

ETHICS: RECENT HISTORIES AND NARRATIVES

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MAXINE SINGER



Dr. Philip Handler, President National Academy of Sciences Washington, DC 20418

Dear Doctor Handler

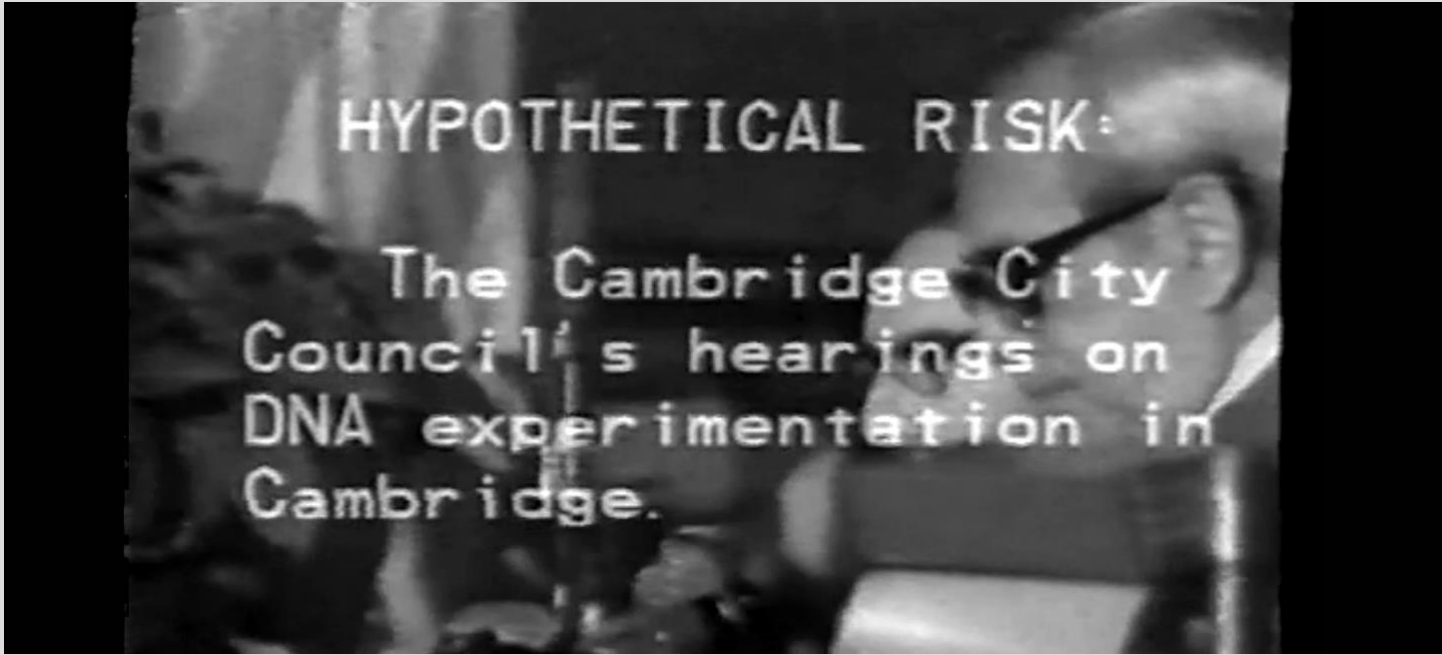
Several of the scientific reports presented at this year's Gordon Research Conference on Nucleic Acids (June 11-15, 1973) indicated that we presently have the technical ability to join together, covalently, DNA molecules from diverse sources. Scientific developments over the past two years make it both reasonable and convenient to generate overlapping sequences, bacteria and animal viruses. Such sequence homologies can then be used in order to combine the diverse molecules by Watson-Crick hydrogen bonding. Application of existing methods then permits covalent linkage of such molecules. In this way new kinds of viruses with biological activity of unpredictable nature may eventually be created. Certain of these hybrid molecules are potentially hazardous to both laboratory workers and the public. This possibility was recognized and agreed upon by a majority of those attending the Conference, who voted to communicate their concern to you and to the President of the National Academy of Medicine (to whom this letter is also being sent). We suggest that the Academies establish a study committee of appropriate individuals to consider this problem and to recommend specific actions or guidelines should that seem necessary. Related problems such as the risks involved in circuit large-scale preparation of animal viruses might also be considered. A list of participants in the Conference is attached for your interest.

Sincerely yours ,

Maxine Singer

Dieter Soll

Gene Clontz



Asiloma

conference
grounds



ASILOMAR



BASIC SAFETY RULES

- Don't insert pathogens
- Don't insert cancer sequences
- Don't insert genes for drug resistance

- Level 4 (!) Containment
- Banned in the city of Cambridge, Massachusetts
- Science self-regulation just in time (HGH; Artificial Insulin, HGF for hemophilia)

The Ethics
of Human
Gene Therapy

LeRoy Walters

Julie Gage Palmer

POINTS TO CONSIDER

- Ethical issues must be a part of research on recombinant DNA
- 1972 Asilomar → RAC → **safety as main concern**
- RAC lead to Appendix M “Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant DNA Molecules into One or More Human Research Participants”
- RAC also led to Biosafety Committees and Guidelines for accidents in the lab

ALL CLINICAL GTR PROTOCOLS CONNECTED
WITH INSTITUTIONS THAT RECEIVE FEDERAL
FUNDING USE CASUISTIC MODEL AT LOCAL AND
NATIONAL LEVEL

- What are potential harms and benefits to research subjects?
- How will potential harms and benefits be communicated so they can consent?
- How will selection among research subjects be made?
- How will privacy and confidentiality be preserved?

(Leroy Walters)

CANONICAL PUBLIC OBJECTIONS

1. DNA as the really real
2. Nature is normative, good and fixed.
3. Suffering and mortality is the main thing that defines our humanity.
4. Slopes are slippery.
5. Dual Use is Inevitable
6. Error is Inevitable.
7. The marketplace will corrupt science
8. The world is already unfair and this will worsen injustice.
9. The world is already inauthentic and *umhiemlich* enough
10. Finitude and Contingency define us, not control—
“mastery” is a mistakenness—

AAAS 1999 CONSENSUS STATEMENT ON INHERITABLE GENETIC MUTATIONS:

- **Are there reasons in principle why performing the basic research should be impermissible?**
- **What contextual factors should be taken into account and do any of these prevent development and use of the research?**
- **What purposes, techniques or applications would be permissible and under what circumstances?**
- **What procedures, structures, involving what policies, should be used to decide on appropriate techniques and uses?**

SO WHAT IS NEW?:

- Viral vector idea was complexly flawed with terrible off target effects and disruption of the immune system
- Tragic flaws -> Gelsinger death
- Thus: Zinc Fingers, TALENS and: CRISPR-Cas 9
- And a turn toward new tools of synthetic biology by engineers whose experience is orthogonal to clinic

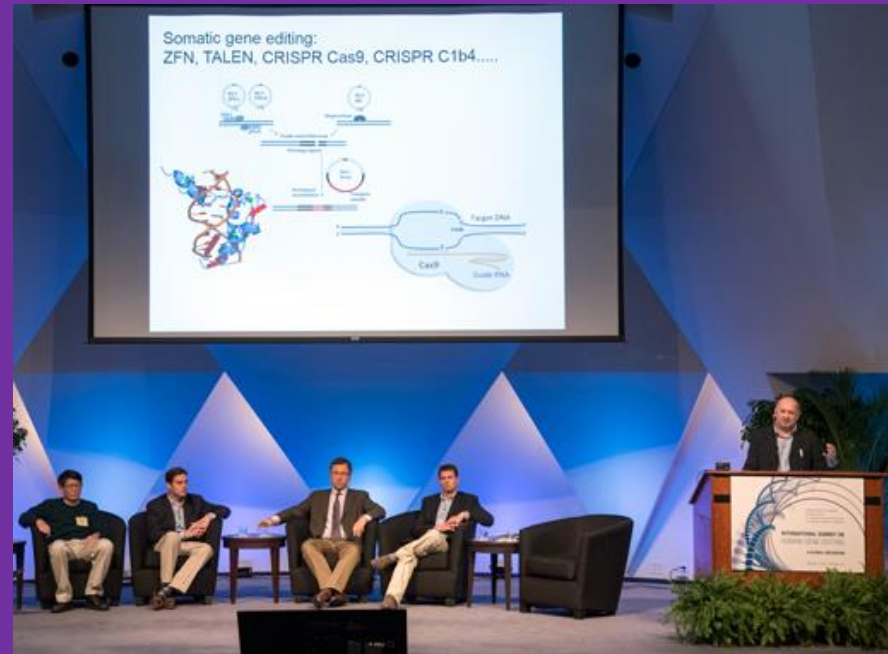
CRISPR-CAS 9 CHARPENTIER AND DOUDNA



6 NEW THINGS

- The marketplace— small, and large, with immediate conflicts— what is a "product" and what is ownership? What is a decent profit? Can conflicts be managed?
- 40 years of failure, hope and hype within the same group of people. "Decaphilia" Problem.
- Growth of patient advocacy and activism with internet connectivity post AIDs
- The deep and fundamental unknowability of modern molecular biology
- The world of environmental catastrophe and significant mistakes
- The reality of terrorism

NATIONAL ACADEMIES OF THE US, UK AND CHINA “ASILOMAR-TYPE” MEETING 2015



MORE TO COME: SYNTHETIC BIOLOGY WILL RAISE NEW ISSUES

- USE OF BIOTEMPLATES AS TOOL
- DE NOVO CREATION AND ONTOLOGICAL QUESTIONS
- LOCUS SHIFTS FROM CLINICAL TRIALS TO PROBLEMS WITH OTHER SCALES: LARGER (ENVIRONMENTAL) AND SMALLER (ENERGY MOLECULES.)

THANKS