Human gene editing and biosecurity

David Relman, Stanford University

International Summit on Human Gene Editing:
A Global Discussion

November 3, 2015

Alan Moses, Berkeley Science Review

Why talk about biosecurity*?

World is much more complex than our immediate experiences (at home and work) might suggest, and getting more complex (less well understood) every day.

*Protection, control of, and accountability for high-consequence biological agents…and critical relevant biological materials and information to prevent…misuse

http://www.whitehouse.gov/administration/eop/ostp/nstc/biosecurity

Topics

- Capabilities
- Motivations
- Misuse of science
- Risk mitigation

Growing power of the individual in the life sciences

- Capabilities of individuals in life sciences expanding dramatically; now comparable to those of large organizations 20 yrs ago
- Barriers to entry (life sciences) are falling
- Costs much reduced
- Processes more efficient, rapid

The packaging of recombinant DNA technology

Knock-out Kit via CRISPR, for Every Human/Mouse gene from OriGene Technologies

Starting a CRISPR/CAS9 project on genome editing? Come to OriGene for a wide selection of tools -

- Gene knockout kit for every human/mouse gene
- pCAS-Guide vectors and gRNA vectors
- gRNA and donor vector cloning services

Features:

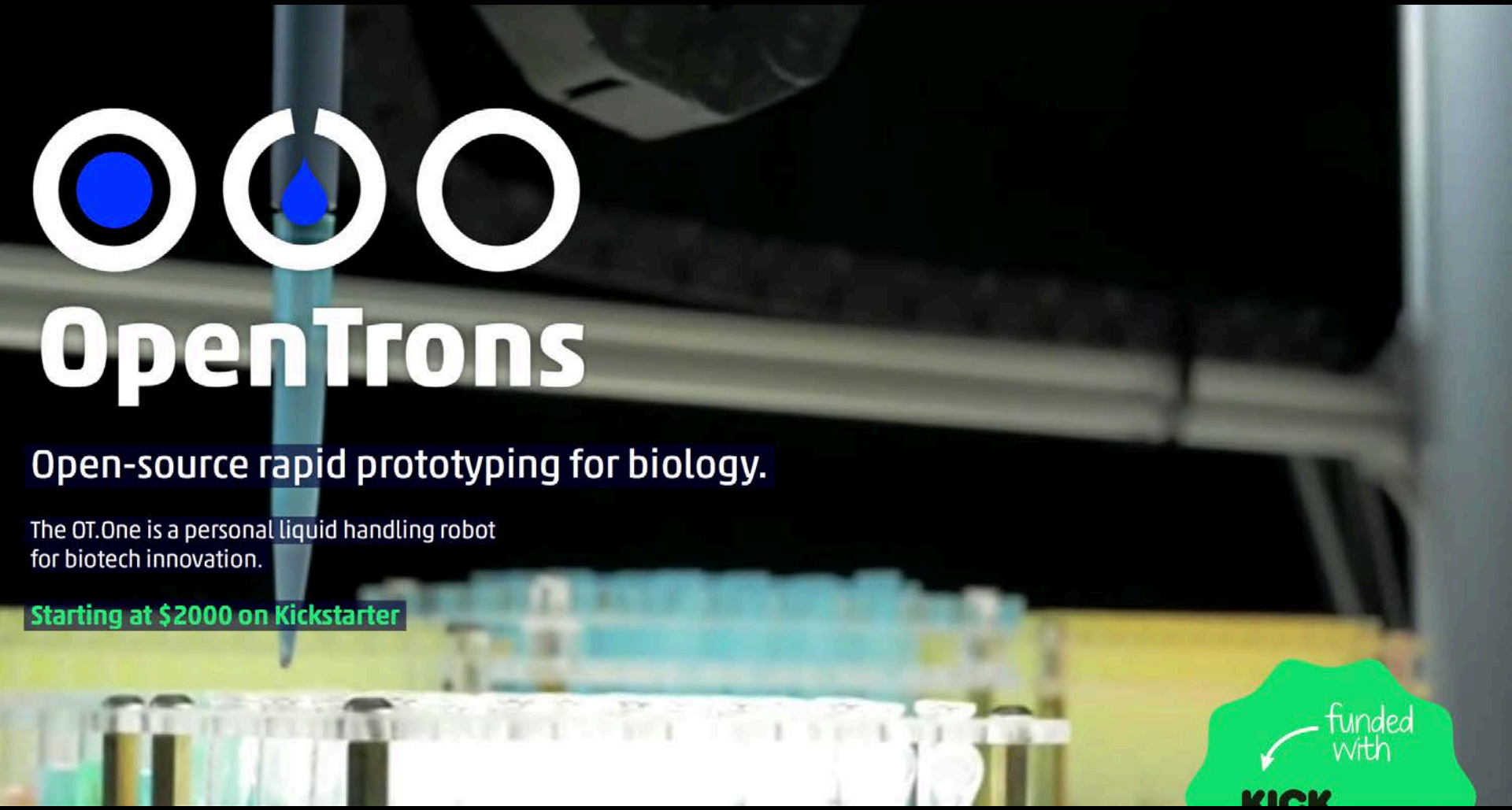
- Complete kit for gene knockout via CRISPR (targeted sites around the 5' end of the ORF)
- 2 guide RNA vectors in pCas-Guide to ensure an efficient cleavage
- Donor vector with predesigned homologous arms
- Knockin GFP-Puro for selection
- pCas-Guide-scramble is also provided as a negative control

Supplier Page

Supplier Page from OriGene Technologies for Knock-out Kit via CRISPR, for Every Human/Mouse gene

ORIGENE
Your Gene Company

Digitalization of biological information and procedures, outsourcing



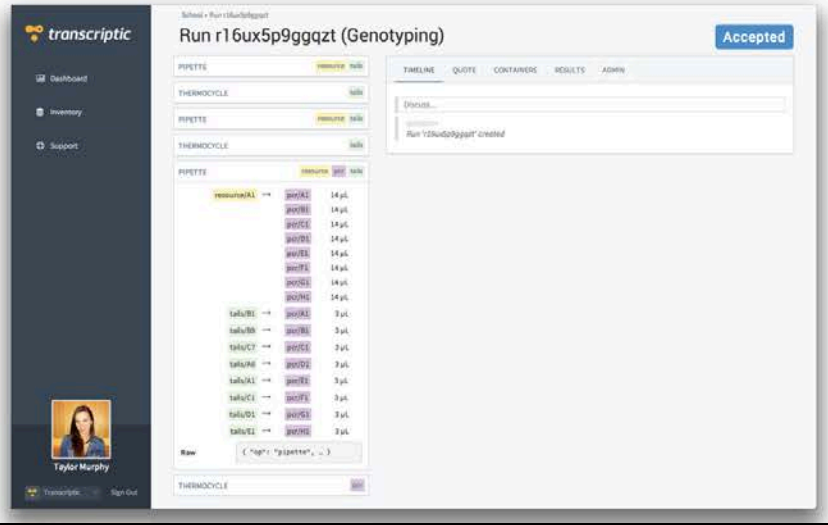
Digitalization of biological information and procedures, outsourcing

transcriptic

SERVICES PRICING PLATFORM PARTNER COMPANY BLOG LOG IN

Welcome to the future.

Never look at the research lab the same way again.



Transcriptic is a web-based, on-demand remote life science research lab powered by advanced, custom robotic automation.

Using Transcriptic can be as easy as a few clicks in the secure web interface, or power users can write their own code to connect directly to our lab systems.

Transcriptic Platform has two principal components: the Foundry and Transcriptic LIMS. The Foundry is the molecular and cell biology execution infrastructure we own and operate from our 10,000-square-foot facility in Menlo Park, California. Transcriptic LIMS is our powerful data management system that keeps track of every container, aliquot, and piece of linked data relevant to your work.

Digitalization of biological information and procedures, outsourcing

transcriptic

HOW IT WORKS | WORKCELLS | PRICING | LOG IN | SIGN UP

RUN YOUR EXPERIMENTS FROM ANYWHERE

DESIGN

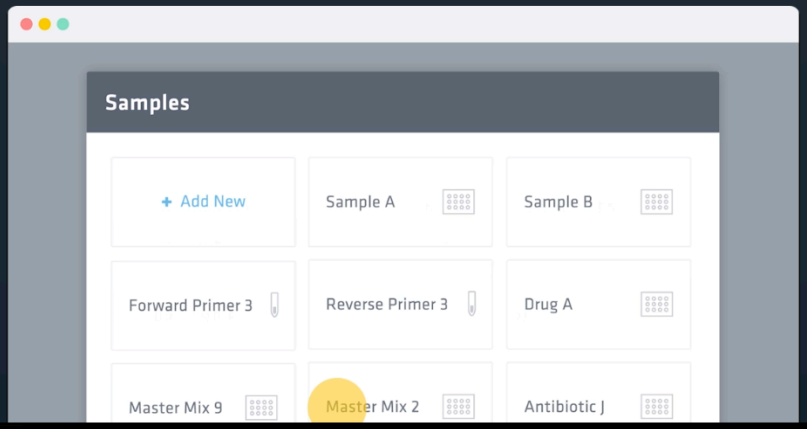
Define every detail of your experiment online.

AUTOMATE

A Workcell performs your experiment in our facilities.

ANALYZE

Get results via email when your experiment completes.



SCIENCE HACK DAY

About How-To Guide Ambassador Program Sponsor Wiki

SCIENCE HACK DAY

50 EVENTS, 30 CITIES, 19 COUNTRIES

Science Hack Day celebrates 50th worldwide event!

Create a Science Hack Day in your city!

Read the How-To Guide

What motivates scientists?

- Quest for knowledge
- Quest to help others (application of knowledge)
- Curiosity
- Fame
- Fortune/livelihood
- Other

Bio2011

Attendees await the opening of the #bio2011 Exhibition Pavilion

By BIO Photos ★ Favorite

BIO Business Forum draws the attendees

By BIO Photos ★ Favorite

Kinds of misuse (of biology)?

Accidental, benign, unwitting
Callous disregard
Deliberate, intentional

Misuse of human gene editing technology (somatic, germ-line)?

Misuse of human gene editing technology (somatic, germ-line)?

- Create disease model?

Misuse of human gene editing technology (somatic, germ-line)?

- Create disease in humans

LETTER

doi:10.1038/nature13902

In vivo engineering of oncogenic chromosomal rearrangements with the CRISPR/Cas9 system

Danilo Maddalo[1], Eusebio Manchado[1], Carla P. Concepcion[1,2], Ciro Bonetti[1], Joana A. Vidigal[1], Yoon-Chi Han[1], Paul Ogrodowski[1], Alessandra Crippa[3], Natasha Rekhtman[4], Elisa de Stanchina[5], Scott W. Lowe[1,6] & Andrea Ventura[1]

Chromosomal rearrangements have a central role in the pathogenesis of human cancers and often result in the expression of therapeutically actionable gene fusions[1]. A recently discovered example is a fusion between the genes echinoderm microtubule-associated protein like 4 (*EML4*) and anaplastic lymphoma kinase (*ALK*), generated by an inversion on the short arm of chromosome 2: inv(2)(p21p23). The *EML4–ALK* oncogene is detected in a subset of human non-small cell lung cancers (NSCLC)[2] and is clinically relevant because it confers sensitivity to ALK inhibitors[3]. Despite their importance, modelling such genetic events in mice has proven challenging and requires complex manipulation of the germ line. Here we describe an efficient method to induce specific chromosomal rearrangements *in vivo* using viral-mediated delivery of the CRISPR/Cas9 system to somatic cells of adult animals. We apply it to generate a mouse model of Eml4–Alk-driven lung cancer. The resulting tumours invariably harbour the *Eml4–Alk* inversion, express the *Eml4–Alk* fusion gene, display histopathological and molecular features typical of ALK$^+$ human NSCLCs, and respond to treatment with ALK inhibitors. The general strategy described here substantially expands our ability to model human cancers in mice and potentially in other organisms.

Genetically engineered mouse models of human cancers have proven indispensable to dissect the molecular mechanisms underlying tumorigenesis[4] and provide powerful preclinical platforms for studying drug sensitivity[5] and resistance[6–8]. Although many gain- and loss-of-function mutations observed in human cancers can be modelled using current gene-targeting technologies, chromosomal rearrangements leading to oncogenic gene fusions have proven challenging to faithfully recapitulate

Nature 2014 (Dec 18/25); 516:423-427

LETTER

doi:10.1038/nature13902

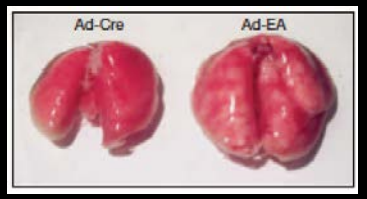
In vivo engineering of oncogenic chromosomal rearrangements with the CRISPR/Cas9 system

Danilo Maddalo[1], Eusebio Manchado[1], Carla P. Concepcion[1,2], Ciro Bonetti[1], Joana A. Vidigal[1], Yoon-Chi Han[1], Paul Ogrodowski[1], Alessandra Crippa[3], Natasha Rekhtman[4], Elisa de Stanchina[5], Scott W. Lowe[1,6] & Andrea Ventura[1]

- Create mouse model of human lung cancer

(NSCLC 2º inversion on chr2, EML4-ALK oncogene)

- Intra-tracheal delivery of 2 sgRNAs, Cas9 on adenovirus vector
- Multiple bilateral lung tumors as early as 4 weeks, 34/34 mice with tumors by 8 weeks



Nature 2014 (Dec 18/25); 516:423-427

Recombinant adenovirus ordered from…

ViraQuest Inc.

Innovative Adenovirus Technologies and Reagents

800-665-4190

help@viraquest.com

Home | Services | Dual Expressers | Products | Confidentiality | Quality Control | Quote | Service Request Form | Questions | References | Contact

Confidentiality

Learn More »

Expert Adenovirus Services

ViraQuest Inc. is a biotechnology company specializing in custom adenovirus production services. Our custom services include the production of novel vectors or the amplification of existing stocks. Quality control is included on every lot number. ViraQuest Inc. retains the exclusive commercial rights to **RAPAd® technology**.

References

Arthritis Bone Metabolism Ca Metabolism Cancer Cancer Vaccine Cardiology Cardiovascular Cell Biology Development Diabetes Dual Expressor Epidermis Extra Cellular Matrix

Nature 2014 (Dec 18/25); 516:423-427

Misuse of human gene editing technology (somatic, germ-line)?

- Create disease in humans
- Reduce disease susceptibility?

Misuse of human gene editing technology (somatic, germ-line)?

- Create disease in humans
- Produce disease susceptibility

Misuse of human gene editing technology (somatic, germ-line)?

- Create disease in humans
- Produce disease susceptibility
- Express missing beneficial factor?

Misuse of human gene editing technology (somatic, germ-line)?

- Create disease in humans
- Produce disease susceptibility
- Express detrimental factor

Misuse of human gene editing technology (somatic, germ-line)?

- Create disease in humans
- Produce disease susceptibility
- Express detrimental factor
- Induce helpful drug expression?

Misuse of human gene editing technology (somatic, germ-line)?

- Create disease in humans
- Produce disease susceptibility
- Express detrimental factor
- Induce harmful drug expression

Misuse of human gene editing technology (somatic, germ-line)?

- Create disease in humans
- Produce disease susceptibility
- Express detrimental factor
- Induce harmful drug expression
- 'Safe harbor'?

Misuse of human gene editing technology (somatic, germ-line)?

- Create disease in humans
- Produce disease susceptibility
- Express detrimental factor
- Induce harmful drug expression
- Covert production site

But given potential difficulties (especially delivery) and other options, if determined to do harm, why bother?

- Covert, diminish likelihood of early recognition, attribution
- Insidious, endogenous, promote fear and uncertainty
- How would we know? Once suspected, fully understood?

But given potential difficulties (especially delivery) and other options, if determined to do harm, why bother?

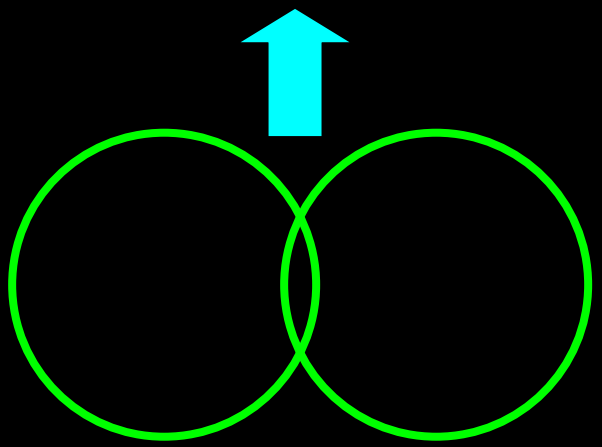
- And what about germ-line of food crops, livestock...?

Misuse of biology: How big a risk?

small number ± [big number] x big number ± [big number] = ??

Likelihood of harmful use

Consequence of harmful use



now

capable individuals

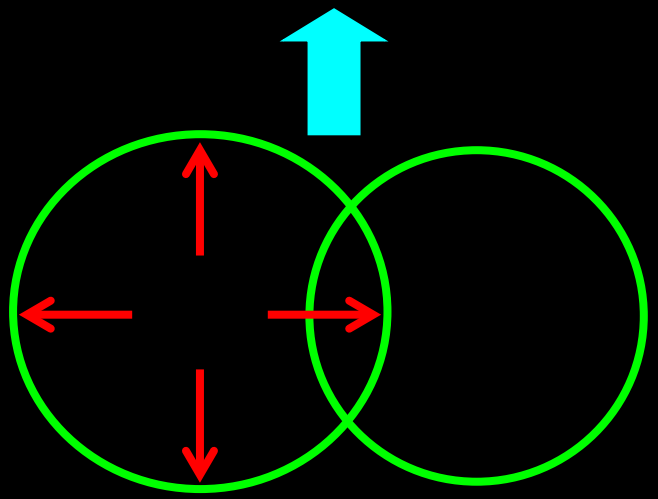
ill-intended or irresponsible individuals

Misuse of biology: How big a risk?

small number ± [big number] x big number ± [big number] = ??

Likelihood of harmful use

Consequence of harmful use



later

capable individuals

ill-intended or irresponsible individuals

وزارة التعليم العالي والبحث العلمي
Ministry of Higher Education & Scientific Research

جامعة الموصل
UNIVERSITY OF MOSUL

Football finals in Mosul University

جرت المباراة النهائية بين فريقي التربية الرياضية و رئاسة جامعة الموصل , وكانت المباراة سجالا بين الفريقين حيث انتهت ... ...

more details

June 5, 2014, 10:06 am - اعلام الجامعة

This university was founded on a strong and solid architecture which is an extension of the rules of this ancient city, founded the first school in Islam at a time when the school has not seen any like this, which was in the city of Mosul humpback .... More

ABOUT UNIVERSITY | COLLEGES | CENTERS | LEAFLETS AND | GRADUATES | COMMUNITY SERVICE | CENTRAL LIBRARY | DIRECTORATES AND

Search Site

Search | In college

Final results

Exams Schedule

Third Scientific Symposium of the Department of Earth Sciences

Tape news

:: Chemistry students / Faculty of Sciences issuing the fourth issue of the ma

Urgent ads

Breaking news

Department of Life Sciences Library / Faculty of Science, received a number of thesis and doctoral theses

... مكتبة قسم علوم الحياة / كلية العلوم تستلم عددا من اطاريح الدكتوراه ورسائل الماجستير

more details

College English

main menu

:: Home
:: Mr. Dean word
:: Mayaklah Science
:: Vision Mission Goals
:: Faculty
:: Organizational structure
:: Curriculum
:: News Archive
:: Photo Archive

Departments

:: chemistry department
:: Department of Science Hayya
:: Department of Earth Sciences
:: Department of Physics
:: Department of Biological Physics
:: S new and renewable energies

Graduate students database

AhlulBayt (a.s.) News Agency
ABNA

ABNA

العربية
Español
বাংলা
Swahili

ISIS executes Head of Physics Department for refusing to develop bioweapons in Mosul

November 14, 2015 - 5:10 PM

A local source in Nineveh province said that ISIS has executed the head of the Department of Physics at the University of Mosul because of his refusal to develop biological weapons.

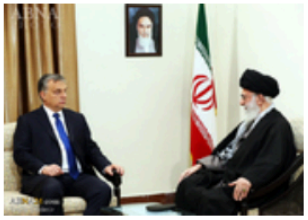
The source said: “militants belonging to ISIS executed the president of the Department of Physics at the Faculty of Science in the University of Mosul,” adding that, “the execution came on the back of his rejection to cooperate with the organization in the development of biological weapons, which ISIS is seeking to possess and use in the fighting against government forces.”

The source, who requested to remain anonymous, noted: “The execution took place in a public square in the center of Nineveh,” pointing out that, “the organization has handed over the body to the forensic medicine department.”

Source : **IraqiNews** News Code : **719877**

A local source in Nineveh province said that ISIS has executed the head of the Department of Physics at the University of Mosul because of his refusal to develop biological weapons.

PICTORIAL



Photos: Ayatollah Khamenei Receives Hungarian PM

December 1, 2015 - 6:46 PM

Photos: Imam Hussein Mourning Ceremony Held by Iranian Pilgrims Near to Karbala

December 1, 2015 - 6:06 PM

Mitigating the risks

- Regulate access to reagents, information?
- Promote awareness, sensitize relevant communities, establish norms
  - role of individuals
  - local (professional orgs, academia, industry)
  - national leadership
  - international organizations (models?, e.g., International Air Traffic Control)
- Anticipate, preempt threats
- Response?

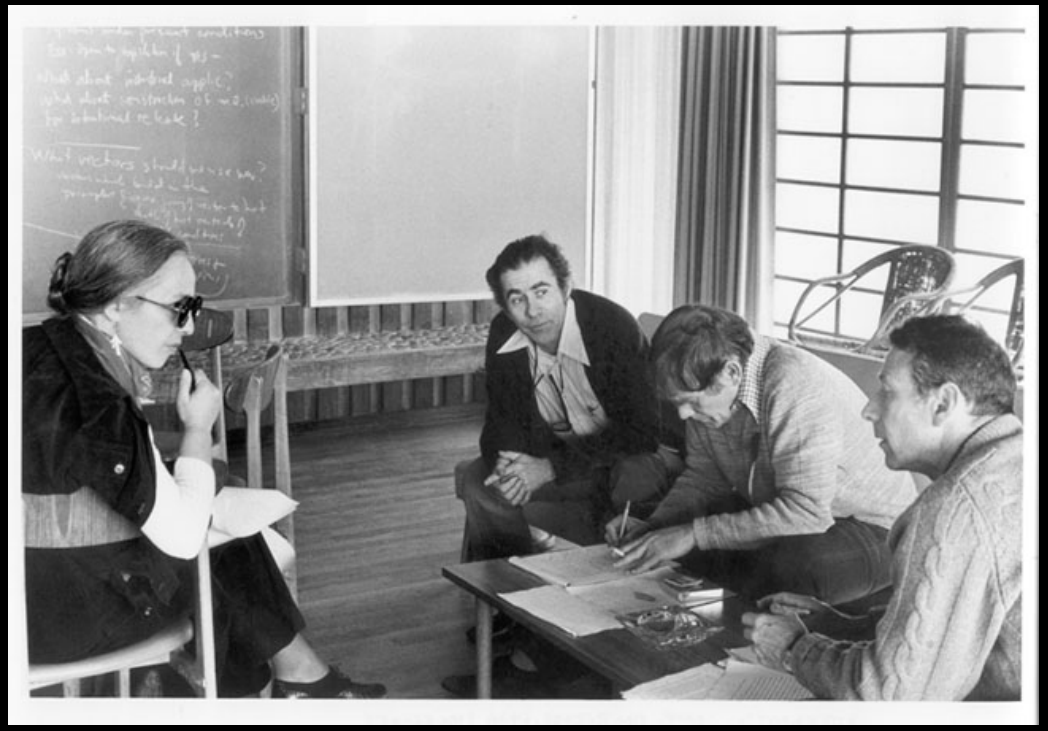
- What are some effective governance models? 'Top down' vs. 'Bottom up'...Both. Scalable, Distributable, Accountable

- How do we sensitize and organize the science communities, so as to detect and minimize risks in the life sciences?

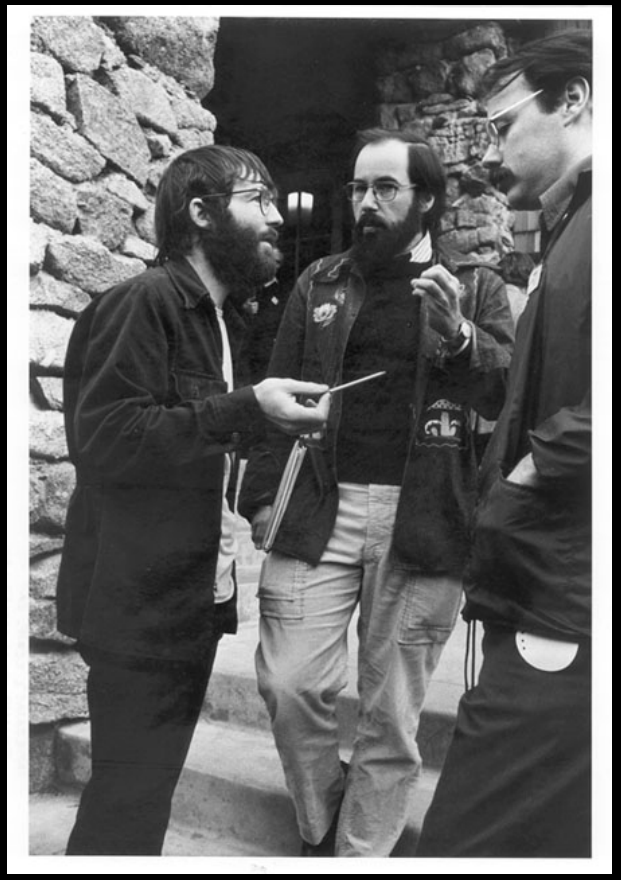
- Partnerships across disciplines, domains of expertise, international boundaries?

Back to the Future?

International Conference on Recombinant DNA Molecules
Asilomar Conference Center, Pacific Grove, California, February 1975



Maxine Singer, Norton Zinder, Sydney Brenner, Paul Berg



Philip Sharp, David Baltimore

http://libraries.mit.edu/archives/exhibits/asilomar/index.html

- We live in the "The Biological Century"
  [Gregory Benford, 1992]
- Unimaginable capabilities, untold benefits, unforeseen issues, significant risks
- There are clear and important risks of misuse of gene editing technologies
- Mitigating the risks: raise awareness, educate, communicate, norms, guidelines, anticipate threats, and promote flexible/agile/rapid/responses