Development of biological technology:

Where the H5N1 flu story fits, and thoughts for after

Roger Brent

Member, Division of Basic Sciences
Fred Hutchinson Cancer Research Center

and

Center for Biological Futures @ FHCRC

1) Survey of continuing development of biological Knowledge and Capability (K&C)

2) Survey of biological K&C pertinent to this workshop

3) Thoughts on policy and ethics pertinent to this workshop

Representative developments in biological Knowledge, Capability, and Governance

1911-1918. T. H. Morgan, Sturtevant, Muller at Columbia develop transmission genetics, (including mapping, crossing over, assortment of traits during meiosis). This genetic understanding used immediately by Pioneer Hi-Bred seed company (founded 1926)

1930. US Congress passes Plant Patent act, limited to plants reproducing asexually.

1933. Warren Weaver at Rockefeller Foundation begins using term "molecular biology"

1953. DNA structure

1960s. DNA replication

1961. mRNA (Brenner, Jacob, Meselson)

1966. Genetic code

1969. Repressor proteins. End of "8th Day of Creation" period for molecular biology

1969. US halts biological warfare program, calls for treaty banning biological weapons.

Representative developments in biological Knowledge, Capability, and Governance

1970. US Plant Variety Protection Act grants 17-year monopoly via "Plant Variety Protection Certificates" for variants that are "distinct", "stable", and "uniform".

1971. Mary Dell Chilton and others form "Seattle Crown Gall Group", begin exploring bacterium-to-plant transmissible plasmid that will enable plant genetic engineering.

1972. Draft Biological Weapons Convention text released.

1973. Working recombinant DNA (Cohen-Chang-Boyer-Helling)

Proc. Nat. Acad. Sci. USA
Vol. 70, No. 11, pp. 3240–3244, November 1973

Construction of Biologically Functional Bacterial Plasmids *In Vitro*

(R factor/restriction enzyme/transformation/endonuclease/antibiotic resistance)

STANLEY N. COHEN*, ANNIE C. Y. CHANG*, HERBERT W. BOYER†, AND ROBERT B. HELLING†

* Department of Medicine, Stanford University School of Medicine, Stanford, California 94305; and † Department of Microbiology, University of California at San Francisco, San Francisco, Calif. 94122

ABSTRACT **The construction of new plasmid DNA species by *in vitro* joining of restriction endonuclease-generated fragments of separate plasmids is described. Newly constructed plasmids that are inserted into *Escherichia coli* by transformation are shown to be biologically functional replicons that possess genetic properties and nucleotide base sequences from both of the parent DNA molecules. Functional plasmids can be obtained by reassociation of endonuclease-generated fragments of larger replicons, as well as by joining of plasmid DNA molecules of entirely different origins.**

This, we called
“molecular cloning”

Representative developments in biological Knowledge, Capability, and Governance

1973-1978. Combinations of plasmids, natural and chimeric promoters, repressors, and chimeric ribosome binding sites needed for high level expression of recombinant proteins in *E. coli* perfected.

1974. Recombinant DNA Moratorium. Start of brief period of self-governance by biologists.

1975. Biological Weapons Convention goes into force after ratification by 22 countries.

1975. Asilomar conference. Conference ends in proposed framework for regulation by handoff to NIH. Beginning of end of self-governance period.

ROLLING STONE, JUNE 19, 1975

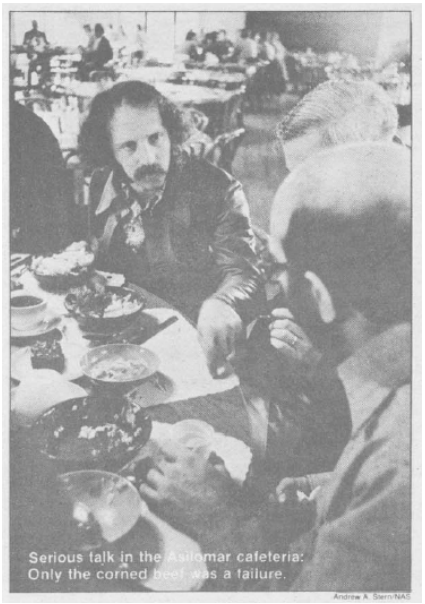
THE PANDORA'S BOX CONGRESS

By Michael Rogers

140 Scientists Ask: Now that We Can Rewrite the Genetic Code, What Are We Going To Say?

...le of molecular biologists, on chapel steps.

Andrew A. Stern/NAS



Serious talk in the Asilomar cafeteria: Only the corned beef was a failure.

Andrew A. Stern/NAS

Rolling Stone article, Michael Rogers, June 1975

By the end of the Asilomar meeting, scientists had devised and endorsed a regulatory regime that combined loose regulation by the NIH with further experimentation to better calibrate the possible risks.

Again, this marked the ending of the brief period of self governance

Representative developments in biological Knowledge, Capability, and Governance

1976. Boyer and Swanson found Genentech. Company signs licensing agreement with City of Hope Medical Center that Genentech will hold patents for synthetic genes encoding human proteins

1976. "Promulgation" of NIH guidelines. Formal end of self-governance, replaced by regulatory framework devised by scientists and controlled by them (they thought).

Review structure consisted of local review committees (Institutional Biohazard Committees) and national overview (the Recombinant Advisory Committee, or RAC)

1976. Chemical (Maxam-Gilbert) and enzymatic (Sanger) DNA sequencing spread pre-publication

1977. Boyer (UCSF, Genentech) and Swanson (Genentech) register as congressional lobbyists.

1977. NIH director Fredrickson insists on public representation on RAC. First reverse for academic scientists on RAC.

1977. Somatostatin produced in *E. coli* from synthetic DNA

Technology

Making Human Hormones With Bacteria

By VICTOR K. McELHENY

New York Times, 7 December 1977

trying to do this.

This group that included Dr. Boyer, Dr. Riggs and Dr. Itakura began by working on a related problem. This was to synthesize an important part of the genetic machinery for bacteria to digest the sugar called lactose and inserting the synthetic DNA into bacteria so that it would be active.

Dr. Itakura synthesized the so-called "operator" for the gene that directs the manufacture of the bacterial protein for cutting lactose into two smaller sugars, galactose and glucose. If the operator is covered by another protein called the repressor, the gene cannot be "read" into a copy that is used

Having obtained expression of the synthetic operator in bacteria, the scientists at the City of Hope Medical Center and the University of California at San Francisco hoped to use the bacteria's genetic machinery for sugar digestion as the way to induce bacteria to make somatostatin.

Dr. Riggs said they chose somatostatin for several reasons. The group wanted a small protein, making it easy to synthesize the entire gene. They wanted a completely synthetic gene to avoid contamination problems.

Representative developments in biological Knowledge, Capability, and Governance

1977-1982. Combination of directed experimentation, lack of evidence of harm, and better understanding of scientific questions leads to great relaxation of and exemption of most experiments from NIH guidelines.

1977. Seattle group isolates, by cloning, "T-DNA" from *Agrobacterium tumifaceans* Crown Gall Ti plasmid

1978. Human insulin produced in *E. coli*

Proc. Natl. Acad. Sci. USA
Vol. 76, No. 1, pp. 106–110, January 1979
Biochemistry

Expression in *Escherichia coli* of chemically synthesized genes for human insulin

(plasmid construction/*lac* operon/fused proteins/radioimmunoassay/peptide purification)

DAVID V. GOEDDEL*†, DENNIS G. KLEID*, FRANCISCO BOLIVAR*, HERBERT L. HEYNEKER*, DANIEL G. YANSURA*, ROBERTO CREA*‡, TADAAKI HIROSE‡, ADAM KRASZEWSKI‡, KEIICHI ITAKURA‡, AND ARTHUR D. RIGGS†‡

*Division of Molecular Biology, Genentech, Inc., 460 Point San Bruno Boulevard, South San Francisco, California 94080; and ‡Division of Biology, City of Hope National Medical Center, Duarte, California 91010

ABSTRACT Synthetic genes for human insulin A and B chains were cloned separately in plasmid pBR322. The cloned synthetic genes were then fused to an *Escherichia coli* β-galactosidase gene to provide efficient transcription and translation and a stable precursor protein. The insulin peptides were cleaved from β-galactosidase, detected by radioimmunoassay, and purified. Complete purification of the A chain and partial purification of the B chain were achieved. These products were mixed, reduced, and reoxidized. The presence of insulin was detected by radioimmunoassay.

Representative developments in biological Knowledge, Capability, and Governance

1978-1979. Genentech plays and wins game of chicken with RAC, grows culture of insulin-producing *E. coli* over 10 liter limit. Second defeat of (or end run around) scientists on RAC.

1979. With funding from Monsanto, Mary Dell Chilton moves to Wash U in St Louis. At Monsanto, Ernie Jarworski forms group to take advantage of T DNA transformation for crop improvement.

1980. US Supreme court decision Diamond vs. Chakrabarty allows patent of deliberately constructed bacterium.

1981. Recovery of live virus from cells transfected with first whole-genome cDNA clone for an RNA virus, for poliovirus, a + strand RNA virus. I'll get back to this.

1982. Genentech and others convince scientists on RAC to vote against greater dismantling of NIH guidelines, preferring loose federal regulation to a possible patchwork of state and local regulations. Third reversal for academic scientists on RAC.

Representative developments in biological Knowledge, Capability, and Governance

1982. Homologous gene replacement in yeast

1982. Chilton group shows "disarmed", high efficiency T DNA from *Agrobacter tumifaceans* can introduce genes into nuclear DNA of a higher plant (tobacco) and transmit to progeny.

1982. Phage lambda genome sequence

1982-1990s. Genentech-Corning joint venture, Genencor, first industrial biotech company, pioneers use of directed evolution methods in industrial applications, for example to make to enzymes that better convert glucose in corn syrup to fructose.

1982. "Molecular Cloning: A Laboratory Manual" from CSH Press, sells >5,000 copies first year.

1983. Mullis at Cetus develops working PCR.

1984. Widespread availability of synthetic DNA machines

Representative developments in biological Knowledge, Capability, and Governance

1984-1985. PCR spreads by word of mouth, used in labs worldwide.

1984-1992. Increasingly effective control of eukaryotic gene expression by partly bacterial and other engineered regulatory proteins.

1985-2000. Gold rush of patent applications for key genetic elements used in various technologies, and for human and other genes. During this period, patents generally issue 5-7 years after application then last for 17 more.

1986. Mullis gets Taq polymerase to work, publishes recombinant Taq polymerase. People worldwide make their own PCR machines.

1987. Current Protocols in Molecular Biology published

"How to clone it" manuals, 2002

In 2002, estimated >100,000 copies of these books including active subscriptions to CPMB

Representative developments in biological Knowledge, Capability, and Governance

1987. Novozyme (now Novo Nordisk) launches Lipolase, first recombinant grease-stain-removing enzyme for laundry pre-soak.

1988. Transformation of yeast (and soon plant) cells by microparticle bombardment (or "gene gun").

1989. Homologous gene replacement in mice

1989-1994. Increasingly effective two-hybrid methods for finding partner proteins and scoring protein-protein interactions. Direct impact on science and pharma industry.

1990. Functional RNA aptamers from combinatorial libraries. Widespread use of random sequence DNA as source of diversity.

1990. RNAi, in petunias. Outside of plants, nobody much notices.

1990s-2012. Perfection of "marker assisted breeding" or "marker assisted selection" allows many plant traits to be introduced quickly by breeding. Interestingly, and increasingly, it allows you tiptoe across a species barrier.

1994. Complete yeast genome sequence.

Representative developments in biological Knowledge, Capability, Drivers, and Governance

1994. Willem Stemmer demonstrates single step synthesis of functional circular plasmid from oligonucleotides. Uses same method in "DNA shuffling" to generate diversity.

1994. Many groups use rounds of diversity generation and *in vitro* evolution to evolve cold adapted subtilisin for detergents.

1996. First release of Pubmed.

1996. Launch of Roundup-Ready soybeans. In US, commercial success despite large public resistance. For soybeans, very last applicable Monsanto owned patent to expire in 2014.

1998. Complete *C. elegans* (nematode) genome sequence.

1998. Launch of Roundup-Ready corn. Commercial success in US.

1998. RNAi in worms. Everybody notices. Use spreads well before knowledge of mechanism.

1999. Celera releases complete *Drosophila* (fruit fly) genome sequence

1999. Jessie Gelsinger becomes first human killed by recombinant DNA, an engineered Adenovirus vector, in a botched gene therapy clinical trial.

Representative developments in biological Knowledge, Capability, and Governance

2000-2012. MAS, perfected, receives greater boost during 2000-2010 when most economically important plant genomes are sequenced. Traits introduced by MAS go along with others by transgene. Increase in rate of yield increase for many human food crops.

2001. si RNAs in mammalian cells. Use spreads immediately, ahead of knowledge of how it works.

2002. Reasonably complete sequences of human genomes available to the public

2010. Total UC faculty and staff 150K, total students 200K, so > 350K people, more than 1% of population of California, have access to Current Protocols (in Molecular Biology and everything else) via University of California Digital library.

2011. Report on NHGRI claims, over 1998-2010, $141 dollars of economic activity per dollar spent on the genome projects, or 3.8 million person-years of employment, or each $1000 spent generated one person-year of employment.

Key general developments over last 10-20 years

1) Increase, then slowdown, then halt in growth of NIH research budget. Minor retrenchment at HHMI, now trending slightly up above $800M / year.

2) General strengthening of institutional, NIH, and HHMI conflict of interest guidelines.

3) Most methods patents and human gene patents expired or will expire 2005-2015

4) Clear signs that The Revolution, or aspects of it, are becoming institutionalized ("1000 dollar genome" project).

I'm saying one sign a revolution is becoming institutionalized is when you can make plans based on its continued progress

The experts look ahead

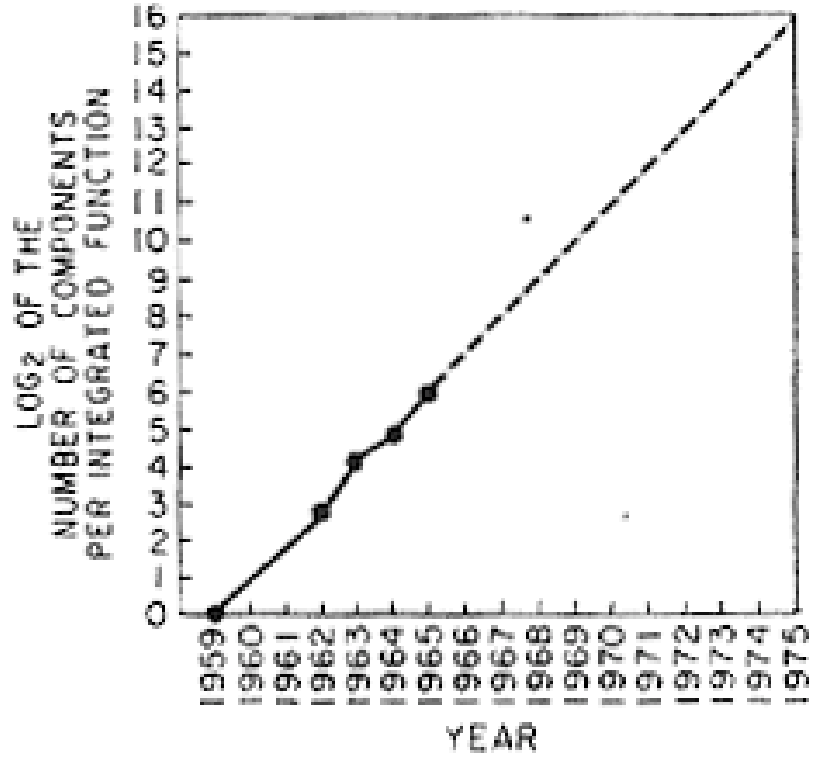
Electronics, Volume 38, Number 8, April 19, 1965

Cramming more components onto integrated circuits

With unit cost falling as the number of components per circuit rises, by 1975 economics may dictate squeezing as many as 65,000 components on a single silicon chip

By Gordon E. Moore

Director, Research and Development Laboratories, Fairchild Semiconductor division of Fairchild Camera and Instrument Corp.



Moore's law and possible future consequences.

Cartoon shows "Home computers", on sale right next to the cosmetics counter!

NHGRI staff initiated work toward "thousand dollar genome" in 2001. Here is ad for Knome, Inc. Menlo Park, October 2011 . This price is for a ten-pack, so 10 human genomes for $50K. Almost there....

Key general developments over last 10-20 years especially relevant to workshop today

1) Near universal conversion of worldwide academic scientists and funding agencies to open access scientific publication.

2) Vast empowerment of scientists at all levels and in all locations by genomic resources, Pubmed, and other online resources.

3) *Very* successful pushback by some members of public in 1990s and 2000s against transgenic plants and animals.

-> Consequence is stalemate for some human foods. During next ten years, it seems likely that there will be no widespread deployment of transgenic wheat, no transgenic pigs, etc.

-> Consequence is a workaround; most traits in plants are now introduced via breeding, via Marker Assisted Selection, rather than by transgenes

Omega-3 pigs,
Lai et al. 2006

Now, to developments in biological Knowledge and Capability important for this workshop

1880s. Pasteur demonstrates and articulates serial passaging for rabies. Nobody has defined viruses yet.

1898. Loeffler and Frosch show that the causative agent for Foot and Mouth disease passes through porcelain filters, and is thus the first "filterable virus" for animals. This isolation of a pathogenic animal virus predates 1911 Peyton Rous isolation of the RSV cancer virus.

1975. Recombinant DNA born in part by successful efforts to engineer genome of SV40, a human, DNA genome, cancer virus.

1981. First whole-genome cDNA clone for an RNA virus, Poliovirus, a + (plus) strand virus.

Cloned Poliovirus Complementary DNA Is Infectious in Mammalian Cells

Abstract. *A complete, cloned complementary DNA copy of the RNA genome of poliovirus was constructed in the Pst I site of the bacterial plasmid pBR322. Cultured mammalian cells transfected with this hybrid plasmid produced infectious poliovirus. Cells transfected with a plasmid which lacked the first 115 bases of the poliovirus genome did not produce virus.*

VINCENT R. RACANIELLO
DAVID BALTIMORE
Center for Cancer Research
and *Department of Biology,*
Massachusetts Institute of Technology,
Cambridge 02139

SCIENCE, VOL. 214, 20 NOVEMBER 1981

Key developments in biological Knowledge and Capability for this workshop

1993. Twelve years after, engineering of minus strand RNA viruses has caught up.

GENETIC MANIPULATION OF NEGATIVE-STRAND RNA VIRUS GENOMES

Adolfo García-Sastre[1] *and Peter Palese*
Department of Microbiology, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, New York 10029

Negative-strand RNA viruses have been refractory to genetic manipulation using recombinant DNA techniques. Recently, new techniques were developed that allowed the rescue of synthetic RNA molecules into influenza A viruses and, subsequently, into other negative-strand RNA viruses. These techniques are presently being used to study the molecular biology of these viruses.... Further development of this methodology has enabled the construction by recombinant DNA techniques of influenza A viruses that contain altered genomes. The phenotypic characteristics and possible applications of these novel transfectant viruses are also discussed.

Annu. Rev. Microbiol. 1993. 47:765–90

Key developments in biological Knowledge and Capability for this workshop

2006-2007. Double stranded RNA viruses catch up. Working reverse genetics allowing recovery of complex double stranded RNA viral genomes from cloned DNA for rotavirus (12 chromosomes) and reovirus (10 chromosomes).

1993-2012. Scientists who create reverse genetic systems for particular types of animal viruses become eminent or consolidate leadership positions in each [small] community of researchers who study a particular virus or viral family.

2007-2012. All major types of animal viruses now have reliable reverse genetic systems.

A Plasmid-Based Reverse Genetics System for Animal Double-Stranded RNA Viruses

Takeshi Kobayashi,[1,2] Annukka A.R. Antar,[2,3,5] Karl W. Boehme,[1,2,5] Pranav Danthi,[1,2,5] Elizabeth A. Eby,[2,3,5] Kristen M. Guglielmi,[2,3,5] Geoffrey H. Holm,[1,2,5] Elizabeth M. Johnson,[2,3,5] Melissa S. Maginnis,[2,3,5] Sam Naik,[2,4,5] Wesley B. Skelton,[1,2,5] J. Denise Wetzel,[1,2,5] Gregory J. Wilson,[1,2,5] James D. Chappell,[1,2,4,*] and Terence S. Dermody[1,2,3,*]

"With the exception of dsRNA viruses, a plasmid-based reverse genetics system exists for all major groups of animal RNA viruses, including bornaviruses, bunyaviruses, coronaviruses, flaviviruses, orthomyxoviruses, paramyxoviruses, picornaviruses, and rhabdoviruses ..... Despite extensive efforts in several laboratories, generation of an animal dsRNA virus entirely from cloned cDNAs has not been achieved. This critical technological gap is perhaps the single most important limitation to studies of these viruses."

2007-2012. Continuing technical improvement and open source publication of "how-to" articles makes all viral reverse genetic systems easier to use and to troubleshoot.

Viral Bacterial Artificial Chromosomes: Generation, Mutagenesis, and Removal of Mini-F Sequences

Hindawi Publishing Corporation
Journal of Biomedicine and Biotechnology
Volume 2012, Article ID 472537, 14 pages
doi:10.1155/2012/472537

B. Karsten Tischer and Benedikt B. Kaufer

Institut für Virologie, Freie Universität Berlin, Philippstraße 13, 10115 Berlin, Germany

Correspondence should be addressed to B. Karsten Tischer, k.tischer@fu-berlin.de and Benedikt B. Kaufer, b.kaufer@fu-berlin.de

Received 15 August 2011; Revised 21 October 2011; Accepted 27 October 2011

Academic Editor: Jiing-Kuan Yee

"Maintenance and manipulation of large DNA and RNA virus genomes had presented an obstacle for virological research. BAC vectors provided a solution to both problems as they can harbor large DNA sequences and can efficiently be modified using well established mutagenesis techniques in *Escherichia coli.* .... In this paper, we provide an overview on the strategies that can be used for the generation of virus BAC vectors and also on systems that are currently available for various virus species. Furthermore, we address common mutagenesis techniques that allow modification of BACs from single-nucleotide substitutions to deletion of viral genes or insertion of foreign sequences. Finally, we review the reconstitution of viruses from BAC vectors and the removal of the bacterial sequences from the virus genome during this process".

Key developments in biological Knowledge and Capability for this workshop

2007-2012. Availability of reverse genetic systems for all main types of animal viruses allows

a) Widespread use of guided evolution in the lab ("passaging"), eg. to change host range, increase transmissibility, or to increase or decrease pathogenticity

followed by

b) DNA sequencing to find candidate mutations,

followed by

c) Easy construction of new genomes containing candidate mutations to test their effects.

-> Again, this ubiquitous access to DNA sequence information, the universal ability to generate new sequence, and the democratization of manipulation/ and reverse genetic technologies, is relatively recent.

-> One of its consequences is to have made key questions about pathogens, questions of virulence, host range, and transmission accessible to a much broader range of scientists, not just members of self-styled elites.

2011. A typical example. Poultry veterinarians. Here, they show us how to make a pigeon strain to cause lethal disease in chickens. Proving... we now live in a world of super empowered veterinarians.

Passaging of a Newcastle disease virus pigeon variant in chickens results in selection of viruses with mutations in the polymerase complex enhancing virus replication and virulence

J. C. F. M. Dortmans,[1,2] P. J. M. Rottier,[2] G. Koch[1] and B. P. H. Peeters[1]

[1]Central Veterinary Institute of Wageningen UR, Lelystad, The Netherlands

[2]Virology Division, Department of Infectious Diseases & Immunology, Faculty of Veterinary Medicine, Utrecht University, The Netherlands

Journal of General Virology (2011), **92**, 336–345 DOI 10.1099/vir.0.026344-0

"Complete genome sequencing of virus obtained after 1, 3 and 5 passages showed the increase in virulence was... accompanied ... by mutations in the L and P replication proteins. The effect of these mutations on virulence was confirmed by means of reverse genetics using an infectious cDNA clone. Acquisition of three amino acid mutations, two in the L protein and one in the P protein, significantly increased virulence as determined by intracerebral pathogenicity index tests in day-old chickens. The mutations enhanced virus replication in vitro and in vivo and increased the plaque size in infected cell culture monolayers...."

Which brings us to H5N1

Cover, le Parisien

Paris, 6 December 2011

Flu scientists have been saying that they were going to try to make human-transmissible H5N1 for years.

Researchers say crossing avian and human flu viruses is crucial to understanding the threat of a new influenza pandemic, but they admit that they might create a monster

Tiptoeing Around Pandora's Box

www.sciencemag.org SCIENCE VOL 305 30 JULY 2004

Martin Enserink

"The aim of reassortment studies, as they're called, would not be to develop new countermeasures, says WHO's principal flu scientist, Klaus Stöhr, because researchers believe current drugs and an H5N1 vaccine in development would work against a pandemic strain as well. But the experiments would provide a badly needed way to assess the risk of a pandemic. If they indicate that a pandemic virus is just around the corner, health officials would further intensify their fight in Asia and go full-throttle in stashing vaccines and drugs; if not, they could breathe a little easier. It's an extremely important question, and we have a responsibility to answer it, insists Stöhr...

...He also downplays concerns that the results, when published, might help those who would unleash a pandemic on purpose. Anyone with the scientific smarts to do so can already find plenty of ideas in the literature, Stöhr asserts. Moreover, the studies are unlikely to produce anything that could not arise naturally, says Osterhaus: 'You could create a monster. But it's a monster that nature could produce as well'....

The studies have been discussed widely with scientists in WHO's global flu lab network and at a recent flu meeting in Lisbon, he says, and have met with nothing but 'overwhelming agreement.' 'If there are other voices, we will take them seriously,' Stöhr adds".

Seven years later, influenza researchers achieved their declared goal.

Scientists Brace for Media Storm Around Controversial Flu Studies

by Martin Enserink on 23 November 2011, 4:48 PM | 67 Comments

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ROTTERDAM, THE NETHERLANDS—Locked up in the bowels of the medical faculty building here and

"' These studies are very important,' says biodefense and flu expert Michael Osterholm, director of the Center for Infectious Disease Research and Policy at the University of Minnesota, Twin Cities. The researchers 'have the full support of the influenza community,' Osterholm says, because there are potential benefits for public health. For instance, the results show that those downplaying the risks of an H5N1 pandemic should think again', he says".

Apparently, last year, for perhaps the first time outside of movies or television, we had a claim that it was important that group of researchers in a scientific subfield decided to make-- and then made-- a new, human-transmissible virus, in order to convince others (Scientists in other subfields? Policy makers? Funding agencies?) of the potential danger from such a virus.

Issues for policy and ethics

H5N1

The Twitter "Fail Whale", since 2007 an icon of failure. Here, failure due to Twitter overload is a metaphor for failure due to not paying attention to things that really matter.

Policy issues for initiating and carrying out future research of this type

1) Any regulation by definition constitutes a burden.

2) Suppose a regulated line of research generate knowledge that could easily be used to cause harm, but also might also be used to achieve some good (for example, aid public health). There is now no system to supply that knowledge to "cleared" individuals worldwide.

3) It is not easy to make either wise general policy or wise specific decisions about initiating particular lines of work when no scientific consensus about right behavior exists. I imagine that most biologists who do not study infectious disease (and most physicists!) might wish this flu work had not been done. The recent split NSABB decision to allow publication after the work was done also reveals lack of consensus, even within that portion-- a distinct minority-- of biologists who work on infectious disease.

4) Any conceivable wise decision about whether to initiate a line of potentially problematic research must somehow weigh the benefits that might come from the new Knowledge and Capability against the danger that the new K&C might be used to cause harm.

-> But one can't know present danger that K&C from any work might be used to cause harm.

-> Even if one could know present danger, one can't possibly know future danger. But, one can reasonably stipulate that, barring catastrophe, some knowledge, such as the five or six or seven mutations to make chicken flu into human transmissible flu, can't be un-made.

-> The more one relies on expert knowledge for a careful weighing of a proposed line of work, the more the experts will tell you of the difficulties in realizing the potential benefits of the work. So, the more careful you are, the more you underestimate your potential benefits.

Ethics issues for initiating and governing future work of this type

1) There is now little engagement by broad scientific community, and no community consensus. I personally find this to be an ethical failure.

2) "Dual use" construct is flawed ethically, or at least incomplete. There are many reasons for this. Here I, will mention two.

-> "Dual use" as used by researchers means that the bad guy is always somebody else.

-> Among other things, the idea that the bad guy is somebody else ignores the fact that the mere existence of a vial of a new virus that requires armed humans to guard it in perpetuity, or the existence of the knowledge of the five (or six) mutations one needs to make the virus transmissible and lethal, is itself a harm.

Anytime humans create something sinister enough to require armed guards in perpetuity, and knowledge about how to make the thing that can never be un-learned, that work casts a kind of shadow onto the future.

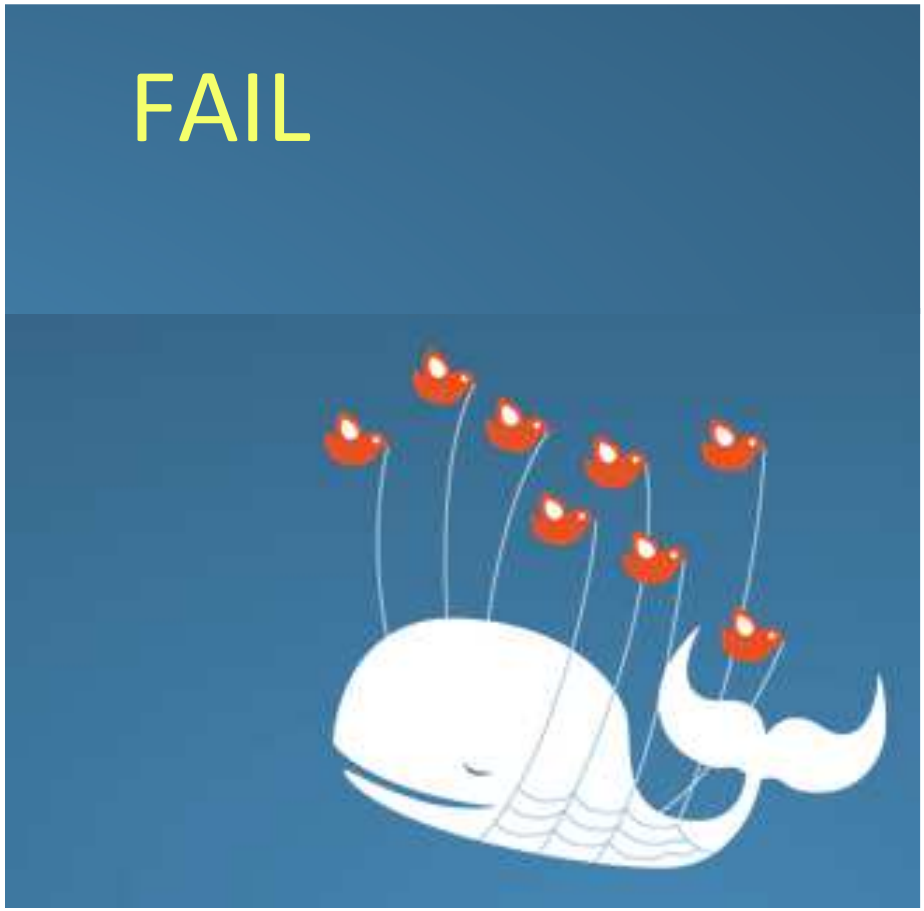
I can easily imagine future situations in which I would consider such work ethically justified, but darned well would like to see researchers articulate, and reviewers review, their reasoning before their proposed work was approved.

Possible policy and ethics paths forward

Policy path ahead

a) Recognize recent White House policy as a good save in a bad situation.

b) Rename it "Life Science Research of Concern" (or whatever); and get on with devising more robust and workable policy appropriate to the demands created by the technical abilities of the world as it actually exists in 2012.



Ethics path ahead

a) Recognize this was an ethical failure.

b) Among other lessons, I think it shows 1) that the scientific community has become too fragmented, and 2) that it will need to step in on issues of this kind in future. For example, if published accounts are true, there have been fairly loose statements that the identity of the five mutations would be important for therapy or prophylaxis, and that knowing their identity would aid disease surveillance. The last idea appears to rest on the idea that the observed path might be only evolutionary path to this change in host range. The truth of that implicit assertion isn't immediately apparent, at least to me. But thousands of scientists, including non-biologists, could have questioned it publically, yet nobody did.

"..the key lesson of the recombinant DNA controversy... [is that] this is precisely how the future will happen, in tiny, incremental 'technical decisions'. The progress of synthetic biology will never again simply involve pure science. Each decision, each new technique, each step forward will carry its own rider of ethics and responsibility."

Michael Rogers, Associate Editor, Rolling Stone, 1977

...and thanks

CBF@FHCRC

Gaymon Bennett
Meg Stalcup
Brent lab members

Elsewhere

Numerous biologists and colleagues in other disciplines