Avian flu and scientific censorship
When should scientists keep their mouths shut?

Tina Liu
Ann Fiegen
Kevin Bonham
Meet H5N1, an avian flu virus

60% mortality rate in documented cases of human infection.
“Deadly Flu Made Airborne”
- The New York Times, Dec 2011

“Dutch lab creates highly contagious killer flu”
- The Independent, Dec 2011

“'Mutant bird flu' sparking terrorist fears”
- The Telegraph, Dec 2011

“Bird Flu strains should be kept secret, government says”
- San Francisco Chronicle, Dec 2011
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Tina Liu – Censorship in the past: recombinant DNA research

Ann Fiegen – Censorship today: A killer flu virus created? How and why?

Kevin Bonham – Weighing the risks: how do we proceed?
US halts one DNA experiment at Harvard
Dec 16, 1977, Boston Globe

Genetic research risk debated in Cambridge
Boston Globe, Sept 30, 1976

Is Harvard the proper place for Frankenstein tinkering?
June 1976, Washington Star
Outline

1. Biological basics.
2. The first recombinant DNA
3. The “Frankenstein factor”: response of science and society
DNA is the blueprint of life
How is the information in DNA used?

DNA (genes) is transcribed to RNA.

“Encyclopedia” → “Messages”
How is the information in DNA “read”? 

DNA (genes) \rightarrow RNA is translated to Protein. 

“Encyclopedia” \rightarrow “Messages” \rightarrow “Workers” 

Changes in DNA lead to changes in protein.
Why is genetic research important?

- **Diabetes**: 1 of 12 people in the U.S. are affected.
- **Cancer**: Responsible for 13% of all deaths worldwide in one year

Understand genetic basis ➔ Develop better treatments
Research isn’t just about doing experiments…
Outline

1. Biological basics.
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3. The “Frankenstein factor”: response of science and society
Biological research, pre-1970

Many disadvantages!
Recombinant DNA: a new, improved tool for biology

Stanley Cohen
Stanford University

Herbert Boyer
UC-San Francisco
Construction of recombinant DNA

Frog DNA $\rightarrow$ Recombinant DNA

Bacterial DNA (plasmid) $\rightarrow$ Recombinant DNA
Construction of recombinant DNA

Bacterial cell

Frog protein

Experiments
Biological research, post-rDNA

Proteins or DNA
Biological research, post-rDNA

Proteins or DNA
Many diabetics lack insulin, a hormone.

Treatment requires regular insulin injections.
Potential of recombinant DNA?

Bacteria

= ?
“Is this the answer to Dr. Frankenstein’s dream?”

-Alfred E. Vellucci, Mayor of Cambridge, 1976
What do you think?

Questions?
Outline

1. Biological basics.
2. The first recombinant DNA
3. The “Frankenstein factor”: response of science and society
Worries of a biologist...

1. Antibiotic resistance genes
2. Toxin genes
3. Cancer genes
Asilomar: first of its kind
Asilomar: who was there?

- Scientists
- Attorneys
- Reporters
Fruits of Asilomar

• NIH Committee

• Rules and proper procedures for rDNA handling
Frankenstein… or not?

- Not as dangerous as suspected
- No public health disasters to this day
- Exchange of DNA between organisms occurs in nature, too!
10 years later...

Gene technology is generally safe, panel concludes

Boston Globe, 1987

Genetic scientists close in on cause of cystic fibrosis

Chicago Tribune, 1985

Despite questions, it’s time to embrace gene therapy

Chicago Tribune, 1990
Uses of rDNA in medicine today

- Vaccines
- Drugs
- Gene therapy
- Diagnostic tools
- And many more…
Outline

1. Biological basics.
2. The first recombinant DNA
3. The “Frankenstein factor”: response of science and society

What about this new avian flu virus?
“Dutch lab creates highly contagious killer flu”
- The Independent, Dec 2011

“Deadly Flu Made Airborne”
- NYTimes, Dec 2011

“mutant bird flu’ sparking terrorist fears”
- The Telegraph, Dec 2011
“This is an Asilomar moment”

- Paul Keim
Chair of the U.S. National Science Advisory Board for Biosecurity
December 2011
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Part II: A dangerous flu virus created? How and Why.

- Influenza virus: parts and life cycle
- Lock and Key: Cellular and Viral Receptors
- Human vs Avian vs Swine Flu
- The ‘censored’ studies
  - The Goal
  - The Experiments
  - The Benefits
- “The Doomsday virus” and Censorship
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Influenza Virus: Parts of a virus

Genome (RNA)

Surface Proteins:
- Hemaglutinin (H)
- Neuraminidase (N)
Influenza Virus: Life Cycle

1. Enter
2. Release Genome
3. Replicate Genome
4. Make Protein
5. Assemble
6. Exit
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Cells have many proteins

DNA $\rightarrow$ RNA $\rightarrow$ Protein

**Inside the cell:**
Building
Transporting

**Outside the cell:**
Hold the cell in place
Detect chemical signals
Which cells does Influenza virus infect?
Which cells does Influenza Virus infect?
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Which cells does Influenza virus infect?

- H5, H7
- H1, H2, H3

Clker.com, virology.ws
Seasonal Flu – easy come, easy go

“Seasonal Flu” (H1, H2, H3)

- Infects upper respiratory tract
- Excellent airborne transmission
- No lung infection – not severe
Avian Influenza – damage in the deep

- **H5N1 “Avian Flu”**
- Difficult to catch because air droplets must get deep
- Severe symptoms due to damaging infection of lungs
- Not transmissible to others, because virus cannot escape lungs
Questions?
Part II: A dangerous flu virus created? How and Why.

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Avian Influenza – the fear of change

H5N1 “Avian Flu”

• Not transmissible between humans
• Severe symptoms

Q: How might Avian Flu change, to gain airborne transmission in humans?
H5N1 Studies: The Goal

“… to understand what it takes for flu to go airborne [in humans].” – Ron Fouchier, Erasmus Medical Center

“To identify novel mutations in avian H5… that confer human-type receptor-binding preference.”

– Yoshihiro Kawaoka, UW-Madison
H5N1 Studies: Ferrets as a model

Ferret infections similar to human infection
Similar cellular receptors as humans
Better than mice or monkeys
H5N1 Studies: The Experiments

1. Begin with H5N1 Avian flu from a sick bird
2. Engineer ‘starter’ changes in virus’s RNA
3. Infect ferrets
4. Collect virus
H5N1 Studies: The Experiments

1. Begin with H5N1 Avian flu from a sick bird
2. Engineer ‘starter’ changes in virus’s RNA
3. Infect ferrets
4. Collect virus
   - check airborne transmission
   - check virulence
H5N1 Studies: The Experiments
“Four [mutations] in H5 ... confer efficient respiratory droplet transmission in ferrets to a virus possessing an H5 HA in a 2009 pandemic H1N1 backbone.”
H5N1 Studies: Benefits

- Surveillance
- Pandemic control
- Virus evolution
- Vaccines
- Drugs

Dual-use Research: “..with the potential for both benevolent and malevolent applications…”
H5N1 Studies: NSABB Censorship

National Science Advisory Board for Biosecurity (NSABB)

- "...the NSABB recommended that the manuscripts **not include** the methodological...**details** that could enable replication of the experiments by those who would **seek to do harm**."
H5N1 Studies: Benefits

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What’s the Harm?

• The danger of an outbreak – worst case scenario (1918)
• How could the virus be released?
  – By scientists (by accident)
  – By terrorists (on purpose)
• What are the dangers of censoring the data?
• Where do we go from here?
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The 1918 Spanish Flu

- Lasted from Jan 1918 to Dec 1920
- Between 50-100 million people killed (3-6% of the world population)
  - About 27% of humans were infected
- ~ 10-20% mortality
Recipe for Danger

Highly transmissible + High mortality = Deadly pandemic
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Highly transmissible + High mortality = Deadly pandemic
Spanish Flu, Bird Flu and “Ferret Flu”

- Highly infectious (transmissible from human to human)
- High mortality rate in humans

- Not transmissible from human to human (yet)
- High mortality rate in humans (as high as 60%*)

- Unknown person-person transmission
- Unknown mortality rate in humans

Wikimedia commons
Brief Interlude on Mortality

\[
\frac{\text{# of deaths attributed to H5N1}}{\text{# of clinically confirmed cases of H5N1}} = \text{H5N1 Mortality (\sim 60\%)}
\]
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Biosafety containment

BSL2

[Image]

BSL3

[Image]

BSL4

[Image]

Wikimedia commons
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What Was Censored?
How do you turn a genetic sequence into virus?

Bits of DNA Sequence → Enzymes → DNA building blocks
How do you turn a genetic sequence into virus?
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How do you turn a genetic sequence into virus?
Is this process easier than repeating serial passage experiment?

- This is possible without knowing anything about the genetic sequence of the virus
- The resulting mutations might be completely different
What’s the Harm?

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Interspecies transmission may happen regardless of human intervention.
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H5N1 Studies: Benefits

- Surveillance
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Science Works Best When Information is Freely Shared

http://undsci.berkeley.edu/article/0_0_0/howscienceworks_02
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The Life of Risky Research

Funding?
Risky Research
Threat of Inaction
Positive outcomes
Negative Consequences
The Path Forward is Up to Us

- Scientists have an obligation to communicate the risks and rewards of their research
- Policy makers and the public should try to stay informed
- Scientists need to be proactive in addressing risk and self-regulating
Summary

• The dangers of pandemic flu are real (though often exaggerated)
• “Ferret flu” research has a risk of releasing dangerous virus (due to accident or malicious intent)
  – Risk is unknown
  – The withheld data does not necessarily eliminate the risk
• There are also dangers to not doing the research
• Scientists must engage with the public and with policy makers to communicate risks and benefits of dual-use research
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Wikimedia commons
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- Pandemic control
- Virus evolution
- Vaccines
- Drugs
Science works as a network
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Timeline from Tina
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Thank you!

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