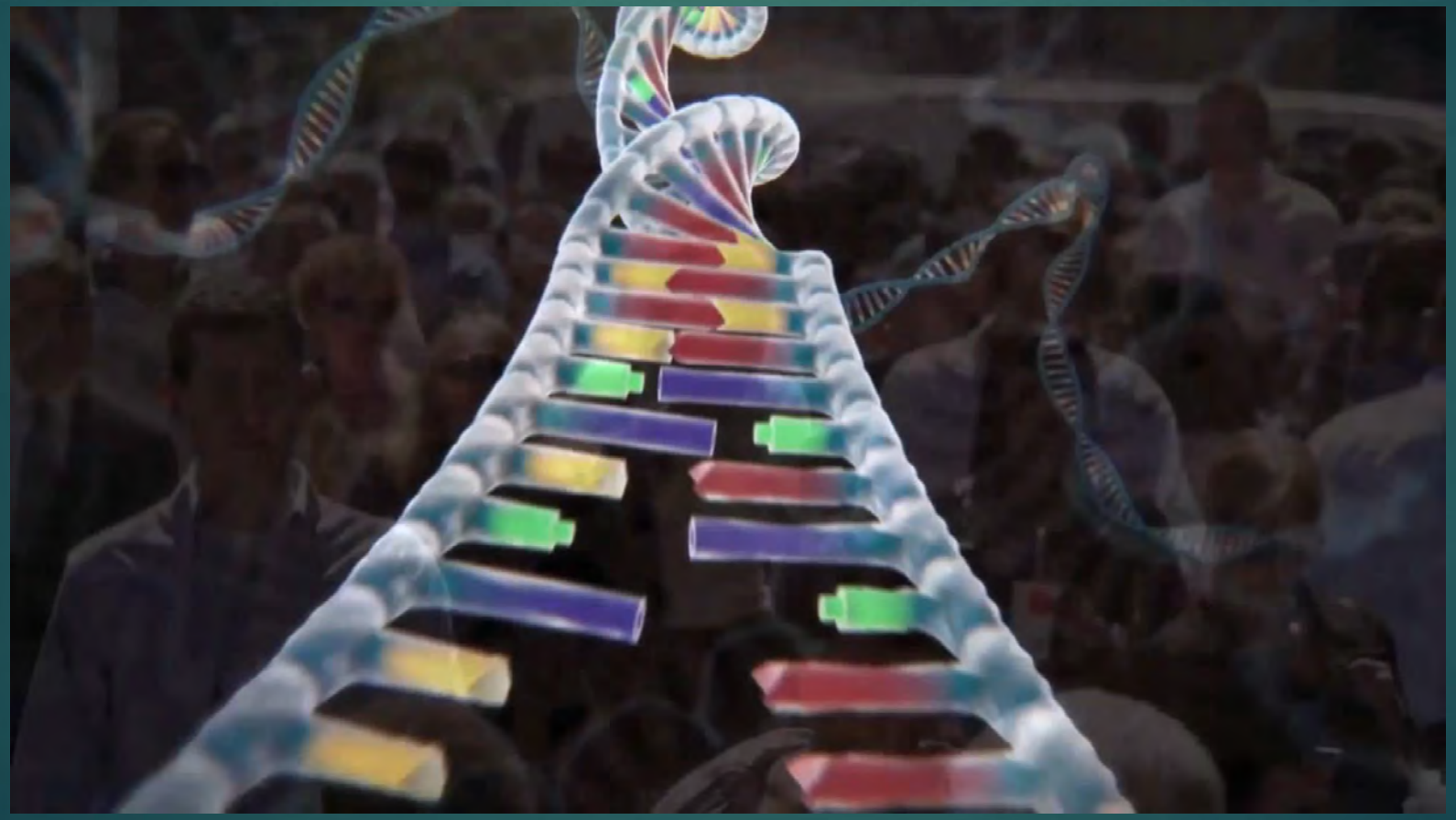
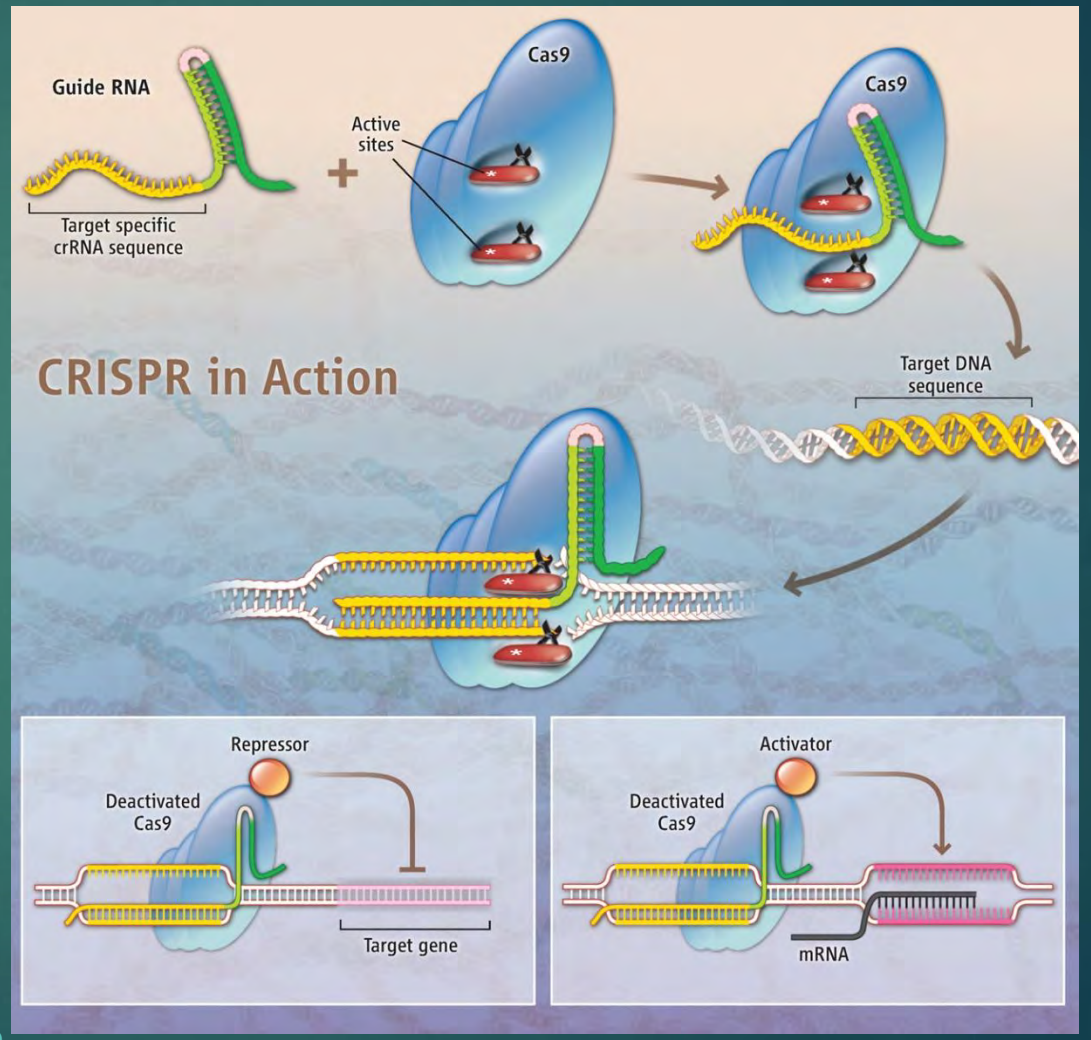
Taking advantage of CRISPR system:



DNA surgeon.

With just a guide RNA and a protein called Cas9, researchers first showed that the CRISPR system can home in on and cut specific DNA, knocking out a gene or enabling part of it to be replaced by substitute DNA. More recently, Cas9 modifications have made possible the repression (lower left) or activation (lower right) of specific genes.

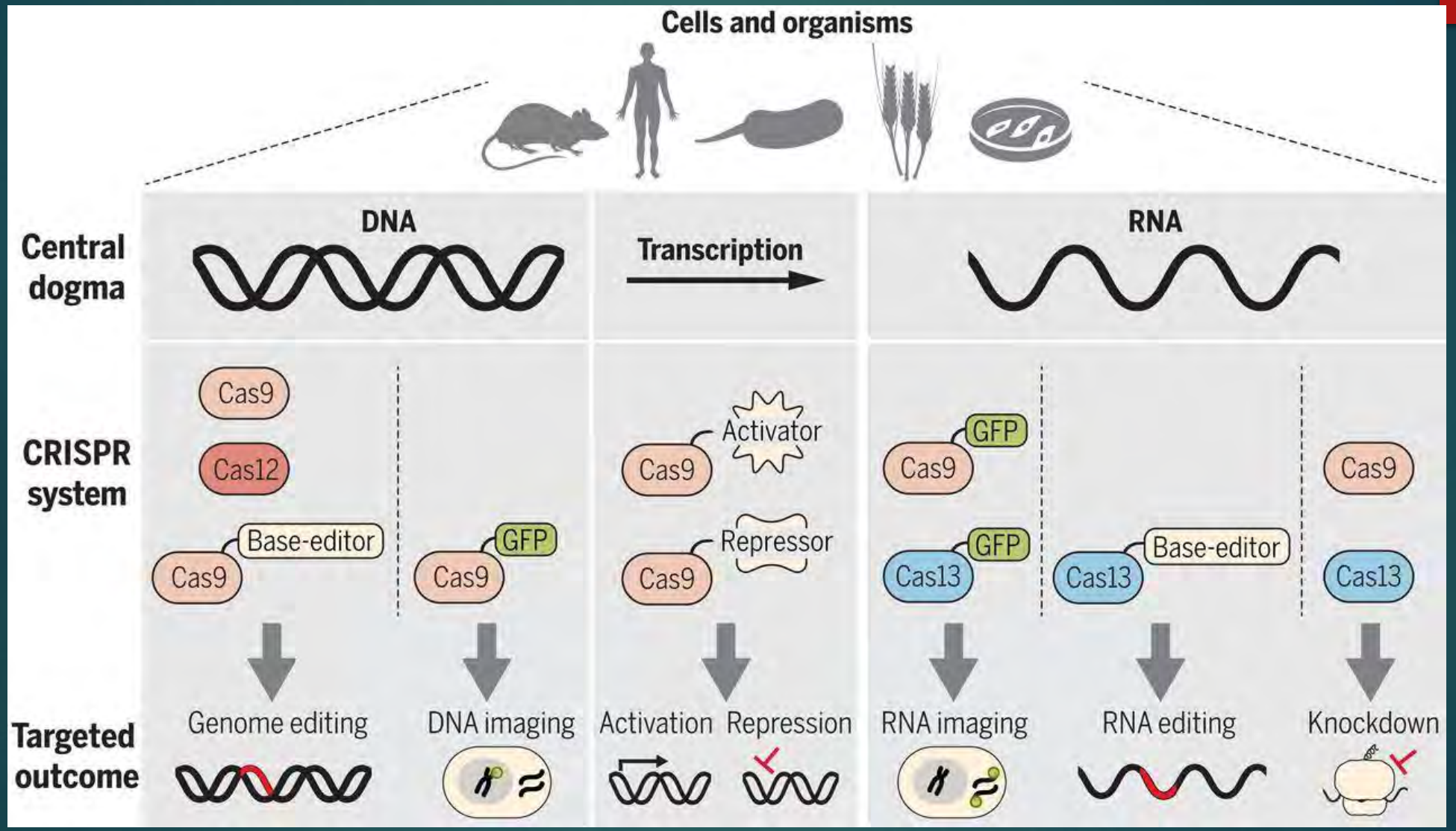


Published by AAAS [Jennifer Doudna explains CRISPR (16 min)]

Elizabeth Pennisi Science 2013;341:833-836

Science AAAS

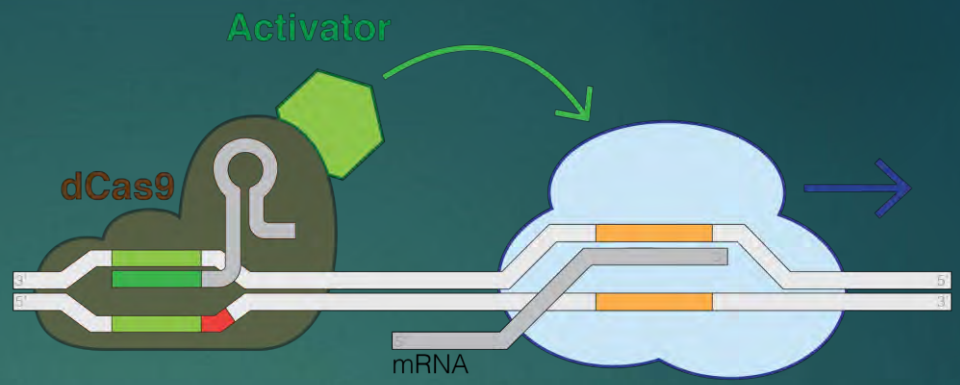
CRISPR-Cas systems allow genetic manipulation across the DNA to protein sequence



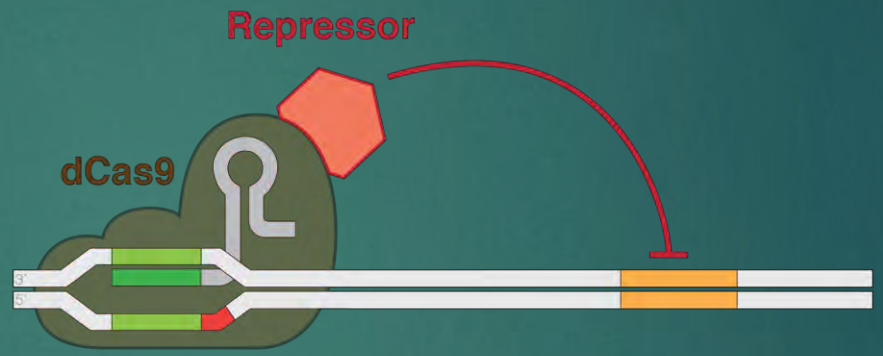
Published by AAAS

Gavin J. Knott, and Jennifer A. Doudna Science 2018;361:866-869

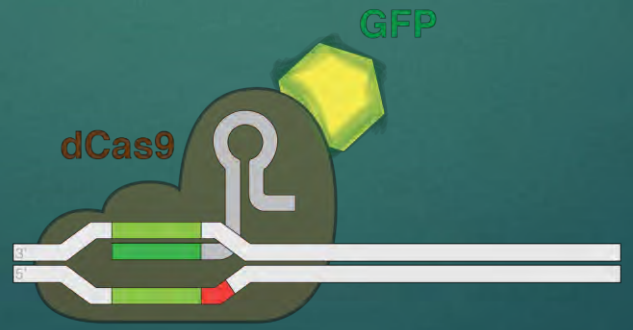
Some Applications of CRISPR in genetic engineering



Gene activation



Gene repression



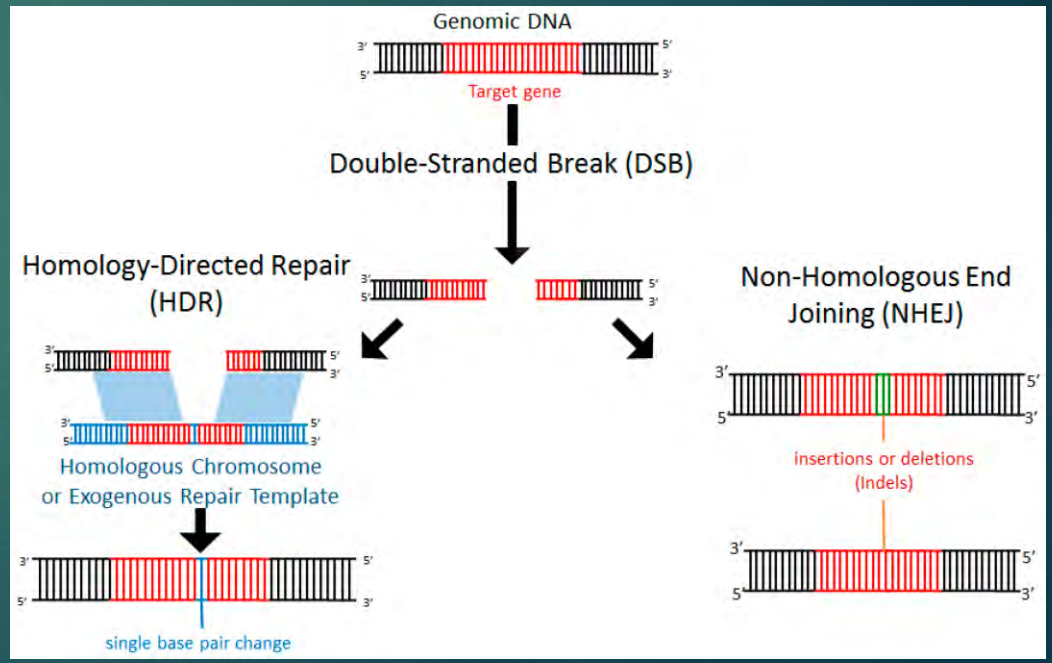
Visualisation

Some Current Applications

- Gene Editing
  - Duchenne muscular dystrophy
    - Editing to induce skipping of defective exon
  - Amyotrophic Lateral Sclerosis (Lou Gehrig disease) and Huntington's
    - Inactivate defective genes
  - Down's syndrome
    - Eliminate extra chromosome in stem cells
  - Endogenous retroviruses in pig cells
    - Make suitable for human transplants
  - Engineered T-cells
    - Activate immune response to cancer cells
  - Sickle-cell anemia

Some problems

- How to deliver CRISPR to targets
  - Virus delivery
    - Can be cell-type specific
    - But CRISPR-Cas 9 and associated DNA/RNA editing proteins are too large for most viruses
  - Nanoparticle delivery
    - Not (usually) cell-type specific
  - Non-Homologous End Joining vs Homology-Directed Repair
    - NHEJ can produce deleterious mutations before HDR can occur
- Off-target effects
  - Due to shortness of sgRNA



The Future Promise of CRISPR

Forbes / Pharma & Healthcare

AUG 10, 2015 @ 07:30 AM 35,772 VIEWS

Bill Gates And 13 Other Investors Pour $120 Million Into Revolutionary Gene-Editing Startup

Matthew Herper
FORBES STAFF

I cover science and medicine, and believe this is biology's century.

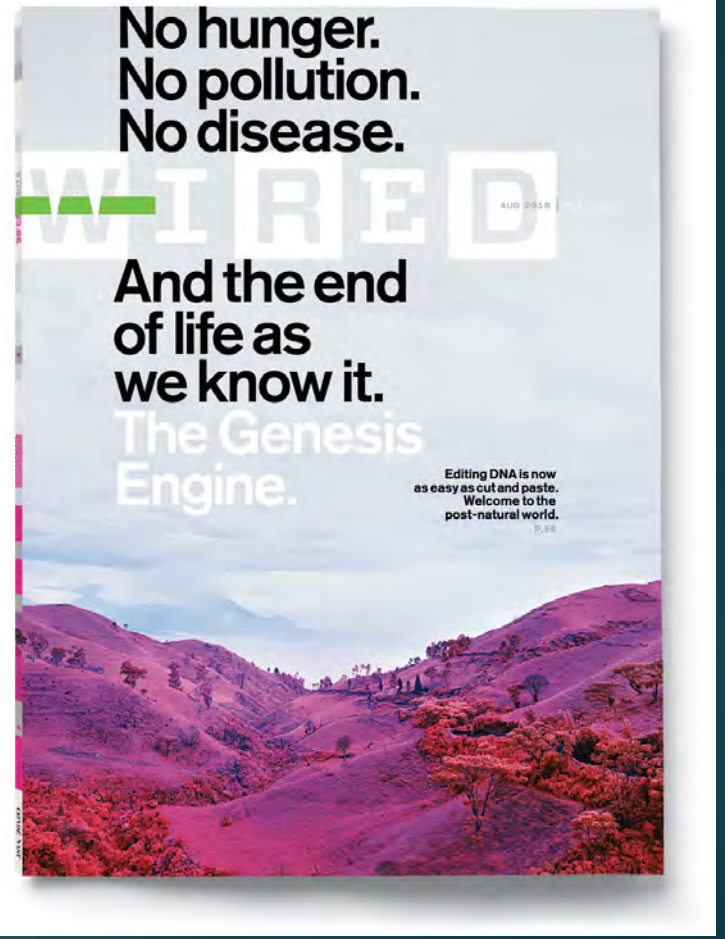
FOLLOW ON FORBES (2029)

FULL BIO >

Four years ago, the protein called CRISPR-Cas9, an enzyme that bacteria use to attack viruses that infect them, was unknown to humans. Now it is ubiquitous in science labs as the most efficient way of cutting-and-pasting DNA yet invented. Wired Magazine, in a breathless cover story, just called it "The Genesis Engine," instructing readers to "buckle up" because the easy DNA editing CRISPR enables will change the world. And now at least one CRISPR-focused company has the cash to back up the hype.

Editas Medicine, based in Cambridge, Mass., already had money. Founded in November 2013 with $43 million from Third Rock Ventures, Polaris Ventures and Flagship Ventures, it was the first big CRISPR effort out of the gate. The company says that money has not been spent. In May, Juno Therapeutics, which is developing cell therapies for cancer, inked a collaboration that gave Editas $25 million upfront and another $22 million in research support. Any products that result could deliver Editas another $250 million.

But those investments are dwarfed by today's announcement, which will put $120 million into the tiny company's bank account – enough, Editas says, to keep it running for a projected three years. The lead investor is a newly created firm called bng0, a select group of family offices led by Boris Nikolic, who was previously a science advisor to Bill Gates. Both Editas and Gates' office confirm that the Microsoft MSFT +0.00% billionaire, who is the world's richest man, is among the bng0 backers.



Top 9 CRISPR Startup Companies Changing the Future of Biotech and Medicine[1]

Inscripta Therapeutics

Plantedit

Beam Therapeutics

eGenesis

Ligandal

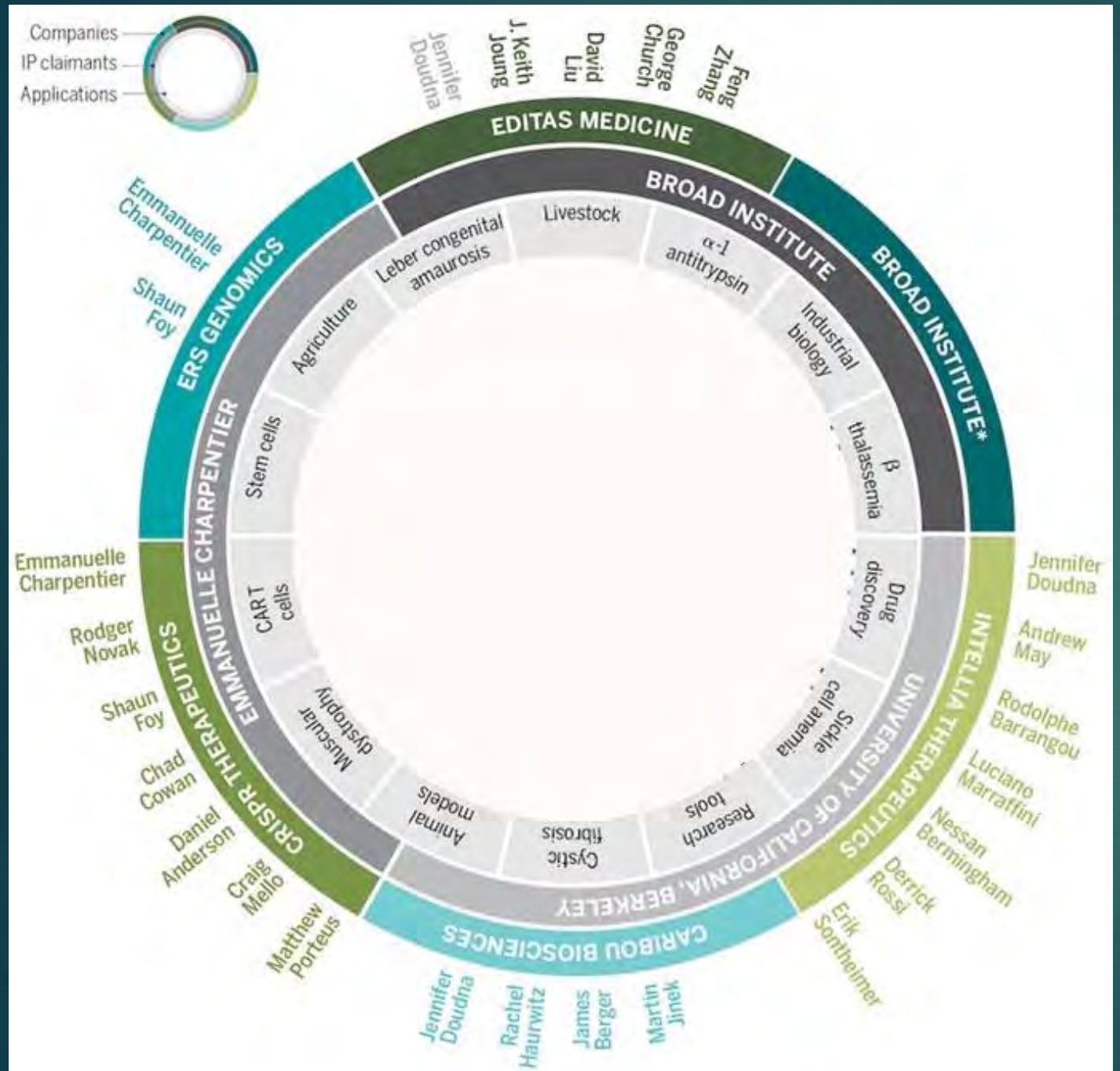
ntrans

Synthetic Genomics

Mammoth Biosciences

Biotech startup companies using CRISPR-Cas9 technology as a main component of their strategy have existed almost since the discovery that CRISPR could be reprogrammed to target essentially any region of any genome. Several CRISPR technology companies, such as CRISPR Therapeutics, Editas Medicine, and Intellia Therapeutics, have already outgrown startup status and are now publicly traded companies.

[1]The Official Synthego Blog where we explore the exciting, rapidly emerging field of CRISPR genome engineering.



Some companies and applications using CRISPR

After https://labiotech.eu/policy-legal-finance/doudna-charpentier-crispr-patent-europe/

- As of March 2015 at least four labs in the US, labs in China and the UK had announced plans for ongoing research to apply CRISPR to human embryos.

- In April 2015, Chinese scientists reported results of an attempt to alter the DNA of non-viable human embryos using CRISPR to correct a mutation that causes beta thalassemia,. The experiments resulted in changing only some genes, and had off-target effects on other genes. (The study had been rejected by both Nature and Science in part because of ethical concerns.)

- In December, following the Chinese studies, Doudna and others urged a worldwide moratorium on applying CRISPR to the human germline, especially for clinical use. "Scientists should avoid even attempting, in lax jurisdictions, germline genome modification for clinical application in humans until the full implications are discussed among scientific and governmental organizations".

- In April 2016 Chinese scientists were reported to have made a second unsuccessful attempt to alter the DNA of non-viable human embryos using CRISPR - this time to alter a gene to make the embryo HIV resistant.

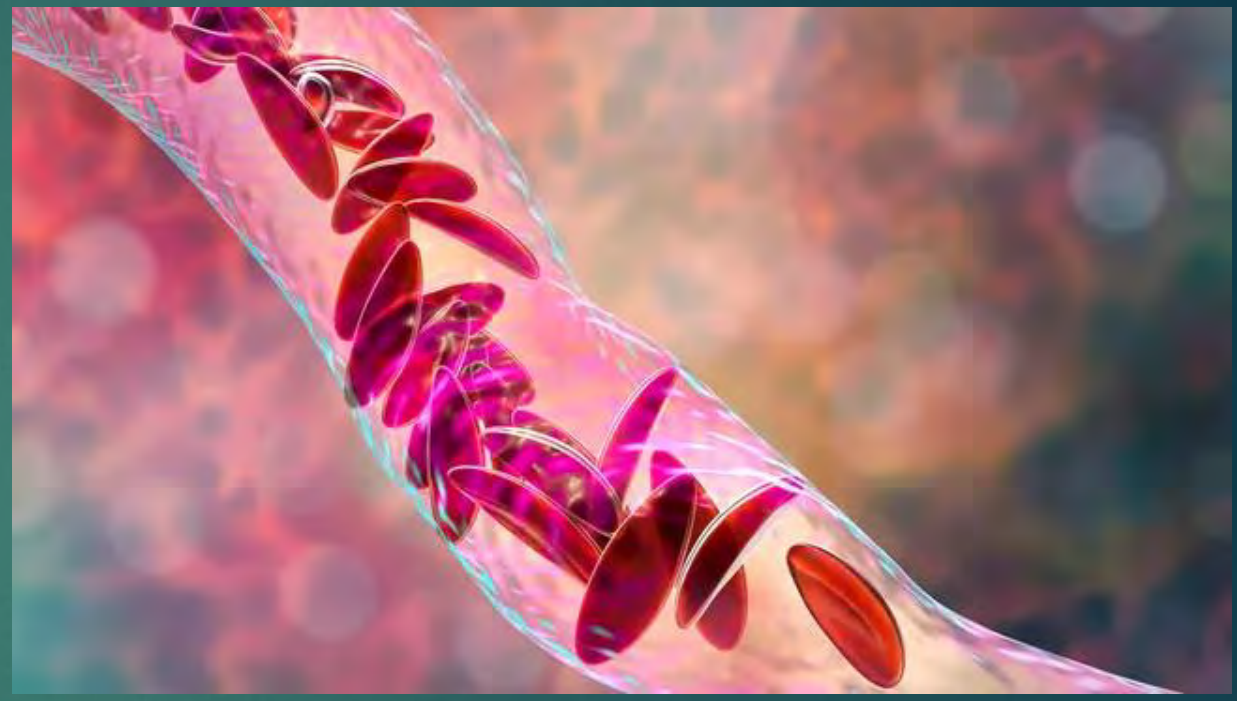
- On Jan 21, 2018, The Wall Street Journal reported that 86 people in China have had their genes edited using CRISPR.

Ethical Implications

- Somatic Gene Therapy
  - Gene replacement therapy
    - Insert "good" gene to replace "bad" one
  - Gene augmentation therapy
    - Insert a functioning gene to provide the protein not produced by a mutated gene.
  - Gene inhibition therapy
    - Inhibits an undesirable gene such as a cancer-causing gene
  - Killing of specific cells
    - Cause cells expressing a certain form of a gene to commit suicide
- Germline Gene Therapy
  - Therapy applied to germ cells and passed on to all subsequent offspring
  - Elimination of inherited diseases

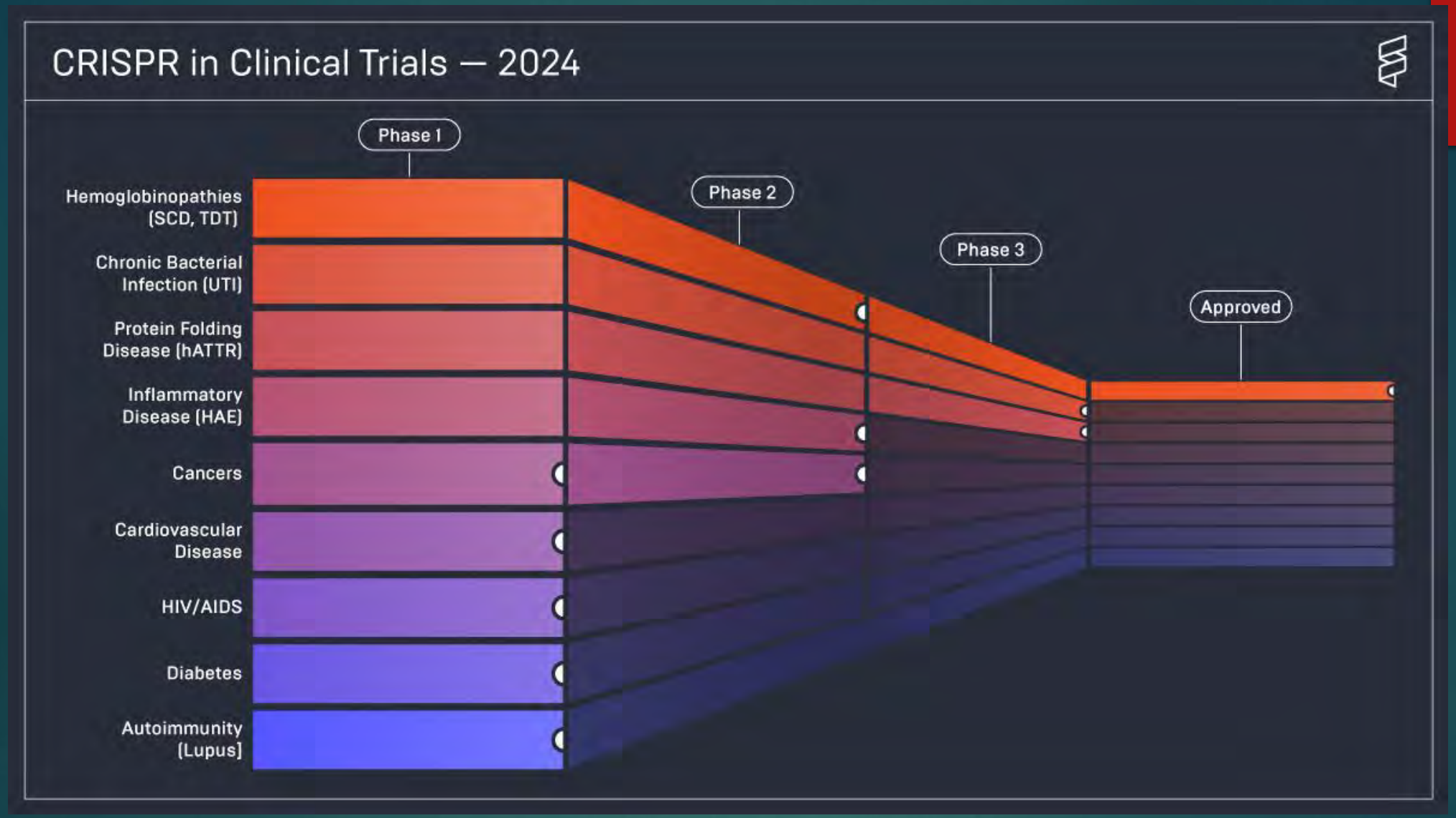
The world's first treatment that uses CRISPR gene-editing technology has been approved.

Exa-cel, also known by its brand name Casgevy, received its first regulatory approval on Nov. 16, 2023 from the U.K. Medicines and Healthcare products Regulatory Agency (MHRA) to treat two debilitating blood disorders: sickle-cell disease and transfusion-dependent beta-thalassemia. The U.S. Food and Drug Administration (FDA) later approved the therapy as a treatment for both disorders.



The regulators' historic decision to approve Casgevy may signal the start of a new era of gene therapy. However, questions remain surrounding the treatment's affordability and its long-term safety.

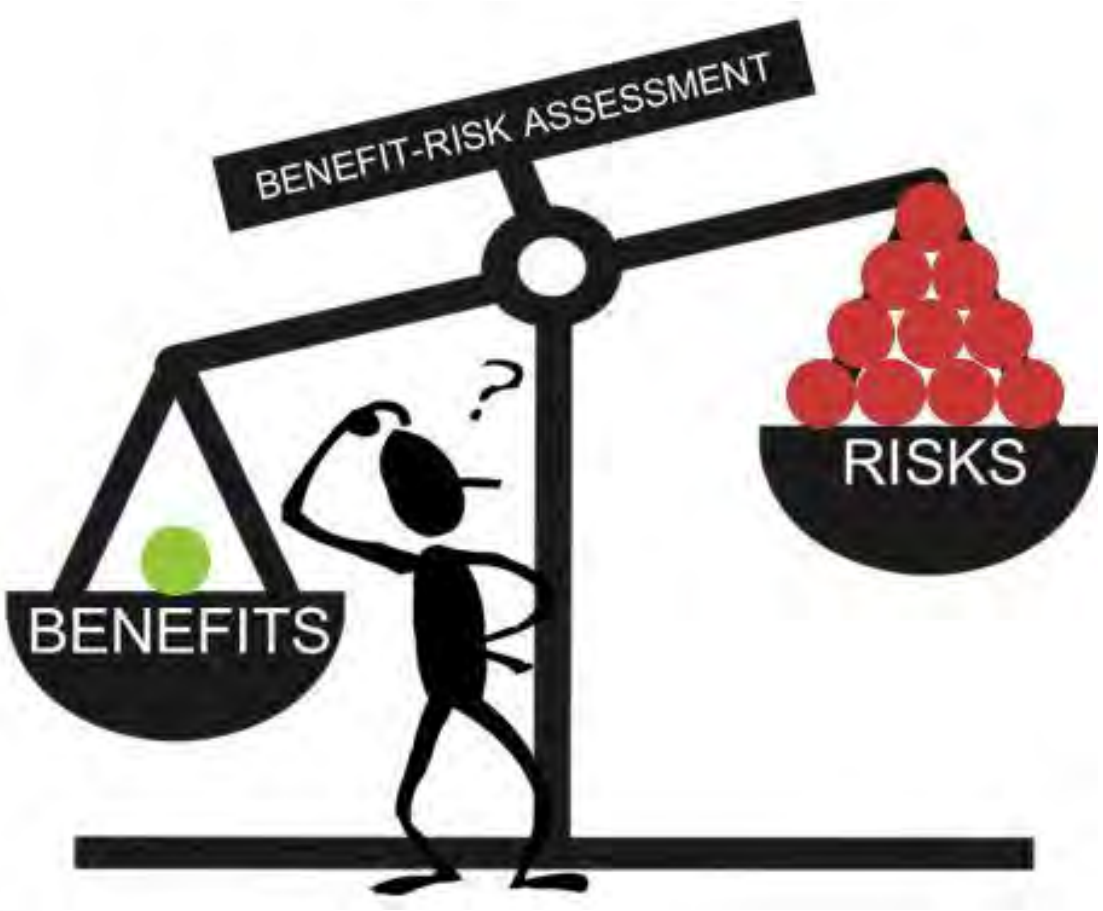
https://www.livescience.com/health/genetics/the-worlds-1st-crispr-therapy-has-just-been-approved-heres-everything-you-need-to-know



https://innovativegenomics.org/news/crispr-clinical-trials-2024/

Where do we stand today???

- Benefits to research into gene functions
- Curing single-gene diseases such as sickle cell anemia
- New agricultural strains, e.g. "golden rice", pest resistance, etc.
- Etc., etc.



- Off-target effects
- Designer babies
- "Frankenveggies" spreading
- Germline editing
- Etc., etc.

Now it's your turn.

THOUGHTS? QUESTIONS?

Open to general feedback and discussion.