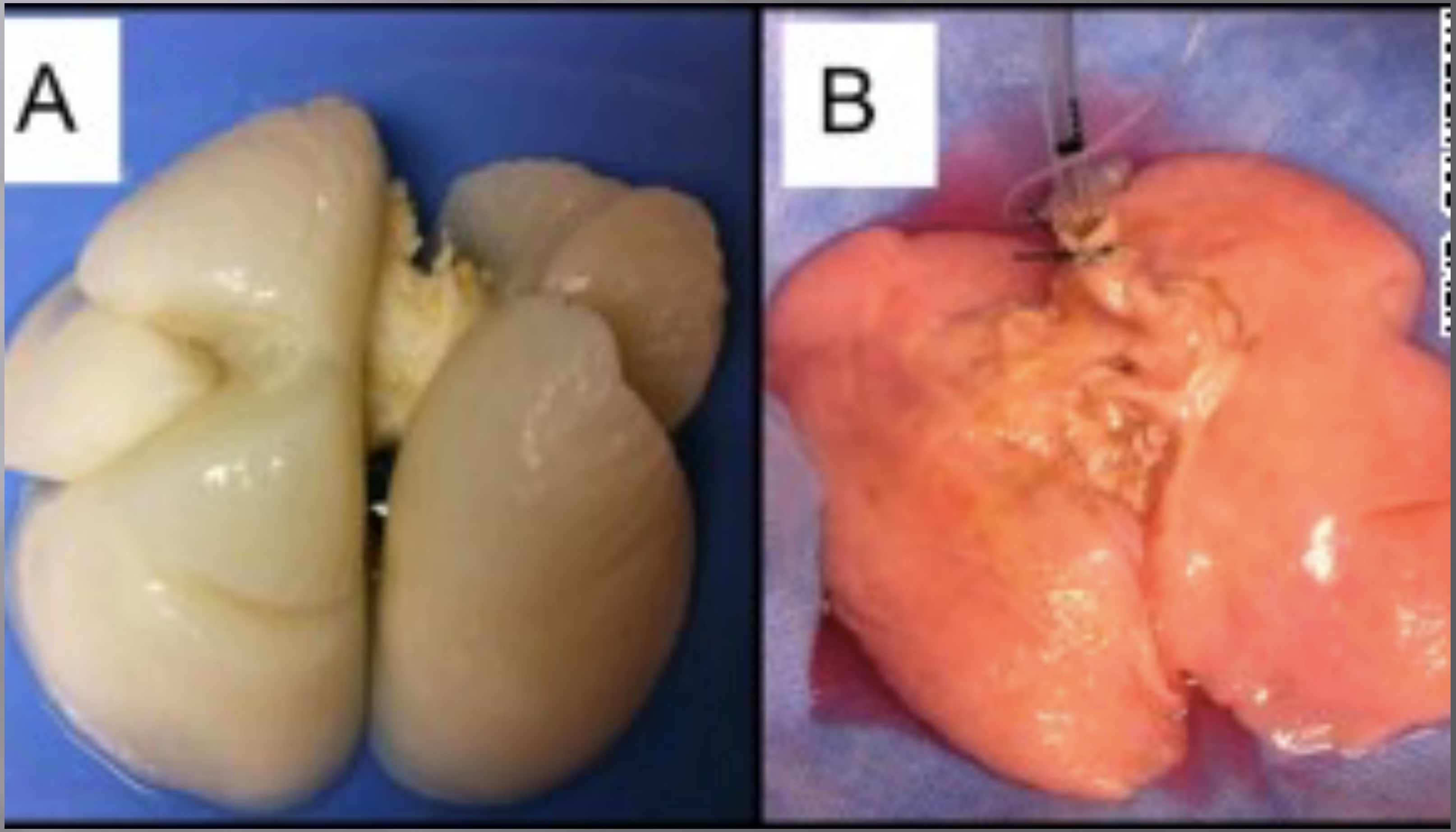
2 Human stem cells are injected into the embryo. They should fill the gap and allow it to grow a human pancreas.

3 The embryo is implanted into the sow and allowed to develop to 28 days.

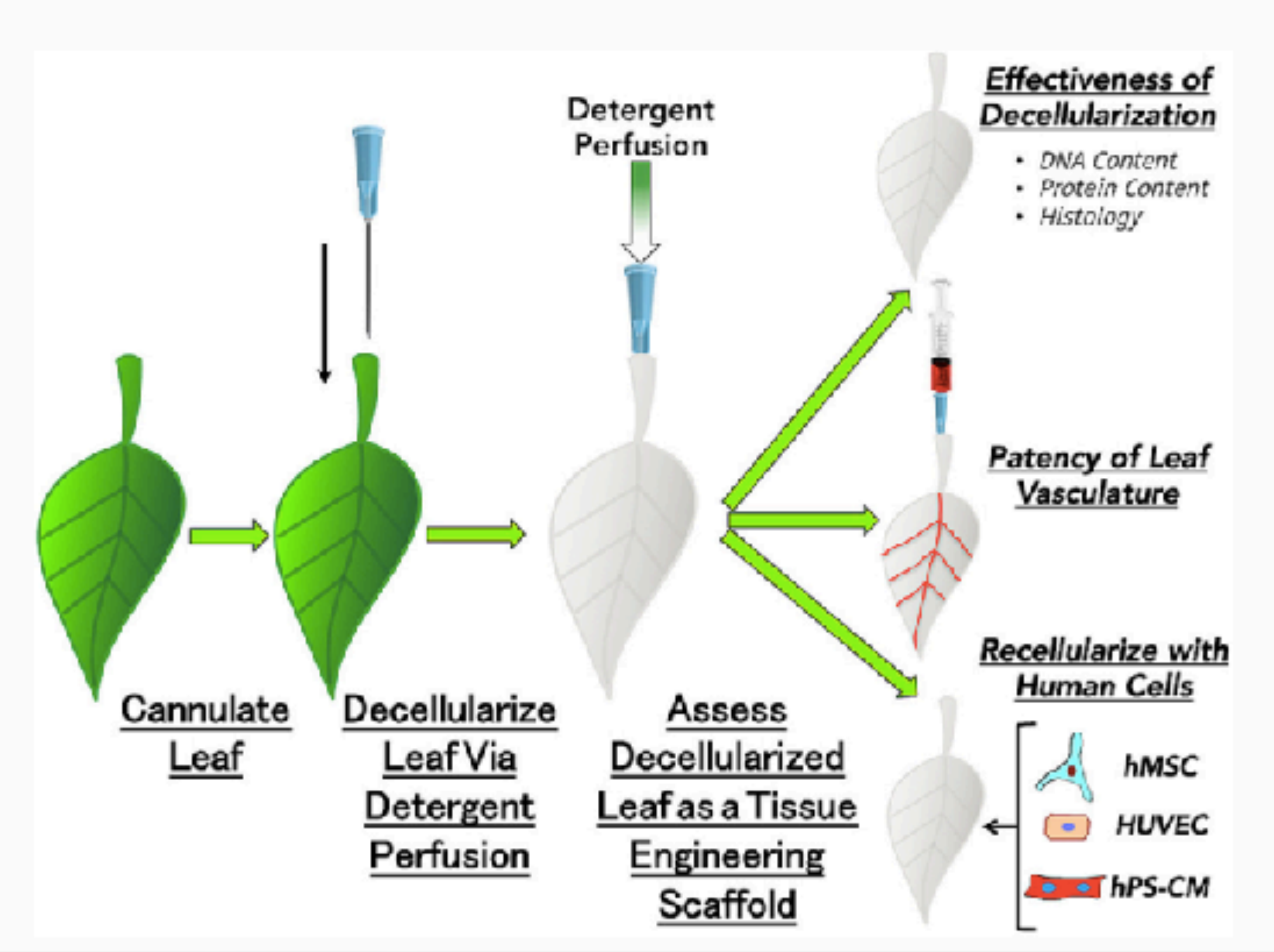




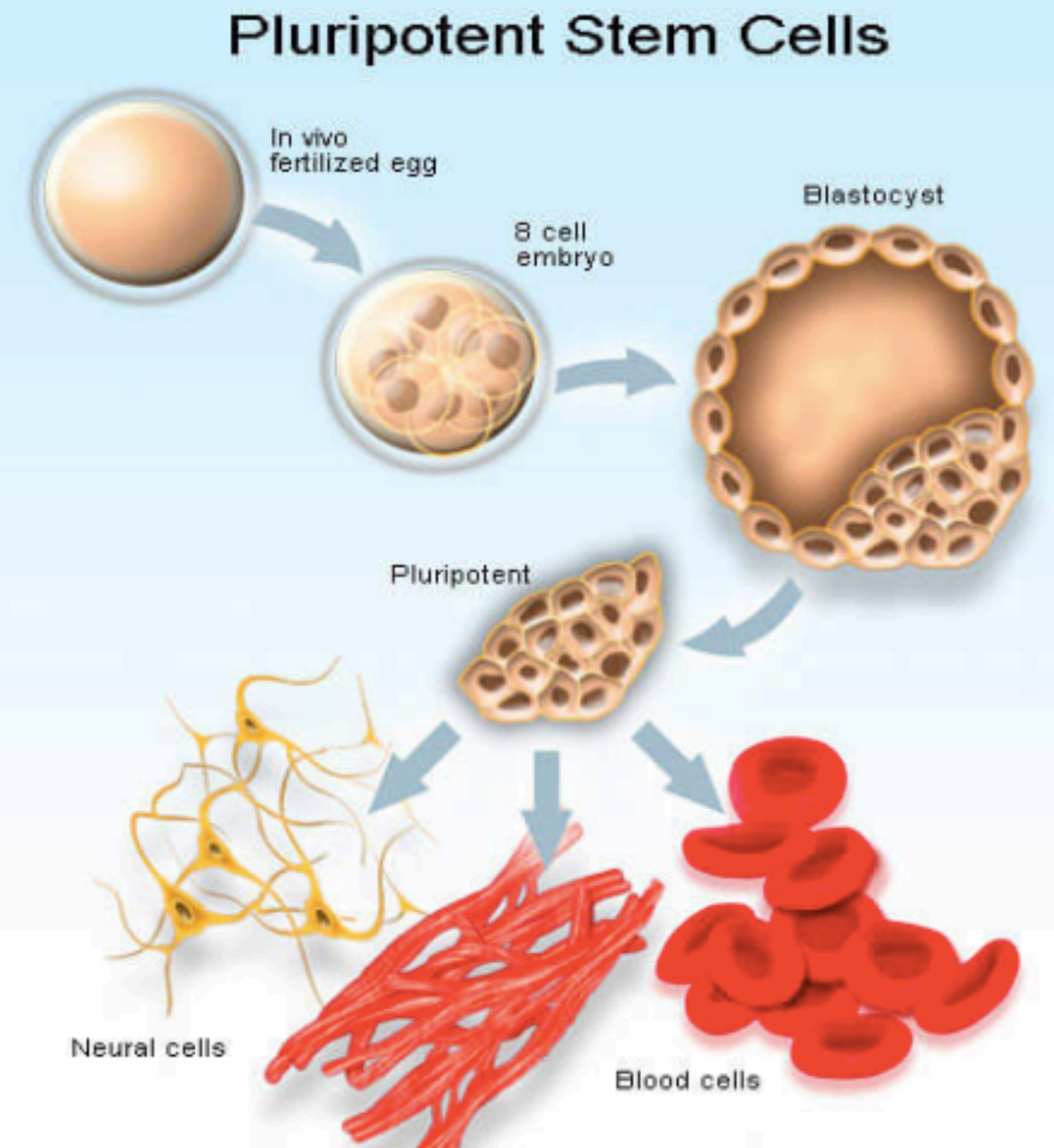
TISSUE CULTIVATION



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.



Detergent Perfusion
Effectiveness of Decellularization
• DNA Content
• Protein Content
• Histology
Patency of Leaf Vasculature
Recellularize with Human Cells
hMSC
HUVEC
hPS-CM
Cannulate Leaf
Decellularize Leaf Via Detergent Perfusion
Assess Decellularized Leaf as a Tissue Engineering Scaffold


Pluripotent Stem Cells
In vivo
fertilized egg
8 cell
embryo
Blastocyst
Pluripotent
Neural cells
Blood cells

SYNTHETIC BIOLOGY

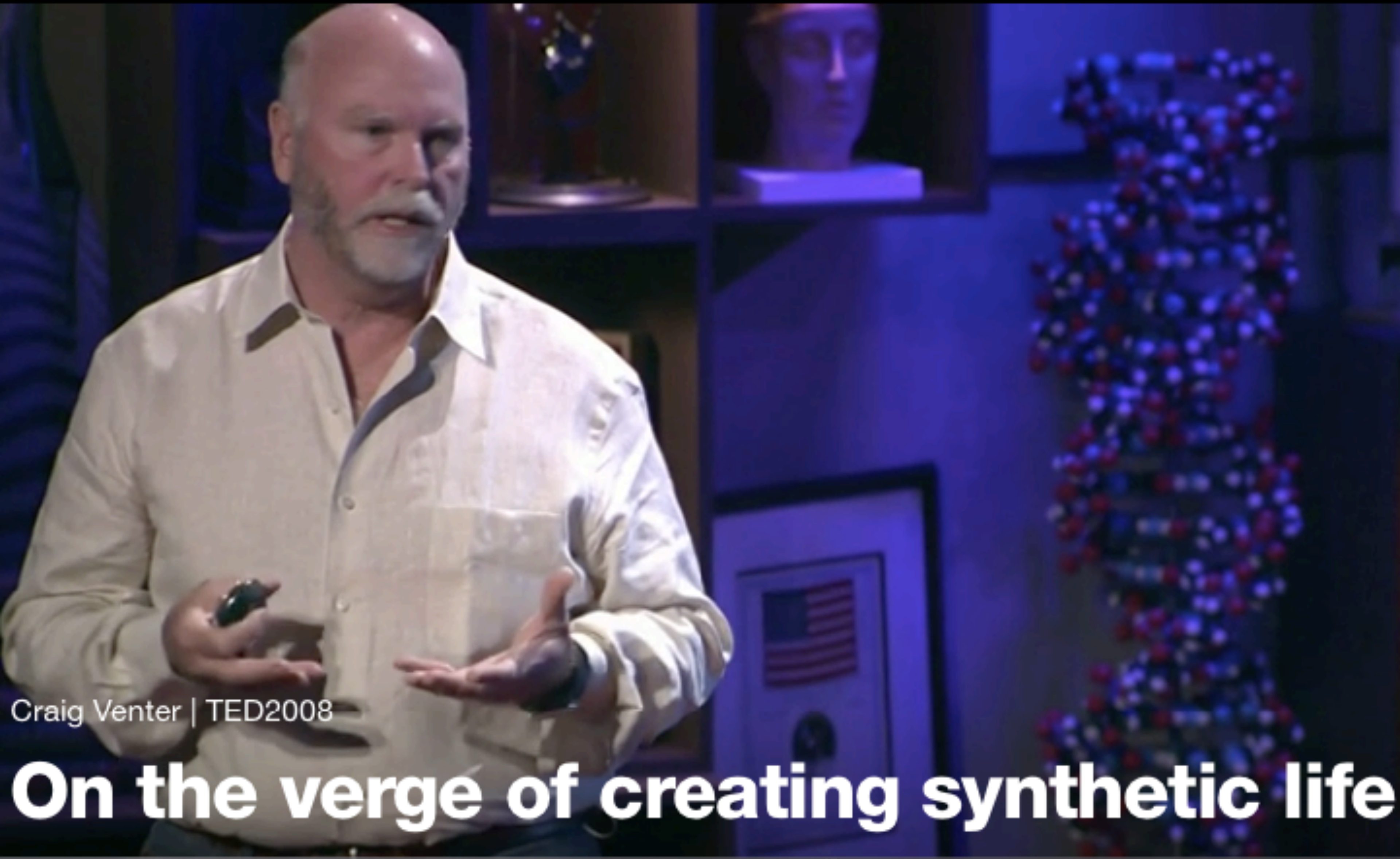
- Tonight's perspective

  - HUMAN GENETICS 1-0-1

  - NEAR TERM DEVELOPMENTS

  - LONG TERM DEVELOPMENTS - Creig Venter

  - PRO ET CON



https://www.ted.com/talks/craig_venter_is_on_the_verge_of_creating_synthetic_life#t-923317

SYNTHETIC BIOLOGY

Also around the corner:
artificial photosynthesis.
gene drives (infertile mosquitos)
editing the *human* genome/biocomputers*
replacement organs, tissue engineering
drug development

About 5-10 years out:
synthetic embryos**
super-viruses
genetic information as the new currency

SYNTHETIC BIOLOGY

* Biocomputer (altered metabolic pathways):
Scientists engineered yeast cells to produce a molecule used to make anti-malaria drugs from sugar

Other teams have made bacteria that convert carbon dioxide into liquid fuels, essentially paving the way for artificial photosynthesis.

Scientists have even managed to link together two *synthetic gene circuits*, (metabolic pathways) allowing teams of bacteria to carry out simple computations.

SYNTHETIC BIOLOGY

Also around the corner:
artificial photosynthesis.
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editing the *human* genome/biocomputers*
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About 5-10 years out:
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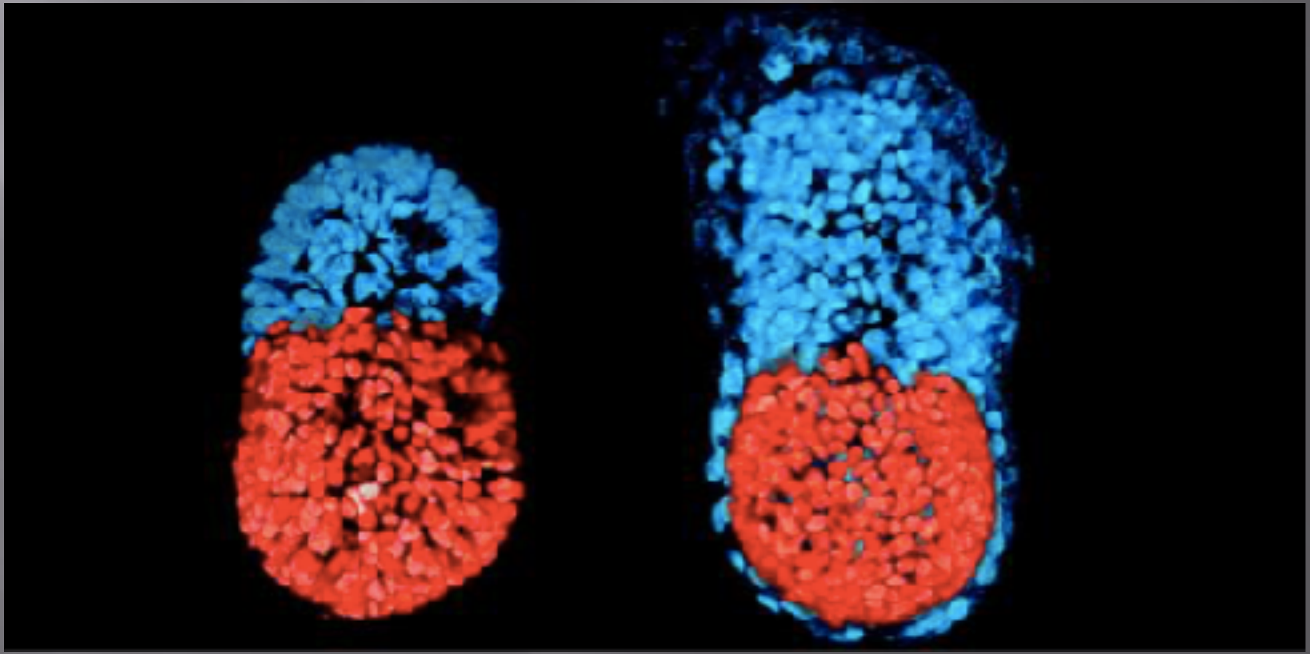
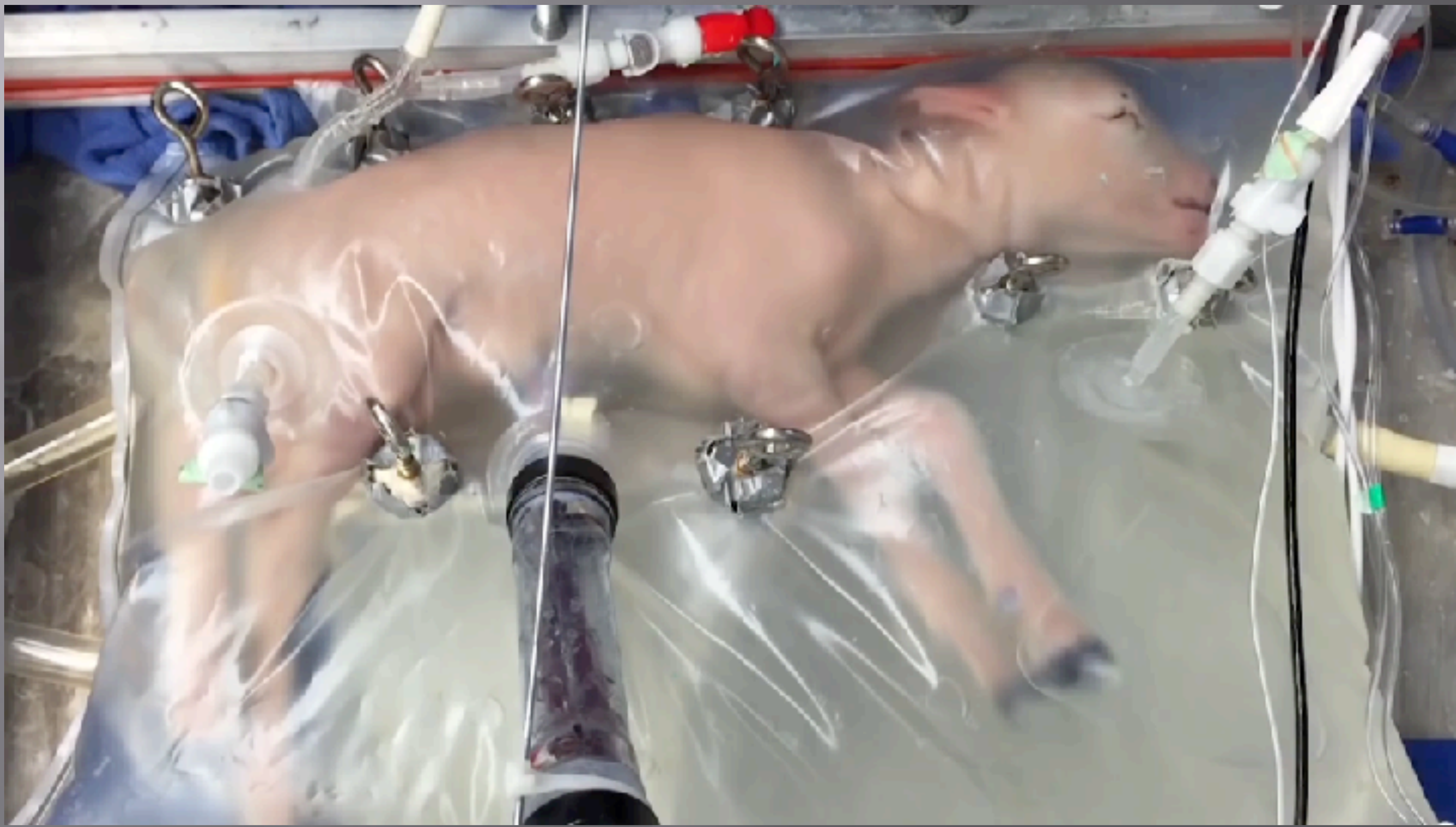
ARTIFICIAL EMBRYO

**By combining genetically modified mouse ESC and extra-embryonic tropoblast stem cells in a 3D- gel scaffold, one research team was able to drive the development of a SYNTHETIC EMBRYO similar to that of natural embryos



ARTIFICIAL UTERUS



SYNTHETIC BIOLOGY

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SYNTHETIC BIOLOGY

The Optimist's 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 comparable only to that of artificial intelligence.

SYNTHETIC BIOLOGY

The Optimist's View

We're standing on the threshold of extraordinary capability in synthetic biology.

CRISPR-Cas9 provide an opportunity to solve problems in food supply, disease, genetics, and—the most tantalizing and forbidden of prospects—modifying the human genome.

Doing so would make us better, faster, stronger, more resilient, and more intelligent: it's a chance to engineer ourselves at a faster rate than natural selection could ever accomplish.

SYNTHETIC BIOLOGY

The Pessimists Views

- some people 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 - and could be limited to only those who can afford it

- concern about unintended consequences

- concern about misuse/abuse (bio-terrorists can make synthetic pathogens)*

SYNTHETIC BIOLOGY

CRISPR may make it possible to create the bioweapons such as smallpox or modify Ebola, and modify it into an epidemiologist's worst nightmare.

Example (2017):

Researchers in Toronto resurrected an extinct strain of the horsepox virus

SYNTHETIC BIOLOGY

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

SYNTHETIC BIOLOGY

Whether
PRO or CON
All agree on one thing:

We are moving fast into
the synthetic biology era.

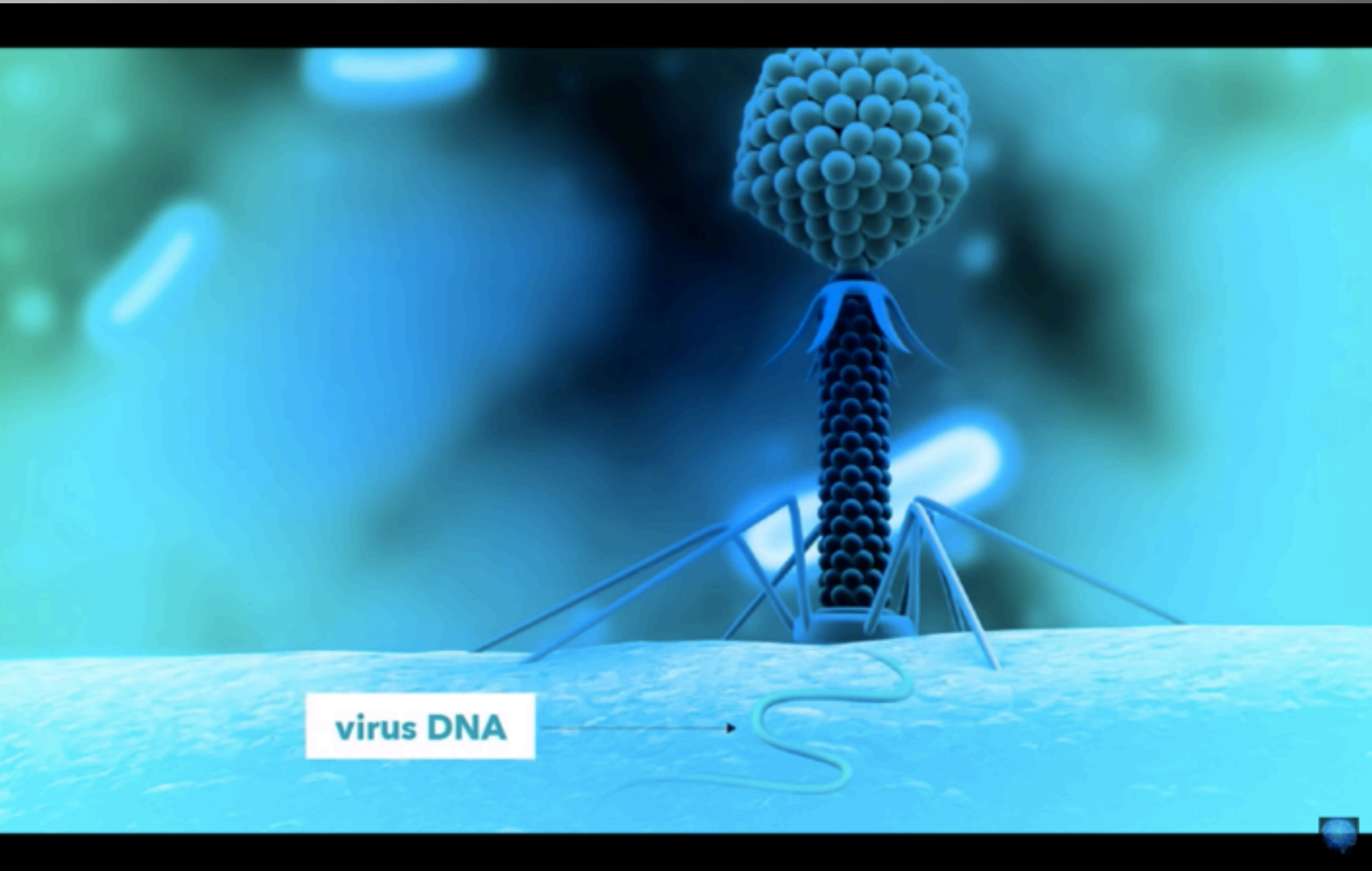
SYNTHETIC BIOLOGY

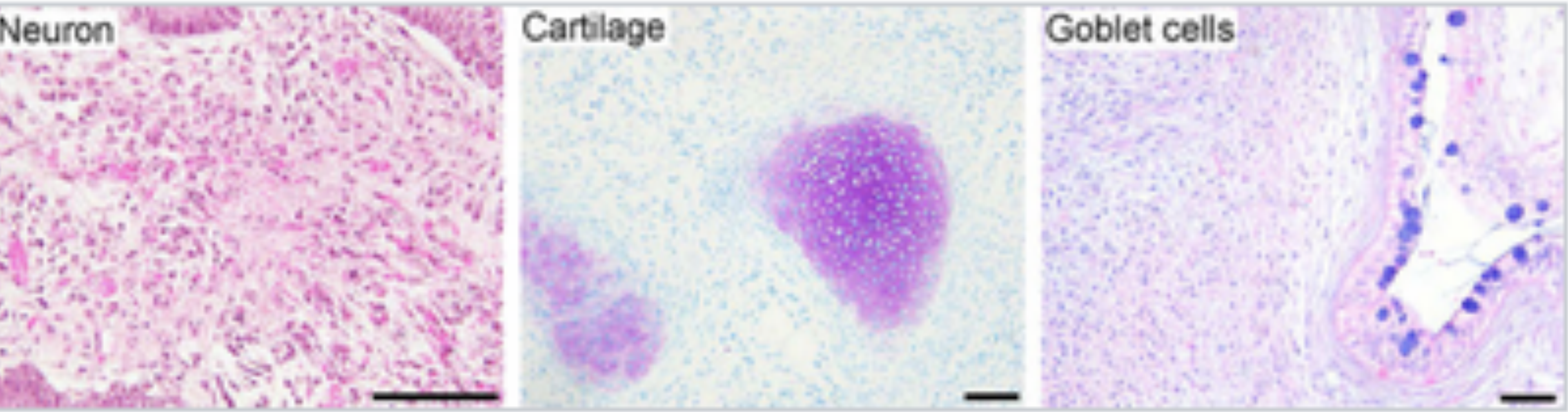
Thank You!

torben.riise@gmail.com

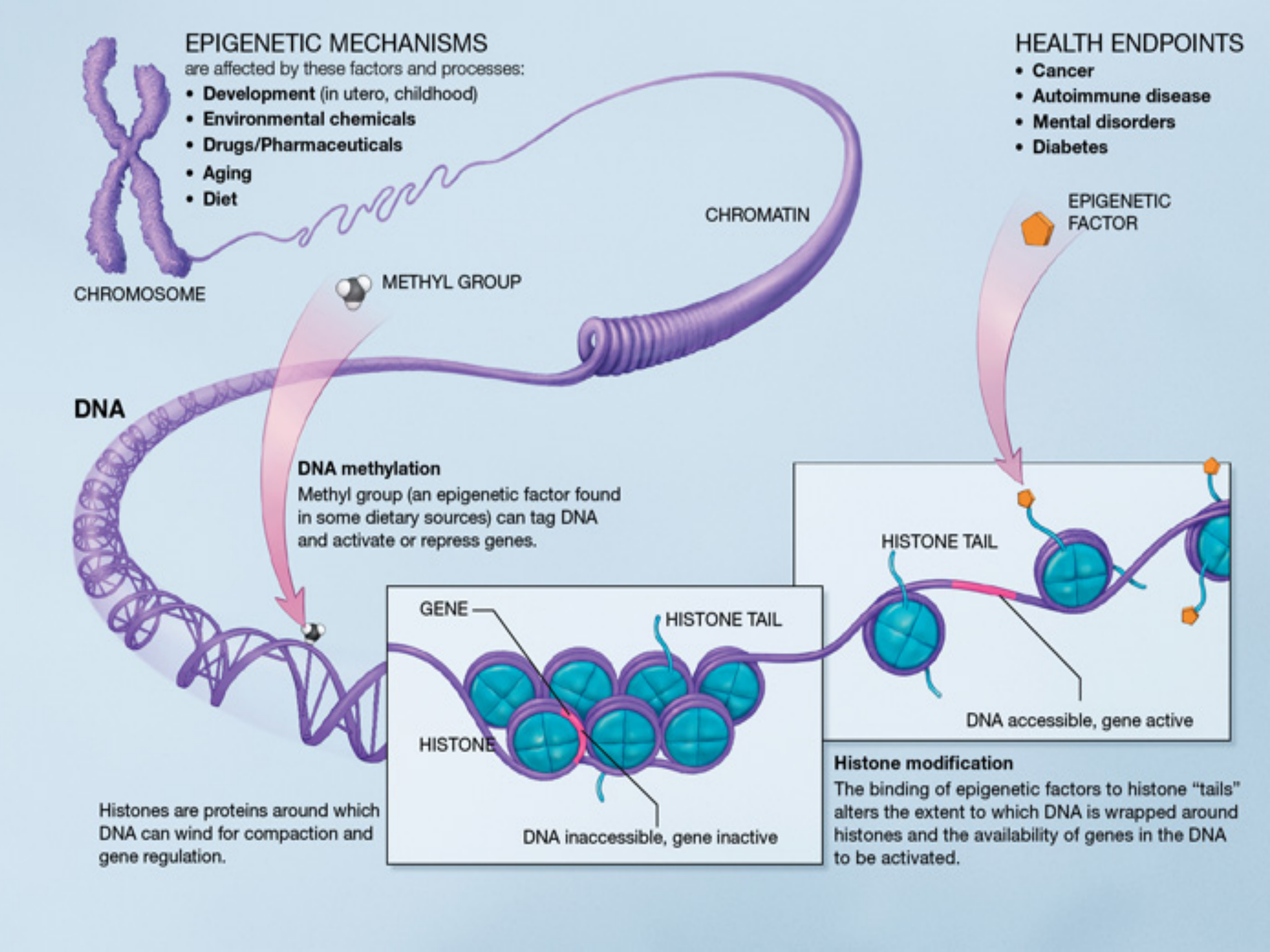
CRISPR Cas9: 4 min
https://www.youtube.com/watch?v=2pp17E4E-O8

Artificial Uterus:
https://www.youtube.com/watch?v=dt7twXzNEsQ


virus DNA



Three germ line cells/tissues differentiated from iPSCs: neurons(ectoderm), cartilage(Soft Bone, mesoderm) and goblet cells in intestine(endoderm).


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 inaccessible, gene inactive
DNA accessible, gene active
Histones are proteins around which DNA can wind for compaction and gene regulation.
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.

USEFUL DEFINITIONS / EXPLANATIONS

- **gene expression** – the process by which information from a gene is used in the synthesis of a functional gene product such as a protein
- **transcription** – the process of making messenger RNA (mRNA) from a DNA template by RNA polymerase
- **transcription factor** – a protein that binds to DNA and regulates gene expression by promoting or suppressing transcription
- **transcriptional regulation** – *controlling* the rate of gene transcription for example by helping or hindering RNA polymerase binding to DNA
- **upregulation**, **activation**, or **promotion** – *increase* the rate of gene transcription
- **downregulation**, **repression**, or **suppression** – *decrease* the rate of gene transcription
- **coactivator** – a protein that works with transcription factors to *increase* the rate of gene transcription
- **corepressor** – a protein that works with transcription factors to *decrease* the rate of gene transcription
- **response element** – a specific sequence of DNA that a transcription factor binds to