



The **First (TvAI) Skyroom**

International **Virtual Congress** on  
the practical Application of Artificial  
Intelligence in **Medical Sciences**

*Date & Time: 1-5 February . 2025 (09:00 Am - 12:00)*

# Artificial Intelligence and Future of Biodesign



**Hosein Shahsavarani, Ph. D**

Principal investigator, Lab. of Regenerative Medicine & Biomedical Innovations

# Biodesign and genome editing in news



Baby mice have been made with **two mums** and **no dad**



**Doctors in China Lead Race to Treat Cancer by Editing Genes**

- Editing patient T cells

- NPR, Feb. 21<sup>st</sup>, 2018

**Russian biologist plans more CRISPR-edited babies**

The proposal follows a Chinese scientist who claimed to have created twin embryos last year.

By [David Cyranoski](#)

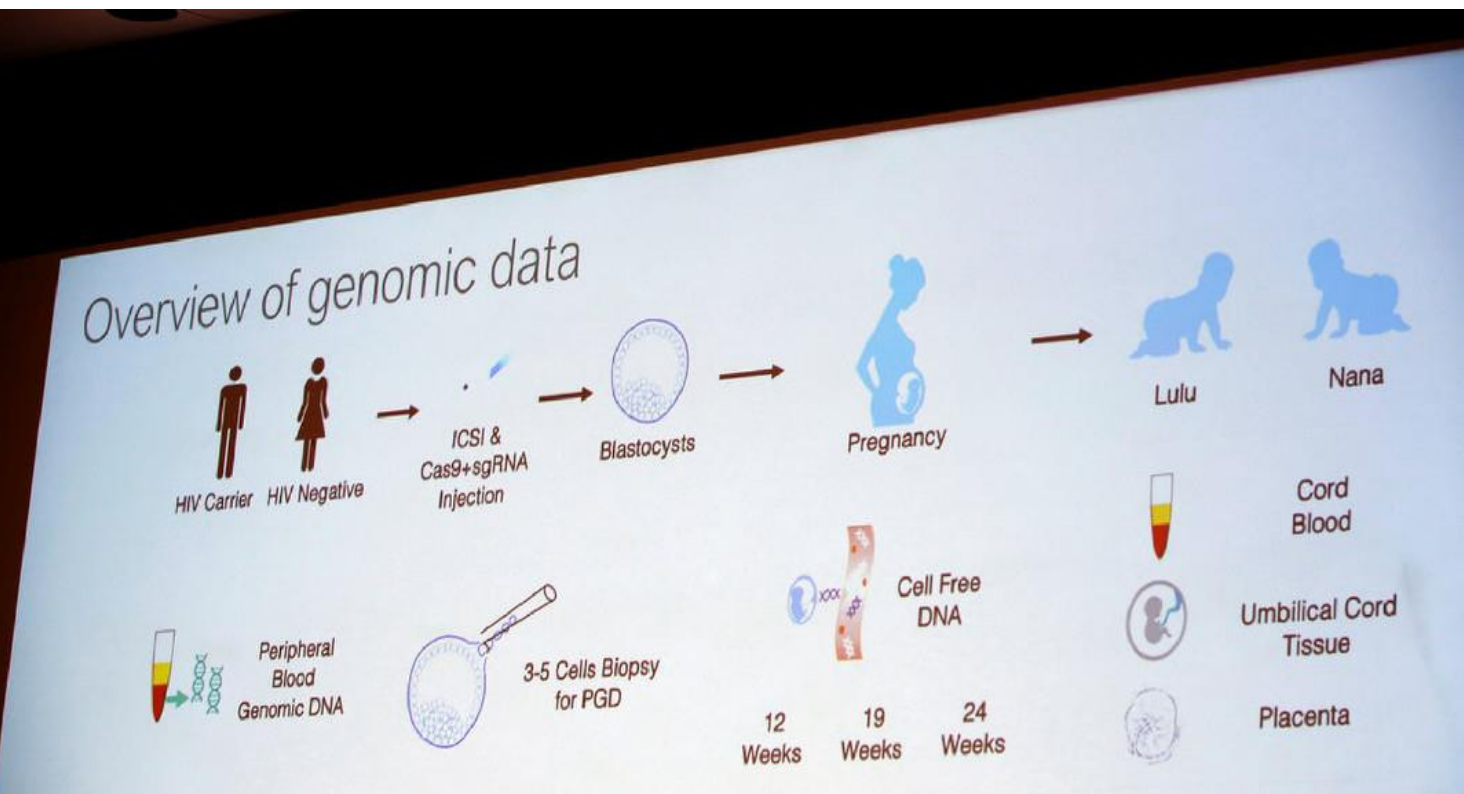
  

A Russian scientist says he is planning to produce gene-edited babies, an act that would make him only the second person known to have done this. It would also fly in the face of the scientific consensus that such experiments should be banned until an international ethical framework has agreed on the circumstances and safety measures that would justify them.

## Chinese scientists report first live birth of chimeric monkey

Source: Xinhua Editor: huaxia 2023-11-14 17:58:15

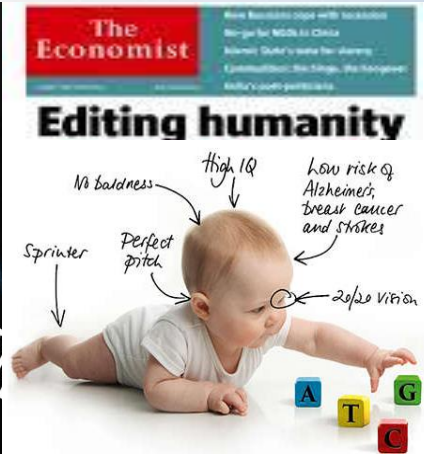
# World's First Genetically Edited Babies Using CRISPR



NEWS • 10 JUNE 2019

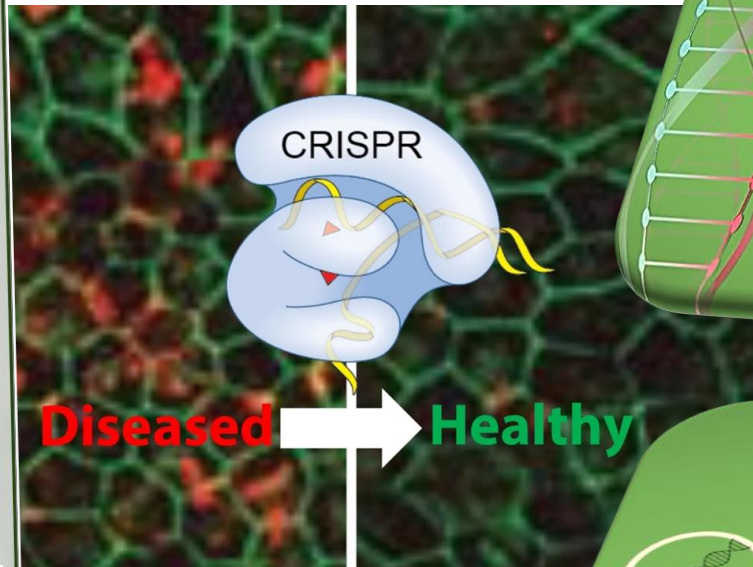
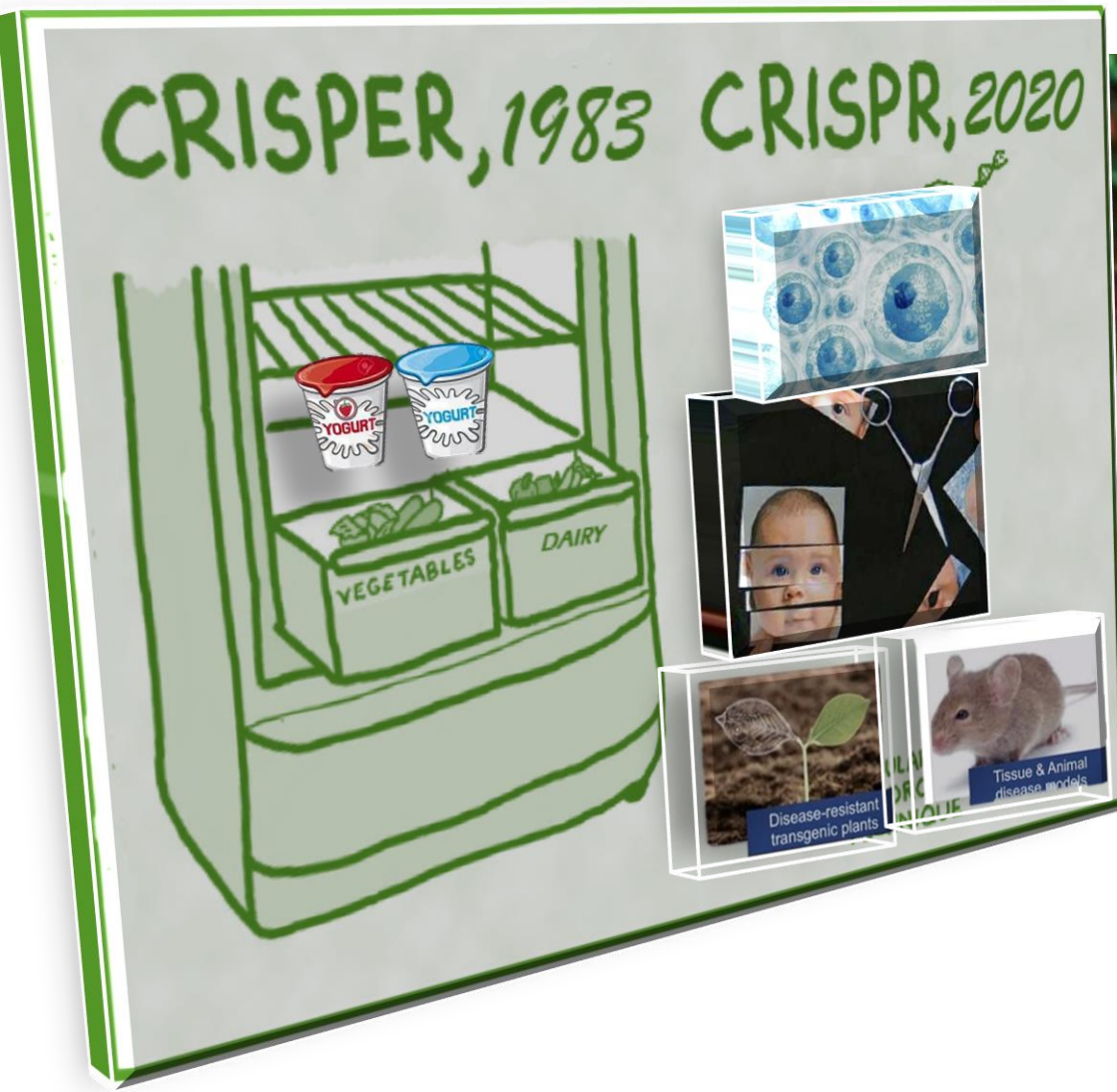
## Russian biologist plans more CRISPR-edited babies

The proposal follows a Chinese scientist who claimed to have created twins from edited embryos last year.



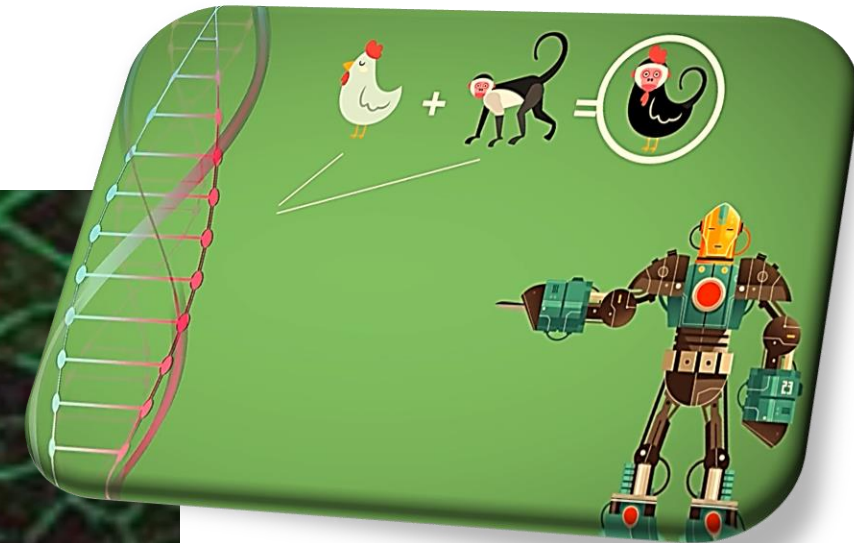
# From bacterial immune system to genome editing

# Future

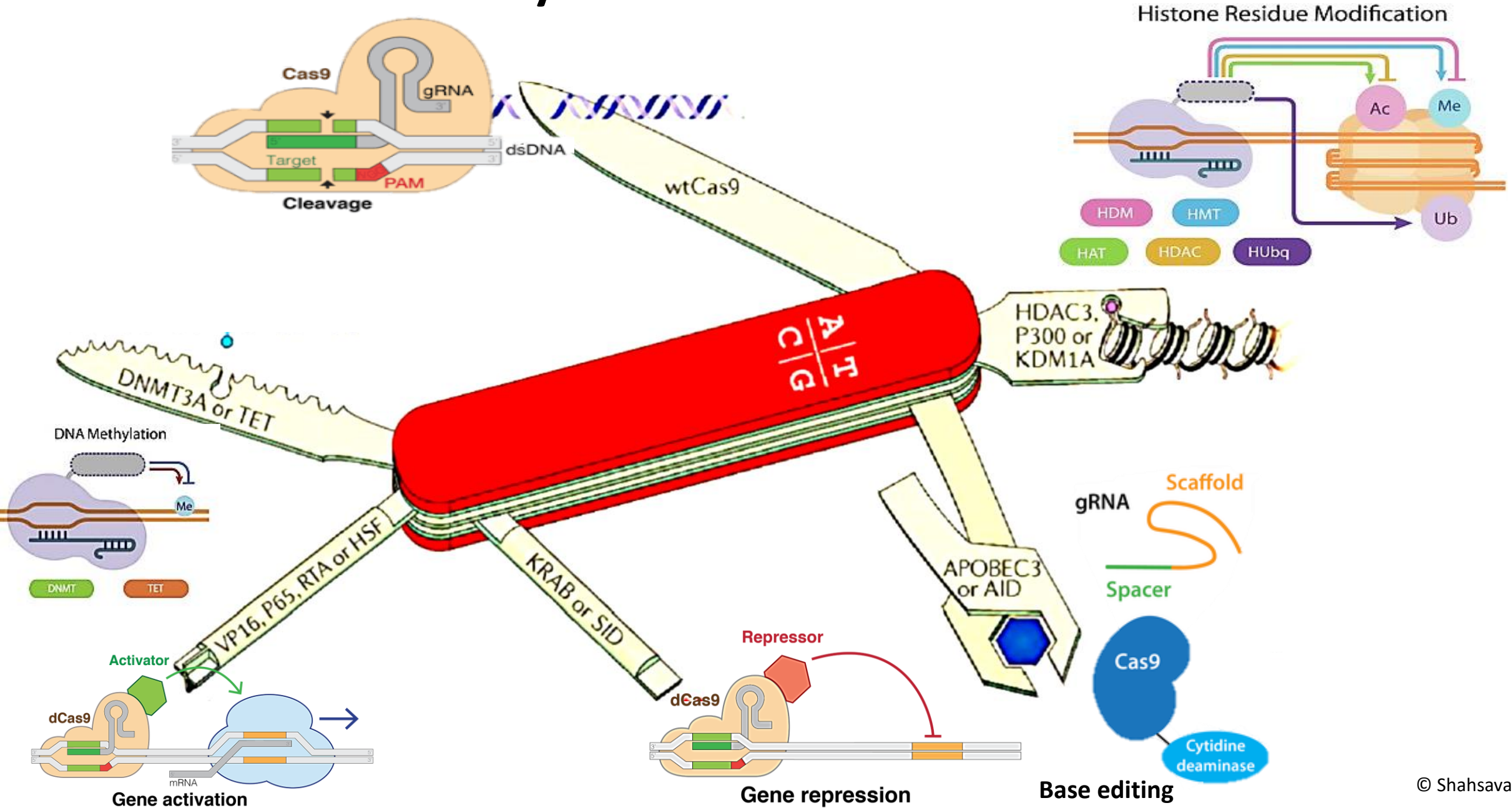


We may be nearing the beginning of the end of inheritable disease.

Jennifer Doudna

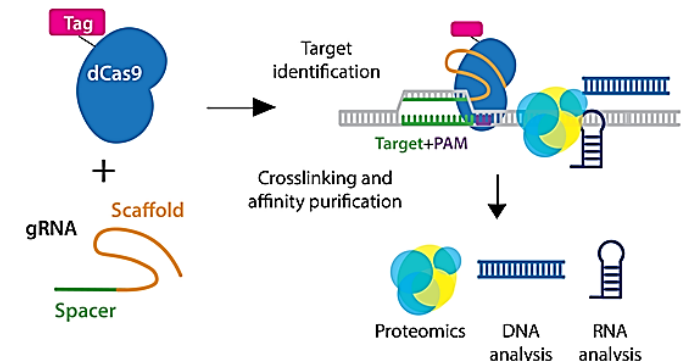
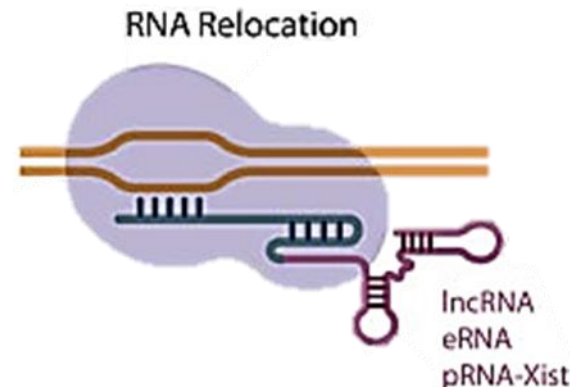
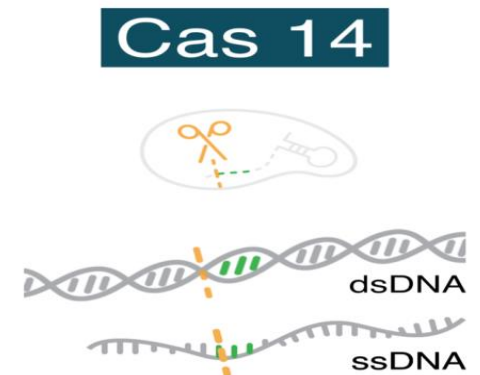
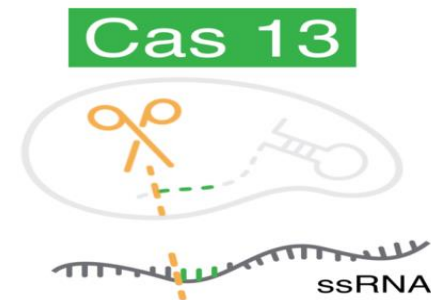
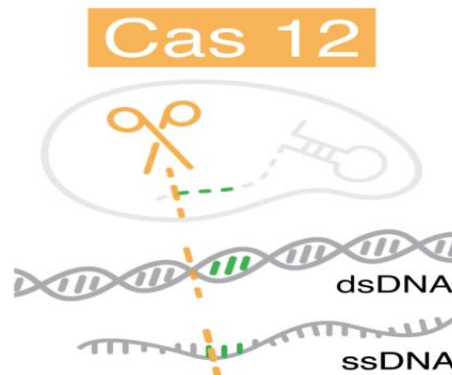
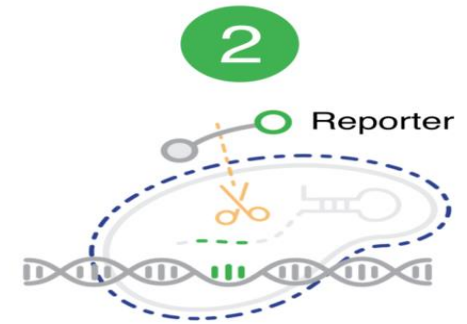
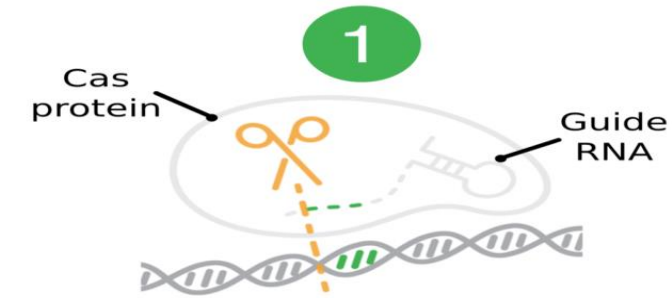
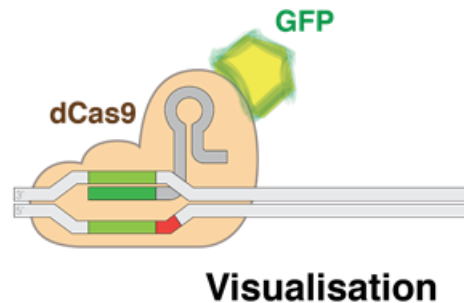
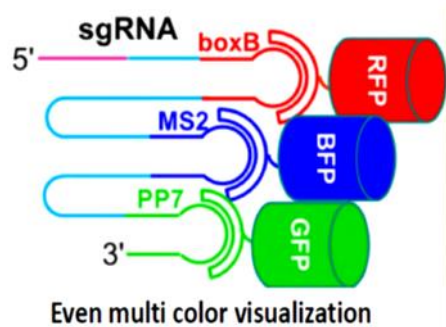


# CRISPR as a swiss army knife in medicine



# New generations and applications of CRISPR

- CRISPRainbow
- Single base editing
- Temporal control of CRISPR
- Multiplexed editing
- RNA editing
- RNA relocation
- enChIP

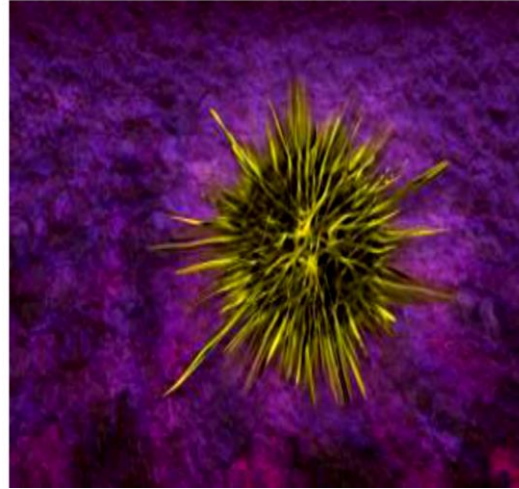


# Clinical Human Applications of CRISPR

## ☐ Viral infections: HIV, HSV, VZV

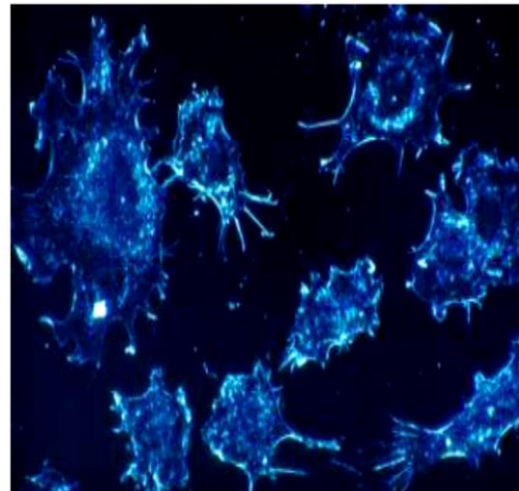
- ✓ Inserted viral genome could be removed by altering immune cells

- ✓ Human embryos: Kang & colleagues inserted the CCR5 $\Delta$ 32 allele into early human 3PN embryos



## ☐ Cancer

Mutation driven cancers



## ☐ Genetic diseases

- ✓ Remove or add the sequence that is causing the disease



## ☐ Transplantation

- ✓ Gene editing of mismatched human or even non-human mammals as potential organ donors
- ✓ Editing will reduce risk of immune responses and rejection when using mismatched organs/tissues/cells



# A Crack in Creation: The New Power to Control Evolution

- ❑ Liang et al using human tripronuclear zygotes cleaved the HBB gene with a CRISPR/Cas9- mediated system
  - Low efficiency and edited embryos were mosaic with off target cleavage

- ❑ Other clinical trials forthcoming:
  - ✓ Editas
  - ✓ CRISPR Therapeutics
  - ✓ Caribou Biosciences
  - ✓ Intellia Therapeutics



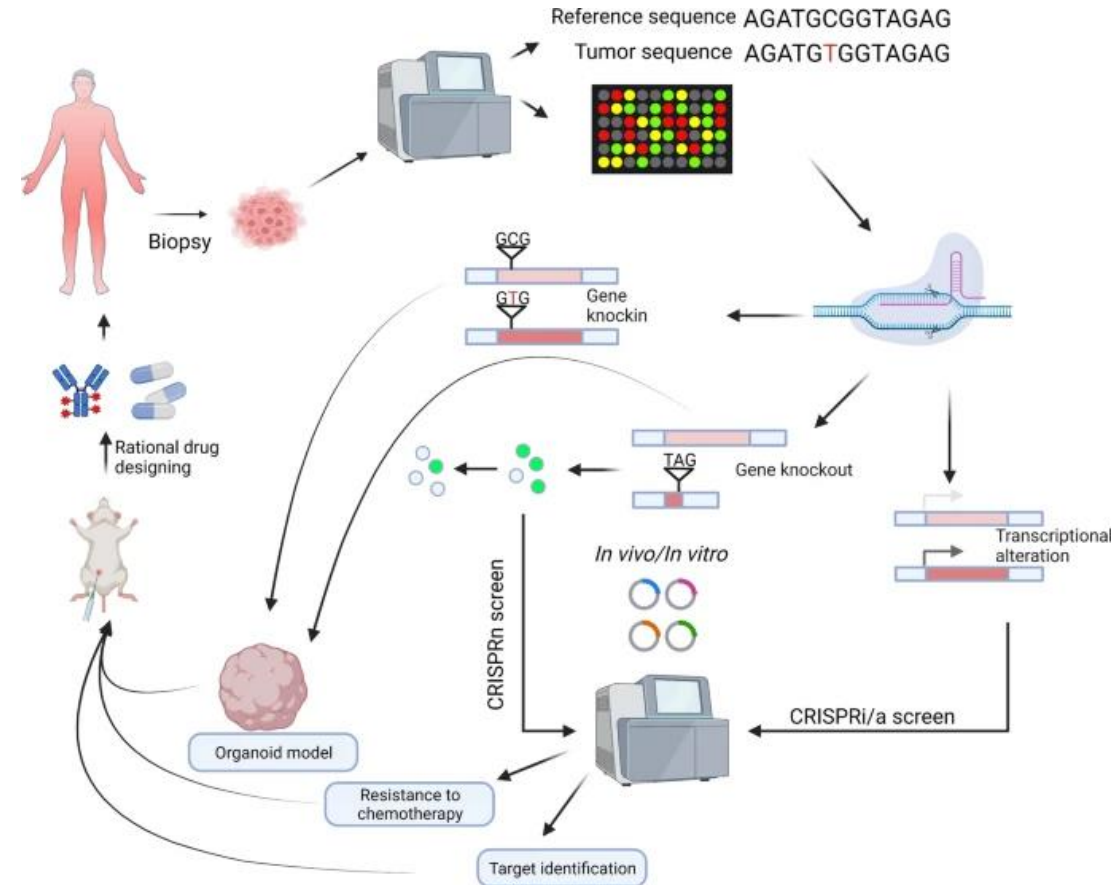
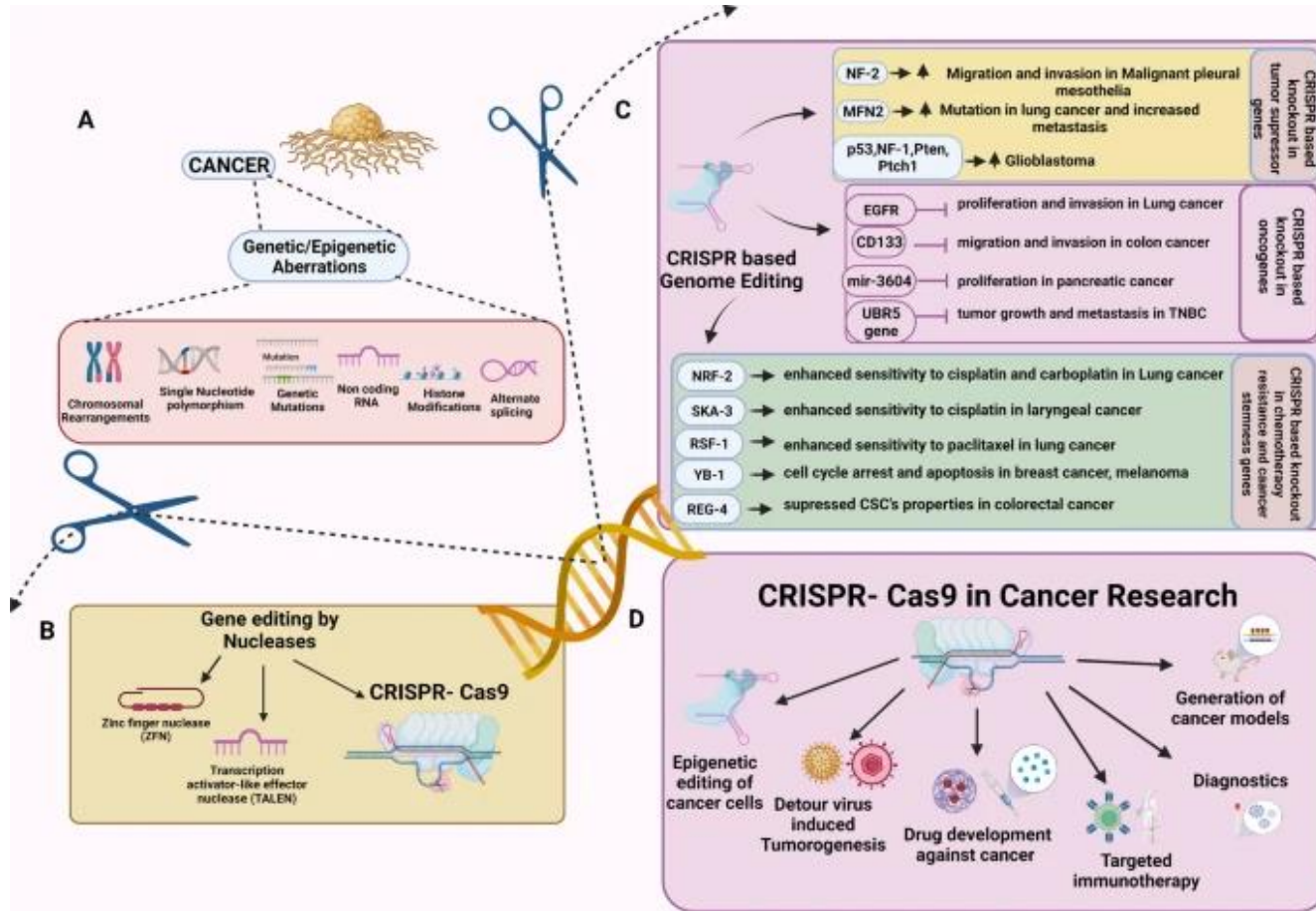
## Cancer trials

|   |                    |                                                                                                                                                                                                                                                          |
|---|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1 | Not yet recruiting | <a href="#">PD-1 Knockout Engineered T Cells for Metastatic Non-small Cell Lung Cancer</a><br><b>Condition:</b> Metastatic Non-small Cell Lung Cancer<br><b>Interventions:</b> Drug: Cyclophosphamide; Other: PD-1 Knockout T Cells; Drug: Interleukin-2 |
| 2 | Not yet recruiting | <a href="#">PD-1 Knockout Engineered T Cells for Castration Resistant Prostate Cancer</a><br><b>Condition:</b> Hormone Refractory Prostate Cancer<br><b>Interventions:</b> Biological: PD-1 Knockout T Cells; Drug: Cyclophosphamide; Drug: IL-2         |
| 3 | Not yet recruiting | <a href="#">PD-1 Knockout Engineered T Cells for Muscle-invasive Bladder Cancer</a><br><b>Condition:</b> Invasive Bladder Cancer Stage IV<br><b>Interventions:</b> Biological: PD-1 Knockout T Cells; Drug: Cyclophosphamide; Drug: IL-2                 |
| 4 | Not yet recruiting | <a href="#">PD-1 Knockout Engineered T Cells for Metastatic Renal Cell Carcinoma.</a><br><b>Condition:</b> Metastatic Renal Cell Carcinoma<br><b>Interventions:</b> Biological: PD-1 Knockout T Cells; Drug: Cyclophosphamide; Drug: IL-2                |

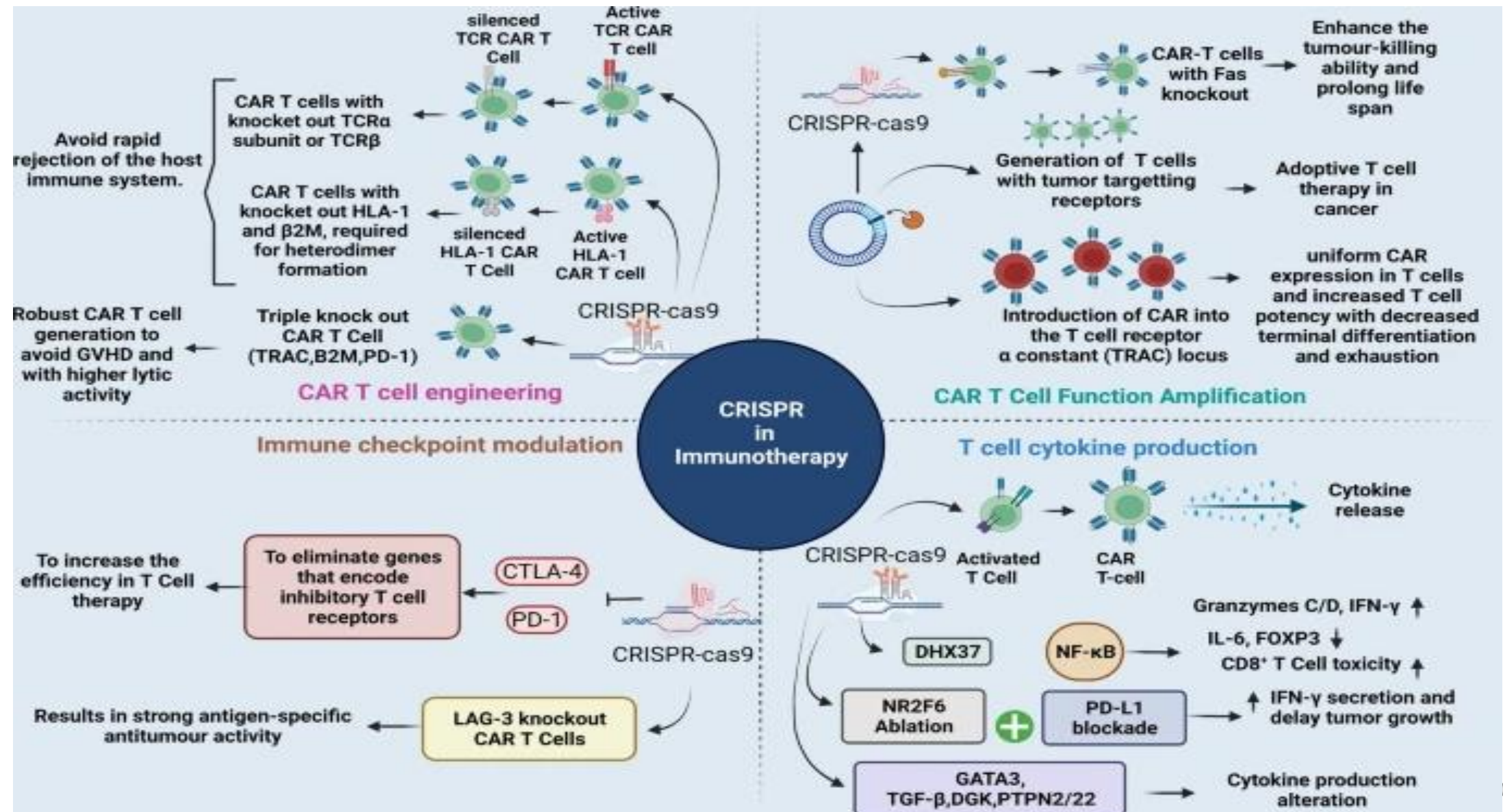
Source: Clinicaltrials.gov, Sept 2016

Liang et al, *Protein and Cell* 2015

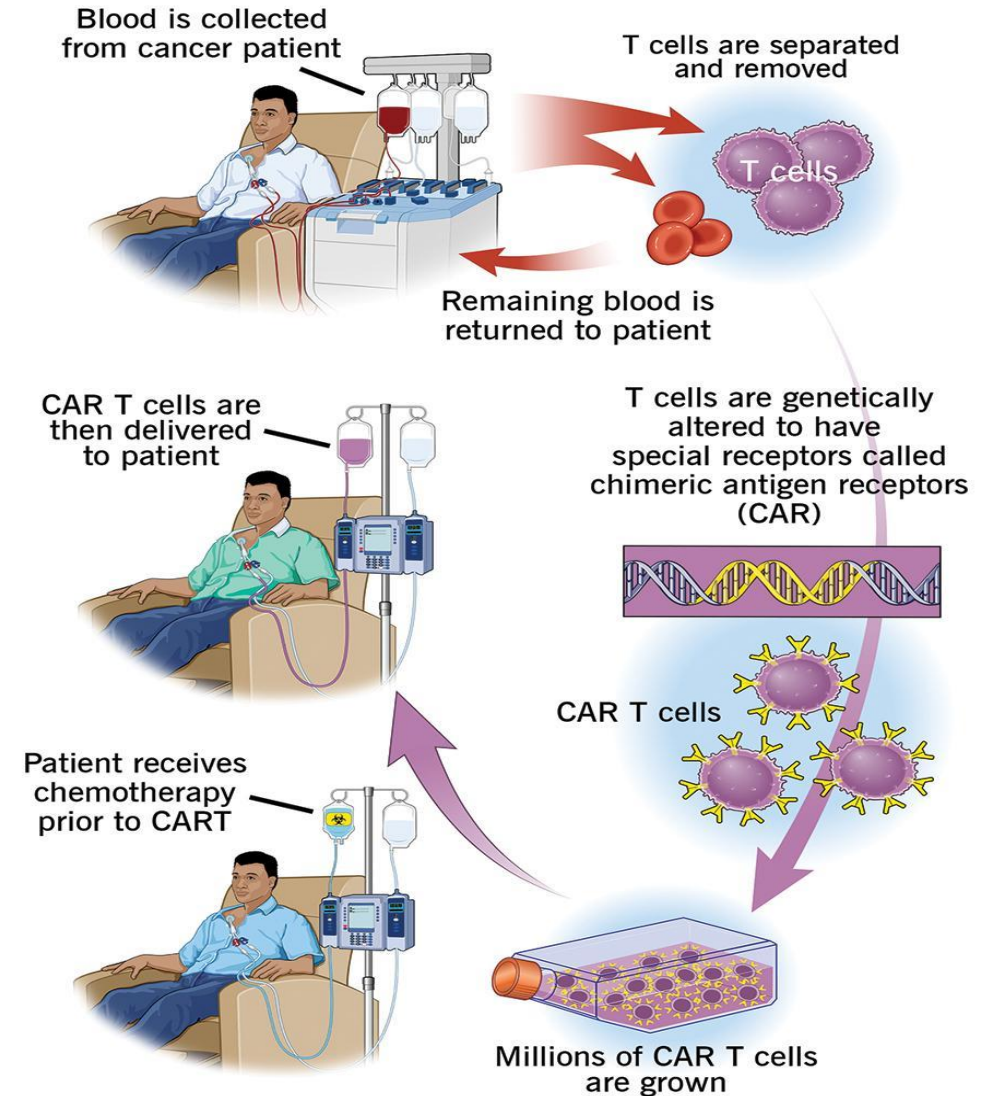
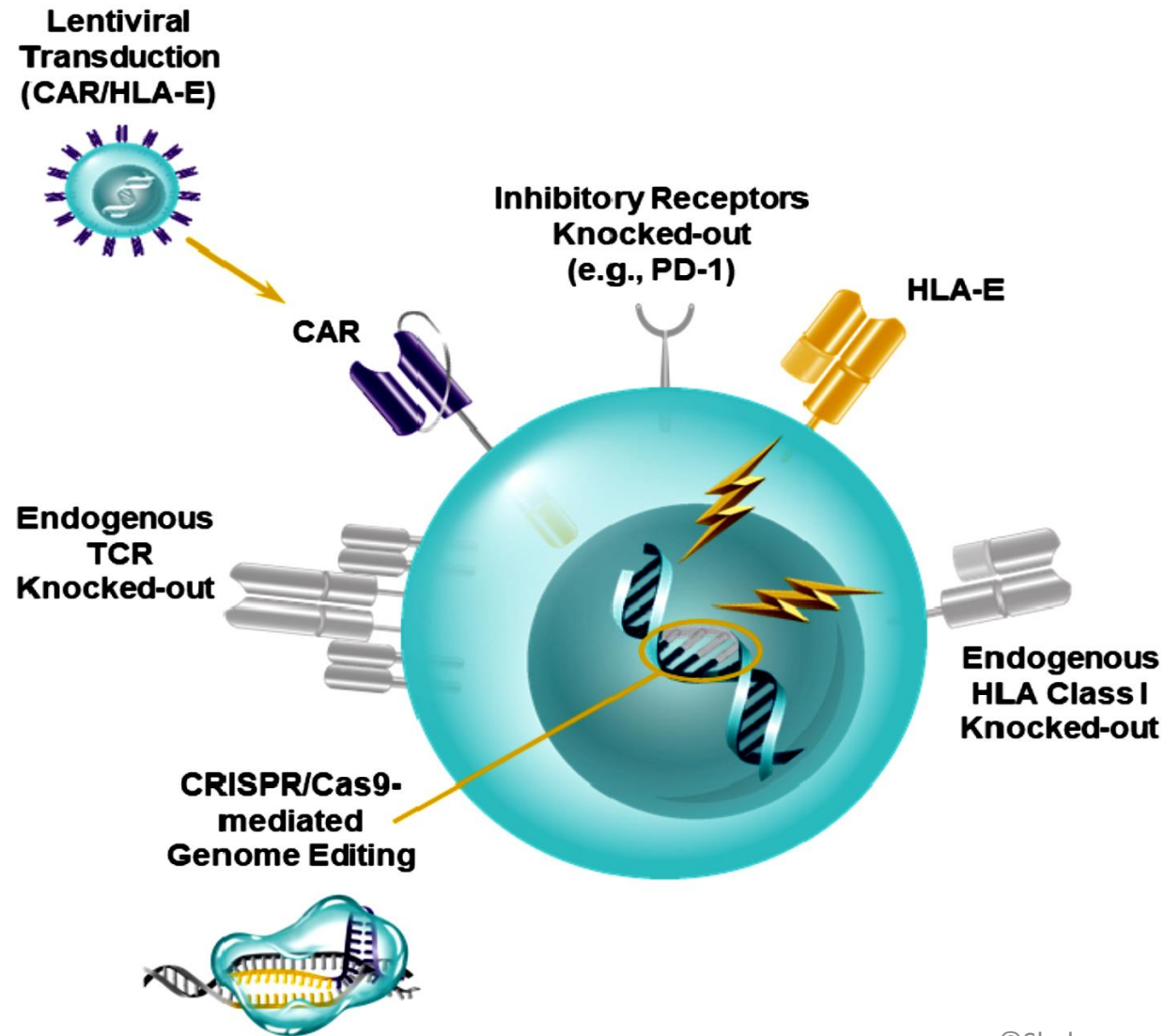
# A paradigm shift in cancer therapeutics

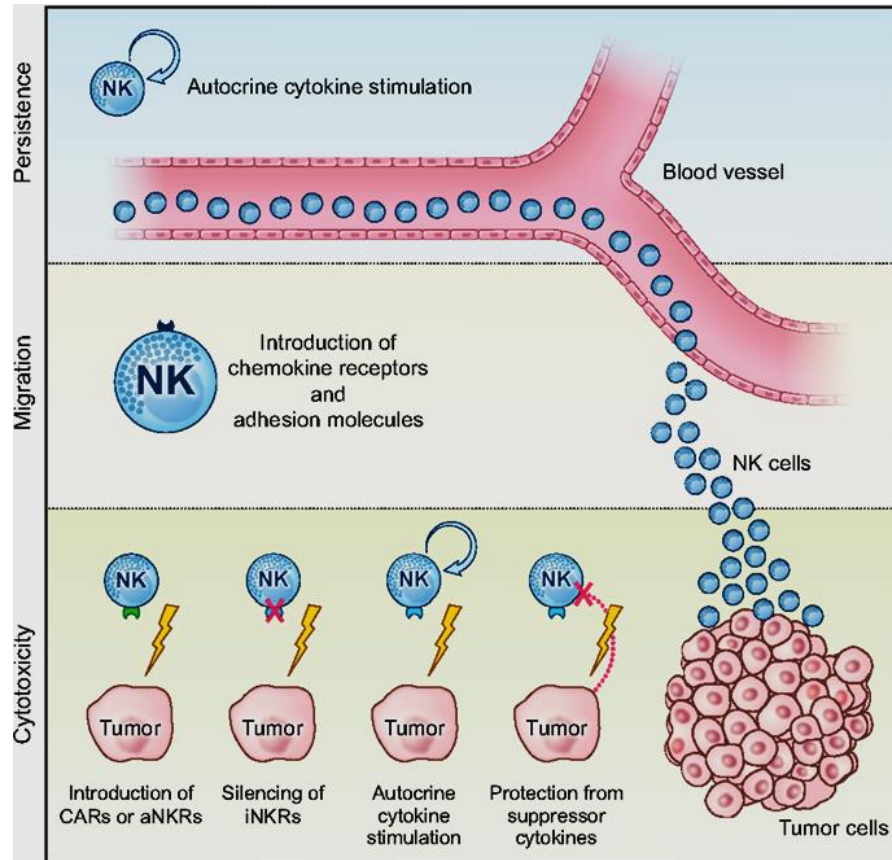


# CRISPR in immune therapy

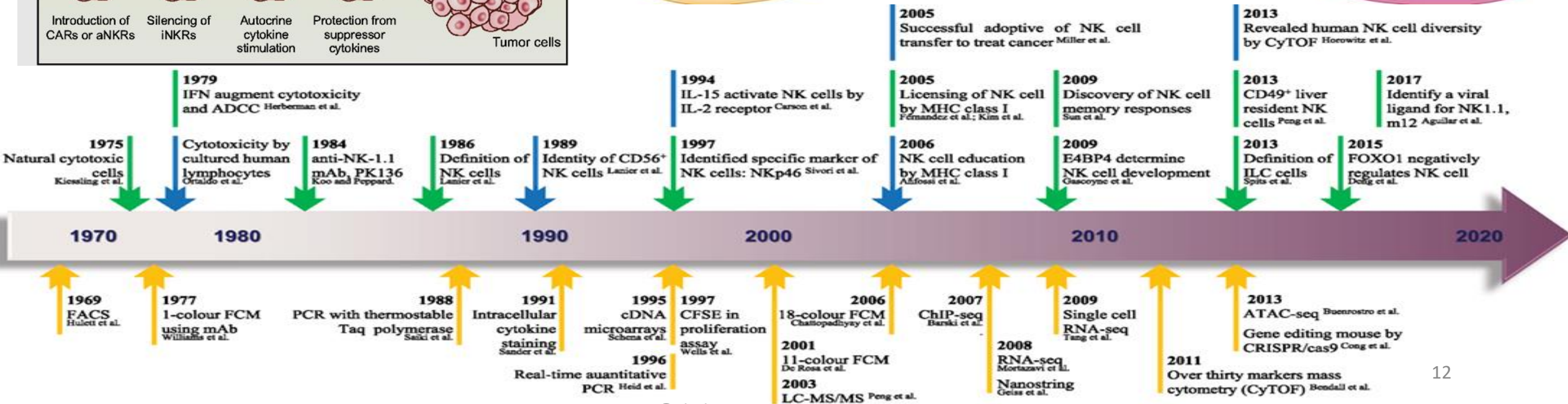
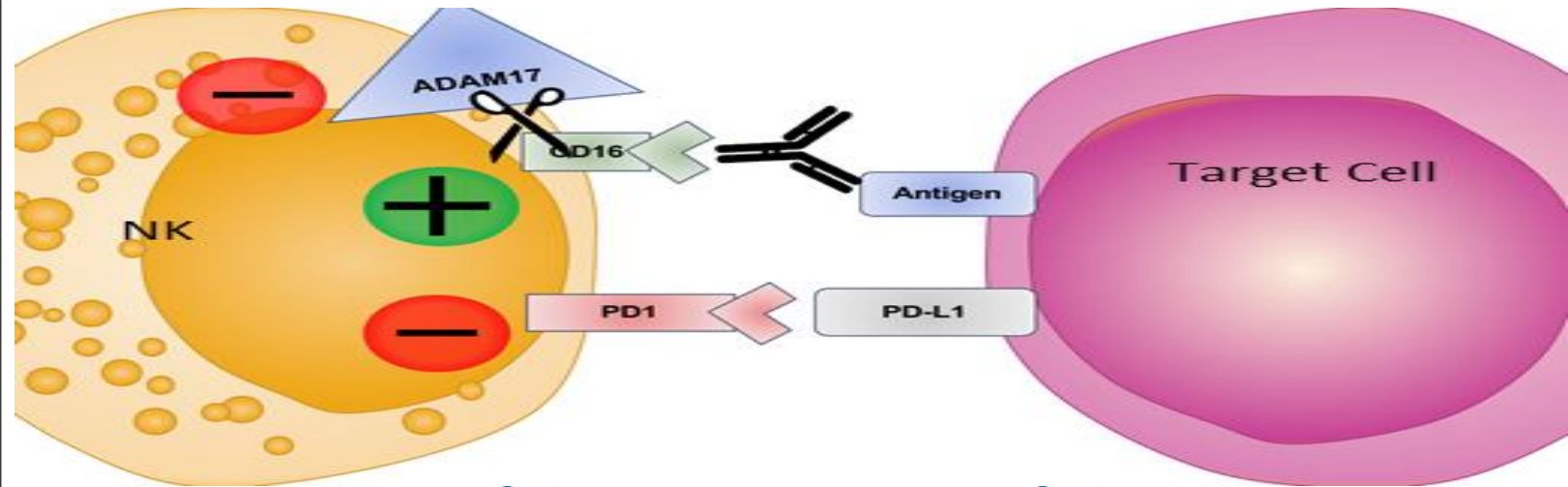


# Advancing CAR T cell therapy with CRISPR/Cas9

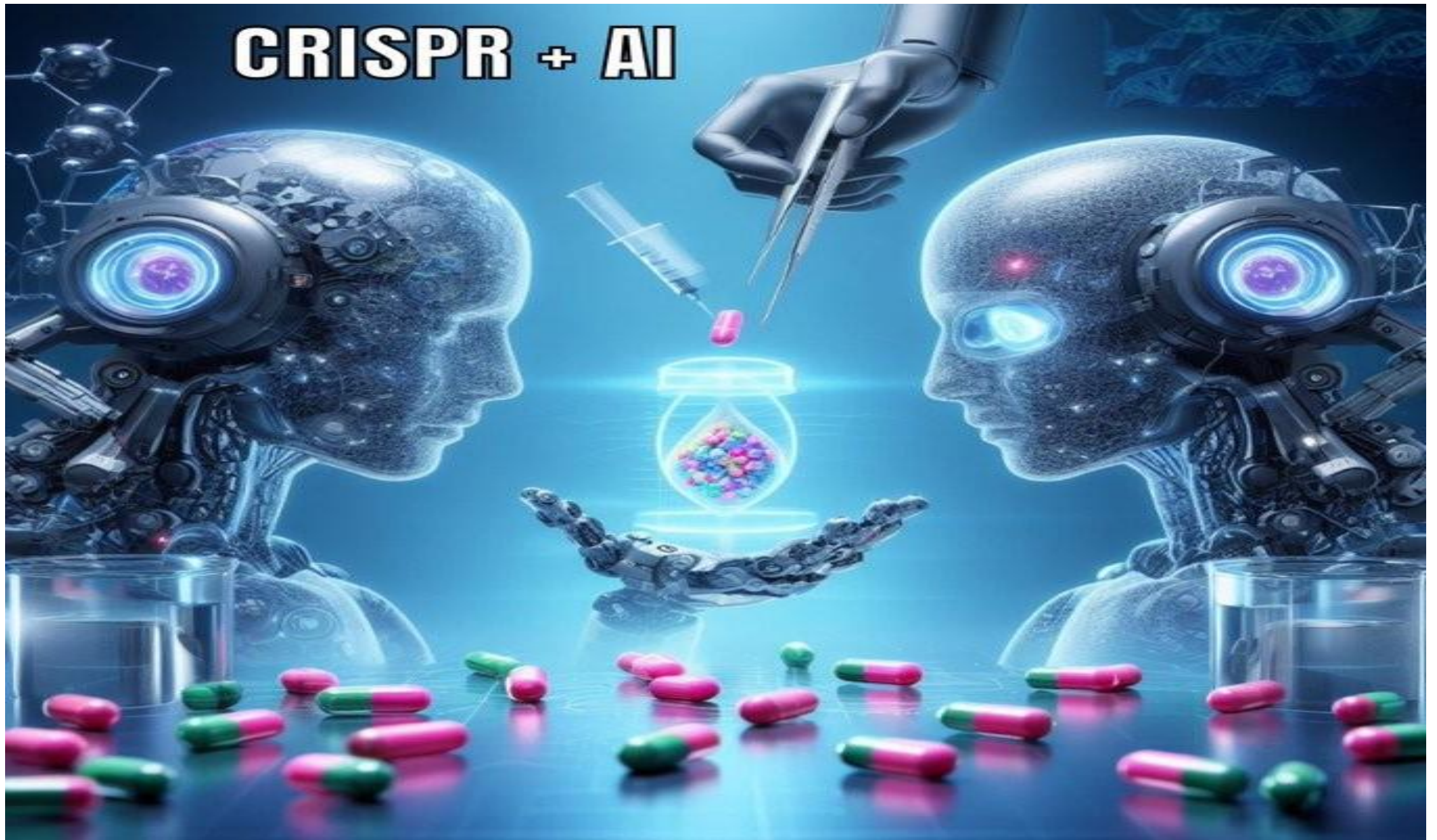




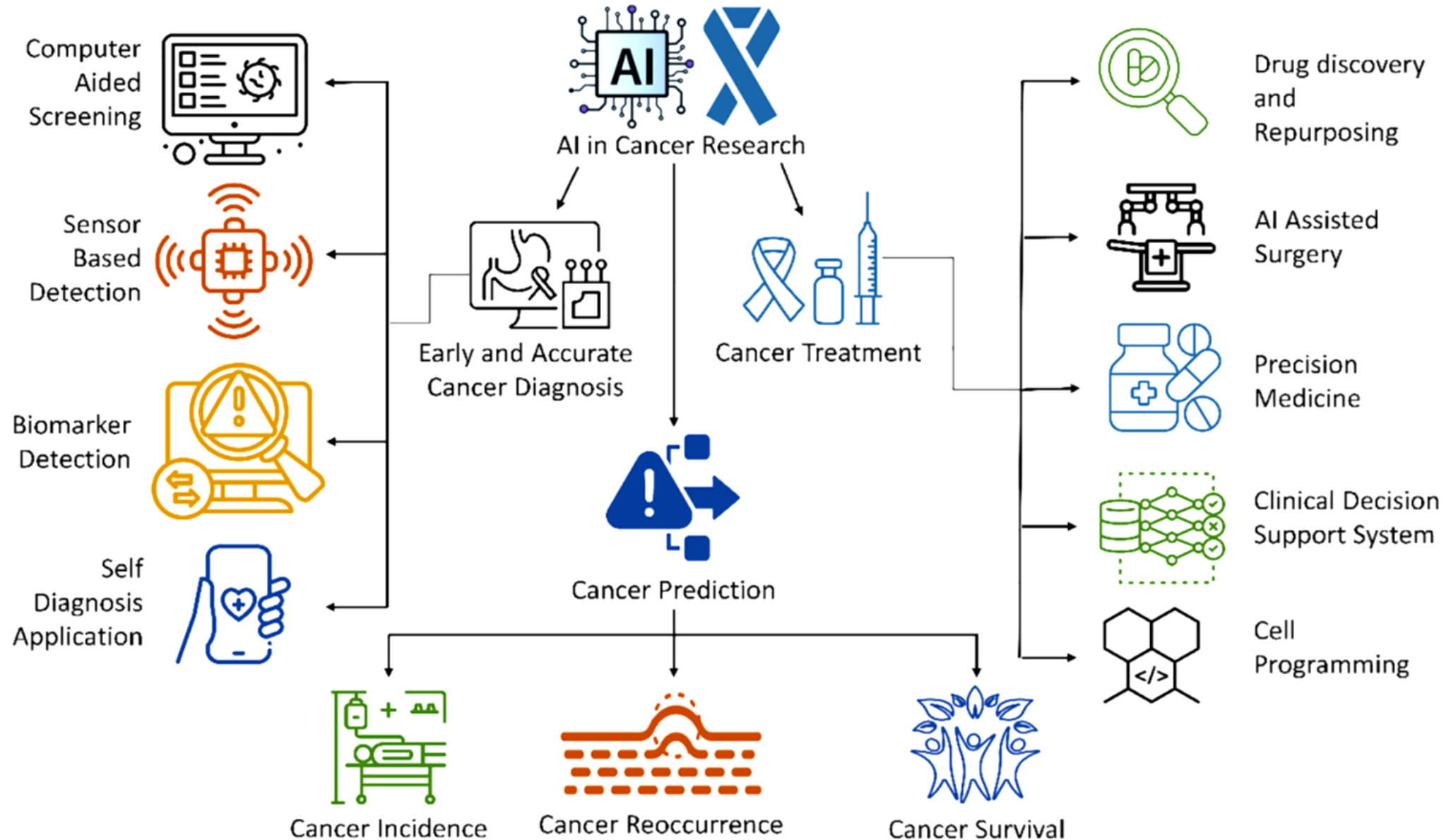
# The next great cancer immunotherapy: CRISPR engineered natural killer cells

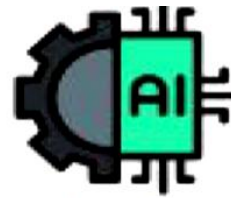


# CRISPR + AI

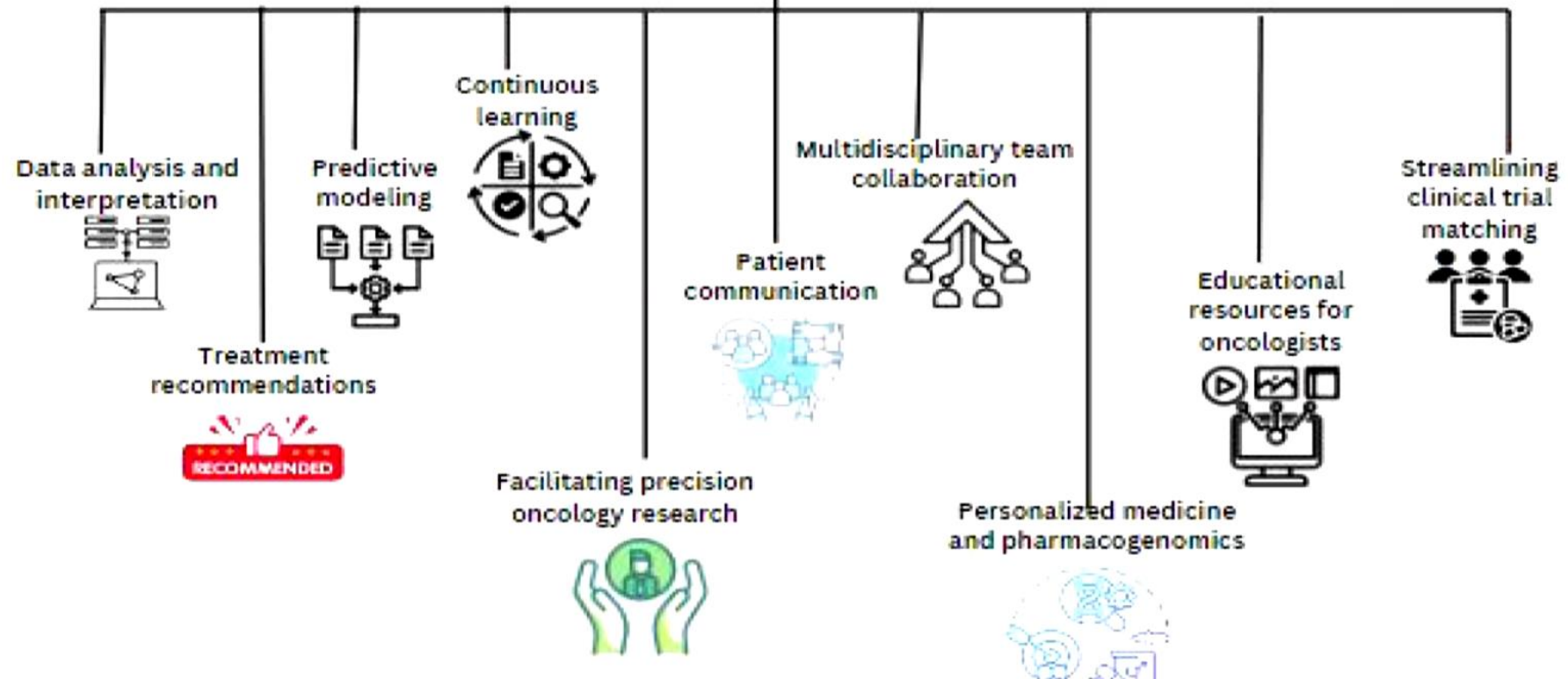


# AI in chimeric antigen receptor-based therapies

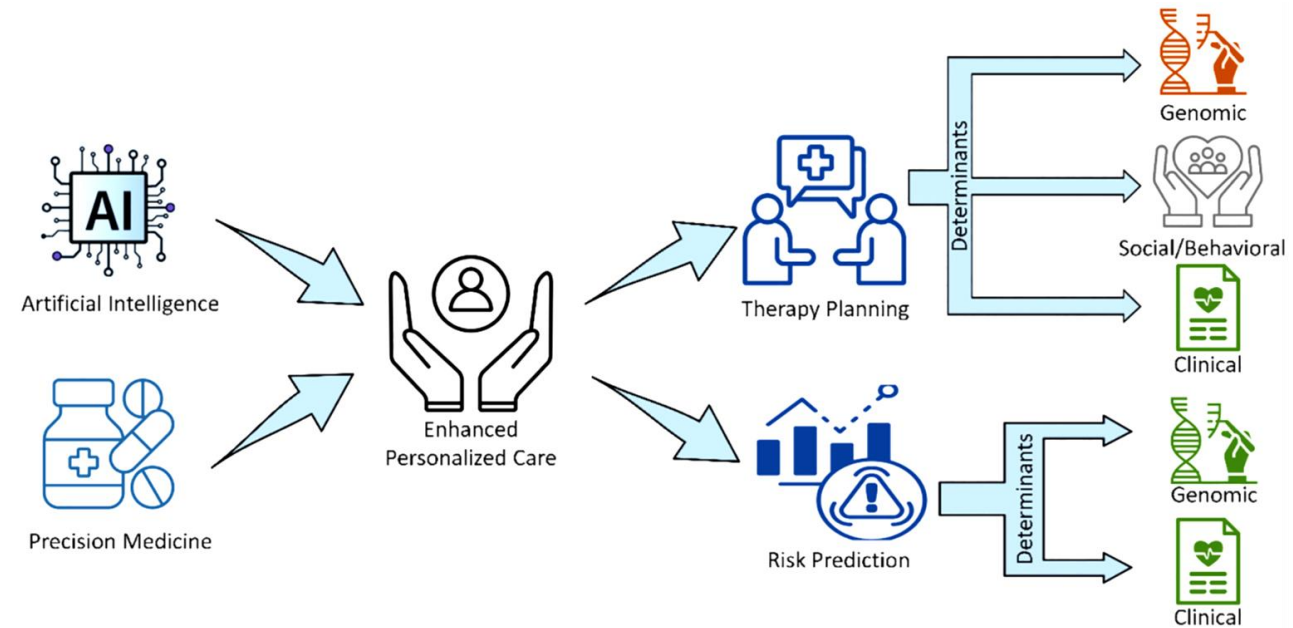
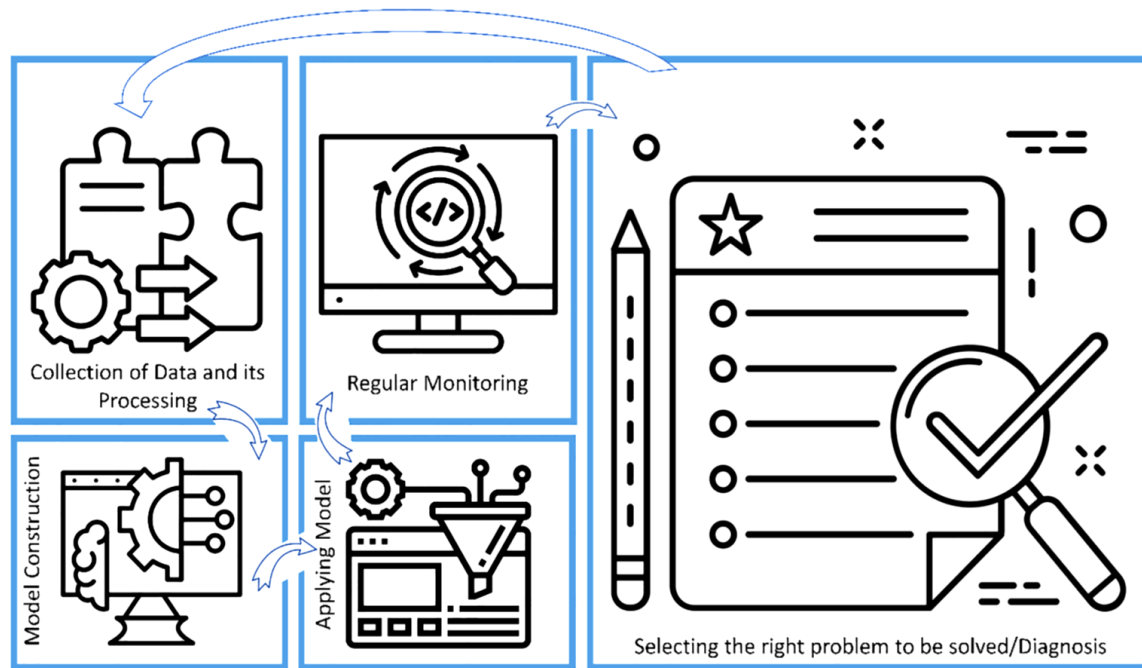




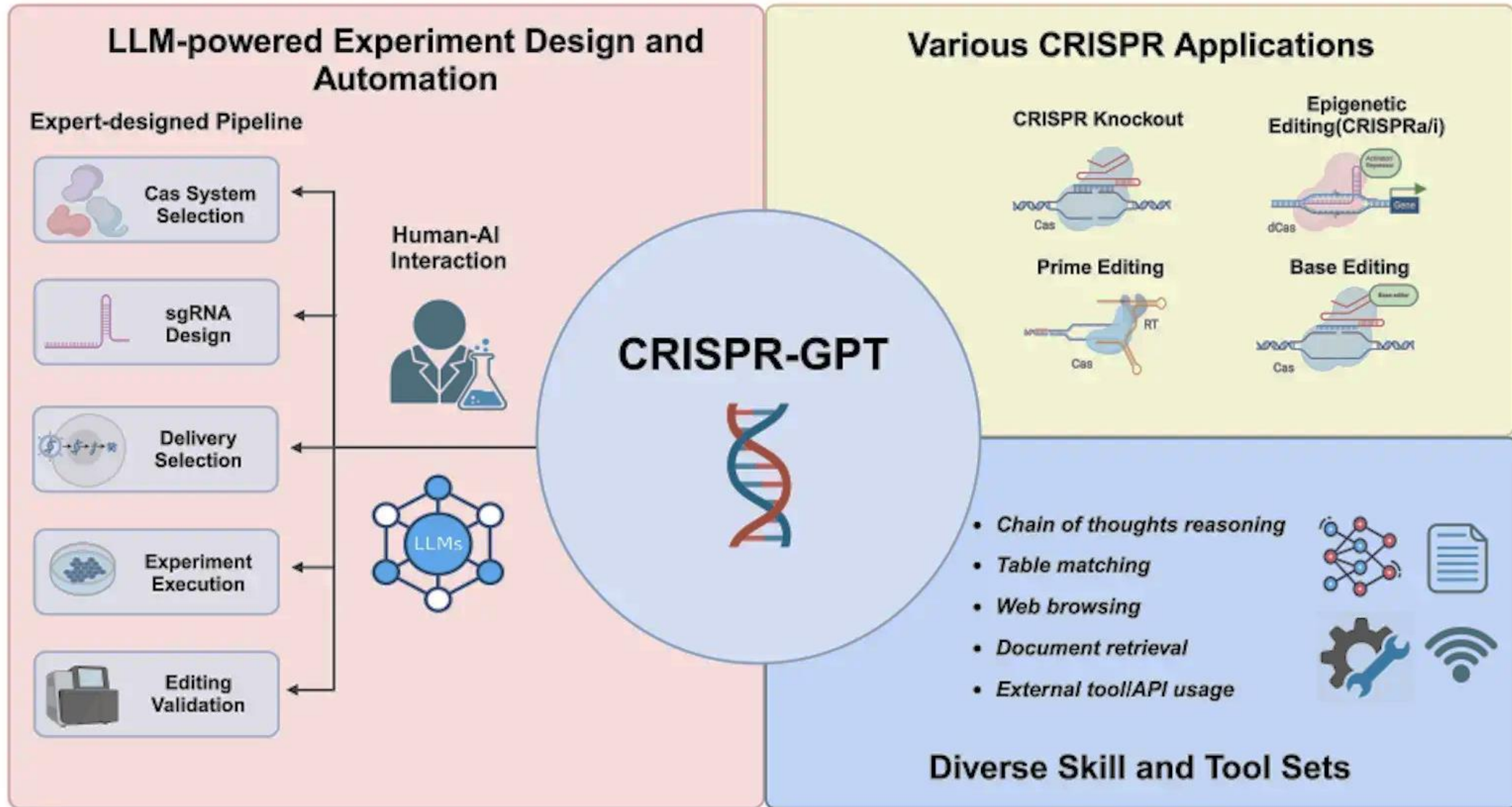
## Molecular Oncology and AI



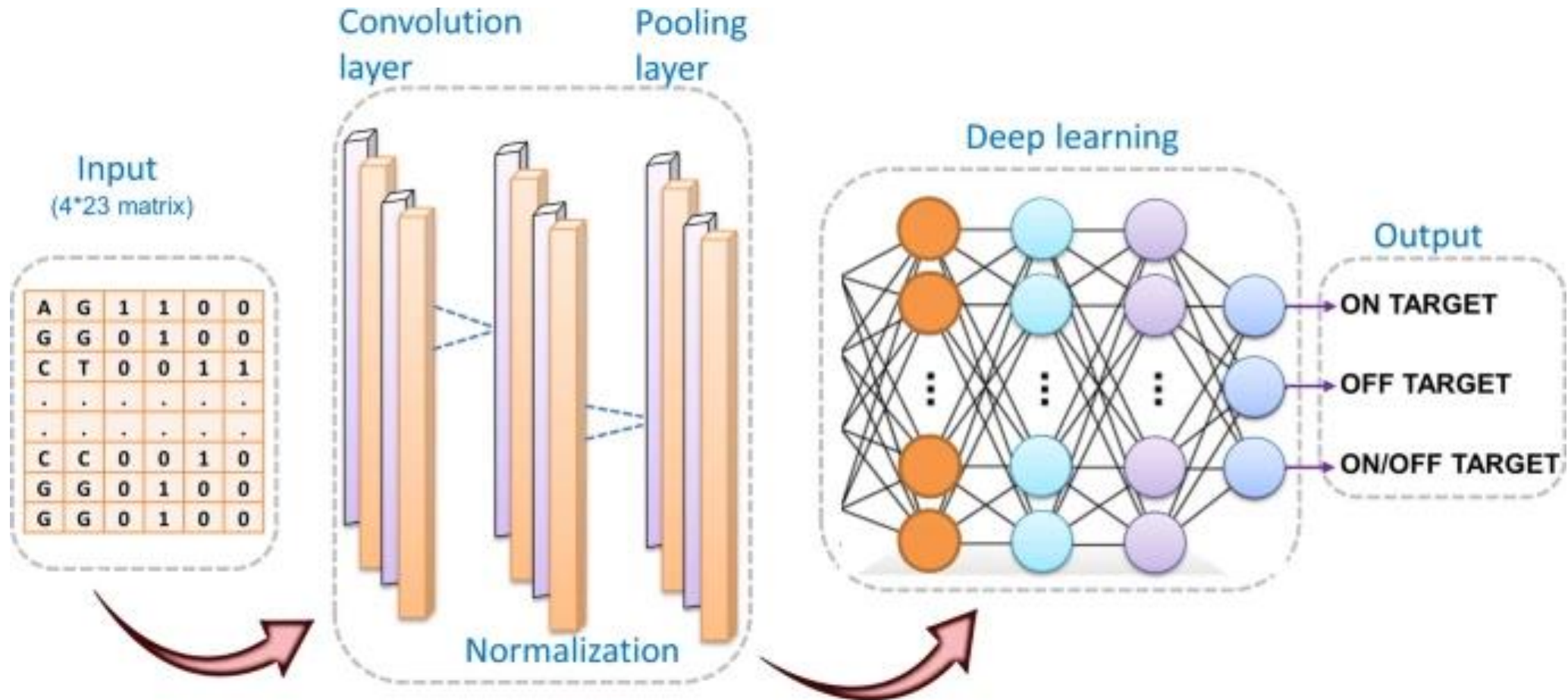
# Steps involved in AI-based models for diagnosis in healthcare.



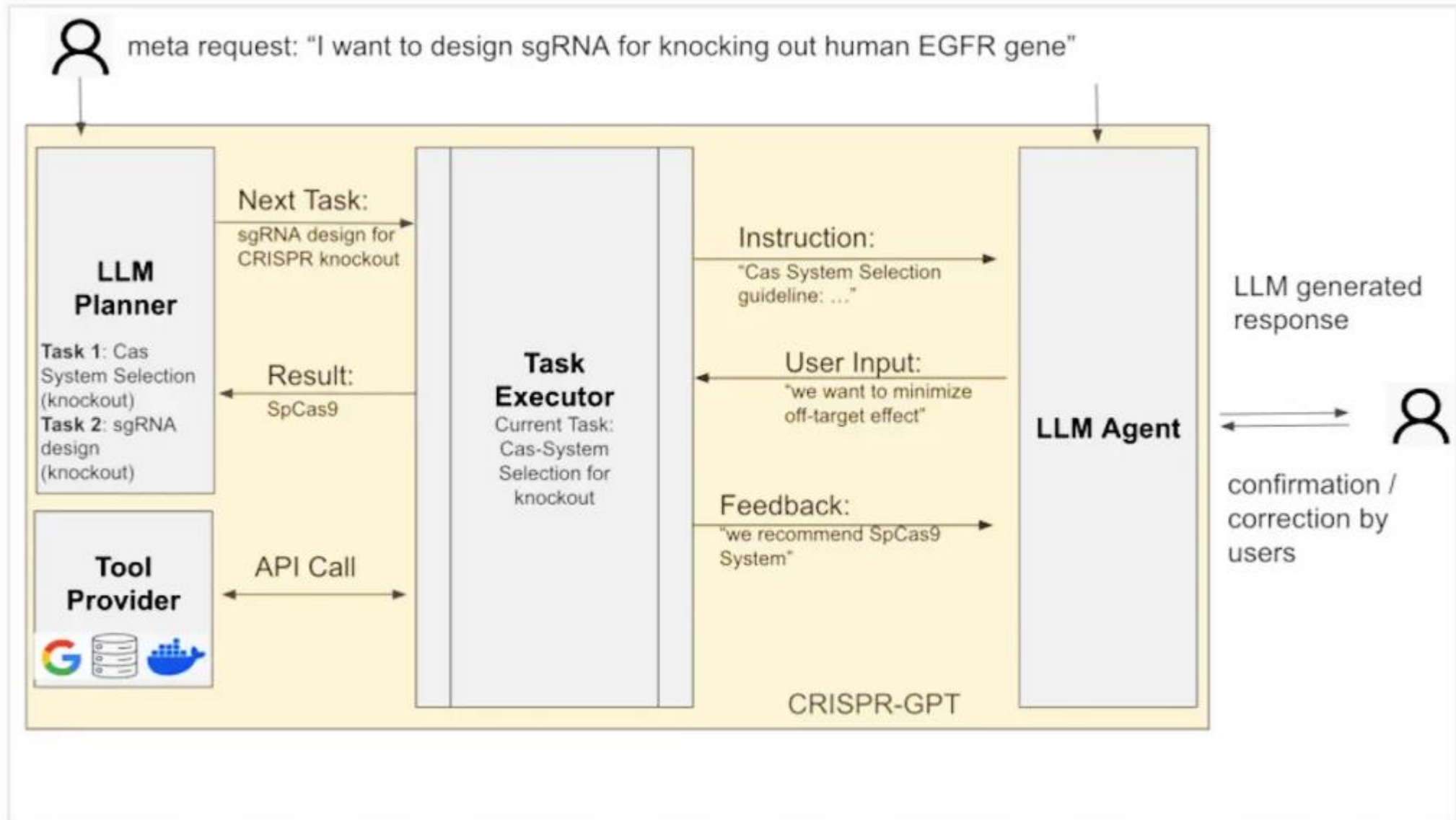
# CRISPR-GPT, the Future of Efficient CRISPR Experiment Design



# CRISPR/Cas9 deep learning architecture.



# Developing apps for beginners



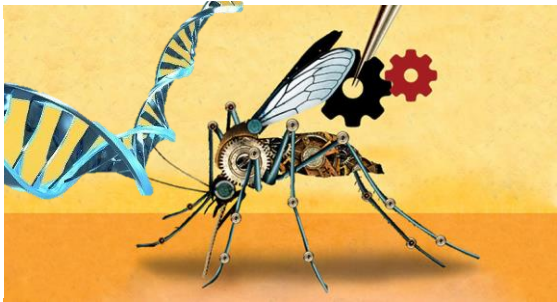
# CRISPR application for eradication of infection disease

MEGAN MOLTENI SCIENCE 09.24.2018 11:00 AM

2018

## Here's the Plan to End Malaria With Crispr-Edited Mosquitoes

Target Malaria hopes to eradicate Africa's malaria-carrying mosquitoes. But when manipulating the fate of a species, moving slowly is a virtue.



The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT September 2019

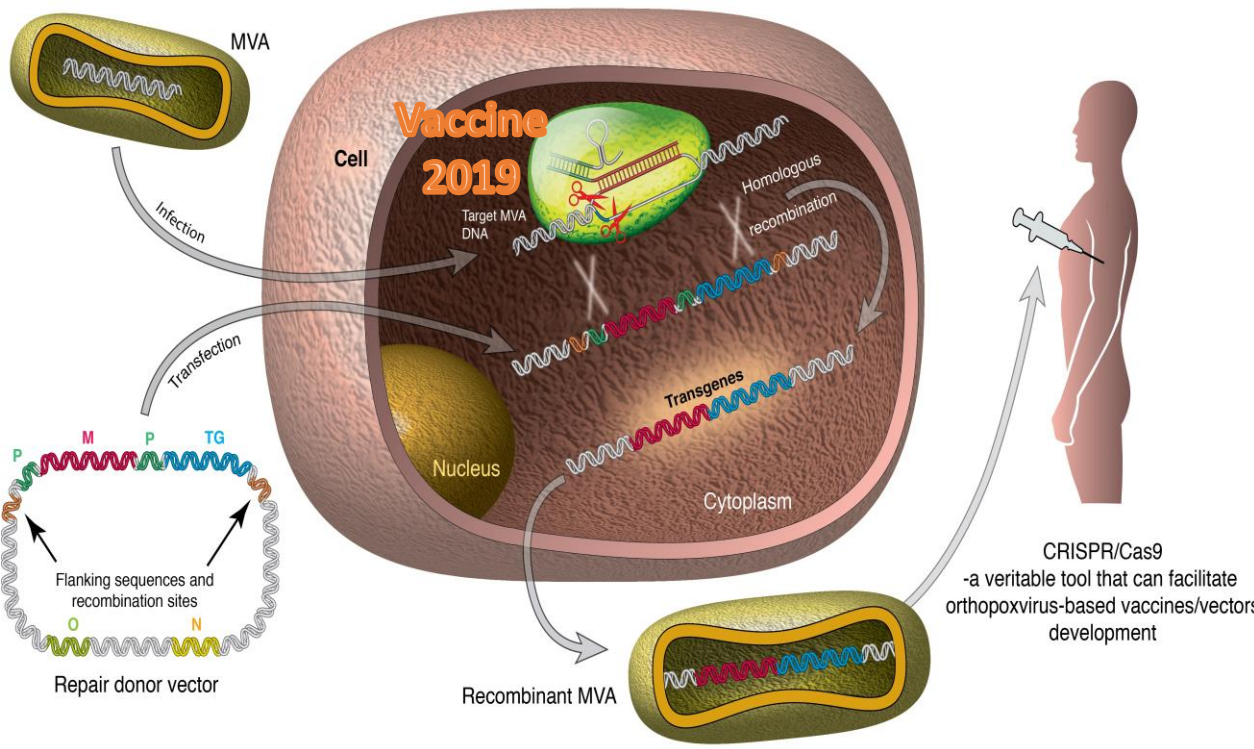
## CRISPR-Edited Stem Cells in a Patient with HIV and Acute Lymphocytic Leukemia

N ENGL J MED NEJM.ORG

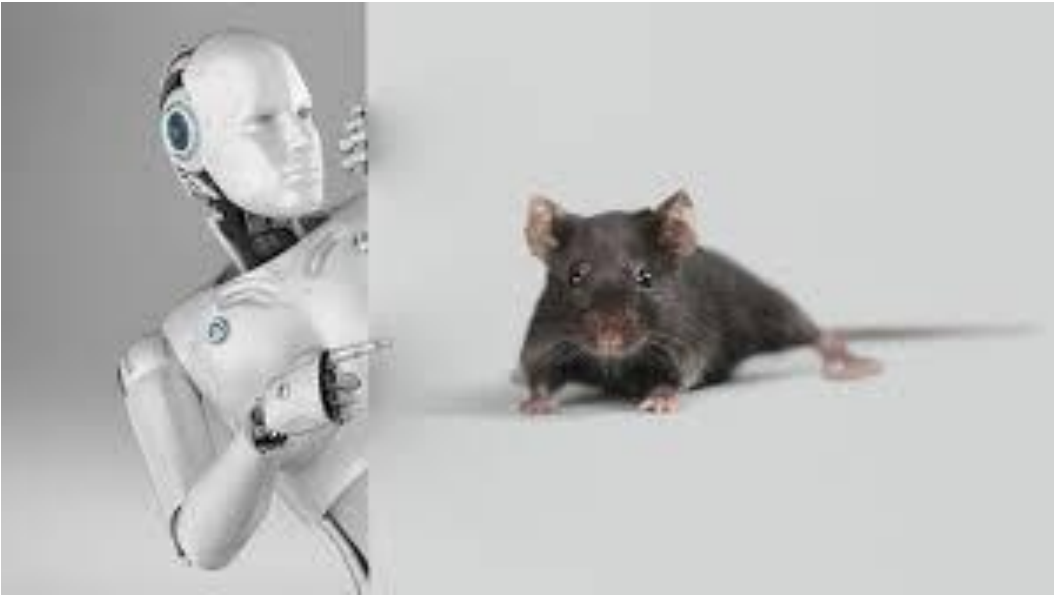
The New England Journal of Medicine

Downloaded from nejm.org at UNIVERSITY OF TOLEDO LIBRARIES on September 12, 2019. For personal use only. No other uses without permission.

Copyright © 2019 Massachusetts Medical Society. All rights reserved.



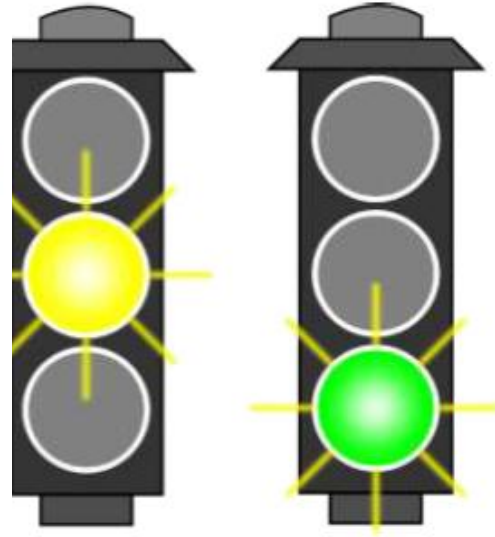
# Artificial Intelligence as a Replacement for Animal Experiments?



# Limitless application

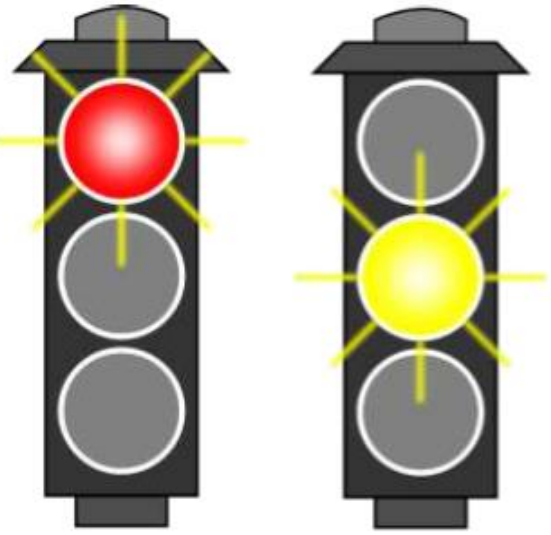
- Drug development – optimize biotech manufacture
- Disease models
- Ecological vector control – mosquito sterilization
- Biofuels
- Agriculture – modification of crop strains or animals

The NIH recombinant advisory Committee has Approved the First US Trial



The University of Pennsylvania:  
combination of PD-1 and  
NY-ESO-1 and LAGE-1  
in human cancer

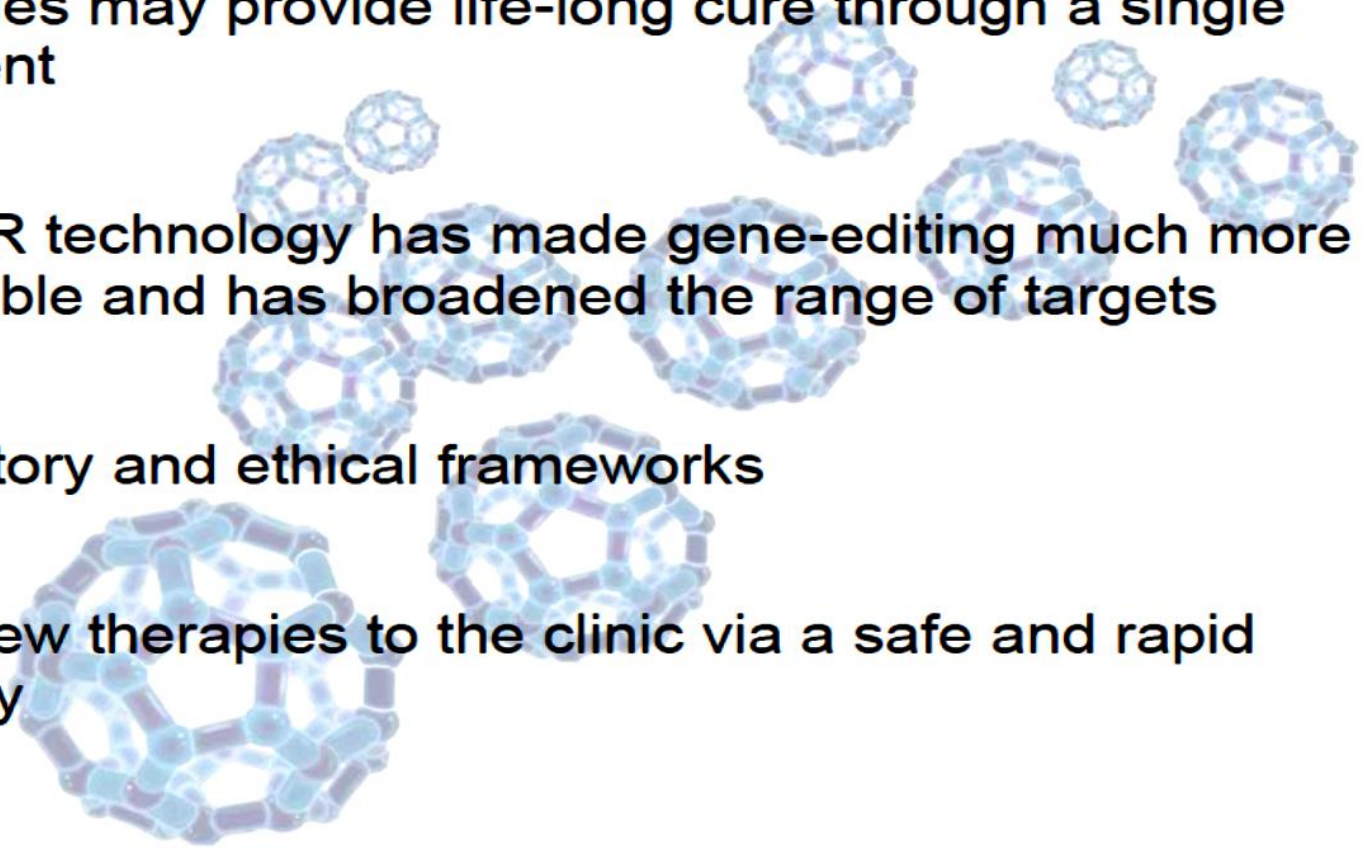




# Clinical Development Considerations for Gene Editing Technology

---

- Therapies may provide life-long cure through a single treatment
- CRISPR technology has made gene-editing much more accessible and has broadened the range of targets
- Regulatory and ethical frameworks
- Bring new therapies to the clinic via a safe and rapid pathway

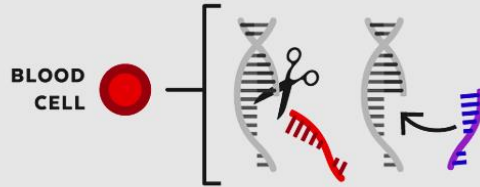


## SOMATIC GENE EDITING

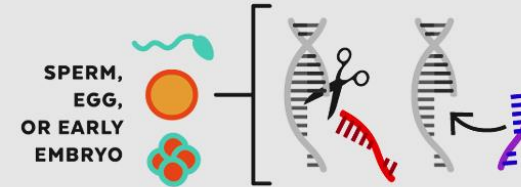
VS.

## GERMLINE GENE EDITING

### EDIT



Somatic therapies target genes in specific types of cells (blood cells, for example).

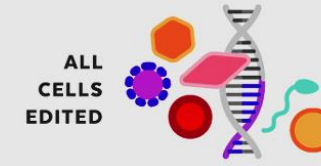


Germline modifications are made so early in development that any change is copied into all of the new cells.

### COPY

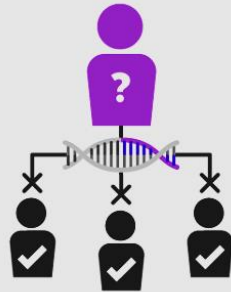


The edited gene is contained only in the target cell type. No other types of cells are affected.

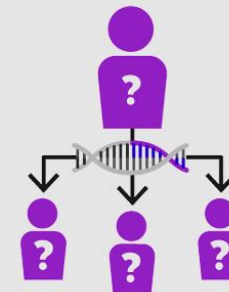


The edited gene is copied in every cell, including sperm or eggs.

### RISKS



Any changes, including potential off-target effects, are limited to the treated individual.



If the person has children, the edited gene is passed on to future generations.

### NEXT GENERATION

### CONSENSUS



Somatic cell therapies have been researched and tested for more than 20 years and are highly regulated.



Human germline editing is new. Heritability of germline changes presents new legal and societal considerations.

# Ethical Concerns

## *Non-Therapeutic Use / Enhancement*

---

- International Summit on Human Gene Editing (Dec 2015)
  - Concerns over germ line editing – need for an ongoing forum
- NAS/NAM Meeting (April 2016)
  - All aspects of human germline editing, consequences, regulation and potential applications
  - Committee assembled to perform a year-long in-depth study
- EU CT Directive (2001/20/EC) does not allow germ line editing (Article 9)
- NIH RAC will not review proposals on germ line editing
- Eugenic practices prohibited:
  - Oviedo Convention
  - Convention on Human Rights and Biomedicine (1997)
  - Article 3(2) of the Charter of Fundamental Rights of EU prohibits eugenic practices

# Regulatory Challenges

## *Somatic Cell Therapies*

- CRISPR/Cas-based gene editing of somatic cell therapies will use in vivo or ex vivo strategies
- Current regulations for gene therapy and cell therapy will regulate CRISPR-based therapies
- Regulators will need to stay up to date with rapid technology advances
- Pathways to market will need to be flexible and allow timely patient access to therapies



# Safety and Efficacy

---

- Off-target effects/genotoxicity
  - Improvements in targeting of CRISPR/Cas9 system
    - Methods to assess genome-wide off-target effects
    - Need to ensure there is no detectable germ line modification
- Efficacy
  - Single administration may be sufficient but need to consider multiple treatments
  - Control of CRISPR/Cas editing
- Animal models
  - Significant area for regulators and companies

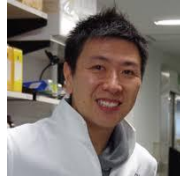
# Acknowledgement



Dr. Kazemi



Dr. Kouichi Hasegawa



Dr. Peter David Gee



Dr. Gursharan Chana



THE UNIVERSITY OF  
MELBOURNE



Dr. Mirella Dottori



Dr. A Kazemi



Dr. Ehsan Shamsi Koushki



TEHRAN UNIVERSITY  
OF  
MEDICAL SCIENCES

آزمایشگاه طب بازساخت و نوآوریها پرشکر  
再生医療学医薬基盤研究室



## Funding supports:



Mirella  
Dottori



JSPS

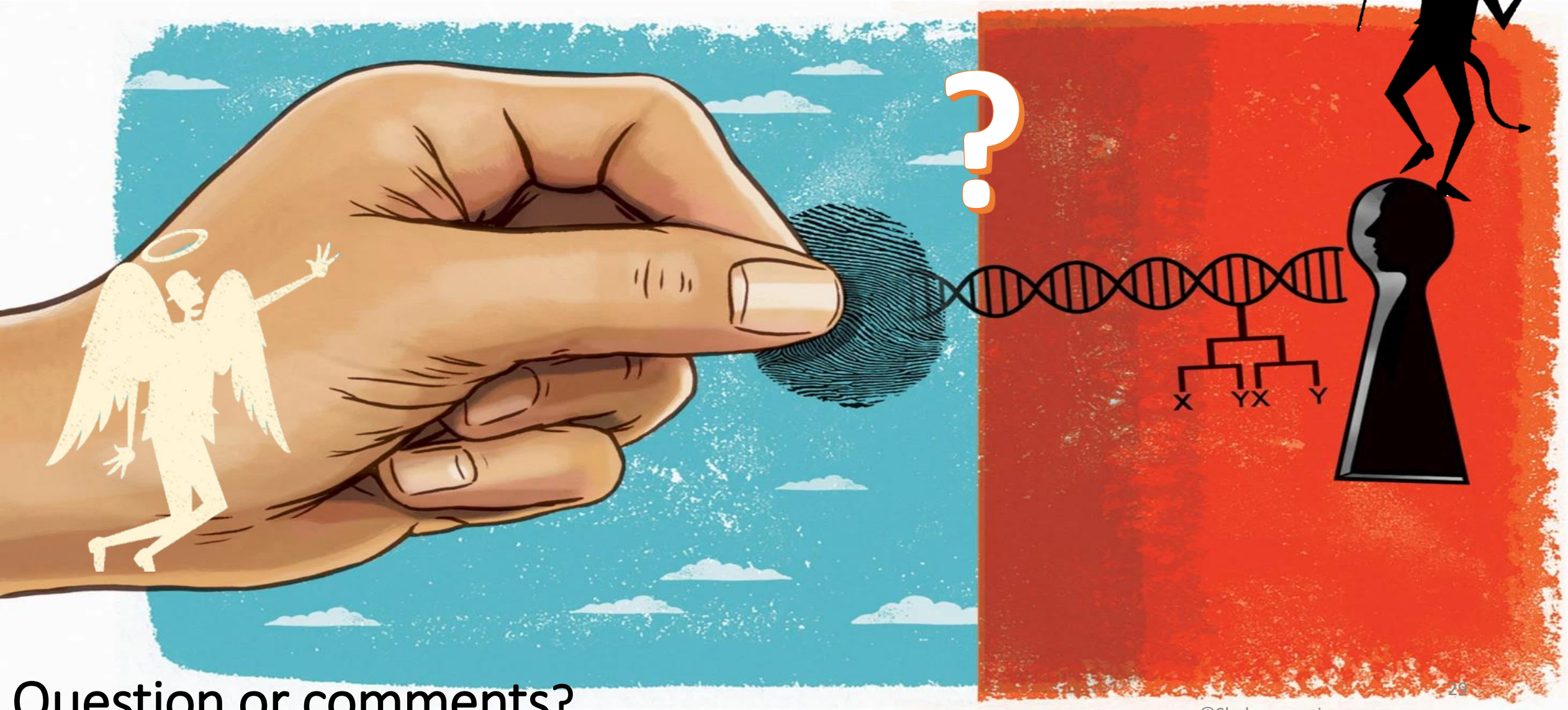
Kouichi  
Hasegawa



Hosein  
Shahsavarani

Iran National Science Foundation

Thank you very much for your kind attention.



Question or comments?