Presentation on

Synthetic Biology:

DIY Tinkering Meets Big Capital

at Shaping San Francisco

by Pete Shanks

13 April, 2016

1964

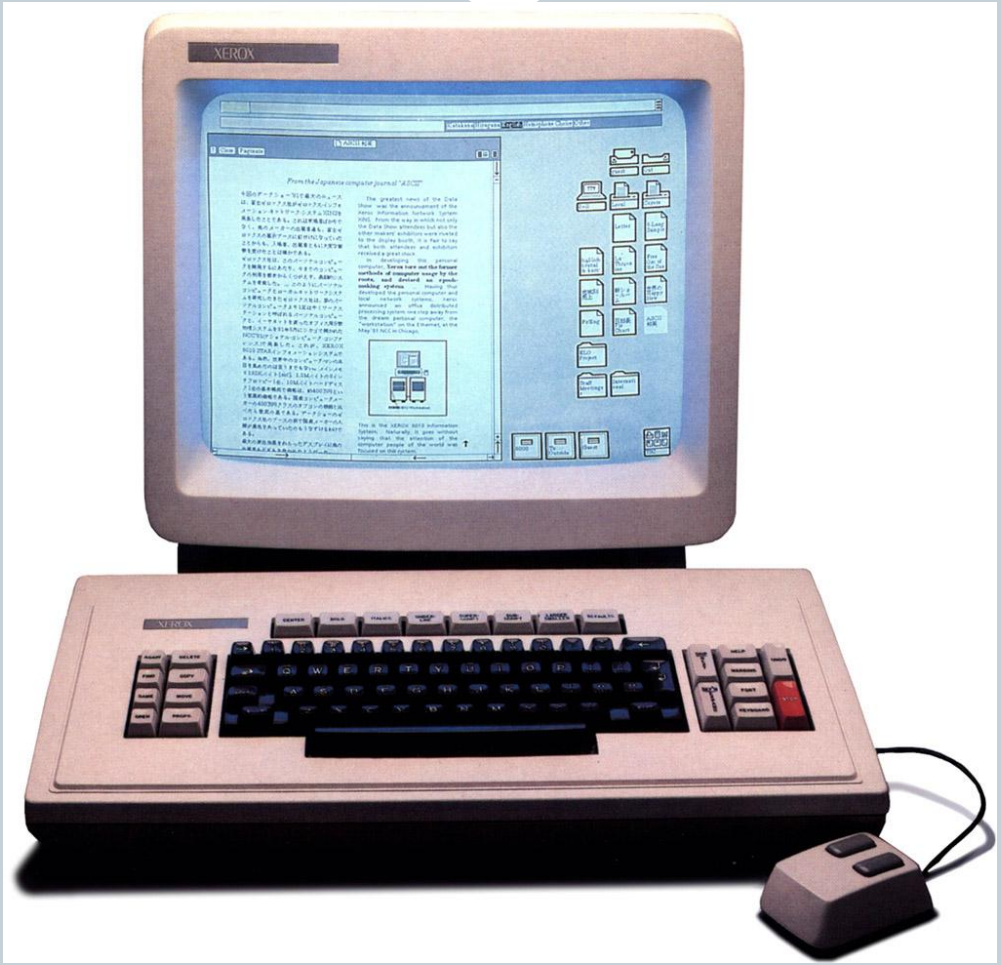
1972

1975

1981

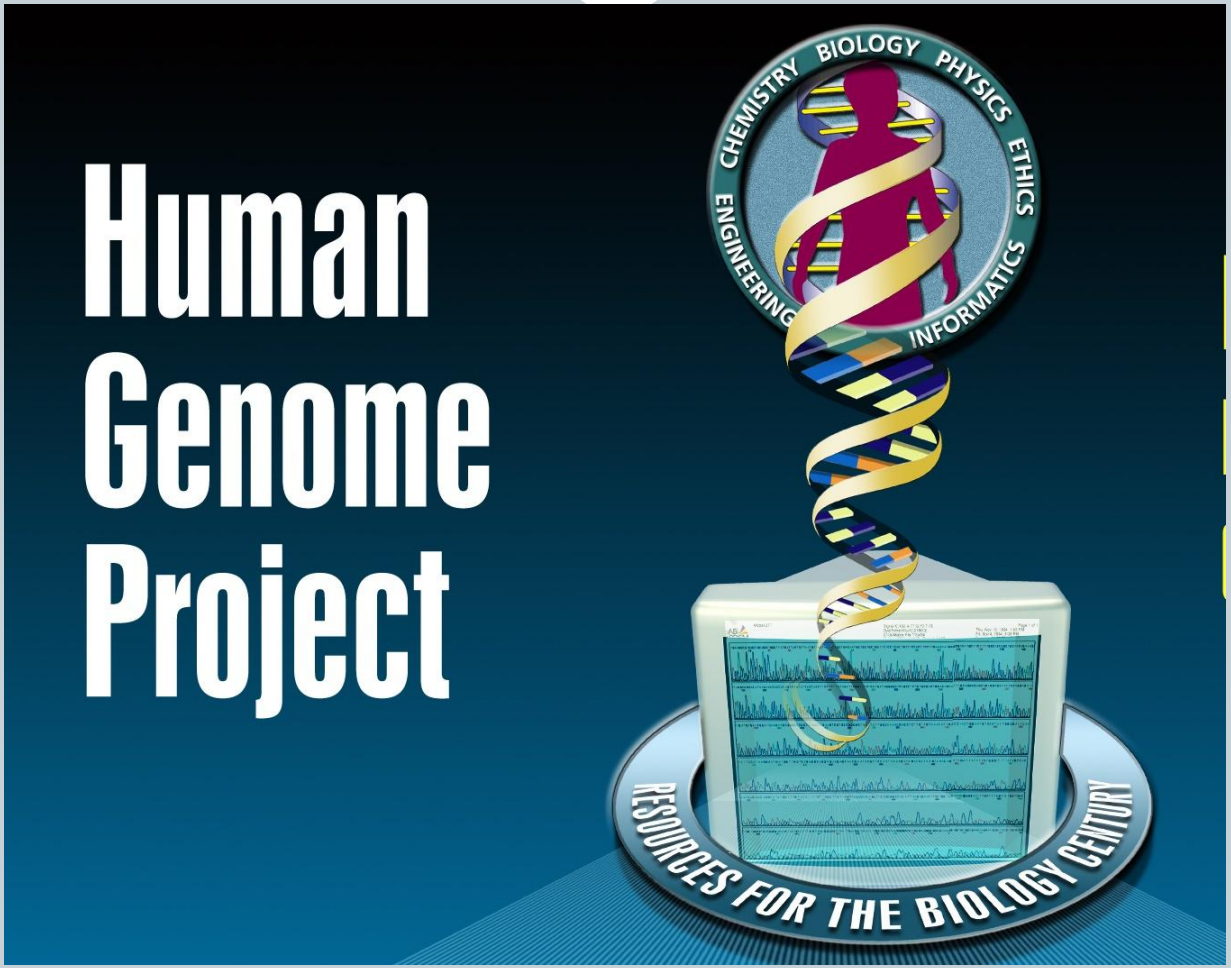
1982

1983



1986

1990–2003


Human
Genome
Project
CHEMISTRY
BIOLOGY
PHYSICS
ETHICS
ENGINEERING
INFORMATICS
RESOURCES FOR THE BIOLOGY CENTURY


GOD... THE HUMAN GENOME CODE'S BEEN UNRAVELLED
DAMN HACKERS!!! NOW, I HAVE TO CHANGE THE PASSWORD

Gene Editing Tools

- 1990s Various targeting vectors
- 2003–5 ZFN: Zinc Finger Nucleases
- 2009–11 TALENs: Transcription Activator-Like Effector Nucleases
- 2012 First CRISPR/Cas9 papers published: Clustered Regularly Interspersed Short Palindromic Repeats [with] CRISPR associated protein 9

Human Experiments (1)

- April, 2015 — Chinese scientists publish an attempt to modify human embryos using CRISPR, being careful not to begin any pregnancies
- The paper was published in *Protein & Cell* after both *Science* and *Nature* refused on ethical grounds
- The experiment failed: only a few embryos were changed, and many had "off-target" effects

Human Experiments (2)

- February, 2016 — British authorities approve in principle experimental genetic editing in embryos
- They will inactivate genes to study the effect on very early development, and stop within 14 days

Human Experiments (3)

- April, 2016 — a second Chinese team reports having edited the genes of human embryos in an attempt to make them resistant to HIV
- 4 of 26 were modified, not all successfully, but the attempt is called a proof of principle

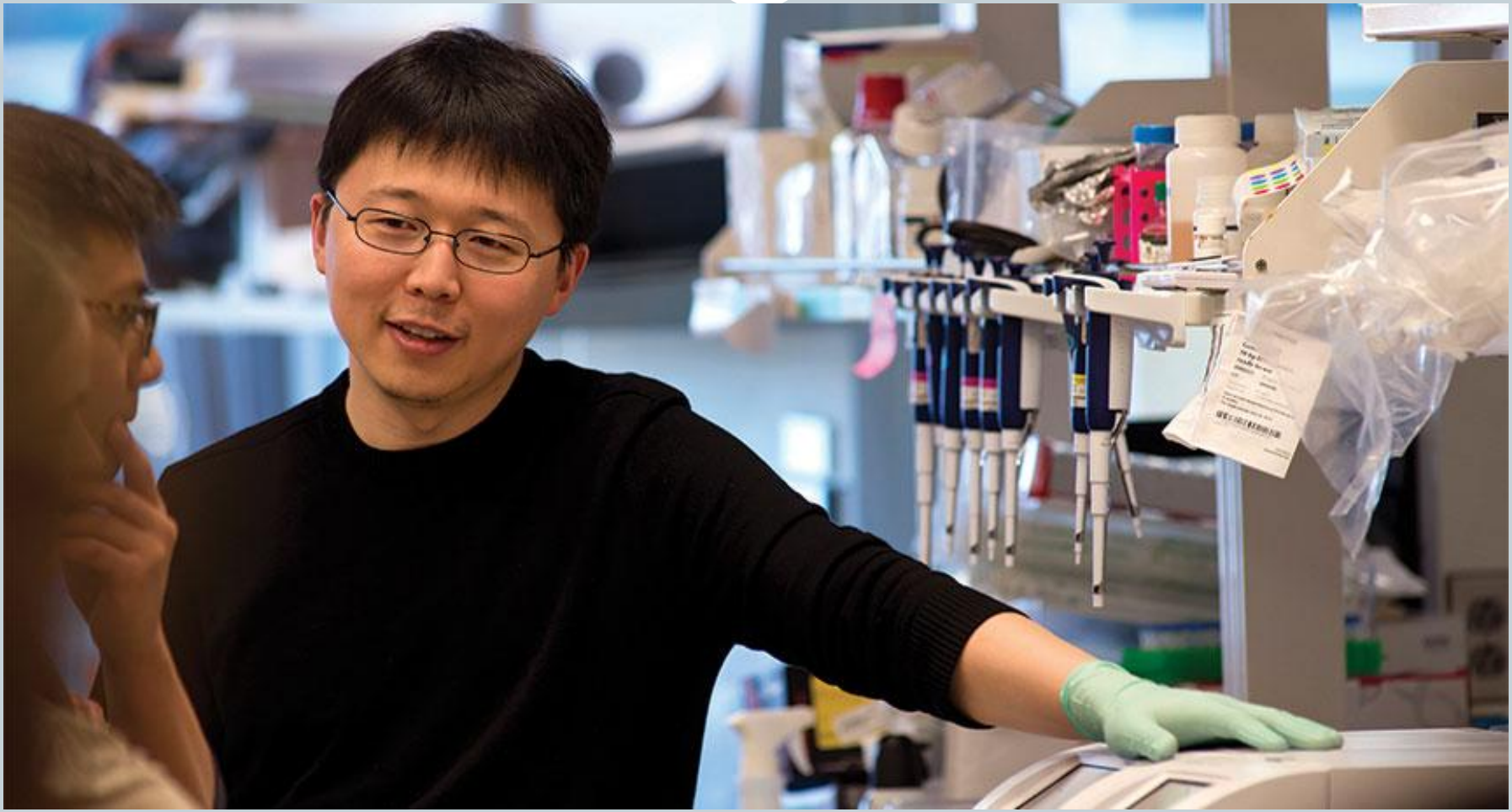
Why CRISPR?

	Rough cost per target gene	Target Validation Time*	Complexity Threshold**	Adoption of Technology	Mode of DNA Recognition	Mode of DNA Modification
Targeting Vectors	jn/a– varies massively	4-12 weeks	1-3	1990s	Vector DNA homology to Host genomic DNA	Host cellular machinery
Zinc Finger Nucleases (ZFNs)	$4000-$7000	8 weeks	Multiple	~2000	Zinc Finger Protein	Zinc Finger fused to Fok1 nuclease***
TALENs	$2500-$4000	8 weeks	Multiple	~2011	Transcription Activator Like Effector (TALE) Protein	TALE fused to Fok1 nuclease
Cas9	$50-$100	2-4 weeks	Multiple	~2013	guide RNA	cas9 intrinsic nuclease activity

From Techcrunch, May 2015

Emmanuelle Charpentier & Jennifer Doudna

Feng Zhang



George Church

A billion here, a billion there …

- These are not hippies in garages, they are tenured professors at UC Berkeley, Harvard and other major institutions
- There is a major patent fight in process, which may be worth billions (or not!)
- All the major players have founded companies, with significant venture capital behind them

editas MEDICINE

- Editas [Zhang, Church et al.] was the first to go public, in early February, raising $94 million
- That's on top of at least $230 million raised earlier; $75 million had been spent by last September
- Early shareholders included at least 7 venture capital funds, which together owned about ¾ of the stock: Flagship Ventures; Third Rock Ventures; Polaris Venture Partners; Bngo (a Bill Gates-affiliated fund) Viking Global; Fidelity; Deerfield

Intellia THERAPEUTICS

- Intellia [Doudna et al.] has important funding from Novartis, Atlas Venture, OrbiMed HealthCare Fund Management, Fidelity Management and Research, Janus Capital Management, Foresite Capital, Sectoral Asset Management, EcoR1 Capita …
- On Monday, Intellia filed for an IPO of $120 million

- CRISPR Therapeutics [Charpentier et al.] is also said to be looking to go public
- Meanwhile, they have a $350 million 5-year deal with Bayer, as well as other substantial funding
- Says CEO Rodger Novak:

Coming late to this party is not very smart

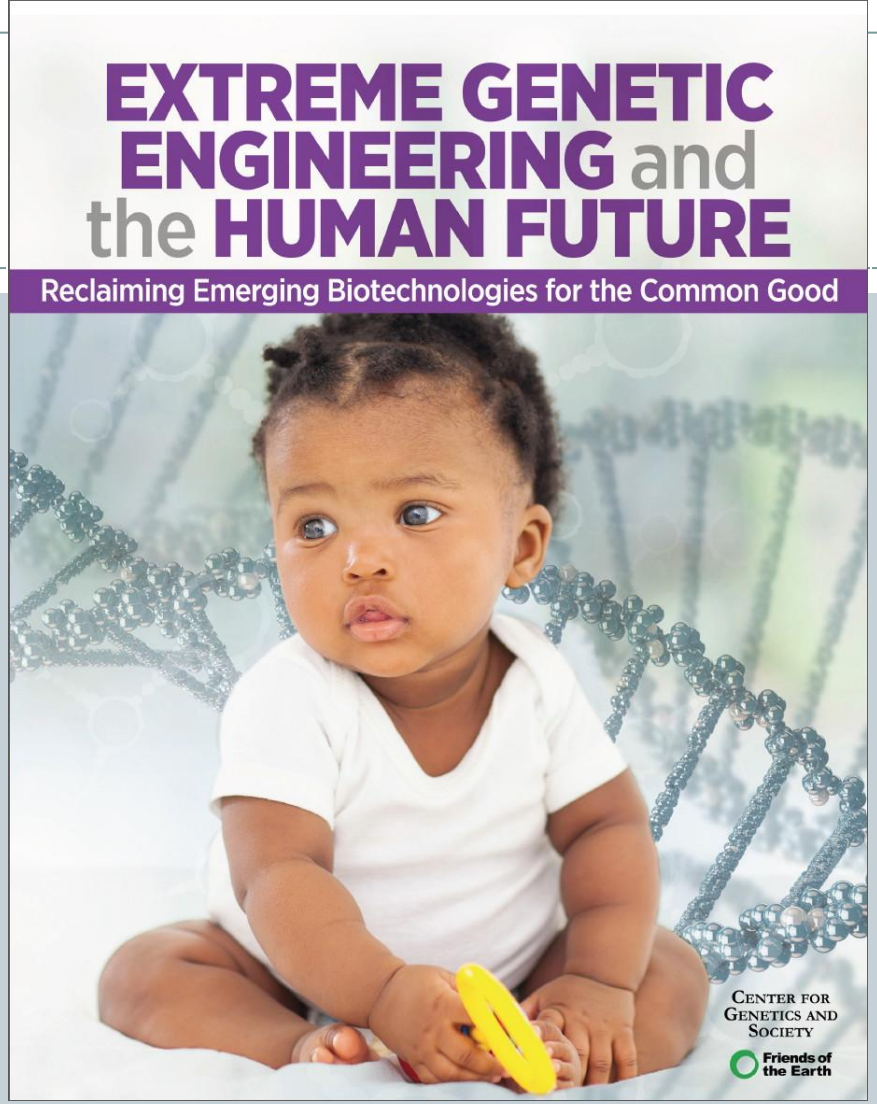

Toto, I've a feeling we're not in Kansas anymore.

Governance,
Regulation
and Control:
Of Which People,
By Which People,
For Which People?

Reasons to Say No to GM Humans

1. Profound health risks to future children
2. Thin medical justification
3. Treating human beings like engineered products
4. Violating the common heritage of humanity
5. Undermining the widespread policy agreements among dozens of democratic nations
6. Eroding public trust in responsible science
7. Reinforcing inequality, discrimination and conflict in the world

Center for Genetics and Society



http://www.foe.org/news/news-releases/2015-11-should-our-children-be-genetically-engineered

http://www.geneticsandsociety.org/article.php?id=9000

“Once the discovery is made, it’s out there. Anybody with basic molecular biology training can use it for genome editing. That’s a bit scary.”

— Jennifer Doudna