



PROJECT

Bioethics

frederickuu.org/fcc

DATE

6 sessions

CLIENT

March 12, 10-11:30am (6 sessions)

Talks about CRISPR



Fredros Okumu

Why I study the most dangerous animal on earth – mosquitoes

Posted Jan 2018



Paul Knoepfler

The ethical dilemma of designer babies

Posted Jan 2017



Ellen Jorgensen

What you need to know about CRISPR

Posted Oct 2016



Jennifer Kahn

Gene editing can now change an entire species – forever

Posted May 2016



Jennifer Doudna

How CRISPR lets us edit our DNA

Posted Oct 2015

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Posted Oct 2015

ted.com/topics/crispr

Covenant

- Use **“I” statements**: *speak from your own experience.*
- **Ask permission before sharing** other participants’ stories outside the group.
- **Lean-in, lean-back**: be conscious of the level of participation that you bring to the conversation. “Share the airspace” to allow everyone a chance to speak before you speak again.
- You always have **permission to “pass.”**



Check-in

- Name
- Why did you sign-up for this course?



Outline

- * **Session #1:** Contemporary Issues, including CRISPR
- * **Session #2 :** Biotechnologies that will boost human physical & mental performance to unprecedented levels
- * **Session #3:** Biotech, part 2
- * **Session #4:**
 - * Moral Reasoning
 - * Paternalism & Autonomy: Before class, please review the "Cases for Evaluation" marked "Ch. 3" ("pages 91-93") of the 21-page PDF.
- * **Session #5:**
 - * Truth-telling & Confidentiality: Before class, please review the "Cases for Evaluation" marked "Ch. 4" ("pages 152-153") of the 21-page PDF.
 - * Informed Consent: Before class, please review the "Cases for Evaluation" marked "Ch. 5" ("pages 206-207") of the 21-page PDF.
 - * Human Research: Before class, please review the "Cases for Evaluation" marked "Ch. 6" ("pages 254-258") of the 21-page PDF.
- * **Session #6:**
 - * Reproductive Technologies: Before class, please review the "Cases for Evaluation" marked "Ch. 8" ("pages 425-427") of the 21-page PDF.
 - * Genetic Choices: Before class, please review the "Cases for Evaluation" marked "Ch. 9" ("pages 557-558") of the 21-page PDF.
 - * Dividing Up Health Care Resources: Before class, please review the "Cases for Evaluation" marked "Ch. 8" ("pages 732-735") of the 21-page PDF.

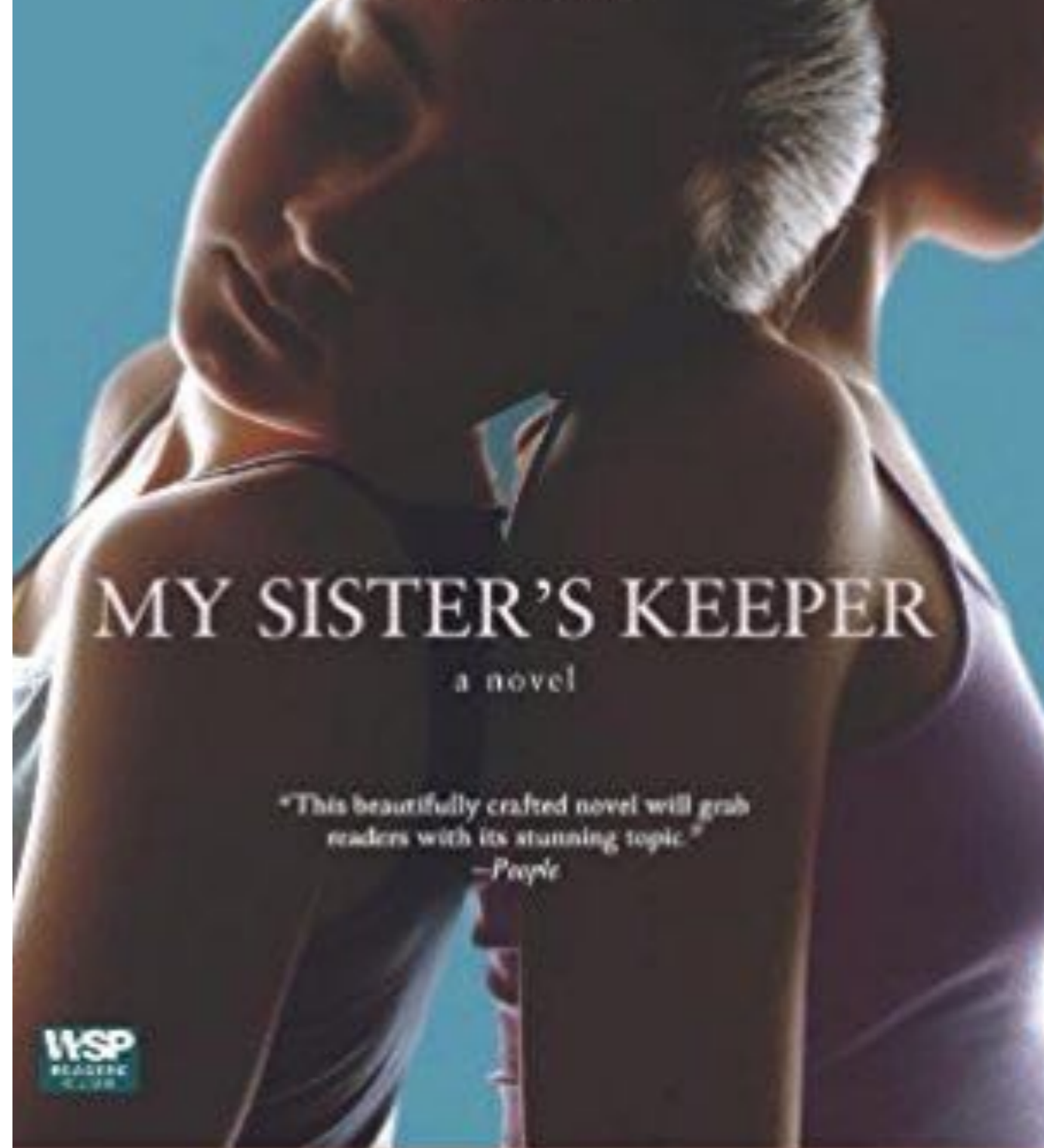
Bioethics Show & Tell

- * A new era of cloning is here — on the **polo** field: <https://www.cbsnews.com/news/a-new-era-of-cloning-is-here-on-the-polo-field/>
- * Senate passes '**right to try**' bill to help terminally ill patients get experimental drugs: https://www.washingtonpost.com/news/to-your-health/wp/2017/08/03/senate-passes-right-to-try-bill-to-help-terminally-ill-patients-get-experimental-drugs/?utm_term=.32ed75fb8352

Bioethics Show & Tell

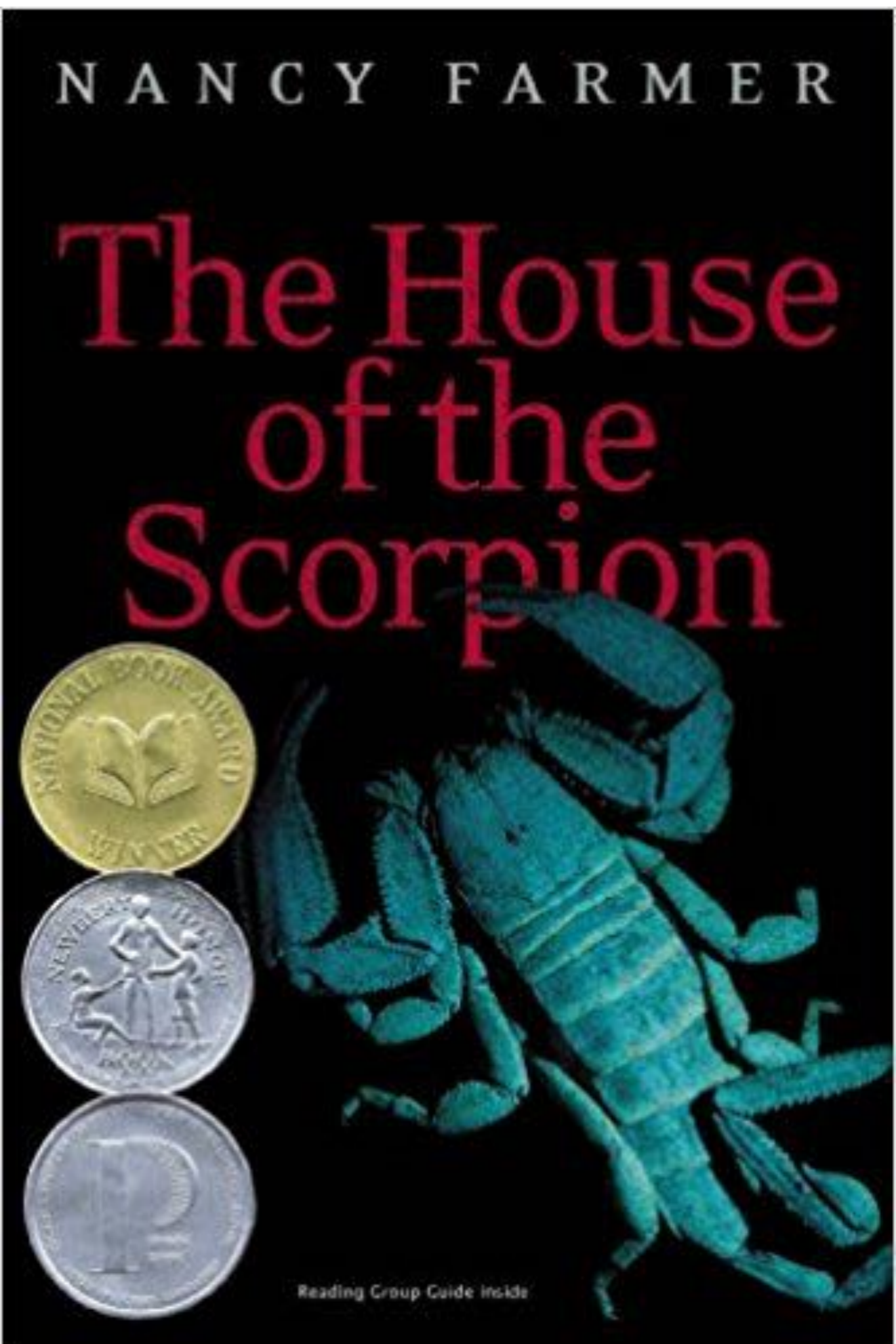
- * A new era of cloning is here — on the **polo** field: <https://www.cbsnews.com/news/a-new-era-of-cloning-is-here-on-the-polo-field/>
- * Senate passes '**right to try**' bill to help terminally ill patients get experimental drugs: https://www.washingtonpost.com/news/to-your-health/wp/2017/08/03/senate-passes-right-to-try-bill-to-help-terminally-ill-patients-get-experimental-drugs/?utm_term=.32ed75fb8352

- Anna is not sick, but she might as well be. By age thirteen, she has undergone countless surgeries, transfusions, and shots so that her older sister, Kate, can somehow fight the leukemia that has plagued her since childhood.
- The product of preimplantation genetic diagnosis, Anna was conceived as a bone marrow match for Kate—a life and a role that she has never challenged...until now. Like most teenagers, Anna is beginning to question who she truly is. But unlike most teenagers, she has always been defined in terms of her sister—and so Anna makes a decision that for most would be unthinkable, a decision that will tear her family apart and have perhaps fatal consequences for the sister she loves.



JODI
PICOULT

- Matteo Alacrán was not born; he was *harvested*. His DNA came from El Patrón, lord of a country called Opium--a strip of poppy fields lying between the U.S. and what was once called Mexico.
- Matt's first cell split and divided inside a petri dish. Then he was placed in the womb of a cow, where he continued the miraculous journey from embryo to fetus to baby.
- He is a boy now, but most consider him a monster--except for El Patrón, who loves him as he loves himself, because Matt is himself.
- Escape is only chance Matt has to survive. But escape is no guarantee of freedom, because Matt is marked by his difference in ways he doesn't even suspect.



In U.S. First, Scientists Edit Genes of Human Embryos

- * **“U.S. First”**: Chinese scientists were the first to experiment with this breakthrough two years ago in mid-2015
- * Not only: should something be tried?
- * But also: what happens if others move forward and we do not?



New York Times
July 27, 2017

In U.S. First, Scientists Edit Genes of Human Embryos

- * **“Scientists Edit Genes of Human Embryos”**
- * Not allowed to develop for more than a few days
- * Never intended to be implanted into a womb.”
- * We are currently holding ourselves back.
- * Should we be?



**New York Times:
July 27, 2017**

F.D.A. Approves First Gene-Altering Leukemia Treatment, Costing \$475,000

- * U.S. Food and Drug Administration “approved the first-ever treatment that genetically alters a patient’s own cells to fight cancer, a milestone that is expected to transform treatment in the coming years.”
- * This particular treatment is for an especially aggressive type of leukemia, but many similar gene therapies are in the pipeline.
- * The half million dollar price tag is because a single-dose must be tailored for each individual, which can make the treatment both effective and expensive.



**New York Times:
August 30, 2017**

F.D.A. Approves First Gene-Altering Leukemia Treatment, Costing \$475,000

- * “First child to receive the therapy was Emily Whitehead, who was 6 and near death from leukemia in 2012 when she was treated....
- * Now 12, she has been free of leukemia for more than five years.”
- * Such possibilities open a whole new world beyond today’s typical regimen of “surgery, radiation, and chemotherapy.”



**New York Times:
August 30, 2017**

New Gene-Therapy Treatments Will Carry Whopping Price Tags

- * There are 34 in the final stages of testing necessary for F.D.A. approval, and another 470 in initial clinical trials
- * One drug, to prevent blindness in those with a rare genetic disease, for example, is expected to cost between \$700,000 and \$900,000 per patient on average



**New York Times:
September 11, 2017**

New Gene-Therapy Treatments Will Carry Whopping Price Tags

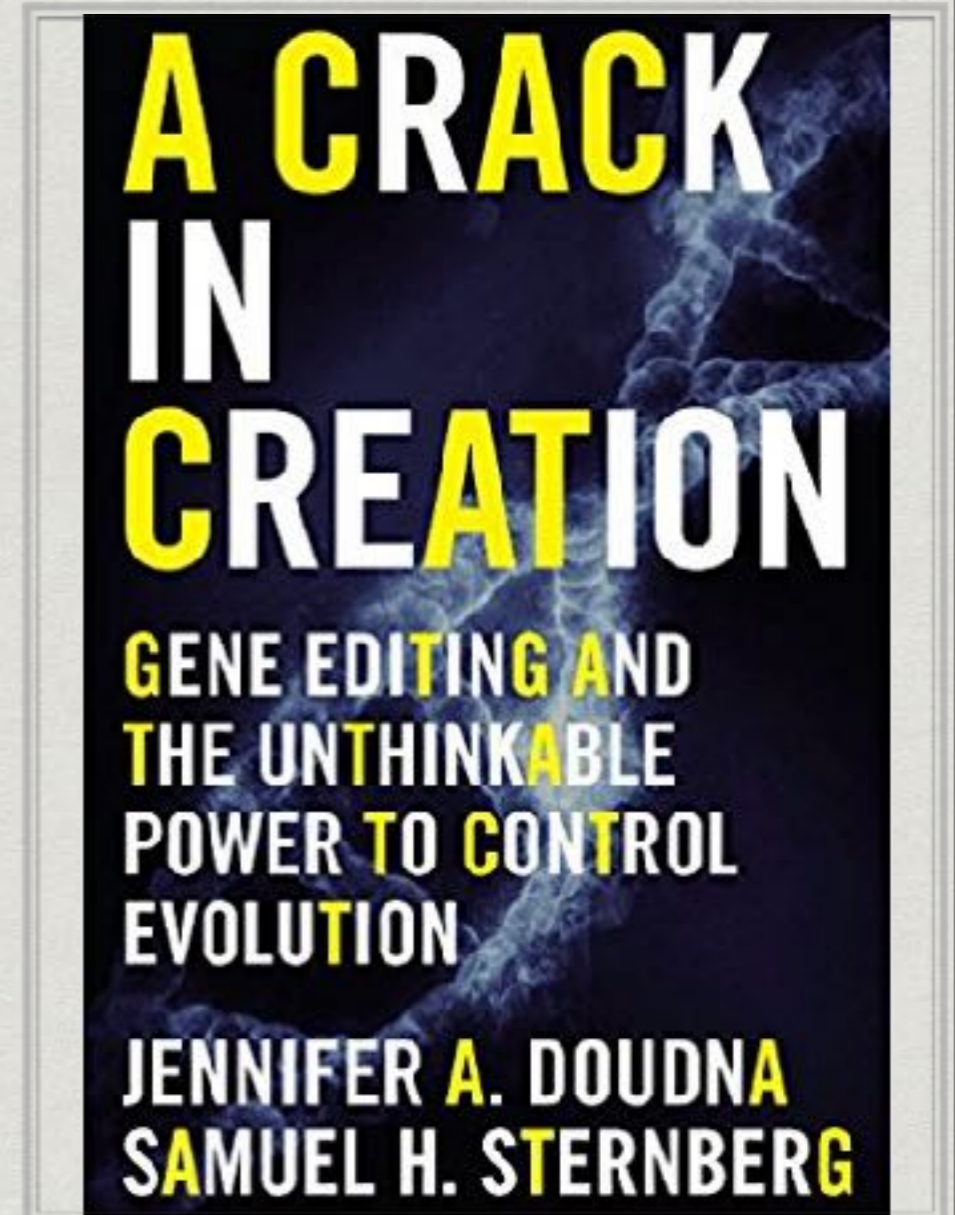
- * Drug makers: prices ought to reflect value of a curative treatment to patient. (*Should be worth a lot to keep your eyesight. “We should be compensated for generating that value.”*)
- * Don't pay the fire department that way. They don't ask, 'How much is it worth to you to put out the fire?'
- * One injection of drug could be expected to replace regular infusions of blood products that can cost \$5 million over 10 years.
- * Industry's warnings that without high reimbursements, field of gene therapy will wither is classic tale “Boy who cried wolf.”



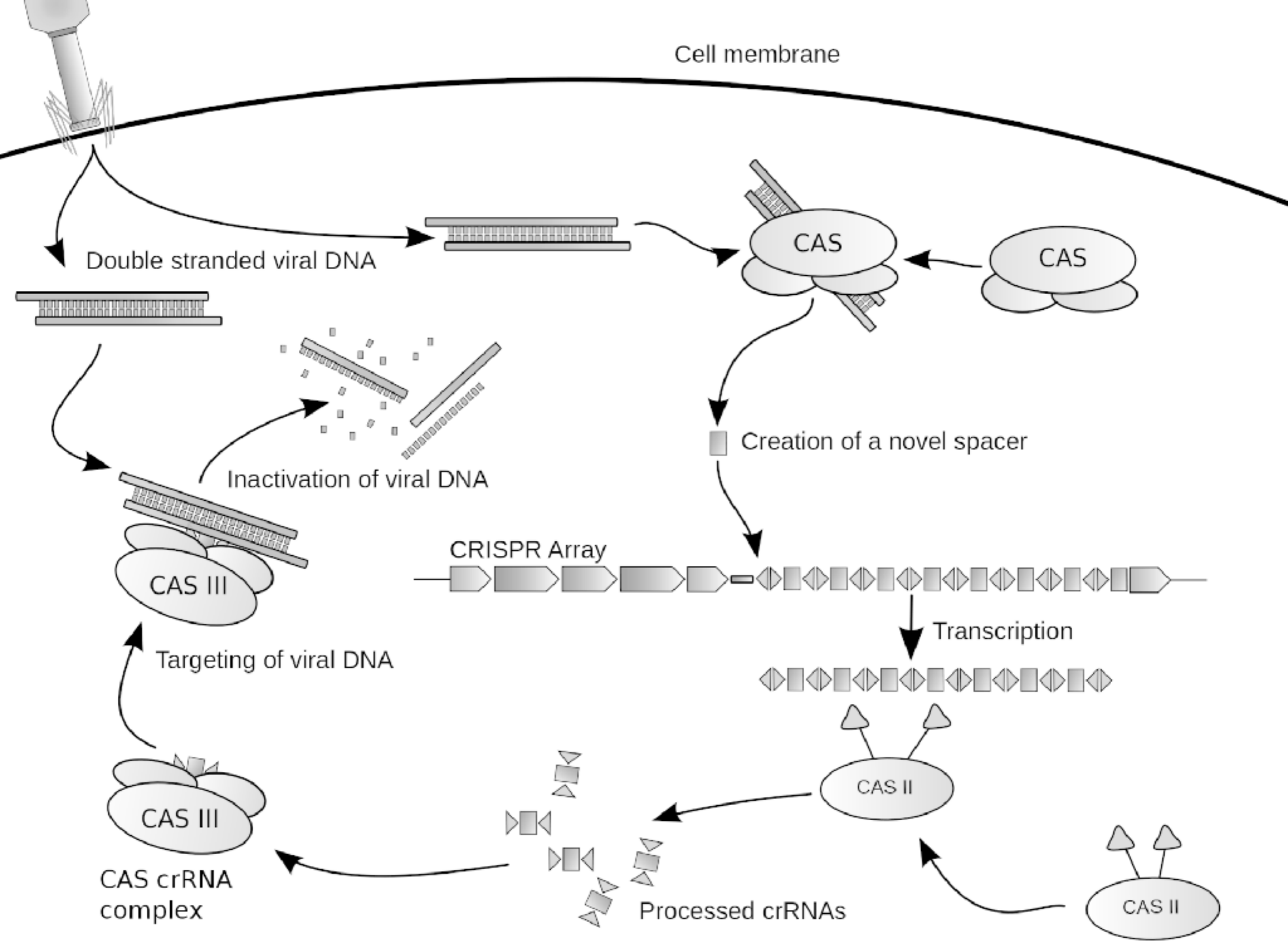
**New York Times:
September 11, 2017**

CRISPR

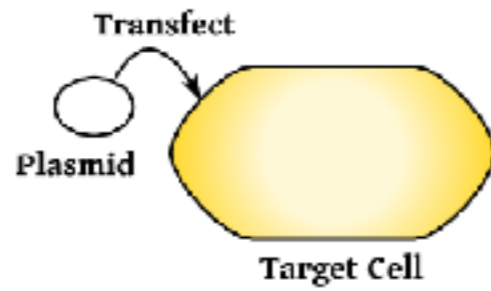
- * Clustered
- * Regularly
- * Interspaced
- * Short
- * Palindromic
- * Repeats



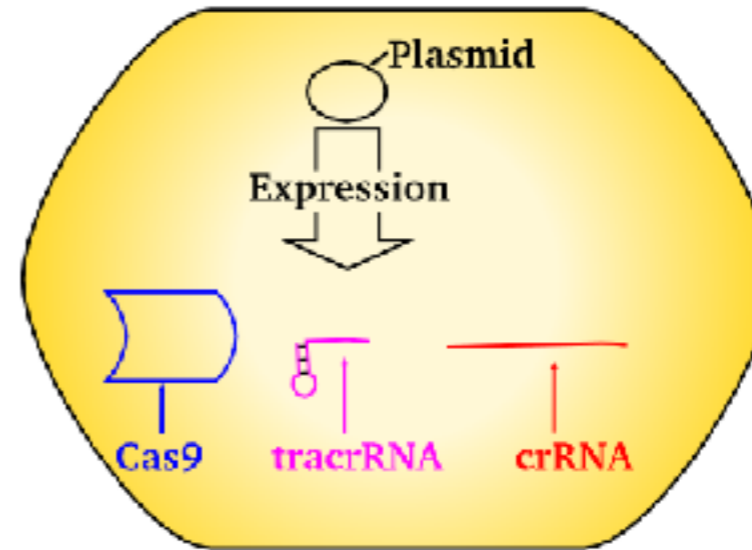
2017



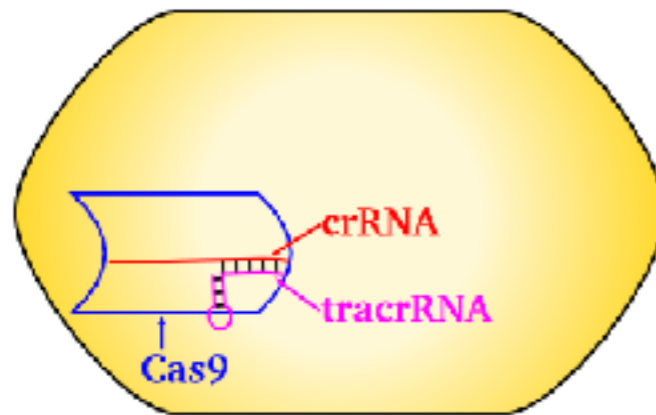
1: Transfection



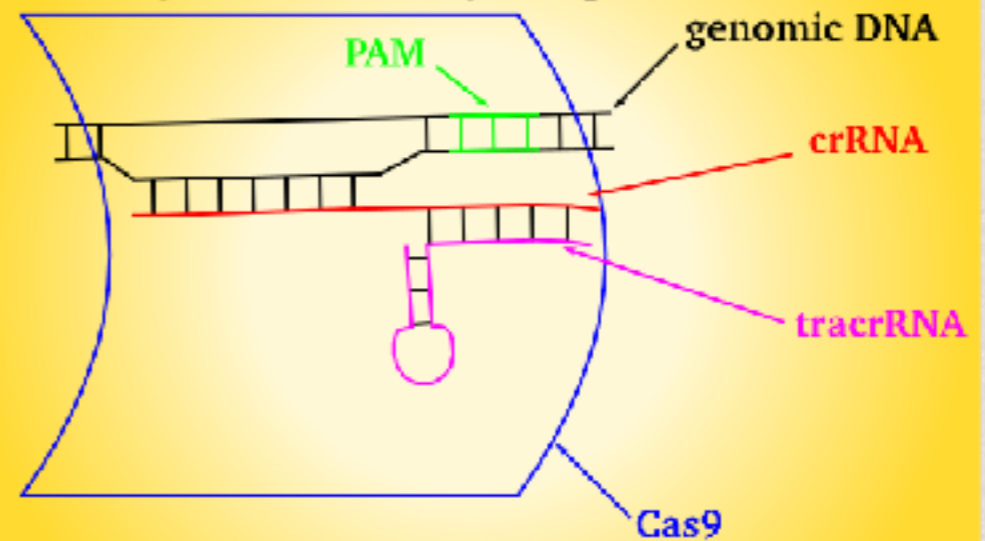
2: Expression of Plasmid



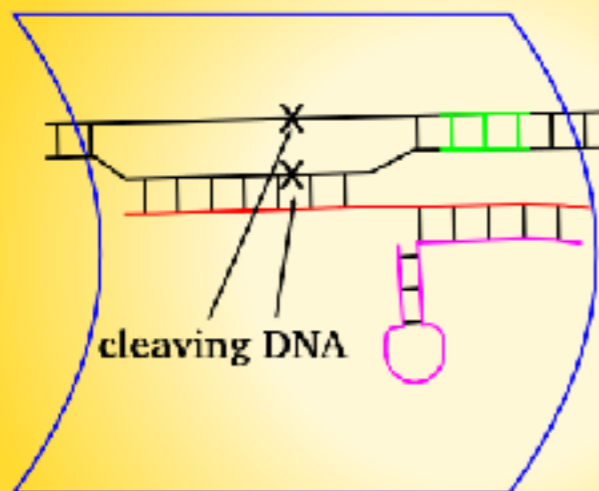
3: Activation of Cas9



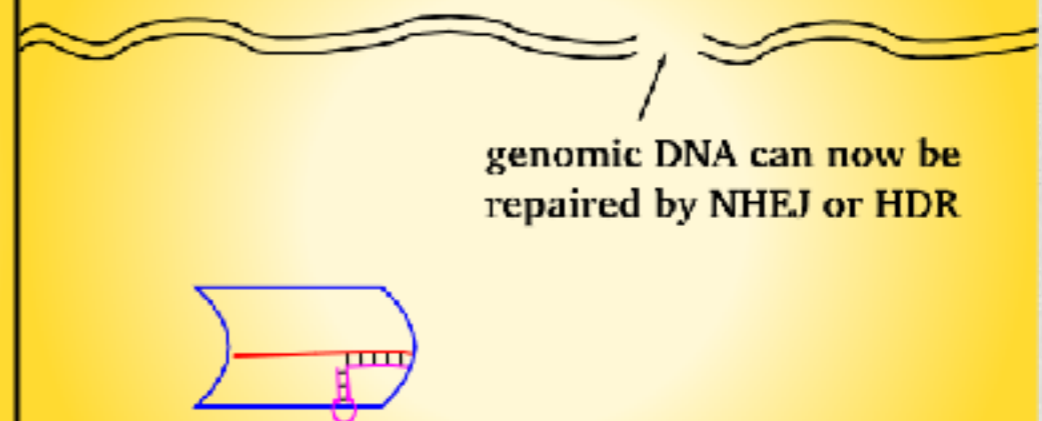
4: Binding to Genome Target Sequence



5: Cleaving Genomic DNA

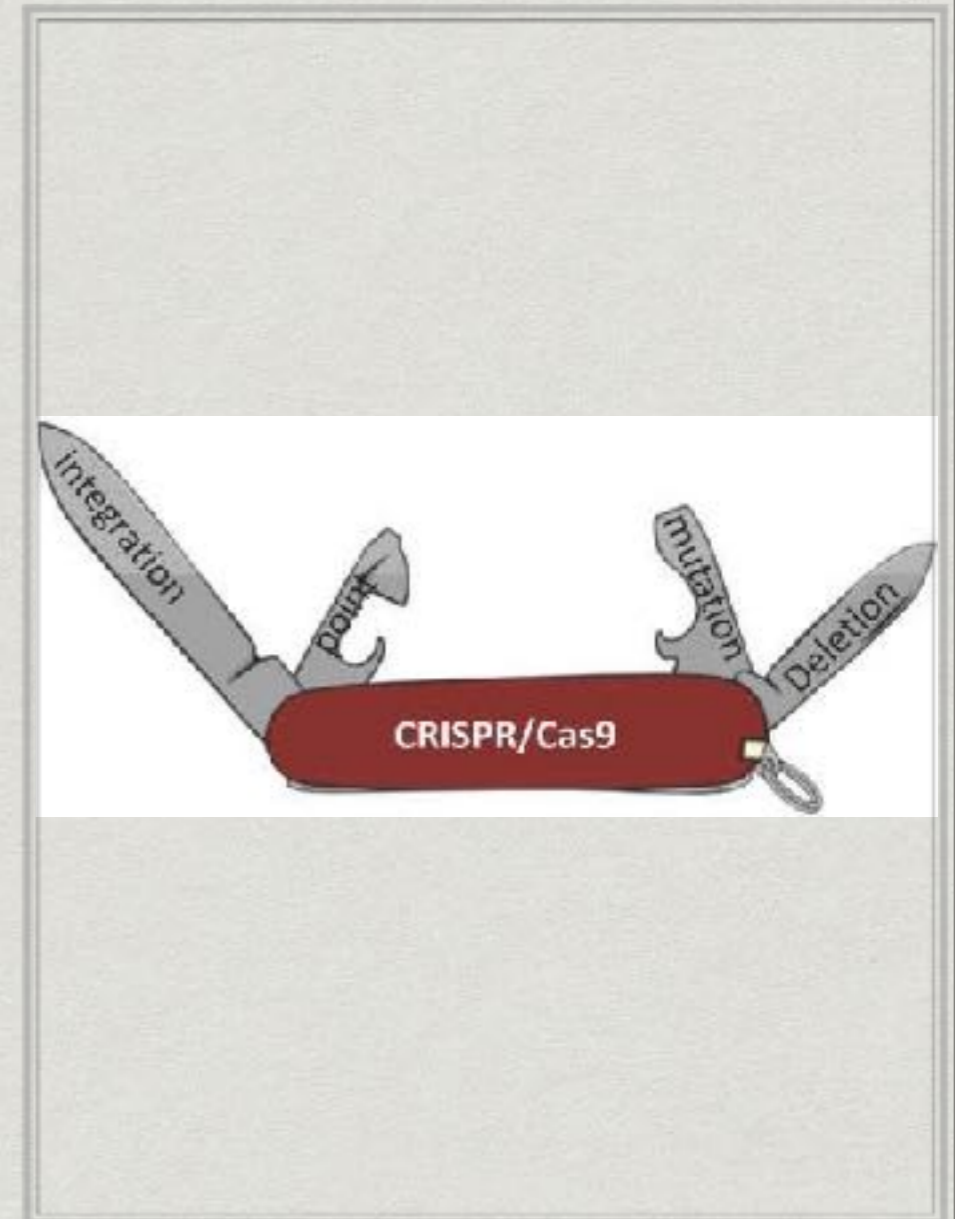


6: DNA is now ready for repair



CRISPR

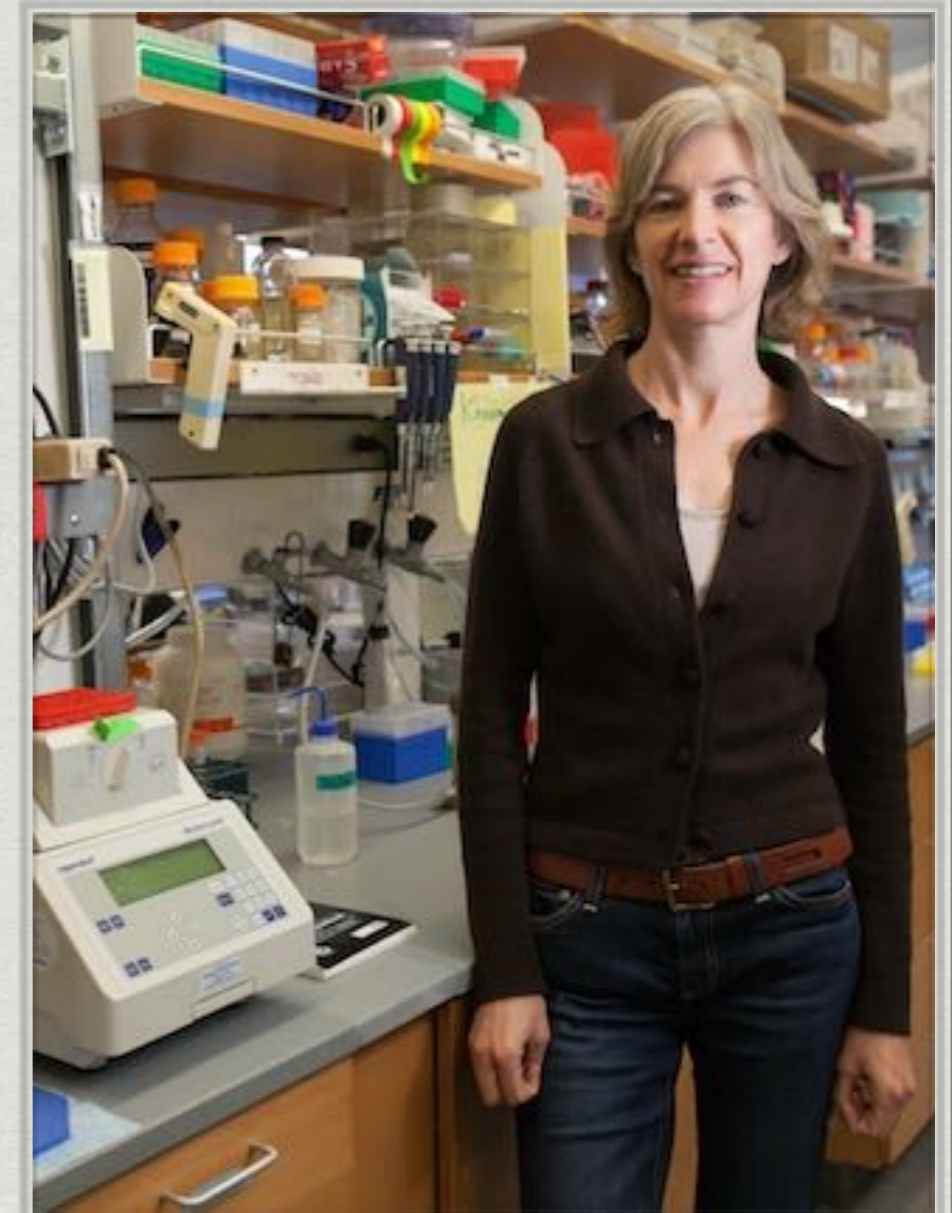
- * **“designer molecular Swiss army knife”**
- * “home in on specific twenty-letter DNA sequences and cut apart both strands of the double helix”
- * What it can do most easily: monogenic [Doudna 160-161]



2017

CRISPR

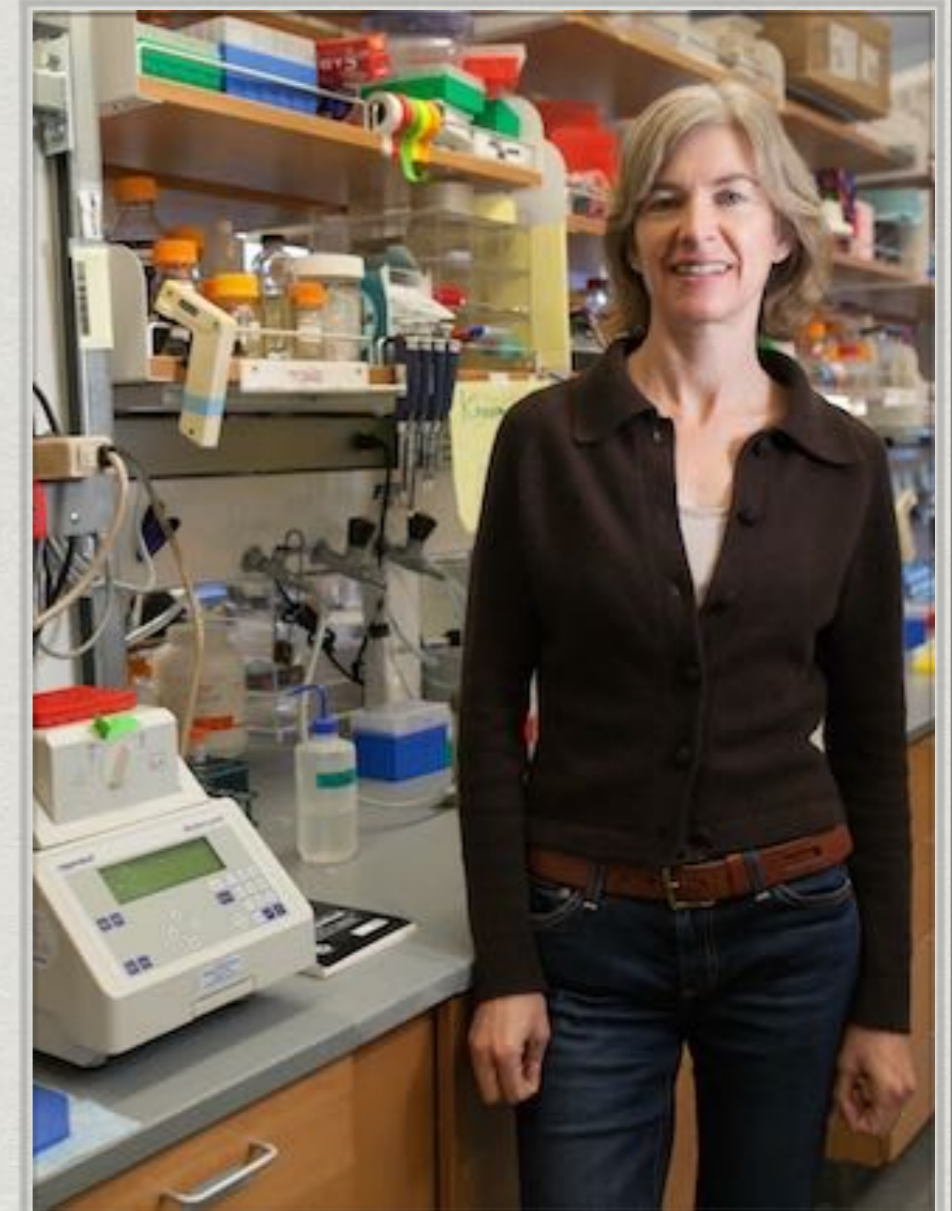
- * Doudna is a professor in the Chemistry and the Molecular and Cell Biology Departments at the University of California, Berkeley.
- * Sternberg is a fellow researcher and doctoral-level biochemist.



2017

CRISPR

- * Research: “way that bacteria defend themselves against viral infection.”
- * Stumbled on: “workings of an incredible molecular machine that could slice apart viral DNA with exquisite precision.
- * Utility of same machine to perform DNA manipulations in other kinds of cells, including human cells, immediately clear
- * *[c.f. 246]*



One's terrorist is another's freedom fighter
One's sacrilege is another's sacred duty

Some: any form of genetic manipulation is a perverse violation of the sacred laws of nature and the dignity of life.

- * Need outright ban on editing the genomes of unborn humans
- * Beware “Law of Unintended Consequences”

Others: genome is software—something we can fix, clean, update, and upgrade—and leaving humans beings at the mercy of faulty genetics is not only irrational, but immoral.

- * forge ahead without restraint.
- * Unethical not to use germline editing to alleviate human suffering

Scientific research is significantly outpacing public awareness of bioethical breakthroughs

- * Scientists have harnessed CRISPR to generate a genetically enhanced version of the beagle, creating dogs with Schwarzenegger-like super-muscular physiques by making single-letter DNA changes to a gene that controls muscle formation.
- * By inactivating a gene in the pig genome that responds to growth hormone, researchers have created micro-pigs, swine no bigger than large cats, which can be sold as pets....
- * Gene-editing experiments have produced disease-resistant rice, tomatoes that ripen more slowly, and soybeans with healthier polyunsaturated fat content....by fine-tuned genetic upgrades involving changes to just a few letters of the organism's own DNA....

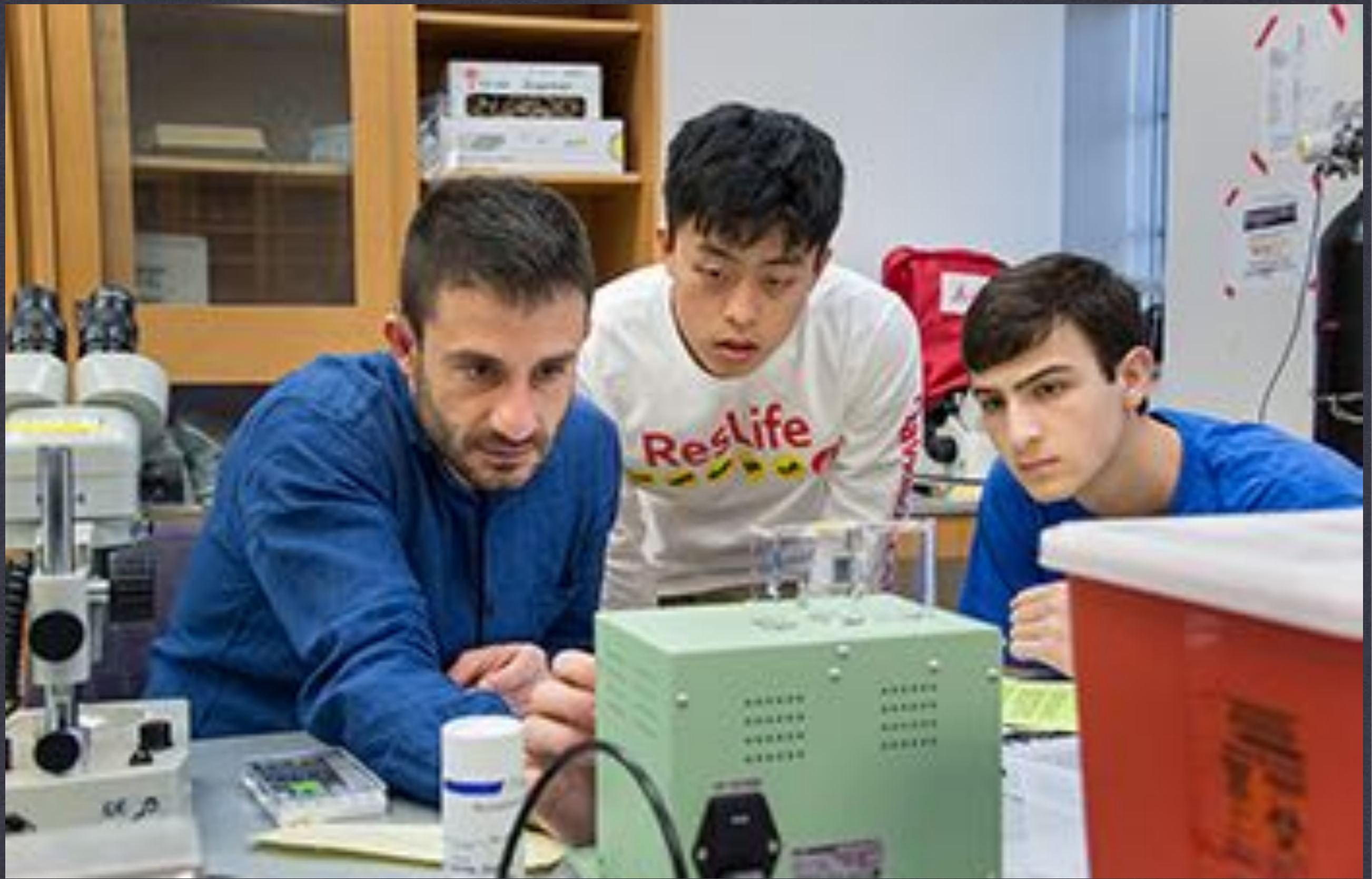
Scientific research is significantly outpacing public awareness of bioethical breakthroughs

- * CRISPR has been used to “humanize” the DNA of pigs, giving rise to hopes that these animals might someday serve as organ donors for humans....
 - * xeno-transplantation (*Doudna 140-142*)
- * In laboratory-grown human cells, this new gene-editing technology was used to correct the mutations responsible for cystic fibrosis and sickle cell disease, among many other disorders. [Doudna 169]



Wave Dream: Title, Theme, Affect, Question (TTAQ)

Doudna xi-xii



Low cost, Ease of use: CRISPR lab for ~\$2,000!

Doudna xi-xii



Precise & Fast compared to conventional breeding methods

Doudna 120-121

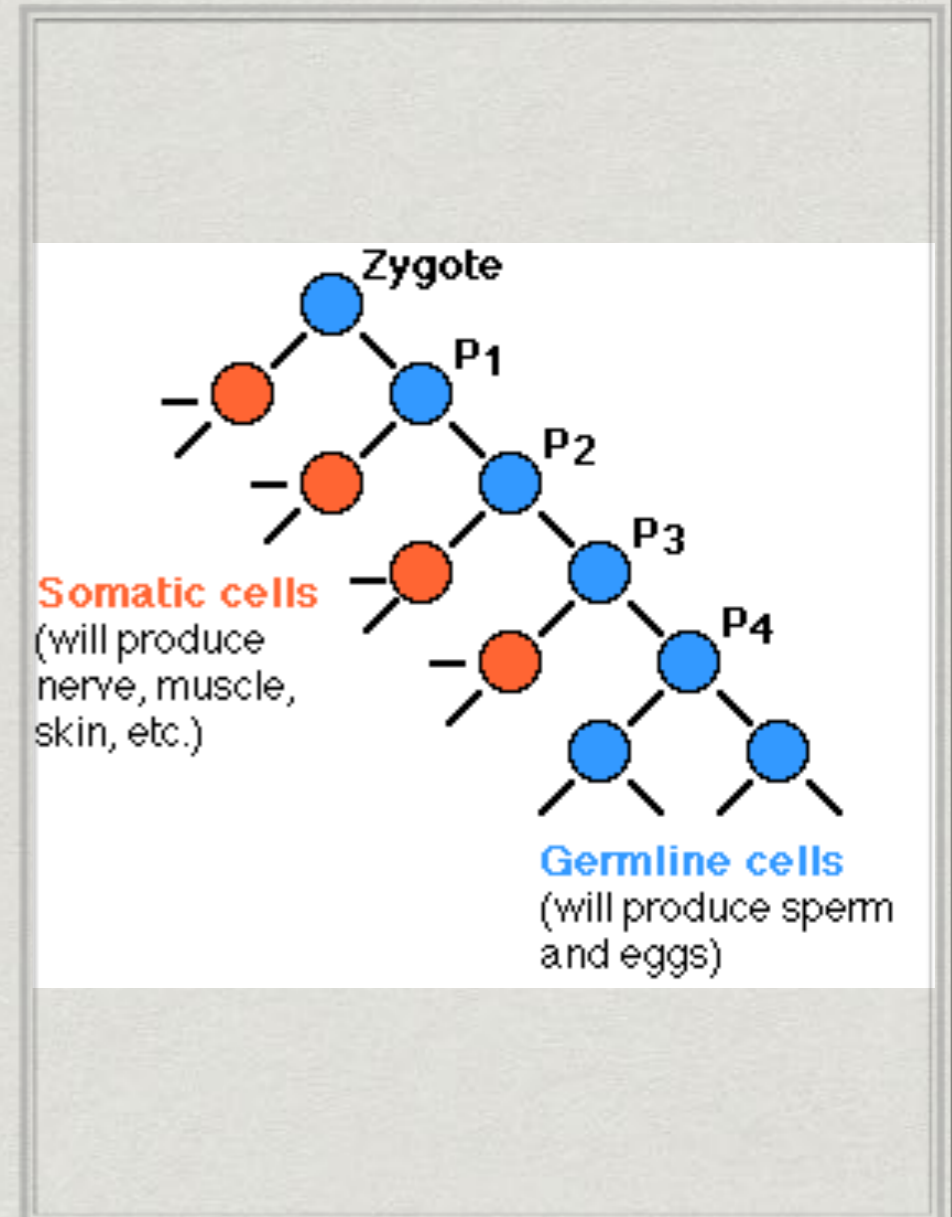
Prometheus

- * Deity in Greek mythology who was the creator of humanity and its greatest benefactor, who stole fire from Mount Olympus and gave it to humankind.”
- * With CRISPR, we are playing with fire with great potential for promise and peril.
- * Dr. Frankenstein’s “monster”?



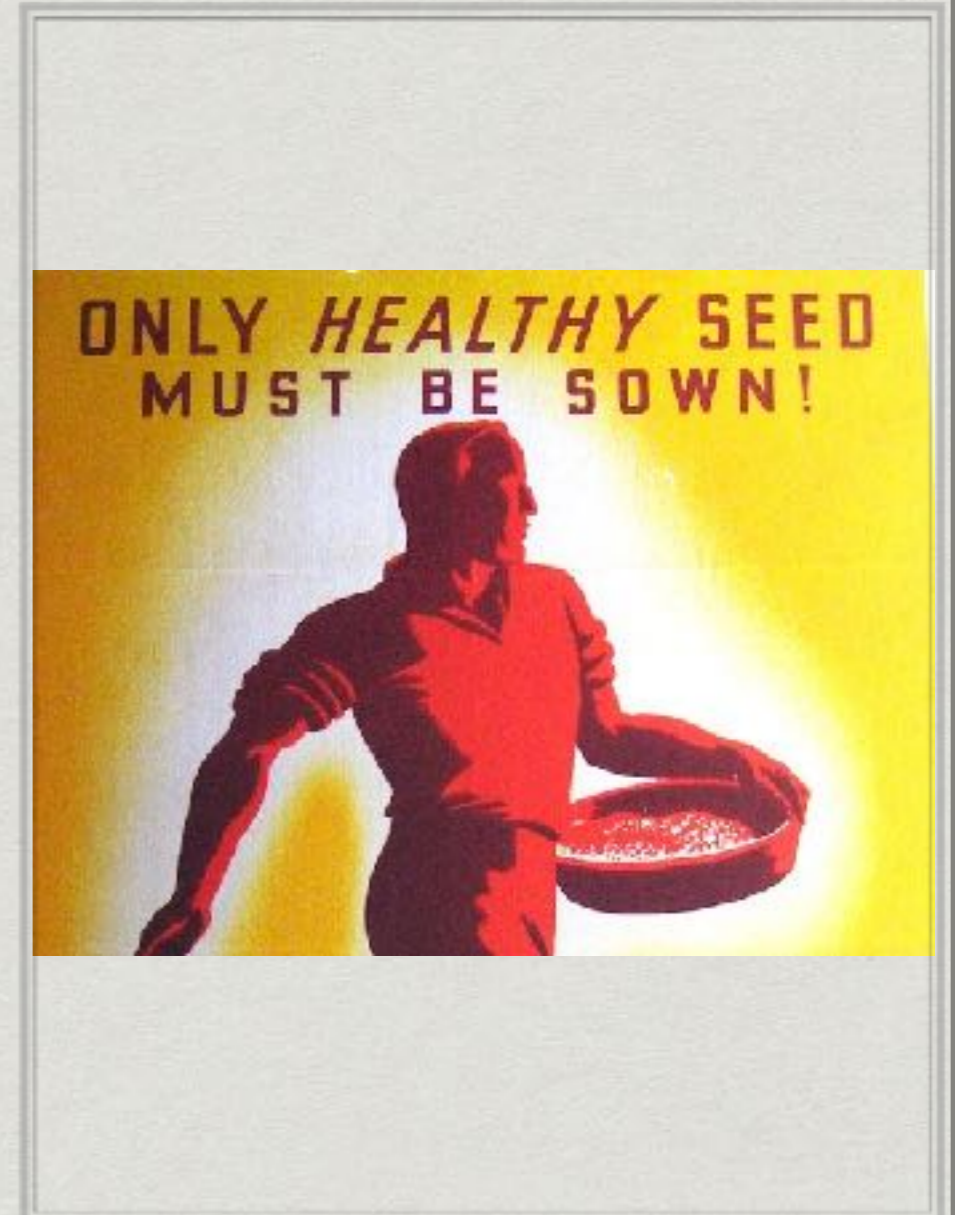
CRISPR

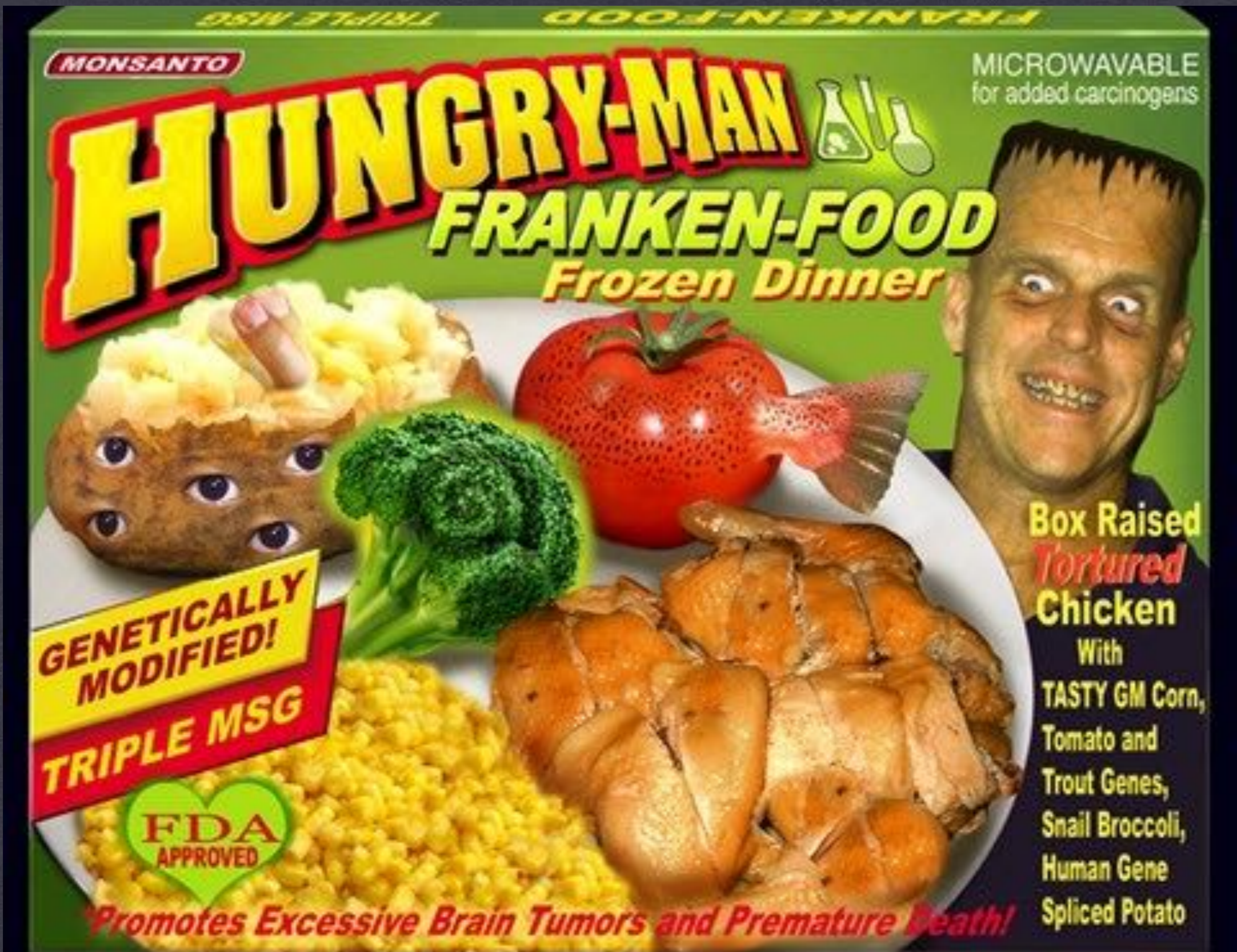
- * Not only alter *somatic* cells (throughout the “body” of individuals)
- * But also *germline* cells, whose traits can be inherited by future generations
- * We humans—ourselves products of the evolutionary process—have the power to micromanage the evolutionary process itself. (“*Stardust become aware of itself.*”)



CRISPR

- * Should we begin editing genes in unborn children to lower their lifetime risk of heart disease, Alzheimer's, diabetes, or cancer?
- * What about endowing unborn children with beneficial traits, like greater strength and increased cognitive abilities, or changing physical traits, like eye and hair color?
- * What about “savior siblings”? [Doudna 195]
- * Or: 3-parent IVF [Doudna 196]





Genetically Modified Organism (GMO): fetischzing “natural”?

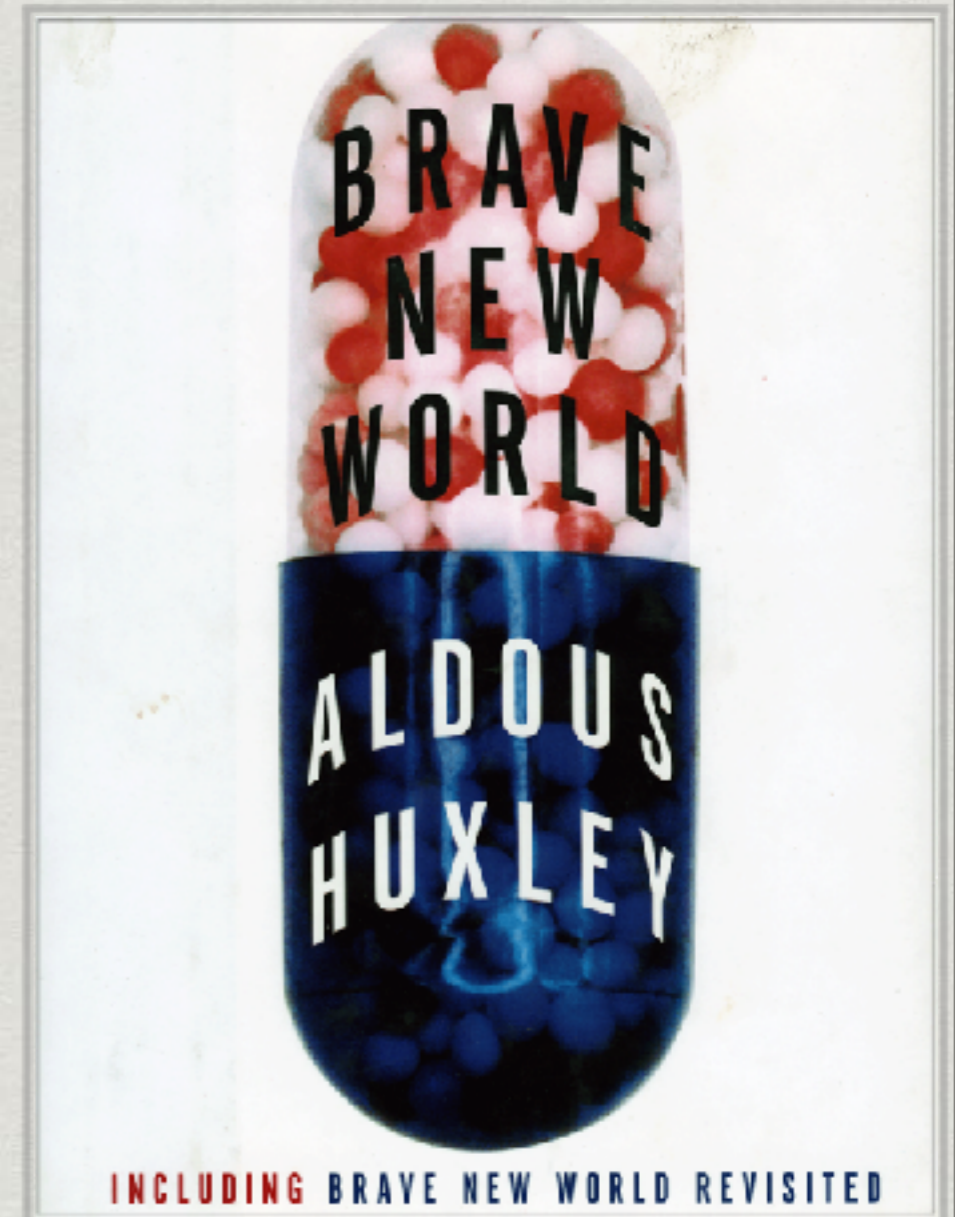


What is “Natural” and is it “best”?

Doudna 227-228

Fictional dystopia: 2540 (632 A.F., “After Ford”)

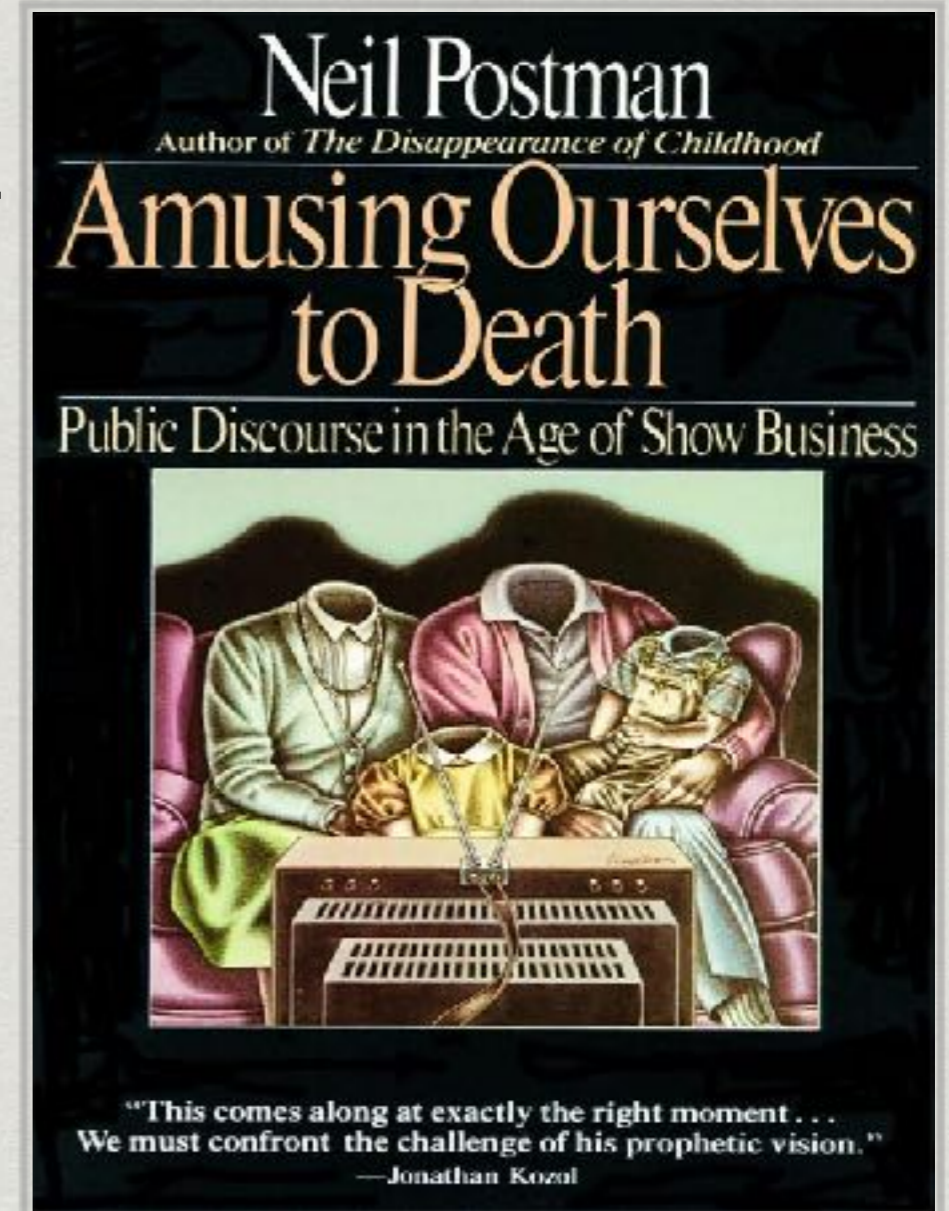
- * Citizens engineered through artificial wombs and childhood indoctrination programs into predetermined classes (or castes) based on intelligence and labour
- * Unlikely that genetic inequality—if it does result from germline editing—will take nearly that long to set in.



1932

Social Critic

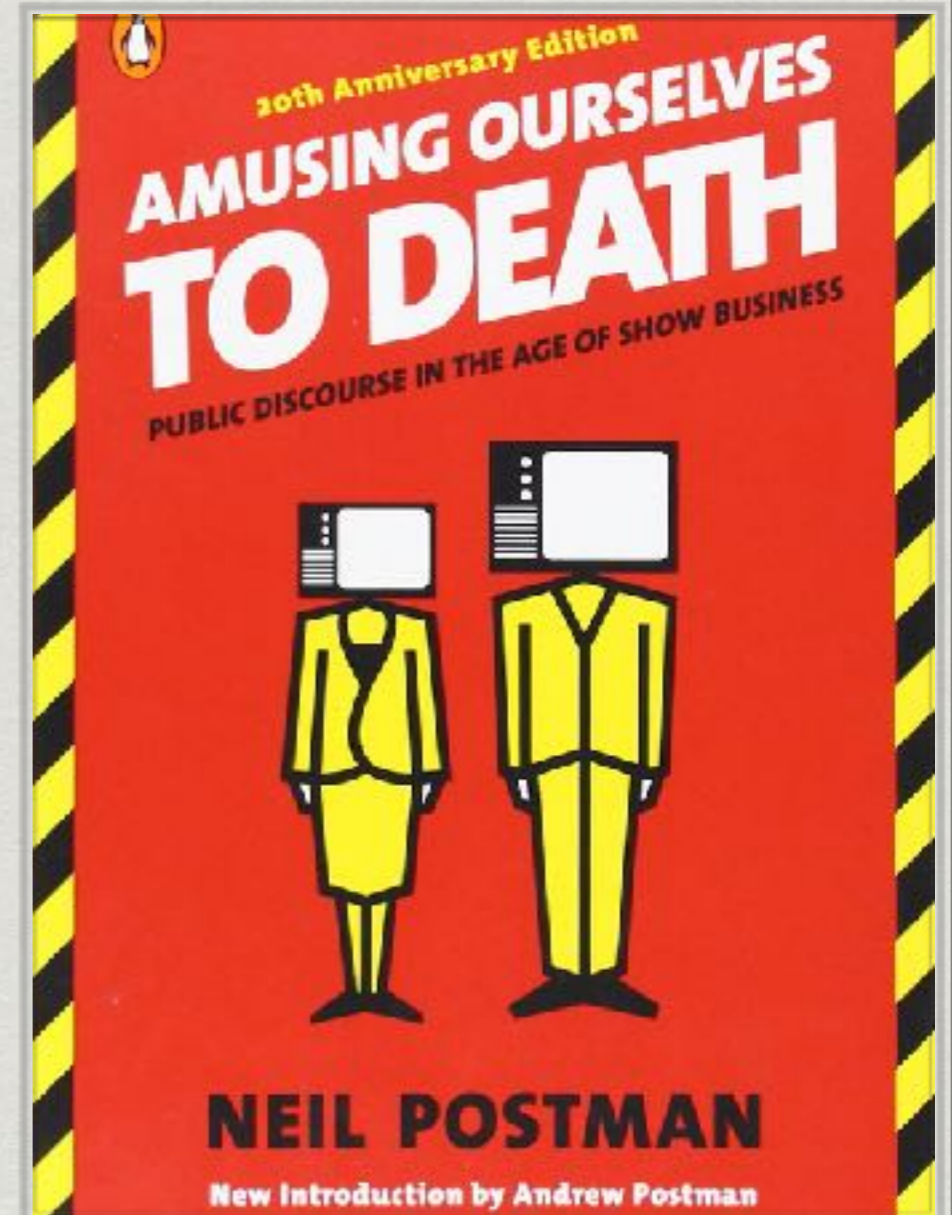
- * What Orwell feared were those who would *ban books*. What Huxley feared was that there would be no reason to ban a book, for there would be *no one who wanted to read one*.
- * Orwell feared those who would *deprive us of information*. Huxley feared those who would *give us so much* that we would be reduced to passivity and egotism.
- * Orwell feared that the truth would be *concealed* from us. Huxley feared the truth would be *drowned* in a sea of irrelevance.



1985

Social Critic

- * Orwell feared we would become a *captive* culture. Huxley feared we would become a *trivial* culture, preoccupied with some equivalent of the feelies, the orgy porgy, and the centrifugal bumblepuppy. Civil libertarians and rationalists who are ever on the alert to oppose tyranny "failed to take into account man's almost infinite appetite for *distractions*."
- * In "1984," people are controlled by inflicting pain. In "Brave New World," they are controlled by inflicting *pleasure*.
- * Orwell feared that our *fear* will ruin us. Huxley feared that our *desire* will ruin us.



1985

Christopher Hitchens: "Why Americans Are Not Taught History"

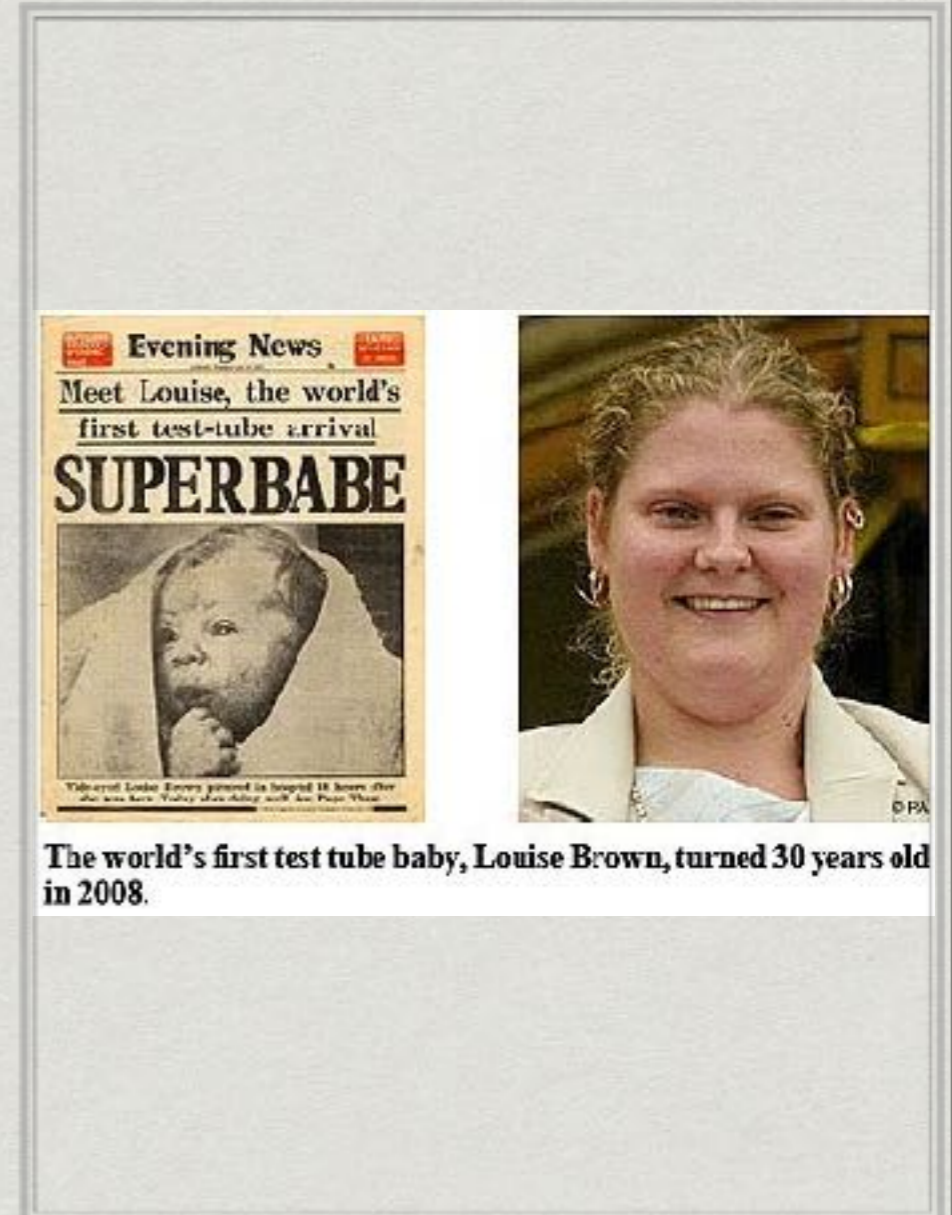
- * We dwell in a present-tense culture that somehow, significantly, decided to employ the telling expression "You're history" as a choice reprobation or insult, and thus elected to speak forgotten volumes about itself.
- * Orwell's was a house of horrors. He seemed to strain credulity because he posited a regime that would go to any lengths to own and possess history, to rewrite and construct it, and to inculcate it by means of coercion. Whereas Huxley ... rightly foresaw that any such regime could break because it could not bend.
- * In 1988, four years after 1984, the Soviet Union scrapped its official history curriculum and announced that a newly authorized version was somewhere in the works. This was the precise moment when the regime conceded its own extinction. For true blissed-out and vacant servitude, though, you need an otherwise sophisticated society where no serious history is taught.



(1949-2011)

1978

- * Louise Brown is born, world's first 'test-tube baby' ...
- * proving that human procreation could be reduced to simple laboratory procedures: the mixing of purified eggs and sperm in a petri dish,
- * fostering of a zygote as it grew into a multicellular embryo,
- * implantation of that embryo in the female womb.
- * In vitro fertilization, or IVF.



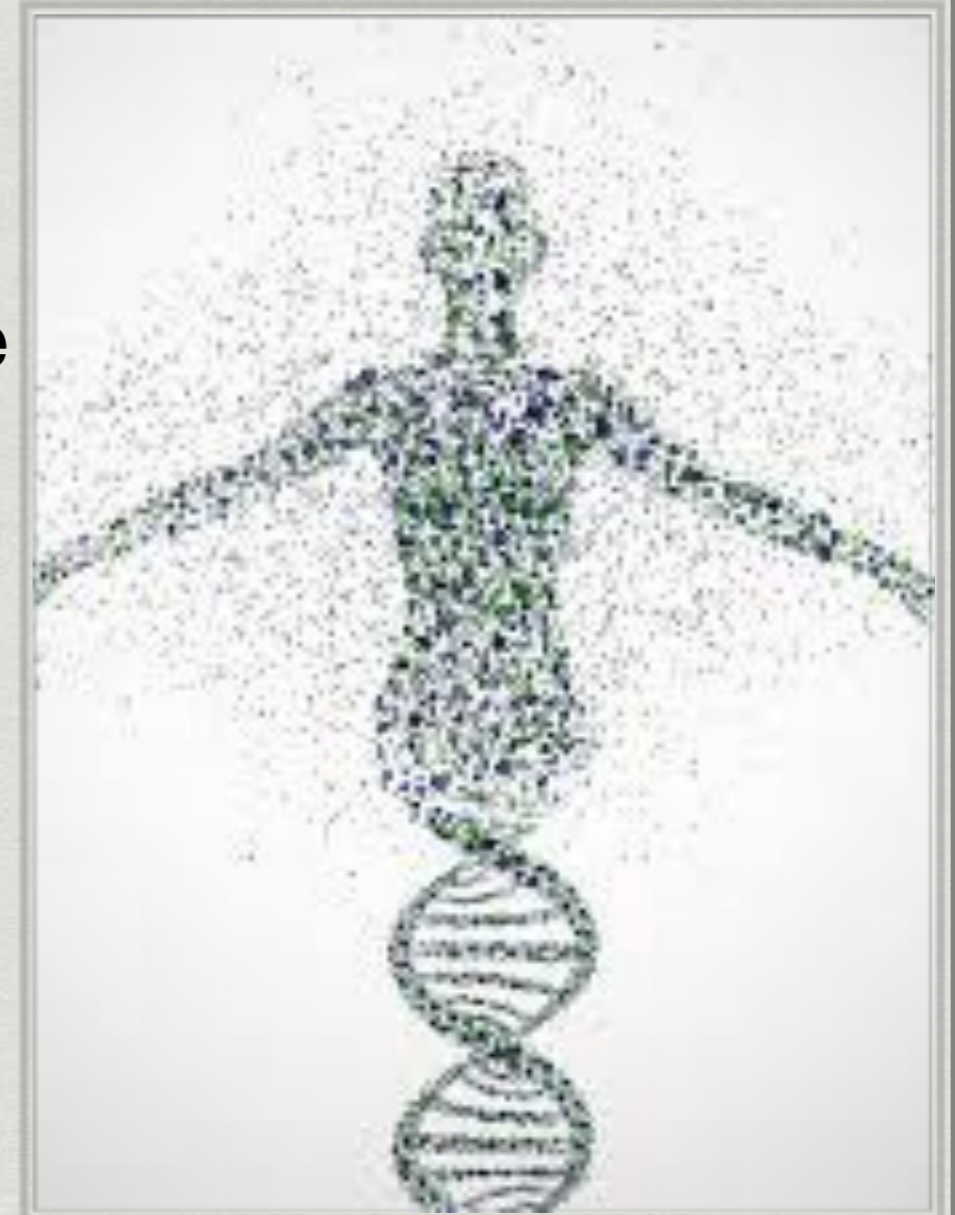
1990s

- * 1990: scientists teaming up around the world to sequence the human genome.
- * 1996: birth of Dolly the sheep, “the first successful cloning of a mammal”



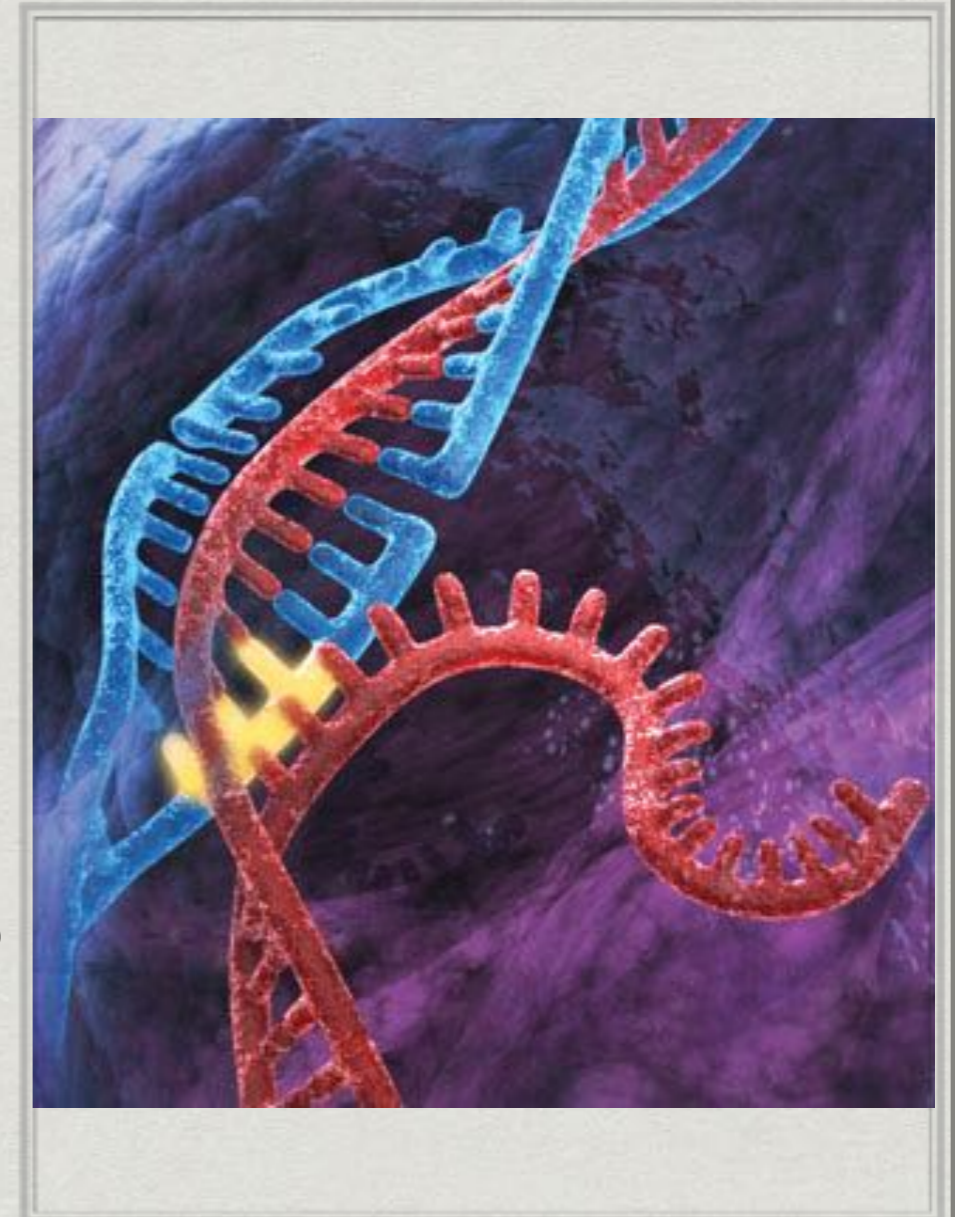
2001

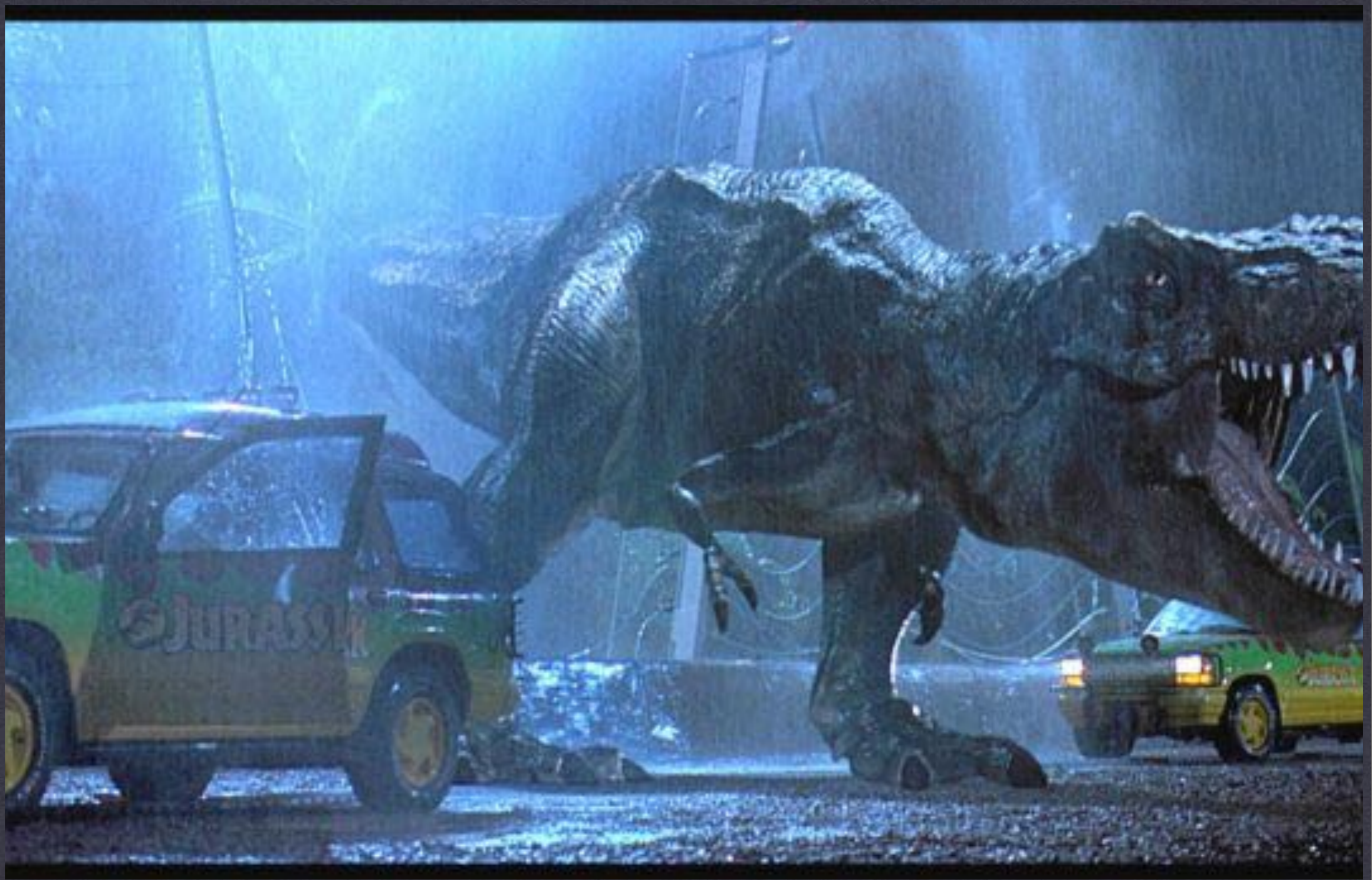
- * After herculean efforts and at a cost of more than 3 billion dollars, the first draft” of the Human Genome Project was completed.
- * Scientists able to edit individual genes at efficiencies of low-single-digit percentages. (Still not every efficient.)



CRISPR

- * Gene editing suddenly “so powerful and multifaceted that it is often referred to” as “genome engineering”
- * making “the human genome as easily manipulable as that of a bacterium”
- * Genome - coined in 1920 by German botanist Hans Winkler (*portmanteau of gene and chromosome*)





De-extinction

Doudna 118-119, 145

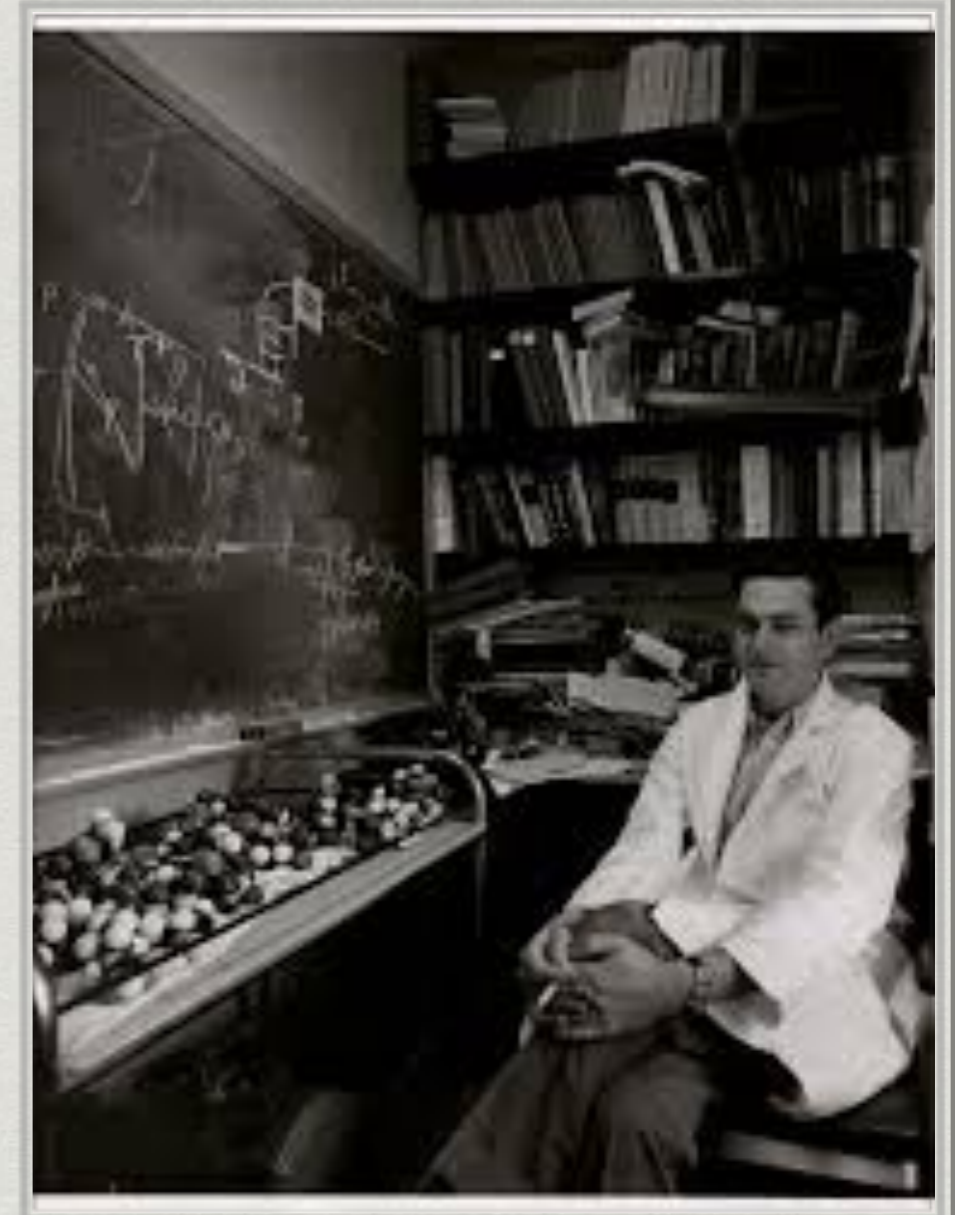
U.S. Senate Armed Services Committee Worldwide Threat Assessment

- * Classified genome editing as one of the six weapons of mass destruction and proliferation that nation-states might try to develop, at great risk to America.
- * (The others were Russian cruise missiles, Syrian and Iraqi chemical weapons, and the nuclear programs of Iran, China, and North Korea.)
- * Parallels: discovery of the atomic bomb.



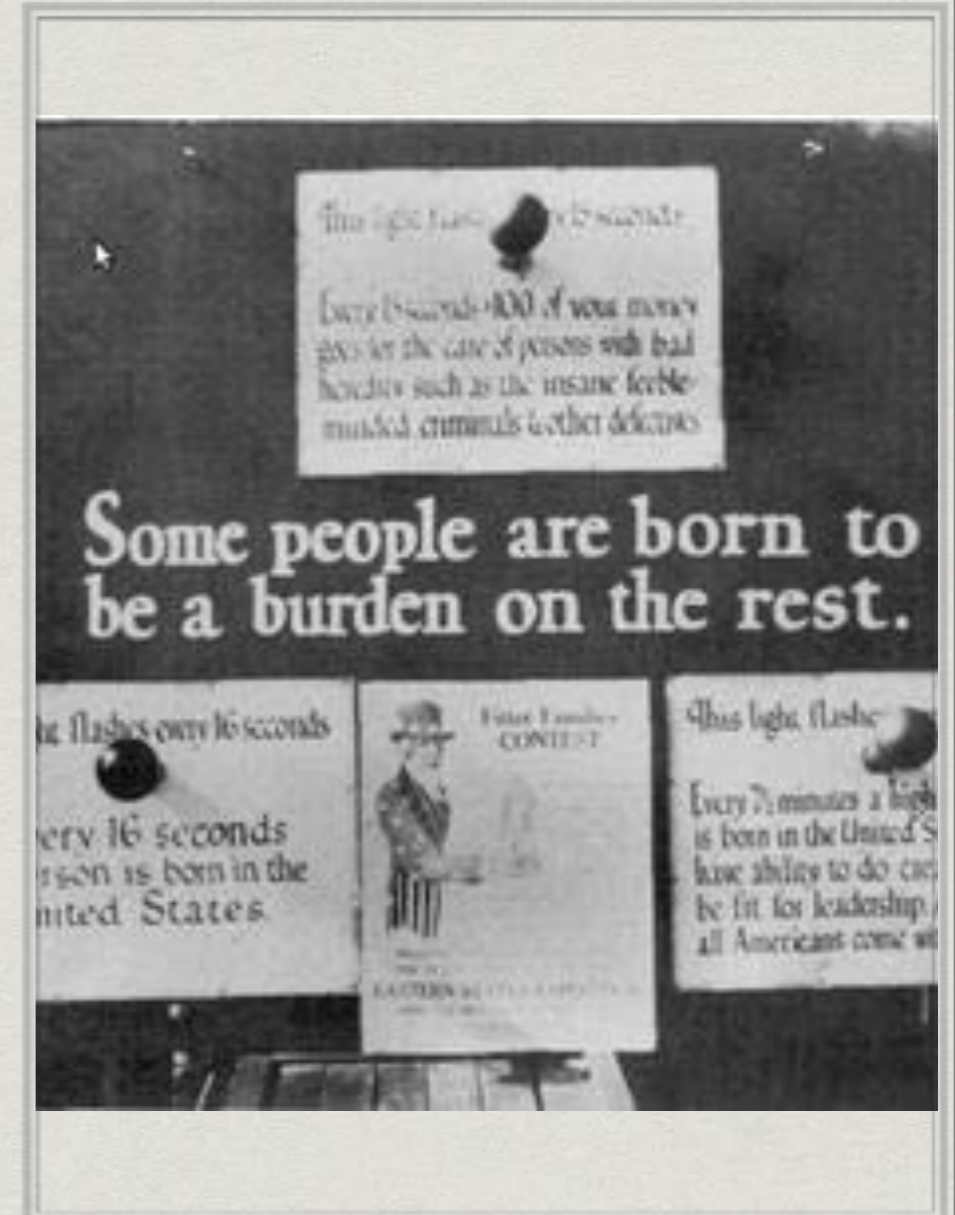
U.S. Senate Armed Services Committee Worldwide Threat Assessment

- * Not “if”
- * But: what, when, how, by whom?
- * Marshall Nirenberg (*shared 1968 Nobel Prize for “breaking the genetic code”*):
“[Humanity’s] [power to shape [it’s] own destiny can be used wisely or unwisely, for the betterment or detriment of [humankind]”



Eugenics?

- * 20th-century Eugenics: racist & repugnant
- * 21st-century bioethics: more complicated
- * Charles Sabine (*lives with Huntington's Disease*): “Anyone who has to actually face the reality of one of these diseases is not going to have a remote compunction about thinking that there is any moral issue at all.”



Ethical Guidelines

Pope Francis's message to Tim Cook, CEO of Apple:

- * “Never has humanity had such power over itself.
- * Yet nothing ensures it will be used wisely.”



Ethical Guidelines

Cook to MIT graduates:

- * Technology is capable of doing great things.
- * But it doesn't want to do great things.
- * It doesn't want anything.
- * That part takes all of us.
- * It takes our values, and our commitment, our love, our belief that all of us are interconnected, our decency, our kindness.

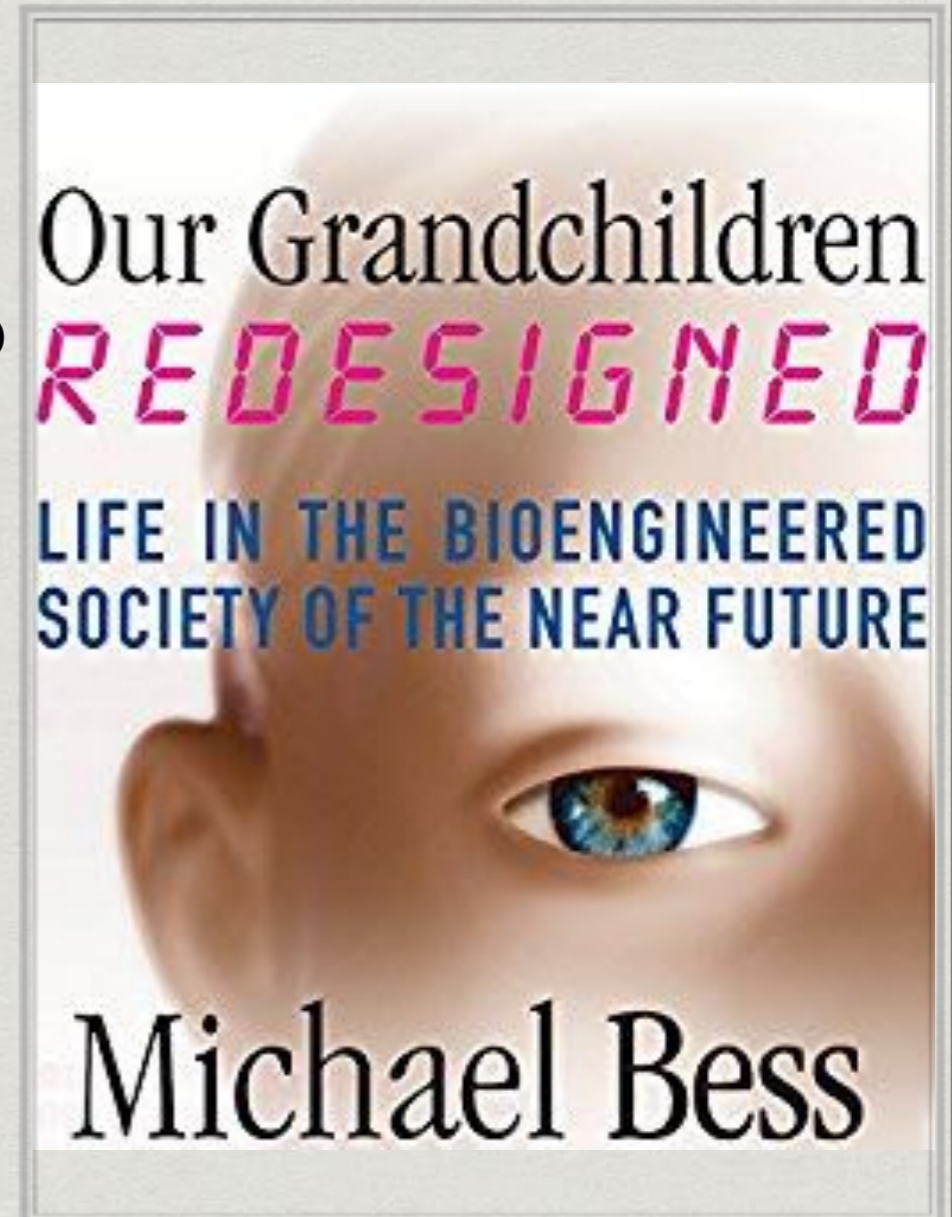


- * Professor of History at Vanderbilt University since 1989
- * Specializations: History of the social and ethical implications of technological change; twentieth-century European history
- * ***Our Grandchildren Redesigned: Life in the Bioengineered Society of the Near Future* (Beacon Press, 2015)**
- * *Choices Under Fire: Moral Dimensions of World War II* (Knopf, 2006);
- * *The Light-Green Society: Ecology and Technological Modernity in France, 1960-2000* (U. of Chicago Press, 2003; French Translation, 2011, Champ Vallon),
- * *Realism, Utopia, and the Mushroom Cloud: Four Activist Intellectuals and Their Strategies for Peace, 1945-1989.*(U. of Chicago Press, 1993).
- * Forthcoming: “What makes us human? From neurons to the Sistine Chapel” — how human personhood emerges from biological & social contexts



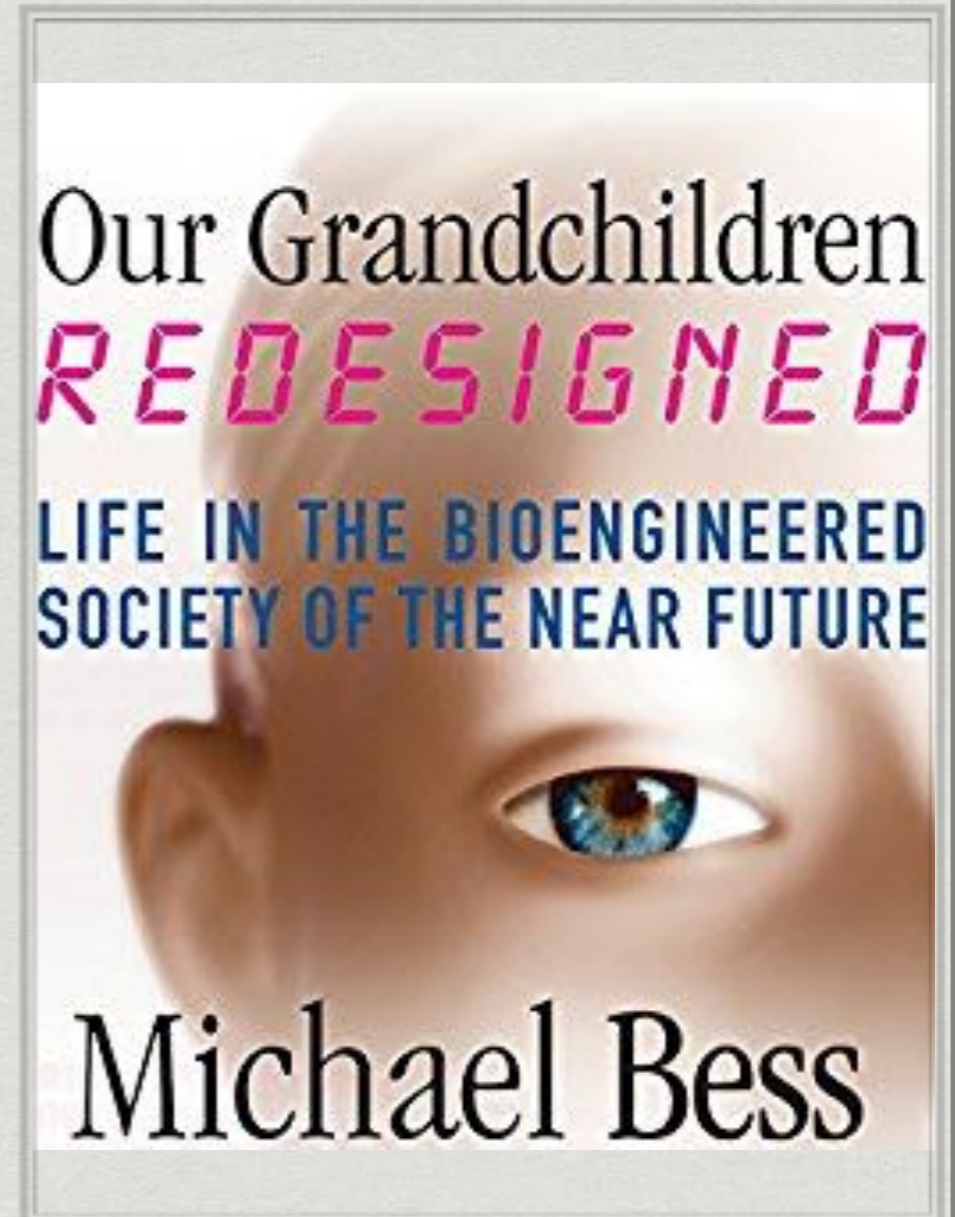
Michael Bess

- * Overview of biotechnologies that can significantly boost human capabilities and the drastic changes these “superhuman” traits could trigger
- * Biotechnology is **moving fast**. In the coming decades, advanced pharmaceuticals, bioelectronics, and genetic interventions will be used not only to heal the sick but to boost human physical and mental performance to unprecedented levels:
- * Pills - make humans stronger and faster,
- * Informatic devices - interface seamlessly with the human brain
- * Epigenetic modifications may allow people to reshape their own physical and mental identities at will.



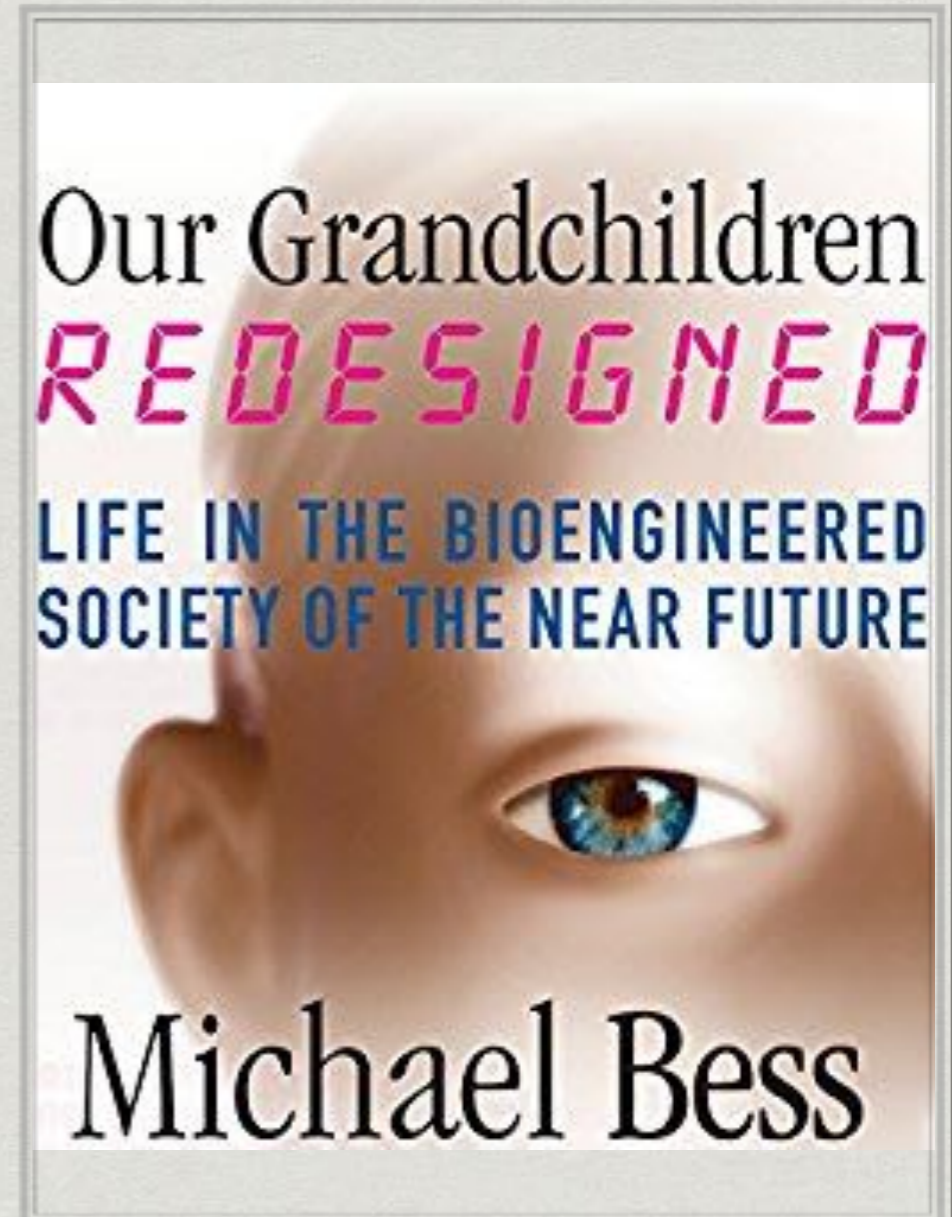
Beacon Press
2015

- * Until recently, such major technological watersheds—like the development of metal tools or the industrialization of manufacturing—came about **incrementally** over centuries or longer. People and social systems had time to adapt: they gradually developed new values, norms, and habits to accommodate the transformed material conditions (?)
- * Contemporary society is dangerously unprepared for the dramatic changes it is about to experience down this road on which it is already advancing at an accelerating pace.
- * Results will no doubt be mixed.



Beacon Press
2015

- * **Live longer, healthier lives**, fine-tune own thought processes, and generate staggeringly complex and subtle forms of knowledge and insight.
- * **Widen the rift between rich and poor**, generate new forms of social and economic division, and force people to engage in constant cycles of upgrades and boosts merely to keep up. [*Brave New World*]
- * Individuals who boost their traits beyond a certain threshold may acquire such extreme capabilities that they will **no longer be recognized as unambiguously human.**



Beacon Press
2015

How should humans respond?

- * Rejuvenation therapies offering **much longer lives** (160+) in full vigor and mental acuity
- * **Cognitive enhancement** through chemical or bioelectronic means (~doubling/tripling IQ scores)
- * Epigenetic tools for altering some genetically influenced traits at any point in lifetime (body shape, athletic ability, intelligence, personality)
- * Bioelectronic devices for **modulating your own brain processes**, including your “pleasure centers” (*potentially non-stop high*)
- * Direct control of machines by thought, and perhaps direct communication with other people, brain-to-brain (*new dimension of sharing & intimacy*)