Converging technologies from the Biotechnologies perspective

Messenger RNA: An emerging biotechnology platform

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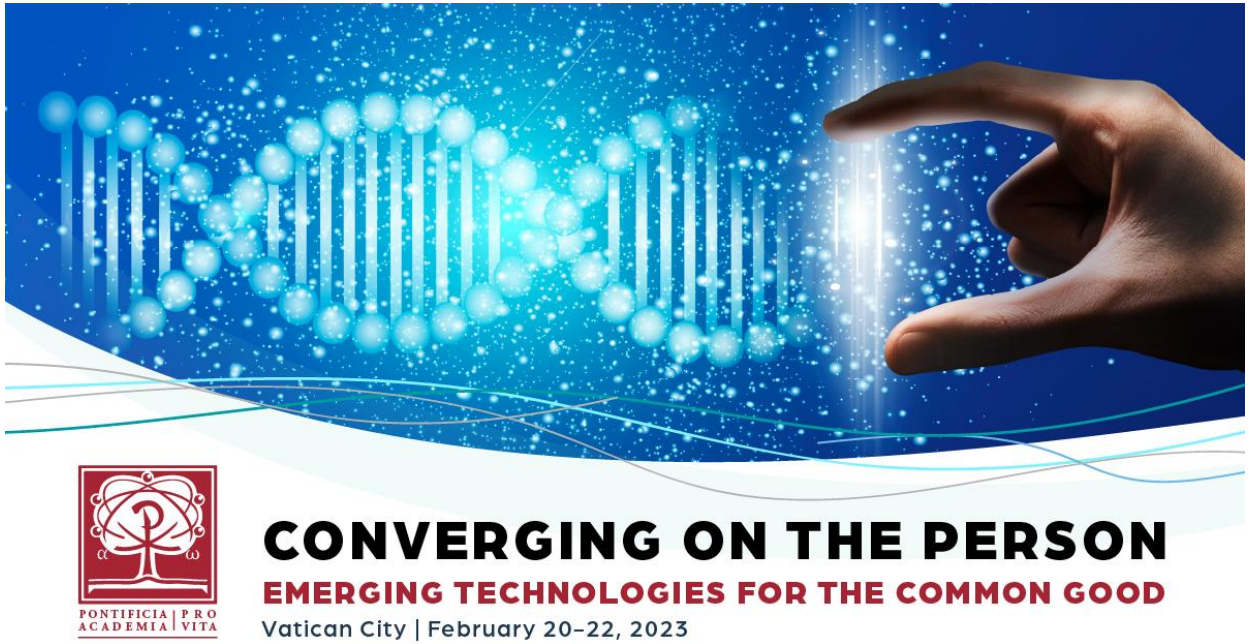
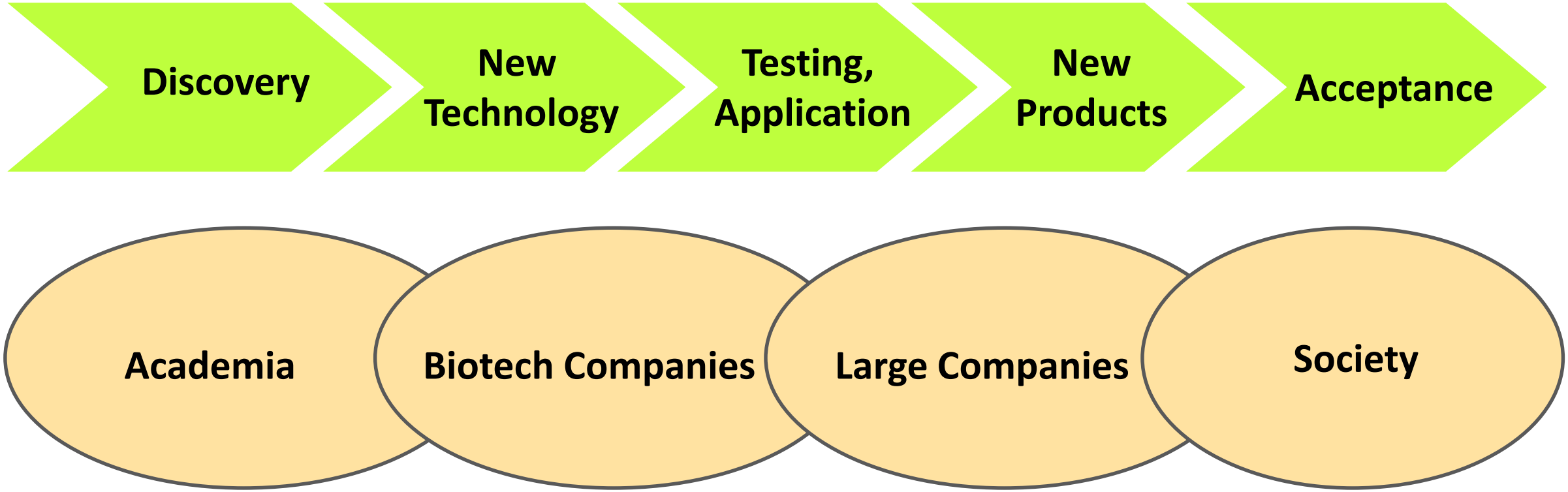


Disclosures

I have securities from BioNTech SE, and serve as consultant for BioNTech SE.
I am inventor on patents and patent applications related to RNA technology.

Emergence of novel biotechnologies



Emerging novel biotechnologies

Genome editing technologies:

- CRISPR-Cas
- TALEN
- Zinc Finger Nucleases

Cell and Gene therapies (FDA: >2,500 trial) **:**

- CAR T cells – Kymriah
- AAV gene therapy – Luxturna

RNA technologies:

- mRNA
- siRNA

Fields impacted by emerging biotechnologies

Genome editing, RNA therapy, cell and gene therapy technologies

Therapeutics:

- Treat human patients: acquired and genetic human disease
- Treat animals – Companion animals, *pets*
  – Farmed animals, *livestock*

Vaccines**:**

- Prevent infections of human and animals

Agriculture:

- Sustainable with improve yield, quality, nutrition of crops

The two most important emerging biotechnologies

CRISPR-Cas-based genome editing technology

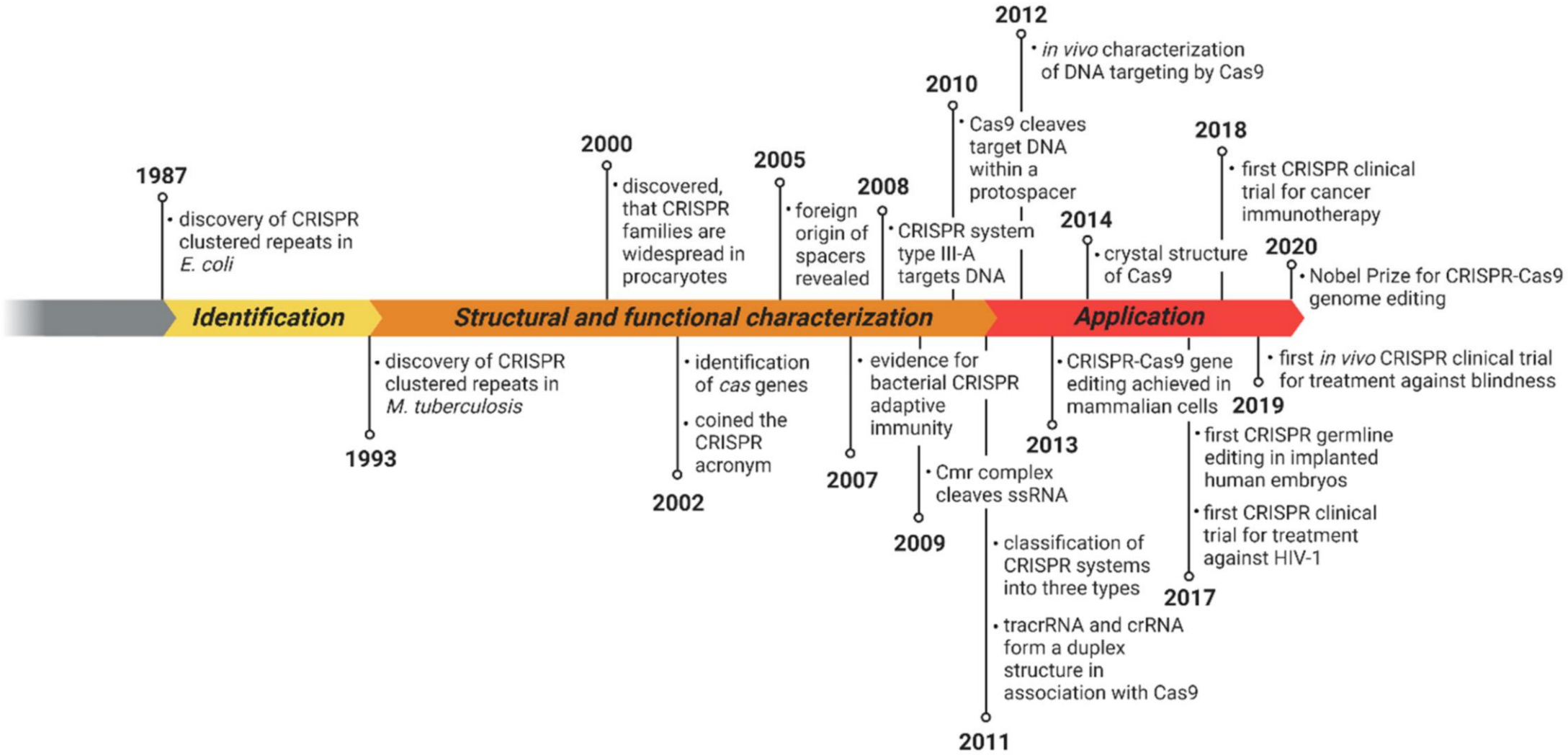
Messenger RNA-based therapy and vaccine technology

The two most important emerging biotechnologies

CRISPR-Cas-based genome editing technology

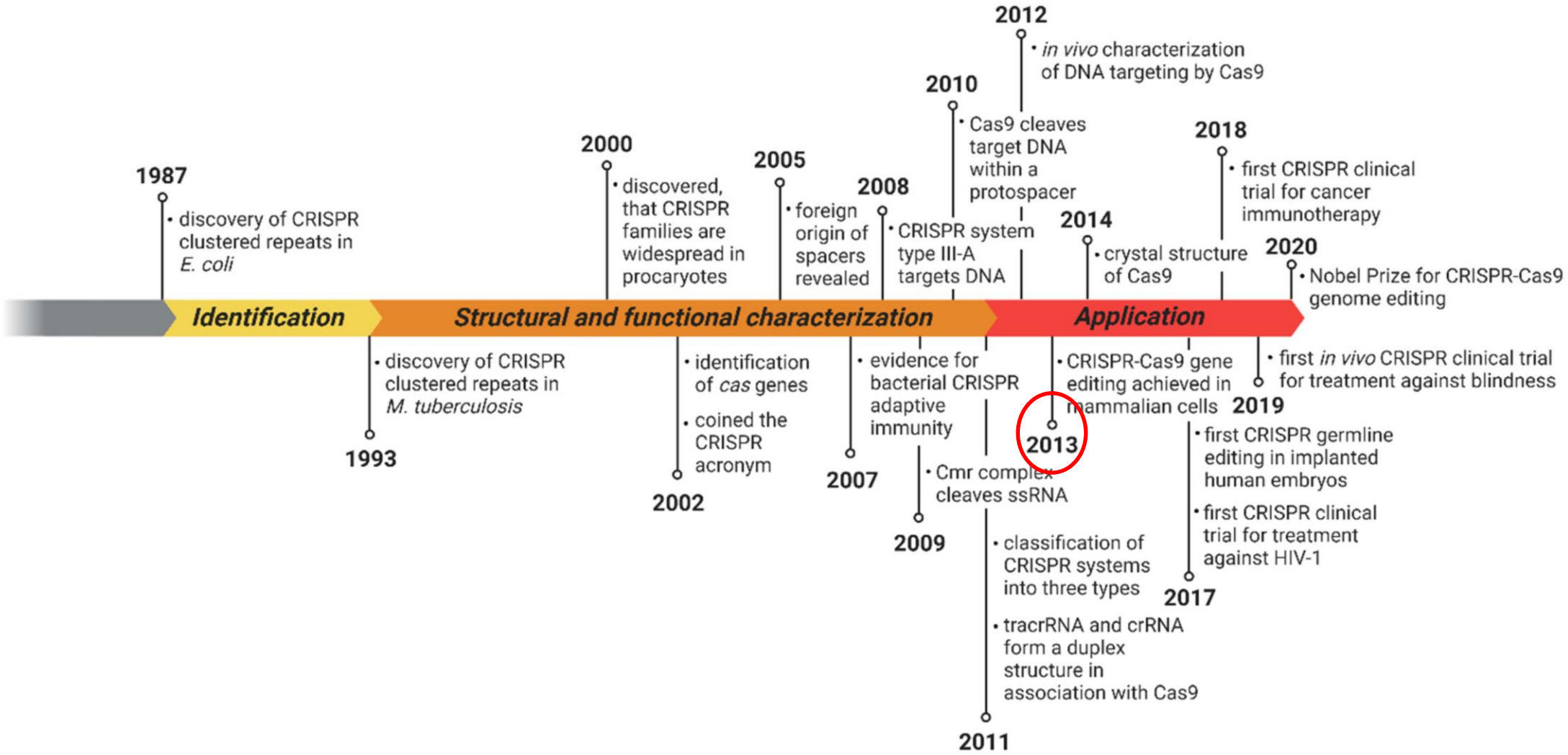
Messenger RNA-based therapy and vaccine technology

Genome editing: Timeline of CRISPR-Cas system with milestones



Int. J. Mol. Sci. **2021**, *22*, 3327

Genome editing: Timeline of CRISPR-Cas system with milestones



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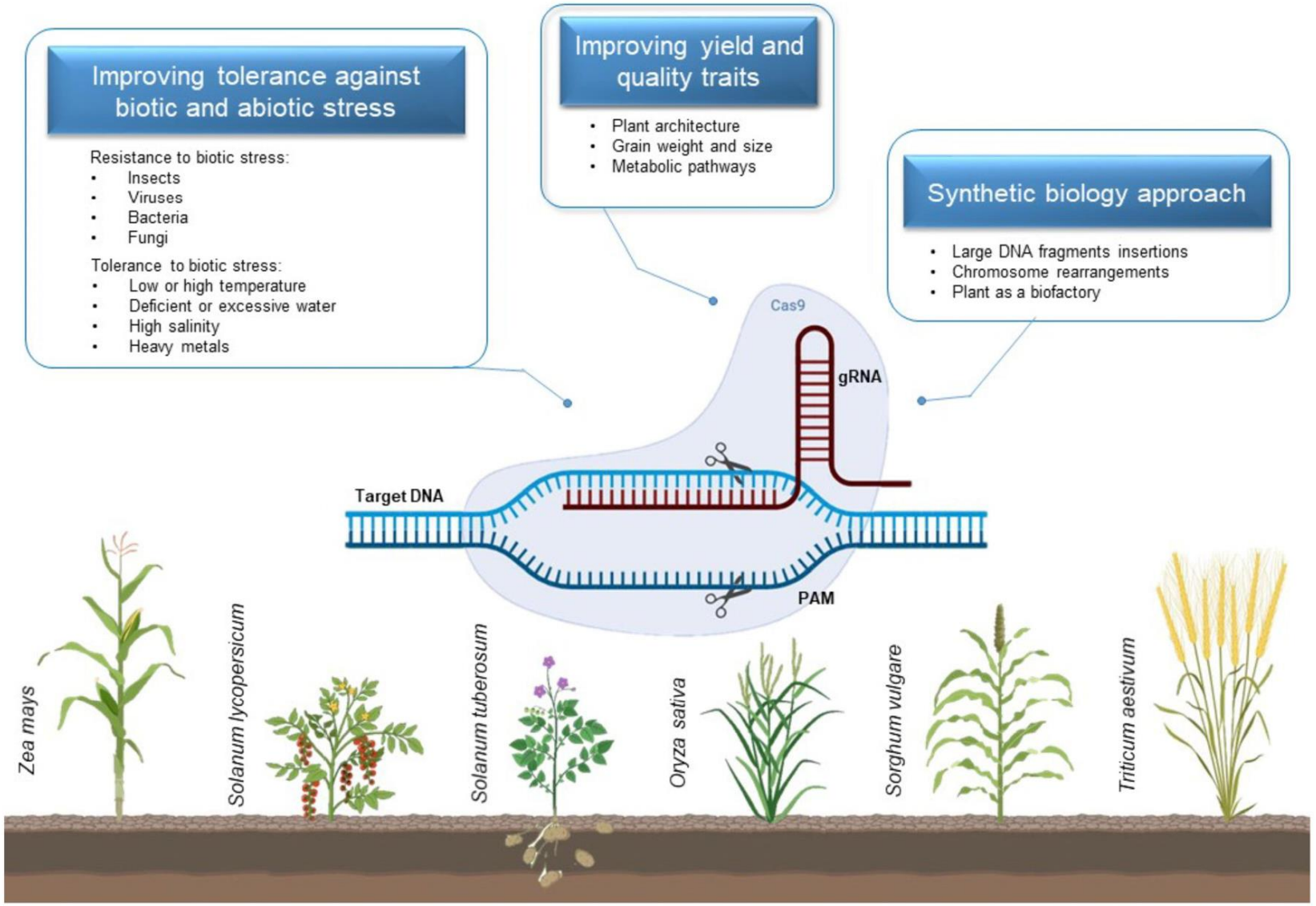
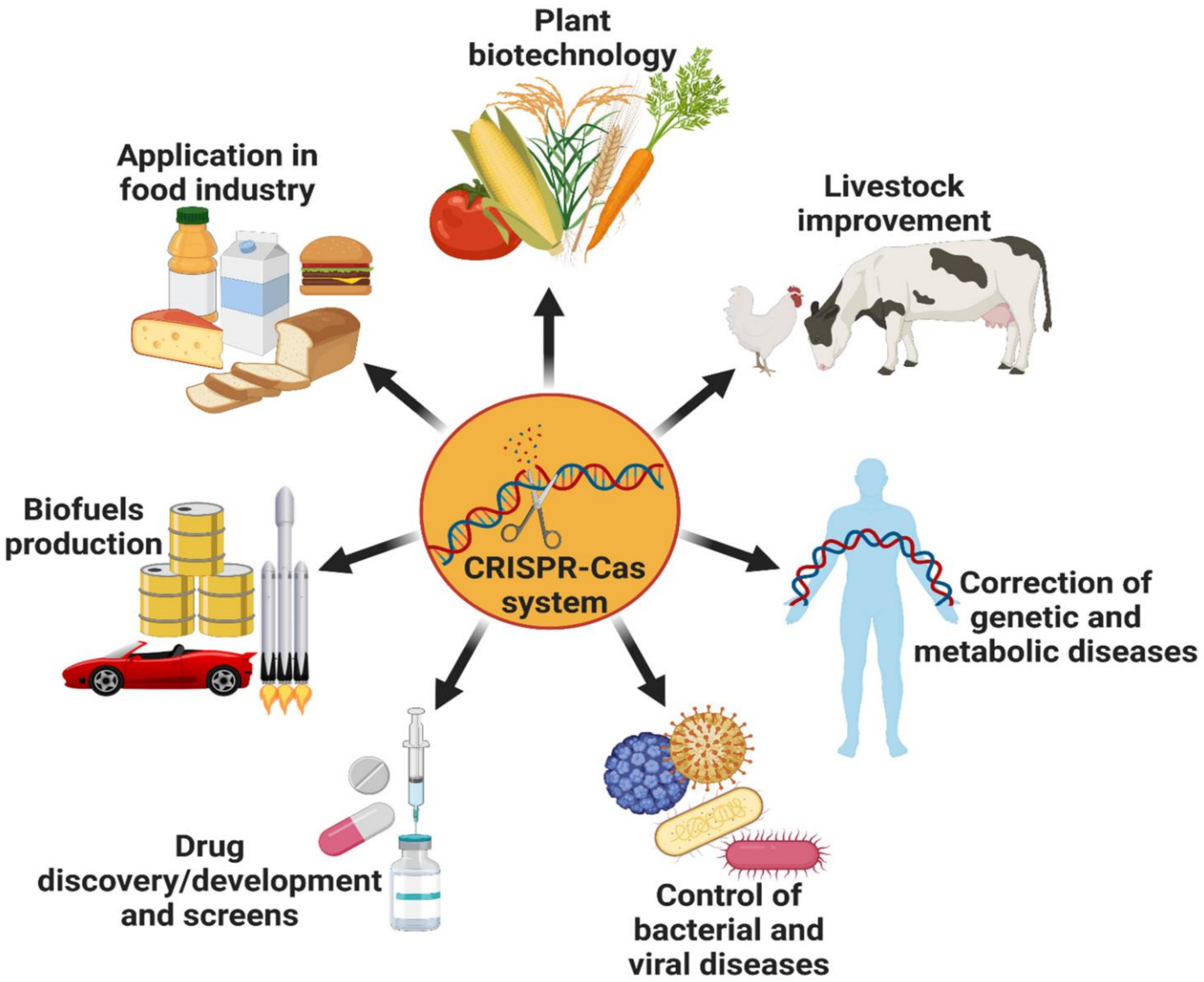
Editing genomes of plants with CRISPR-Cas9 enzyme system



Encyclopedia 2022, **2:** 538

Emerging genome editing in biotechnology: CRISPR-Cas



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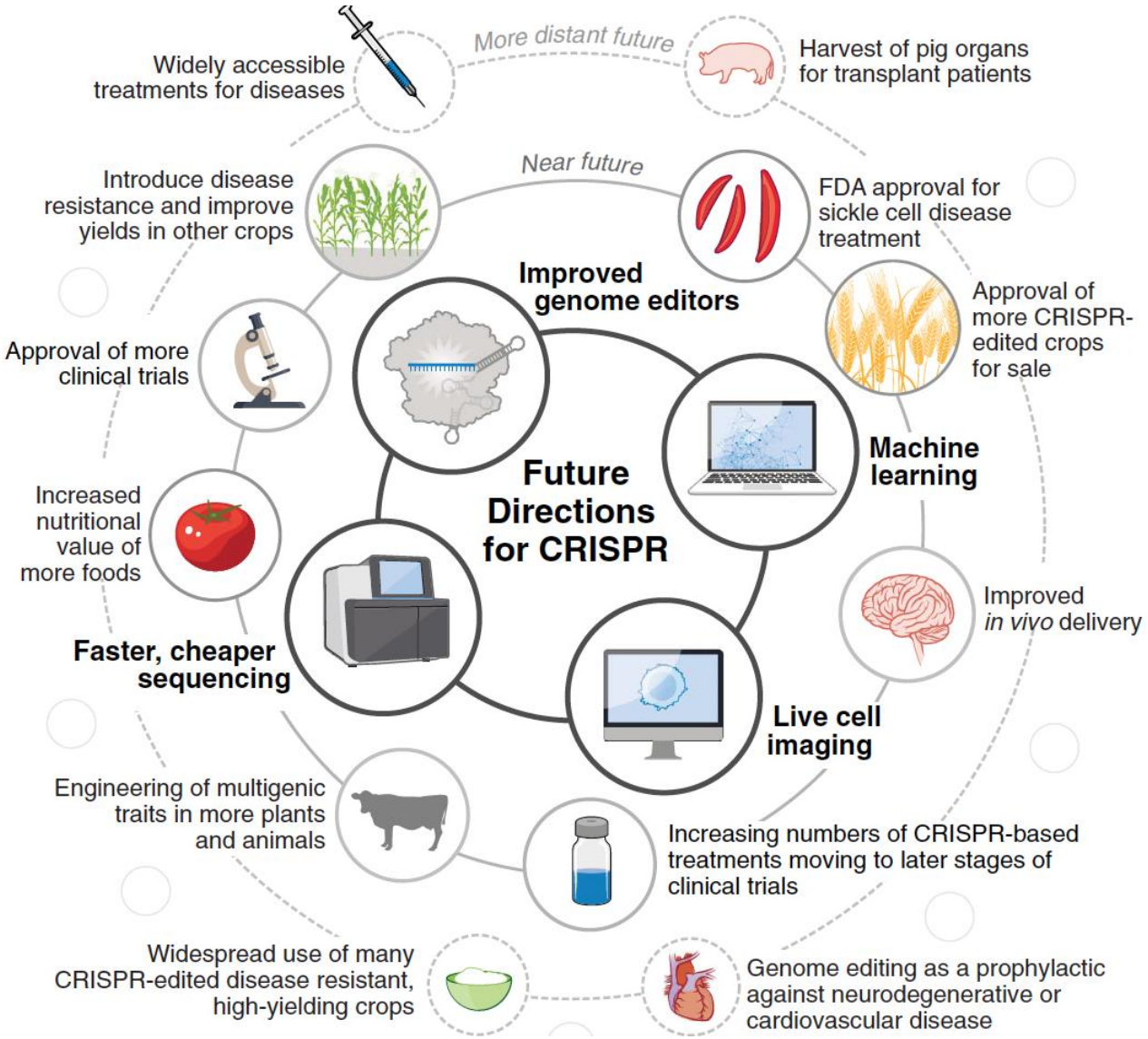
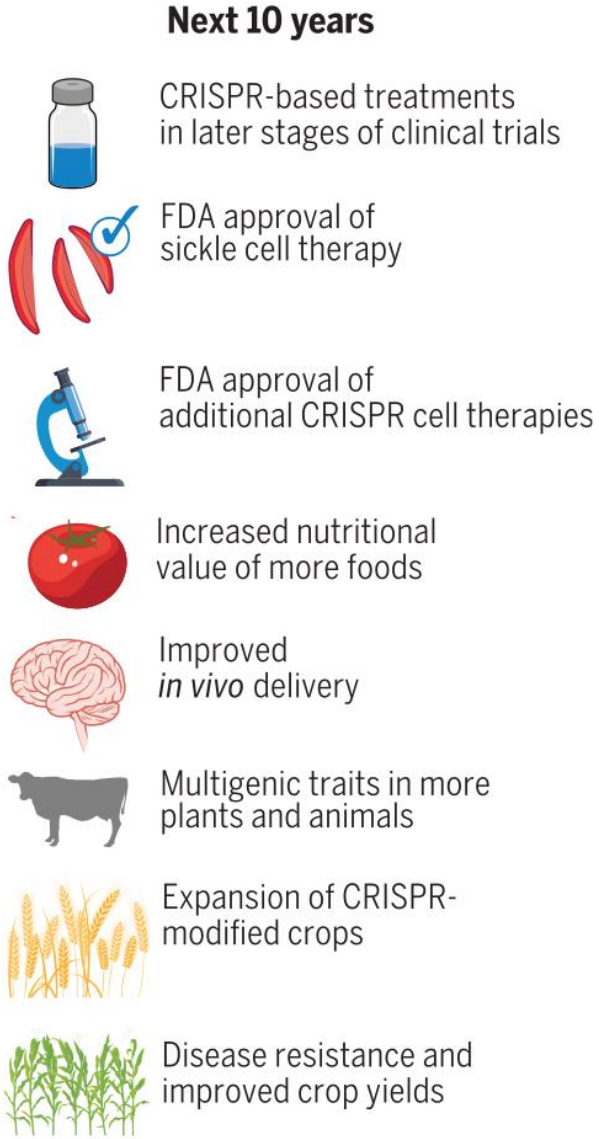
A decade of genome editing with CRISPR-Cas technology





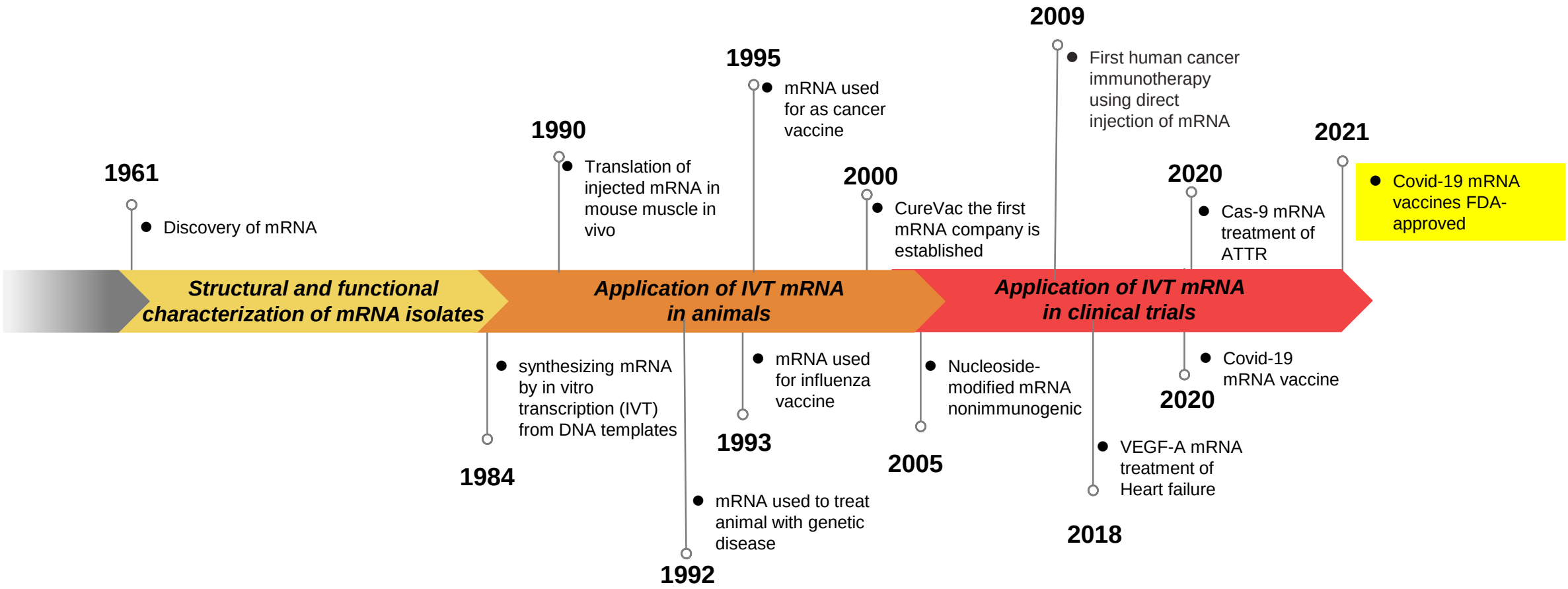
Science **379**, 251 (2023)

The two most important emerging biotechnologies

CRISPR-Cas-based genome editing technology

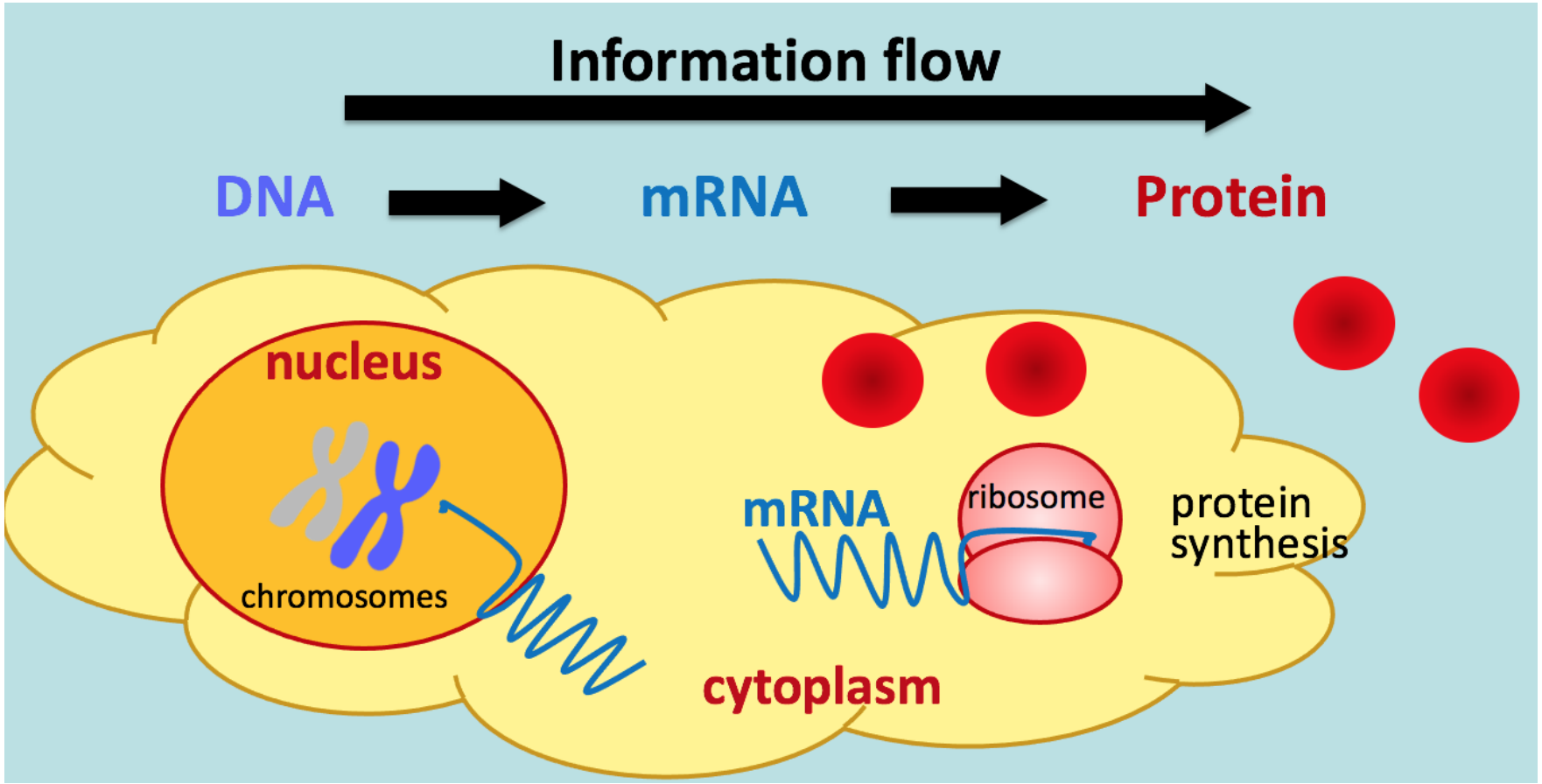
Messenger RNA-based therapy and vaccine technology

Milestones of mRNA development for therapy



Information flow in all cells

mRNA: the labile intermediate carrying the information from the DNA to ribosome



Therapeutic proteins are the new medicines

❖ >100 therapeutic proteins FDA-approved - purified, recombinant
Fastest growing group of therapeutics

Hormones, cytokines, enzymes: replacing proteins missing, deficient, abnormal

- insulin, growth hormone, EPO, cytokines (IFN-α, IFN-β, IL-2)
- enzymes (GLA, alpha-1-antitrypsin, DNase, tPA, uPA)
- blood coagulation factors (FVIII, FVIIa)

Monoclonal antibodies: Targeting TNF-α, cancer antigen, infectives

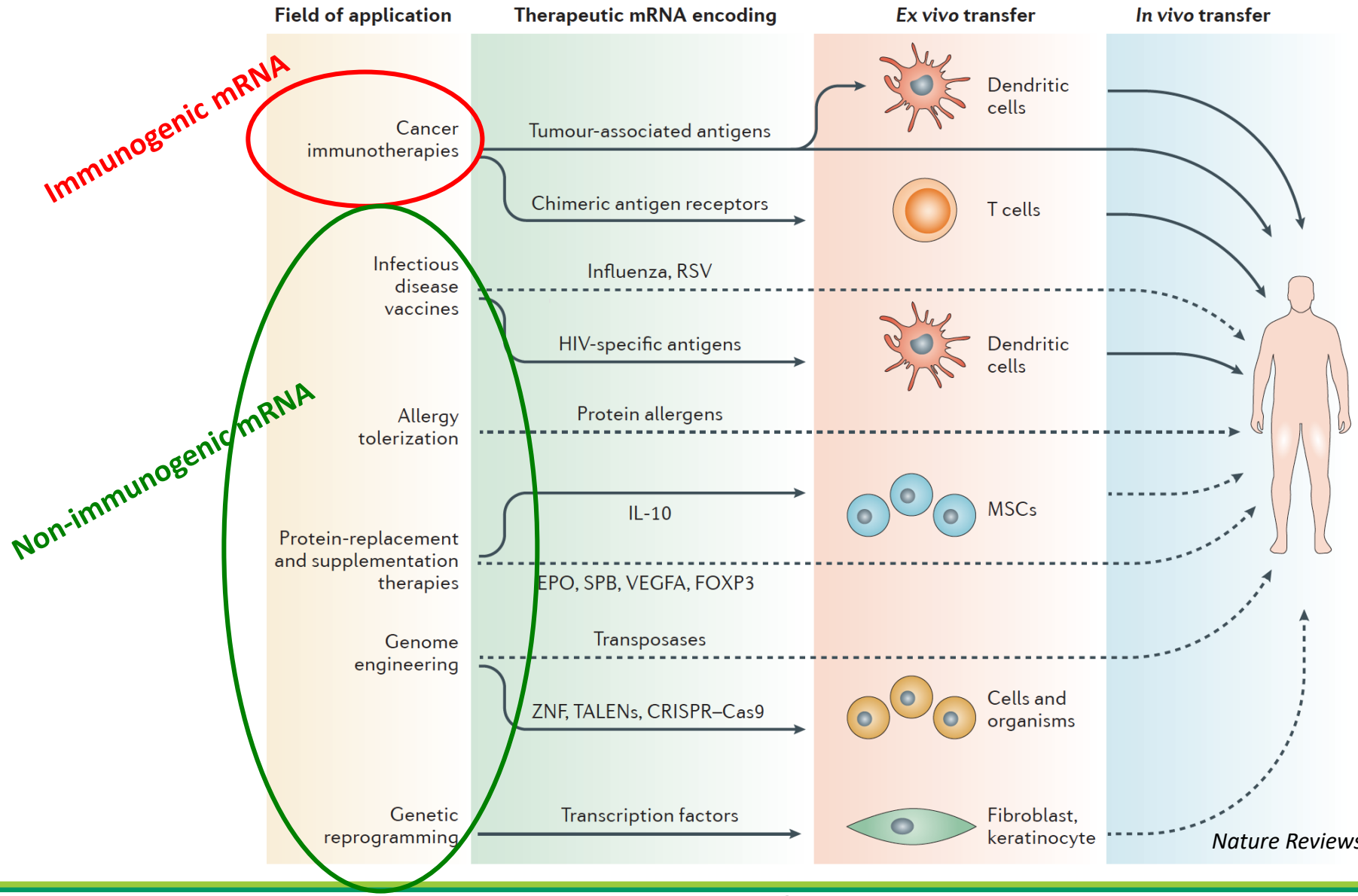
- 1986 Anti-CD3, 1995: Reopro

Advantage of IVT mRNA

mRNA vs. recombinant protein

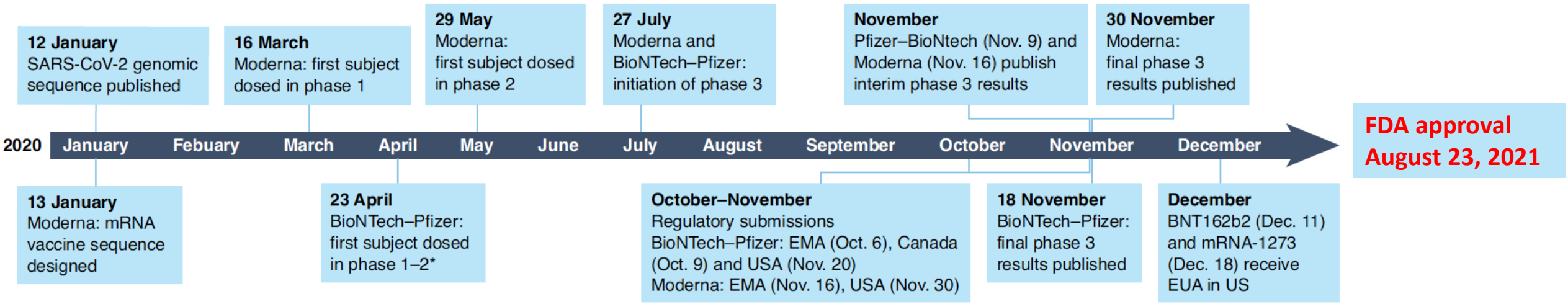
- no need to purify the protein
- speed up drug development using mRNA - easy to make, cheap
- the protein has proper structure
- continuous in vivo supply of encoded protein from the delivered mRNA
- production of intracellular proteins is possible with mRNA

mRNA-based therapeutics — developing a new class of drugs



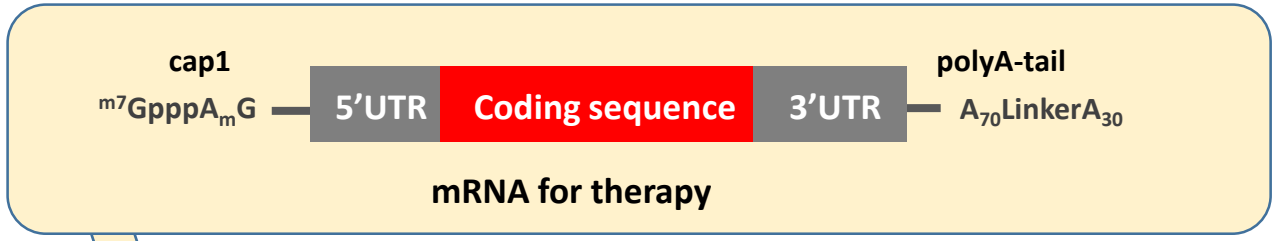
Nature Reviews Drug Discovery 2014, 13: 759

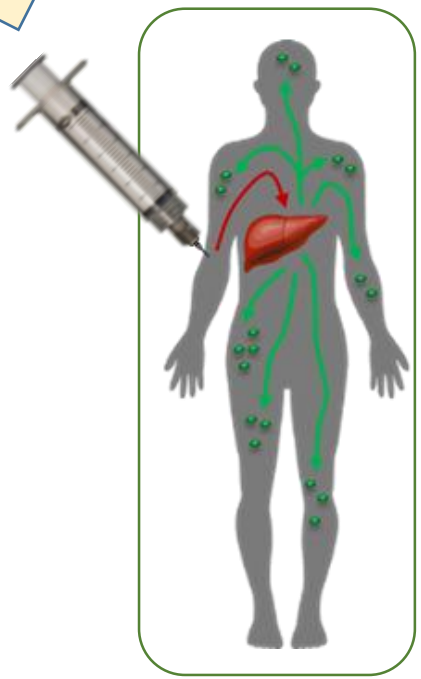
Timeline: development of mRNA vaccines against SARS-CoV-2



Barbier et al. *Nature Biotechnology* 2022

2023 and beyond - mRNA is a new class of medicine

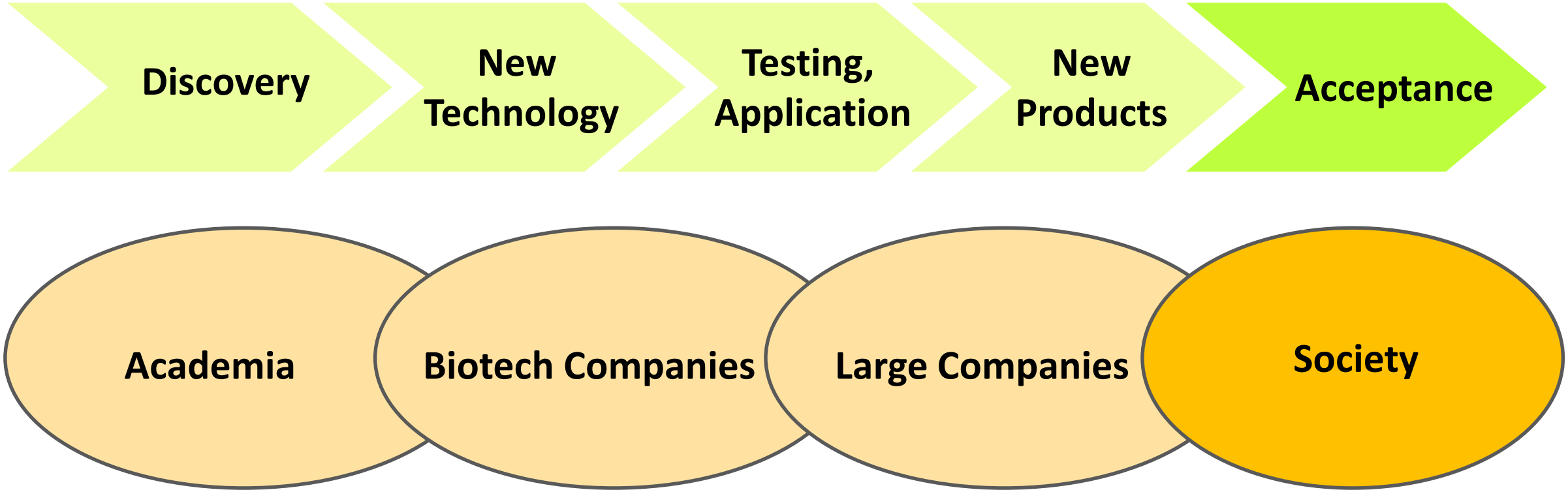




mRNA in clinical trials to prevent or treat

- **infectious disease**
  - RSV, Flu, HIV, ZKV, HSV, EBV, HMPV, CMV, Nipah, malaria
- **cancer**
  - vaccines, antibodies, CAR-T cells, intratumor injection of cytokine mRNAs
- **acute diseases**
  - VEGFA mRNA heart falilure, wound healing
- **genetic diseases**
  - OTCD, Propionic acidemia, methylmalonic acidemia, glycogen storage disease, genome editing (Cas9 mRNA), cystic fibrosis, sickle cell anemia

Acceptance of the new biotech products by society is needed

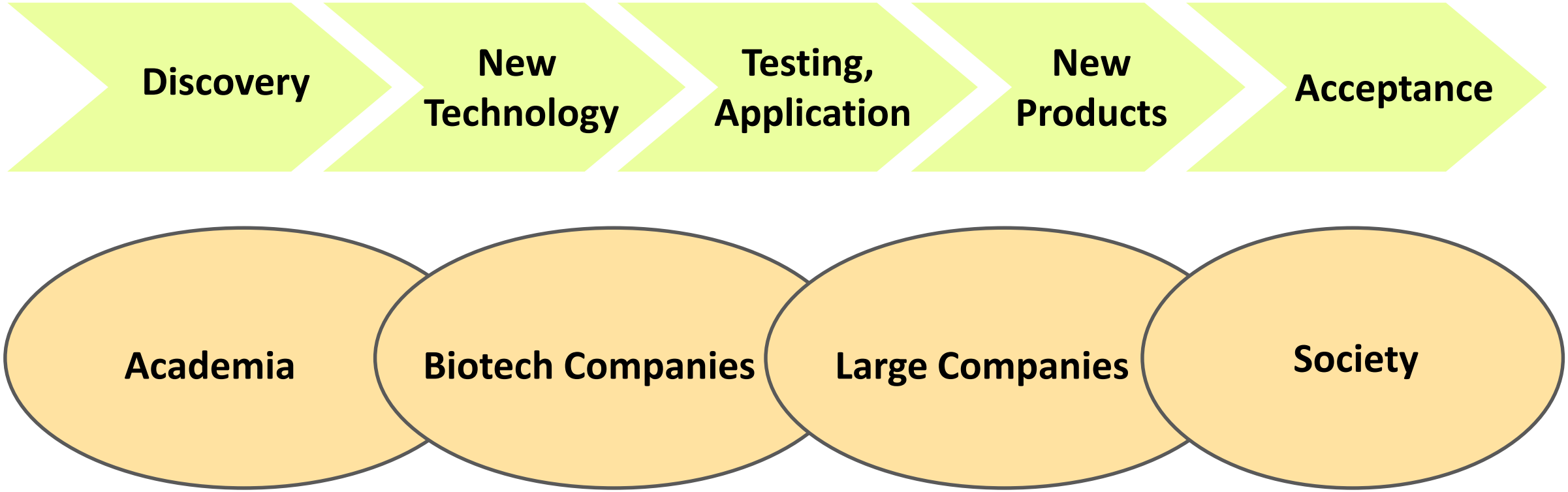


Acceptance of new products by society

Public relation:

- Public engagement, education, debates, transparency
  - concerns, skepticism, vaccines hesitancy
  - fighting misinformation
  - values, benefits
- Regulatory path
  - Safety, efficacy
  - Risk : benefit ratio

Biotechnology is serving the common good



- **Thanks for your attention**