THE CONVERGENCE OF SCIENCE, BIOSAFETY, AND SECURITY

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FBI/WMD Directorate
Biological Countermeasures Unit

Chesapeake Area Biological Safety Association
Gaithersburg, MD Sept 12, 2017
"May you live in interesting times"
Expression attributed to a collection of short stories from the 17th Century.

寧為太平犬莫做亂離人

DNA-Encoded Movie Points Way to ‘Molecular Recorder’
Posted on July 18, 2017 by Dr. Francis Collins

Credit: Seth Shipman, Harvard Medical School, Boston
HOUSTON, [DO] WE HAVE A PROBLEM

- WHY ARE WE HERE?
- IS THERE A PROBLEM?
- WHOSE PROBLEM IS IT?
- ARE THERE SOLUTIONS?
- WHAT DO WE WANT TO ACCOMPLISH?
- WHAT DO WE NEED TO ACCOMPLISH?
- WHEN DO WE NEED SOLUTIONS?
The Weapons of Mass Destruction (WMDD) was established in 2006 to build a cohesive and coordinated approach to the prevention, response, and investigation of threats involving chemical, biological, radiological, or nuclear (CBRN) weapons.

The WMDD ensures a strategic approach to combating the continuously evolving WMD threat.

To address the unique nature of the WMD threat, the WMDD maintains a dedicated workforce with CBRN-specific expertise and experience.

WMDD Mission

Lead the efforts to deny state and non-state sponsored adversaries access to WMD materials and technologies, to detect and disrupt the use of WMD, and to respond to WMD threats and incidents.
Integrated Sections of the WMDD

1. Countermeasures Operations
2. Investigative and Operations
3. Intelligence Analysis

FBI Divisions

- Counterintelligence
- Counterterrorism
- Criminal
- Cyber

Program Focus

- Countries
- People & Groups
- Criminal Enterprises
- Computers & Networks
The FBI Field Offices allow the United States to counter biological threats at the local level while utilizing federal FBI expertise and resources.

The FBI has three regional WMD ALATs that support international partners to counter WMD threats.
WMD Coordinator

• At least one WMD Coordinator in all of the FBI’s 56 Field Offices

• Contacted by state and local Emergency Responders when confronted by a WMD threat or incident

• Act as a conduit to FBIHQ and the Federal Government for technical information, advice, and assistance

• Emphasis on pre-event planning and prevention

• Liaison with Federal regional counterparts, state, county and local response agencies, private industry and academia
FBI WMD Biological Countermeasures Unit Objectives

✓ Build national and international bioterrorism threat detection, identification, and reporting capabilities

✓ Improve bioterrorism assessment and investigative capabilities

✓ Enhance scientific, industry, and academic outreach
Biosafety and Biosecurity

**BIOSAFETY**
The application of knowledge, techniques, and equipment to prevent personal, laboratory, and environmental exposure to biological and other hazards.

**BIOSECURITY**
The application of knowledge, techniques, and equipment to protect biological materials, expertise, information, and technology from illegal access and use.
Spectrum of Biological Risks

Accidental Release
Cyber Attacks
IP and PI Theft
Malicious Misuse

Bioterrorism

Biosafety - Institutions

Biosecurity – Law Enforcement
Whole-of-Community Approach

- Managing Biological Risks
- Science Community
- Institution Leadership
- Government/Policy Makers
- Enforcement – Police/Security
Working Toward the Same Goals

- Different missions that are all vitally important that contribute to national security and resilience.

<table>
<thead>
<tr>
<th>SCIENCE/HEALTH (PH+Ag)</th>
<th>SECURITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>• DETECT/INVESTIGATE DISEASES</td>
<td>• DETECT/INVESTIGATE CRIMES</td>
</tr>
<tr>
<td>• DEVELOP MEDICAL COUNTERMEASURES</td>
<td>• COUNTER TERRORISM</td>
</tr>
<tr>
<td>• PREVENT/MITIGATE DISEASES AND OUTBREAKS (NATURAL OR INTENTIONAL)</td>
<td>• PREVENT/MINIMIZE DISTRUPTIONS TO WAY-OF-LIFE</td>
</tr>
<tr>
<td>• INPUT TO NATIONAL ECONOMY</td>
<td>• PROTECTION OF NATIONAL SECURITY AND ECONOMY</td>
</tr>
<tr>
<td>• INCREASE RESILIENCE</td>
<td>• INCREASE RESILIENCE</td>
</tr>
</tbody>
</table>
This Guy Does NOT Exist

- No such thing as zero-risk
- Hinders progress
- Too expensive

Minimization of Risk
Striking the Proper Balance

THE GOAL

BIOSAFETY  BIOSECURITY
## Threats: Actors and Consequences

<table>
<thead>
<tr>
<th><strong>Actors</strong></th>
<th><strong>Consequences</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-state Actors/Extremist Groups</td>
<td>Bioterror Event</td>
</tr>
<tr>
<td>Insiders</td>
<td>Disruption of Services</td>
</tr>
<tr>
<td>Criminal Organizations</td>
<td>Economic Loss</td>
</tr>
<tr>
<td>Cyber</td>
<td>Loss of Trust</td>
</tr>
<tr>
<td>Hacktivists</td>
<td>Excessive Regulations</td>
</tr>
<tr>
<td>Competitors</td>
<td>Disruption of Research</td>
</tr>
<tr>
<td>State Actors</td>
<td>$$$$</td>
</tr>
</tbody>
</table>

- Bioterror Event
- Disruption of Services
- Economic Loss
- Loss of Trust
- Excessive Regulations
- Disruption of Research
- $$$
Aafia Siddiqui sought by FBI for questioning since 2004


Search of computer data included references to Plum Island ADC, as well as other information regarding chemical and biological materials.

Convicted on charges of assault and attempted murder charges in February 2010

FBI Director Robert Mueller briefs during DOJ press conference August 2004
And any jihadi organization contemplating a bioterrorist attack will face many difficulties: Al Qaeda tried unsuccessfully for years to get its hands on such weapons, and the United States has devoted massive resources to preventing terrorists from making just this sort of breakthrough. The material on this laptop, however, is a reminder that jihadists are also hard at work at acquiring the weapons that could allow them to kill thousands of people with one blow.

http://www.foreignpolicy.com/articles/2014/08/28/found_the_islamic_state_terror_laptop_of_doom_bubonic_plague_weapons_of_mass_destruction_exclusive
That incident prompted the brokering of a deal by major powers that dismantled much of Syria’s chemical weapons stockpiles, but attacks using chlorine have since continued in the country. Moreover, Islamic State has also deployed chlorine and mustard agent in attacks on opposition and anti-ISIS fighters.
Insider Threats
Merial managers allegedly smuggled influenza viruses into Italy, stuffed in their carry-on luggage, or had the samples sent to them in DHL packages. The viruses were then handled illegally in makeshift labs and even stored in home fridges.

“Did we buy it?” apparently referring to the virus. “Yes, we did,” the colleague answered. “We bought it in Padua. We paid for it handsomely, as we did with all the strains we bought from her.”

Perhaps the most explosive charge is that Candoli and others deliberately spread bird flu viruses from 1999 on in an attempt to create a market for vaccines and pressure the government to approve them.

Science 5 September 2014:
Vol. 345 no. 6201 pp. 1105-1106
DOI: 10.1126/science.345.6201.1105
Italy
Cyber Security

WannaCry: What You Need to Know About Global Ransomware Attack

Learn the origins of – and how to protect yourself against – the vicious malware, which has so far infected 200,000 computers in over 150 countries.

Impact
- 150 countries
- UK and Indonesia hospital – shut down
- German railway affected
- Industries and government agencies affected in Spain, Brazil, Russia, Ukraine, Japan, India
- Nearly 30K Chinese academic institutions affected

Get your stuff back – Just $300 in Bitcoins

AROUND THE WEB
The Untold Truth of Coachella
TheList.com

Start Download
www.driverupdate.net
1. Click to Start Download
2. Run and Install DriverUpdate™
3. Scan for Drivers

DOWNLOAD NOW
DriverUpdate™
Unfortunate Cyber Issue – Round 2

• Alleged State-sponsorship
• Affected
  – Manufacturing
  – Finance Sector
  – Global Transport
  – >12,000 Ukrainian computers infected
• Cost
  – >130M USD (to one company alone)
• Still not operation normal
U.S. Healthcare Data Losses

• Community Health Systems Inc, 4.5 million patient records (Aug. 2014)

• Anthem Blue Cross Blue Shield, 80 million patient records (Jan. 2015)

• Premera Blue Cross Blue Shield, 11 million patient records (Mar. 2015)*

• UCLA Health System, 4.5 million patient records (Jul. 2015)*

• Quest Diagnostics, 34,000 patient records (Dec 2016)**

• ~ 7 million health records lost in 2017
The Challenge of Progress

Graph showing the increase in MtCO₂e/y from 1850 to 2010, comparing Global CO₂ & CH₄ emissions and Total Carbon Majors.
What About Scientific Progress

Science Progress

International/National Regulation/Policy

RATE

TIME

2017
Lower Cost

1. Customer Screening
2. Sequence Screening
3. Government Notification

- Reconstruction of the influenza A (H1N1) orthomyxovirus responsible for the 1918 "Spanish flu" pandemic
- RNA genetic code comprised of approximately 13,500 nucleotides

<table>
<thead>
<tr>
<th>Year</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>$7965</td>
</tr>
<tr>
<td>2017</td>
<td>$945</td>
</tr>
</tbody>
</table>
Dual-Use Conundrum – 2000 to 2012

Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox

RONALD J. JACKSON,1,* ALISTAIR J. RAMSAY,2,* CARINA D. CHRISTENSEN,2 SANDRA BEATON,1 DIANA F. HALL,1,3 and IAN A. RAMSHAW2
Pest Animal Control Cooperative Research Centre, CSIRO Sustainable Ecosystems, and Division of Immunology and Cell Biology, John Curtin School of Medical Research, Australian National University,4 Canberra, Australia

Received 25 July 2000/Accepted 13 November 2000

Genetic resistance to clinical mousepox (ectromelia virus) varies among inbred laboratory mice and is characterized by an effective natural killer (NK) response and the early onset of a strong CD8+ cytotoxic T-lymphocyte (CTL) response in resistant mice. We have investigated the influence of virus-expressed mouse interleukin-4 (IL-4) on the cell-mediated response during infection. It was observed that expression of IL-4 by a thymidine kinase-positive ectromelia virus suppressed cytolytic responses of NK and CTL and the expression of gamma interferon by the latter. Genetically resistant mice infected with the IL-4-expressing virus developed symptoms of acute mousepox accompanied by high mortality, similar to the disease seen when genetically sensitive mice are infected with the virulent Moscow strain. Strikingly, infection of recently immunized genetically resistant mice with the virus expressing IL-4 also resulted in significant mortality due to fulminating mousepox. These data therefore suggest that virus-encoded IL-4 not only suppresses primary antiviral cell-mediated immune responses but also can inhibit the expression of immune memory responses.

TRACES OF TERROR: THE SCIENCE; SCIENTISTS CREATE A LIVE POLIO VIRUS

By ANDREW POLLACK JULY 12, 2002

Scientists reported yesterday that they had constructed a virus from scratch for the first time, synthesizing a live polio virus from chemicals and publicly available genetic information.

The work, conducted by scientists at the State University of New York at Stony Brook, was financed by the Pentagon as part of a program to develop bio warfare countermeasures. The scientists constructed the virus using its genome sequence, which is available on the Internet, as their blueprint and genetic material from one of the many companies that sell made-to-order DNA.

H5N1 Causes Controversy Concerning Balance Between Scientific Discovery And Public Safety

30 Jan 2012 Click to Print

After scientists have engineered a new strain of H5N1, commonly known as bird flu, which is readily transmitted between humans, the Annals of Internal Medicine, the principal journal of the American College of Physicians, has published two perspectives online in advance, in which concerns are raised as to whether or not this research should be continued, and how the data should be shared for the benefit of public health.

The H5N1 virus that is circulating at present has an extremely high mortality rate, killing approximately 60% of the more than 500 confirmed human incidents, but in comparison to seasonal flu, this strain has not has not spread easily amongst humans. Two research teams, who bear no relationship with the perspective of Annals authors, have recently engineered the H5N1 virus to make it readily transmissible between ferrets, meaning that it may also be able to make it easily transmissible between humans. Their research has raised controversy in terms of safety factors and appropriateness.

A recommendation to publish the H5N1 research by The National Science Advisory Board for Biosecurity (NSABB) has evoked strong reactions amongst the scientific community. Particularly, the recommendation for journals to publish the work without detailed methodology, to eliminate the risk of replication and purposeful misuse. This has caused a division amongst the scientific community into those who are for censorship, and those who oppose it.

The first Annals perspective writes about Thomas V. Inglesby, MD, CEO and Director of the Center for Biosecurity of University of Pittsburgh Medical Center perspective, who states that the possible consequences of an engineered human transmissible H5N1 strain are devastating. Should the newly engineered strain escape the laboratory, regardless of whether
Dual-Use Conundrum - 2017

"The world just needs to accept the fact that you can do this and now we have to figure out what is the best strategy for dealing with that"

David Evans, University of Alberta

- 212,000 bp (~ 30X poliovirus)
- 6 months
- Team of scientists

An unpublished study suggests that making variola, the virus that causes smallpox, is neither expensive nor difficult.

How Canadian researchers reconstituted an extinct poxvirus for $100,000 using mail-order DNA

By Kai Kupferschmidt | Jul. 6, 2017, 5:00 PM

More Science is Needed for Better Defense

Direct economic impact of selected infectious disease

Leveraging Bioinformatics
Computer Aided Design

Archetype

Genomic Discovery Suite
2010 Screening Guidance
- Screens against genome databases
- Flags raised if hit against list of Biological Select Agents and Toxins

There is no 2017 Screening Guidance
Better Tools – Gene Editing Technologies

Zinc Finger Nuclease (ZFN)

Transcription activator-like effector nucleases (TALEN)

Clusters of regularly interspaced short palindromic repeats (CRISPR)

NgAgo (Argonaute endonuclease)
More Information Available

Graphic attributed to Francois Houllier, President of the French National Institute for Agricultural Research
James Clapper, the Director of National Intelligence, said in a report released Tuesday that Genome Editing poses as great a threat to U.S. National security as weapons of mass destruction (WMD) and proliferation, while scientists debate using the same technology to eradicate the Zika virus.
Zachary Quinto Is Returning to TV for a Biohacker Drama

By Megan Vick | Jul 7, 2016 3:56 PM EDT

New gene-editing trick discovered just in time for J-Lo’s “CRISPR” TV series

By Joel Achenbach  October 26
Kevin Esvelt, the pioneering Harvard University biologist working with Crispr and gene drives to engineer malaria-resistant mosquitoes, told me that he’d like to see the culture of ethics and safety that exists in the DIY bio world move into institutional science.
Germany launches a legal battle against the DIYbio CRISPR-Cas9 kit

Published 4 April 2017 by Ewen Chardronnet

The incredible story of The Odin’s CRISPR-Cas9 gene-editing kit, which travels across the Atlantic and sets off the first legal-sanitary counter-attacks.
### Bavarian Government found Contaminants

<table>
<thead>
<tr>
<th>Isolate</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>isolate 1</td>
<td>dissolved lyophilisate</td>
<td>open, but not dissolved lyophilisate</td>
<td>originally sealed aliquot</td>
</tr>
<tr>
<td></td>
<td>(17-0042151-001-01)</td>
<td>(17-0042151-002-01)</td>
<td>(17-0042151-003-01)</td>
</tr>
<tr>
<td>isolate 2</td>
<td><em>Kluyvera intermedia</em></td>
<td><em>Klebsiella pneumoniae</em></td>
<td><em>Klebsiella pneumoniae</em></td>
</tr>
<tr>
<td></td>
<td>(Ampicillin resistant)</td>
<td>(phenotypically Extended- β-lactamase-formers = ESBL)</td>
<td>(phenotypically Extended- β-lactamase-formers = ESBL)</td>
</tr>
<tr>
<td>isolate 3</td>
<td><em>Kluyvera intermedia</em></td>
<td><em>Enterobacter spp.</em></td>
<td><em>Enterococcus faecalis</em></td>
</tr>
<tr>
<td></td>
<td>(Ampicillin resistant)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>isolate 4</td>
<td><em>Enterobacter spp.</em></td>
<td>Representatives of <em>Enterobacter cloacae</em>-group</td>
<td><em>Klebsiella pneumoniae</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(phenotypically Extended- β-lactamase-formers = ESBL)</td>
<td>(phenotypically Extended- β-lactamase-formers = ESBL)</td>
</tr>
<tr>
<td>isolate 7</td>
<td><em>Klebsiella pneumoniae</em></td>
<td></td>
<td><em>Klebsiella pneumoniae</em></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(phenotypically Extended- β-lactamase-formers = ESBL)</td>
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<tr>
<td>isolate 8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>isolate 9</td>
<td></td>
<td></td>
<td>Bacteria of the <em>B. cereus</em> group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(no formability for human medically relevant toxins Cereulide, NHE, HBL and cytotoxin K)</td>
</tr>
<tr>
<td>isolate 10</td>
<td></td>
<td></td>
<td></td>
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</table>
“We hadn’t really anticipated how much of an impact this would have,” Almquist said. She said she was relieved that they didn’t end up assembling the complete gene drive: “We are maybe not experienced enough to be dealing with [this technology].”

Meanwhile, sophomore Ajinkya Limkar said that the controversy inspired by their project has only motivated him further.
Concerns include:
Ethical, Environmental, Cultural, Society, Economics
### Mitigation Strategies – Scientifically Derived

#### Potentially stringent confinement strategies for gene drive research

Multiple stringent confinement strategies should be used whenever possible.

<table>
<thead>
<tr>
<th>TYPE</th>
<th>STRINGENT CONFINEMENT STRATEGY</th>
<th>EXAMPLES</th>
</tr>
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</table>
| Molecular   | Separate components required for genetic drive  
                          Target synthetic sequences absent from wild organisms               | sgRNA and Cas9 in separate loci (8)                                     |
| Ecological  | Perform experiments outside the habitable range of the organism  
                          Perform experiments in areas without potential wild mates             | Anopheles mosquitoes in Boston                                            |
| Reproductive| Use a laboratory strain that cannot reproduce with wild organisms                                | Drosophila with compound autosomes*                                       |
| Barrier     | Physical barriers between organisms and the environment  
                          • Remove barriers only when organisms are inactive  
                          • Impose environmental constraints  
                          • Take precautions to minimize breaches due to human error             | Triply nested containers, >3 doors (6)  
                          Anesthetize before opening (6)                                           |
|             |                                                                                                 | Low-temperature room, air-blast fans  
                          Keep careful records of organisms, one investigator performs all experiments (6) |

*An example of reproductive confinement would be Drosophila laboratory strains with a compound autosome, where both copies of a large autosome are conjoined at a single centromere. These strains are fertile when crossed inter se but are sterile when outcrossed to any normal or wild-type strain because all progeny are monosomic or trisomic and die early in development.

Akbari, et al., Biosafety, August 2015
Narcotic drugs could soon be manufactured by yeast

Though this prototype yeast was not particularly efficient, some further tweaking converted it into a veritable drug factory—capable of cooking up 131mg of opioids (the equivalent of about 26 medical doses of diamorphine) per litre of culture over a four-day manufacturing cycle.

Importance of Partnerships

**Science and Security Collaboration**

- Science Progress
- Self-Governance
- Informed Policy Development
- International/National Regulation/Policy

**TIME**

2017
## Emerging Applications

<table>
<thead>
<tr>
<th>AGRICULTURE</th>
<th>GM Crops and Livestock</th>
<th>N Fixation, Glowing Plants, Aquabounty</th>
</tr>
</thead>
<tbody>
<tr>
<td>INDUSTRY</td>
<td>Synthesis of Organic Materials</td>
<td>Fuel, Flavors, Drugs</td>
</tr>
<tr>
<td>MEDICINE</td>
<td>Regenerative Medicine, Somatic and Germline Cell Therapy</td>
<td></td>
</tr>
<tr>
<td>ENVIRONMENT</td>
<td>Remediation; Control Vector Borne Disease and Invasive Species</td>
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*Slide courtesy of Dr. Kenneth Oye, MIT*
Summary

• Science and biotechnologies pose unique safety and security challenges
• However, they also provide the solutions
• Risk assessments need to be wholistic
  • Not only about pathogens-of-concern
  • Need to know the threats (inside and out)
  • Multi-sectoral approach (not only about the science)
IF ONLY

GO BACK. WE F*% UP EVERYTHING.
THANK YOU