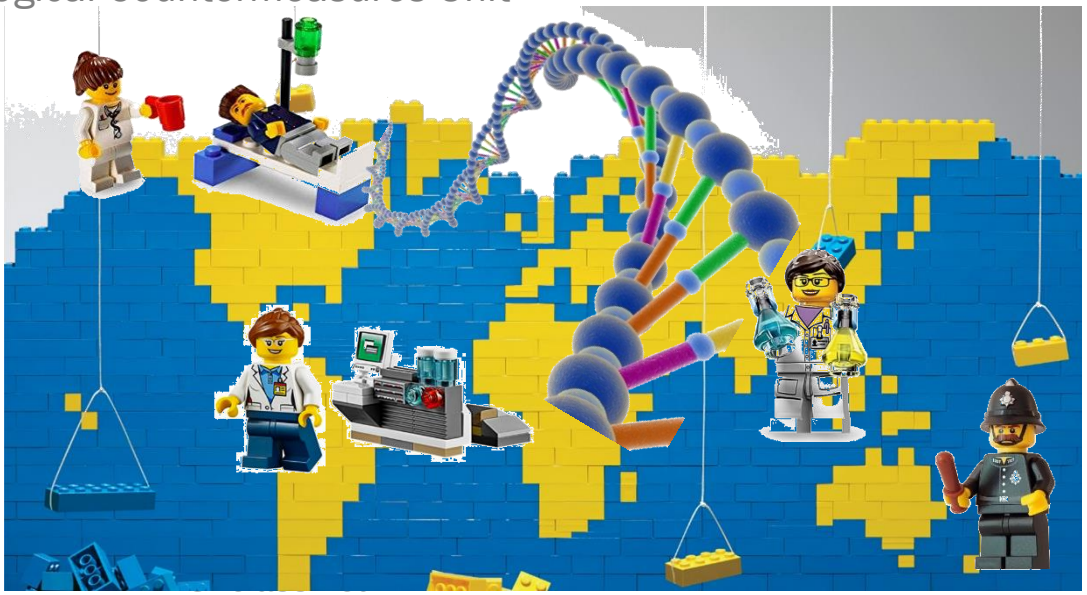
THE CONVERGENCE OF SCIENCE, BIOSAFETY, AND SECURITY

William So
Policy & Program Specialist, Ph.D.
FBI/WMD Directorate
Biological Countermeasures Unit

Chesapeake Area Biological Safety Association
Gaithersburg, MD Sept 12, 2017



Blessing or Curse

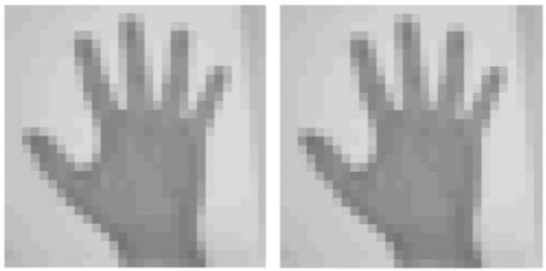
“May you live in interesting times”

Expression attributed to a collection of short stories from the 17th Century.

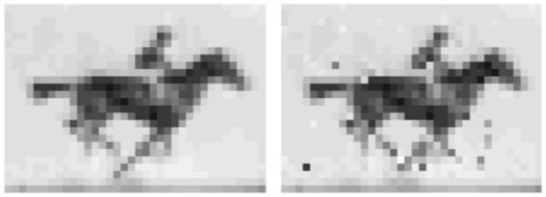
寧為太平犬莫做亂離人

DNA-Encoded Movie Points Way to ‘Molecular Recorder’

Posted on July 18, 2017 by Dr. Francis Collins



Original Image | Image Reconstructed From Bacteria



Original Image | Image Reconstructed From Bacteria

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 Directorate

WMDD Mission

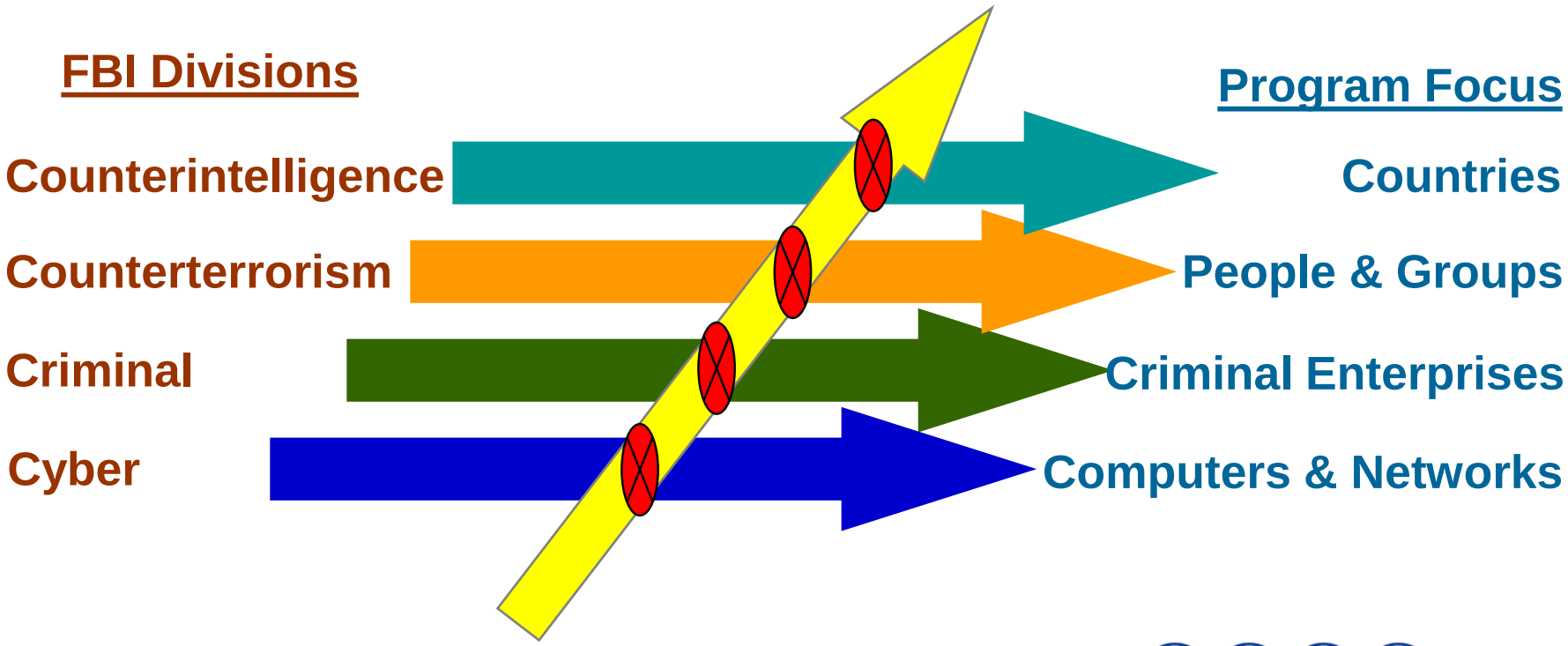
Lead the efforts to deny state and non-state sponsored adversaries access to WMD materials and technologies, to detect and disrupt the use of WMD, and to respond to WMD threats and incidents.

- 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**.

Weapons of Mass Destruction Directorate

Integrated Sections of the WMDD

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



FBI WMD Coordinators

The FBI Field Offices allow the United States to counter biological threats at the local level while utilizing federal FBI expertise and resources.

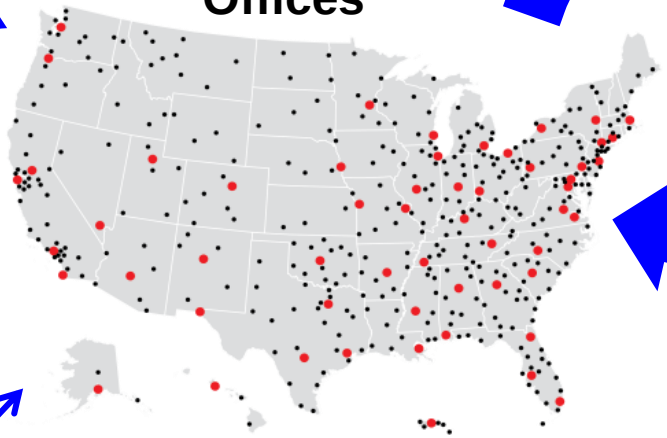
FBI Headquarters

Academic Researchers

Amateur Biologists

Clinicians/ Veterinarians

FBI Field Offices



Biotech Companies

General Public

Diagnostic Laboratories

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

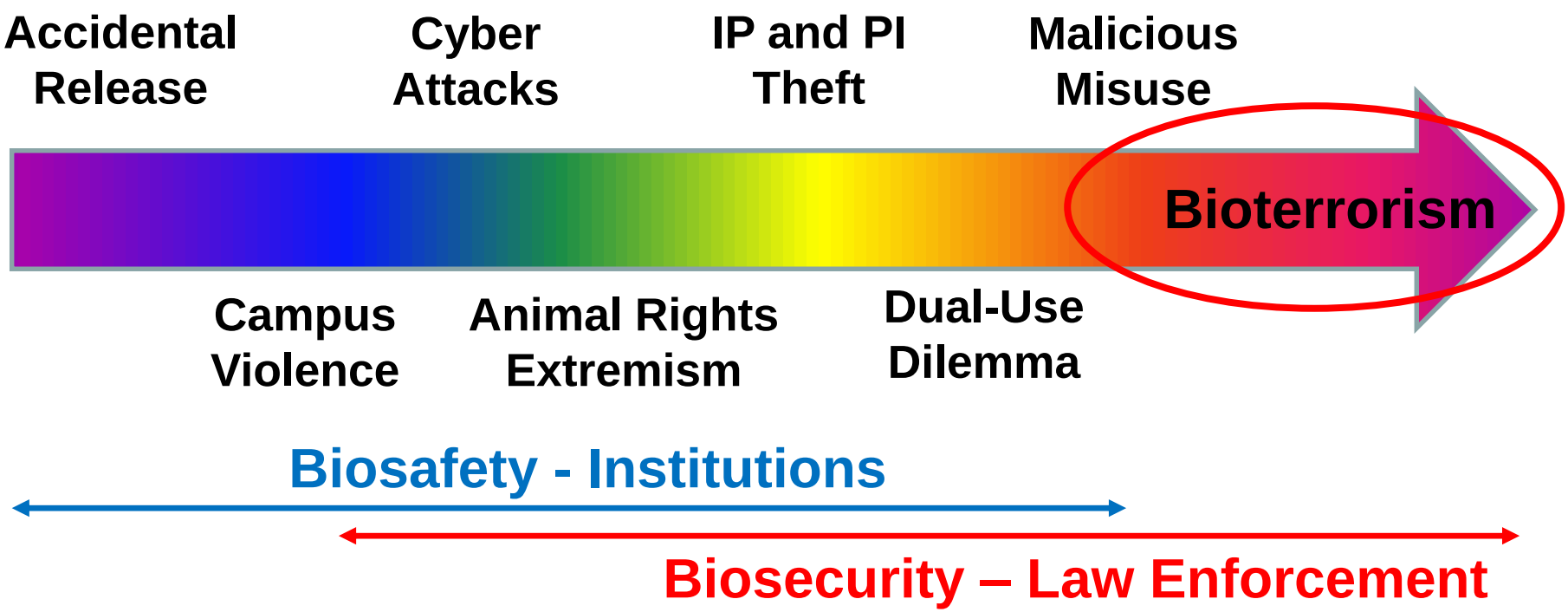
BIOSAFETY

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

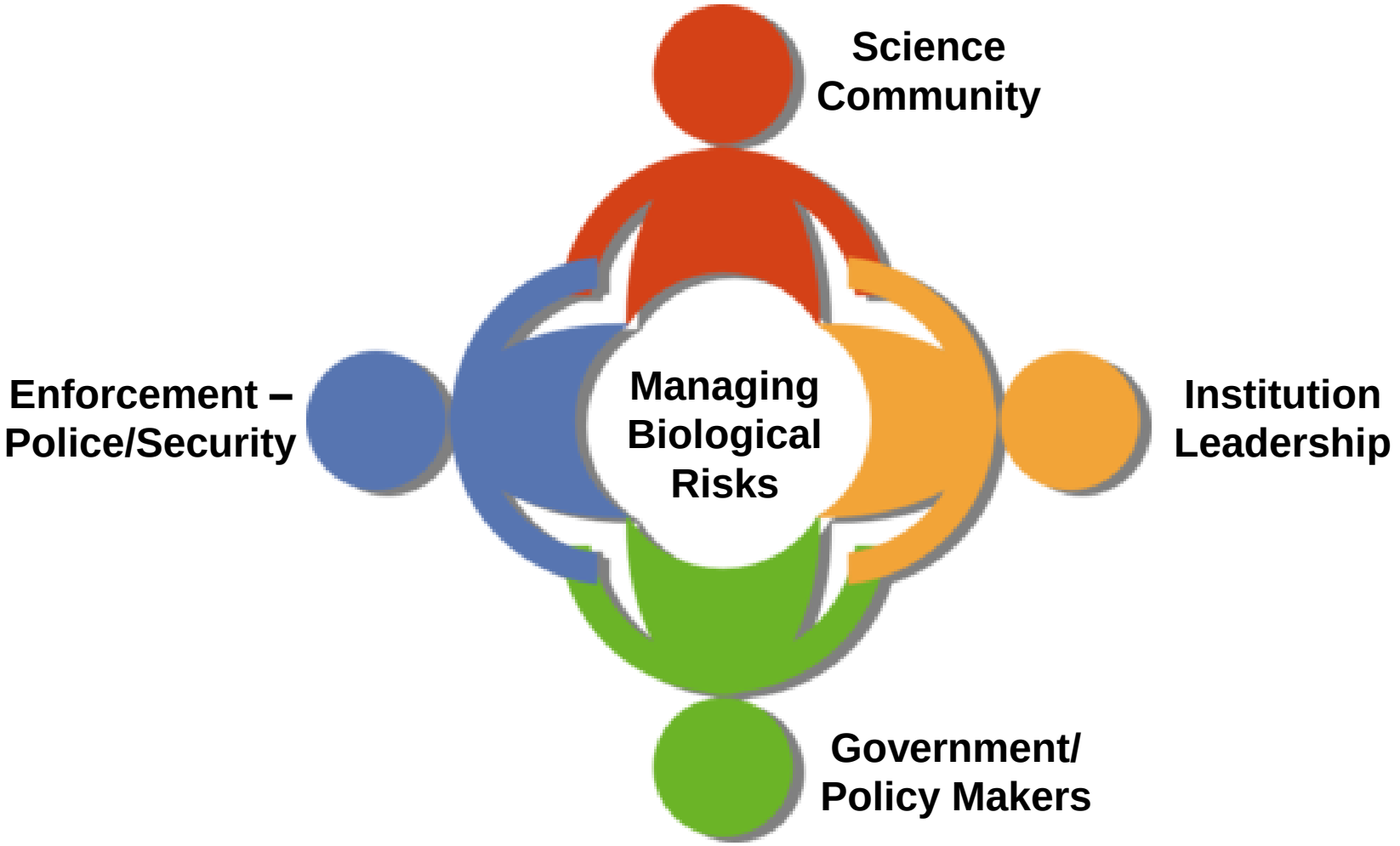
BIOSECURITY

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

Spectrum of Biological Risks



Whole-of-Community Approach

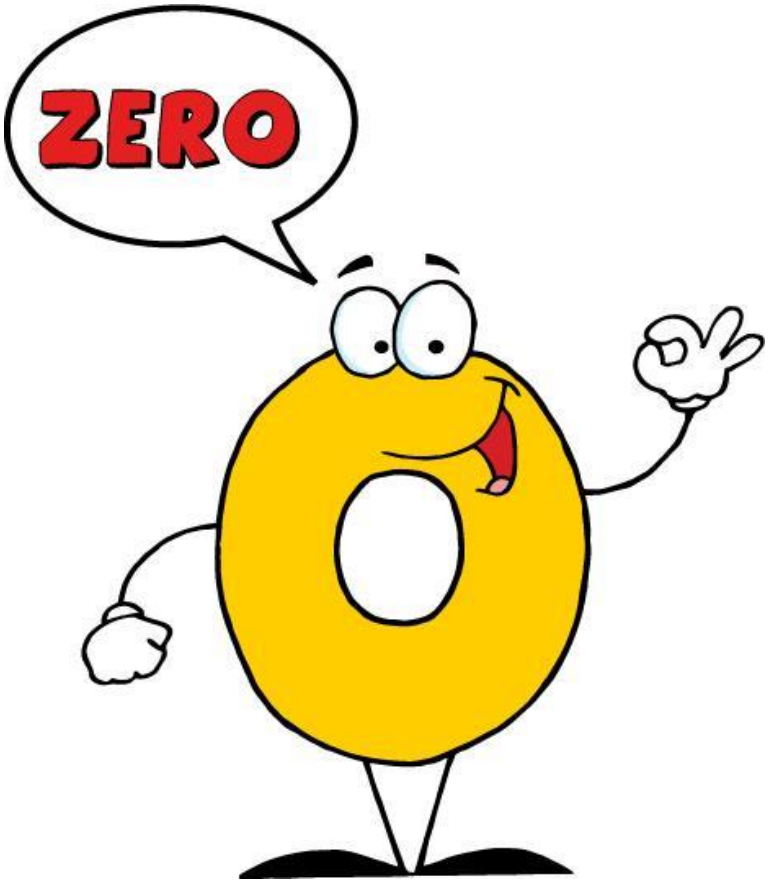


Working Toward the Same Goals

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

SCIENCE/HEALTH (PH+Ag)	SECURITY
• DETECT/INVESTIGATE DISEASES • DEVELOP MEDICAL COUNTERMEASURES • PREVENT/MITIGATE DISEASES AND OUTBREAKS (NATURAL OR INTENTIONAL) • INPUT TO NATIONAL ECONOMY	• DETECT/INVESTIGATE CRIMES • COUNTER TERRORISM • PREVENT/MINIMIZE DISTRUPTIONS TO WAY-OF-LIFE • PROTECTION OF NATIONAL SECURITY AND ECONOMY
• **INCREASE RESILIENCE**	• **INCREASE RESILIENCE**

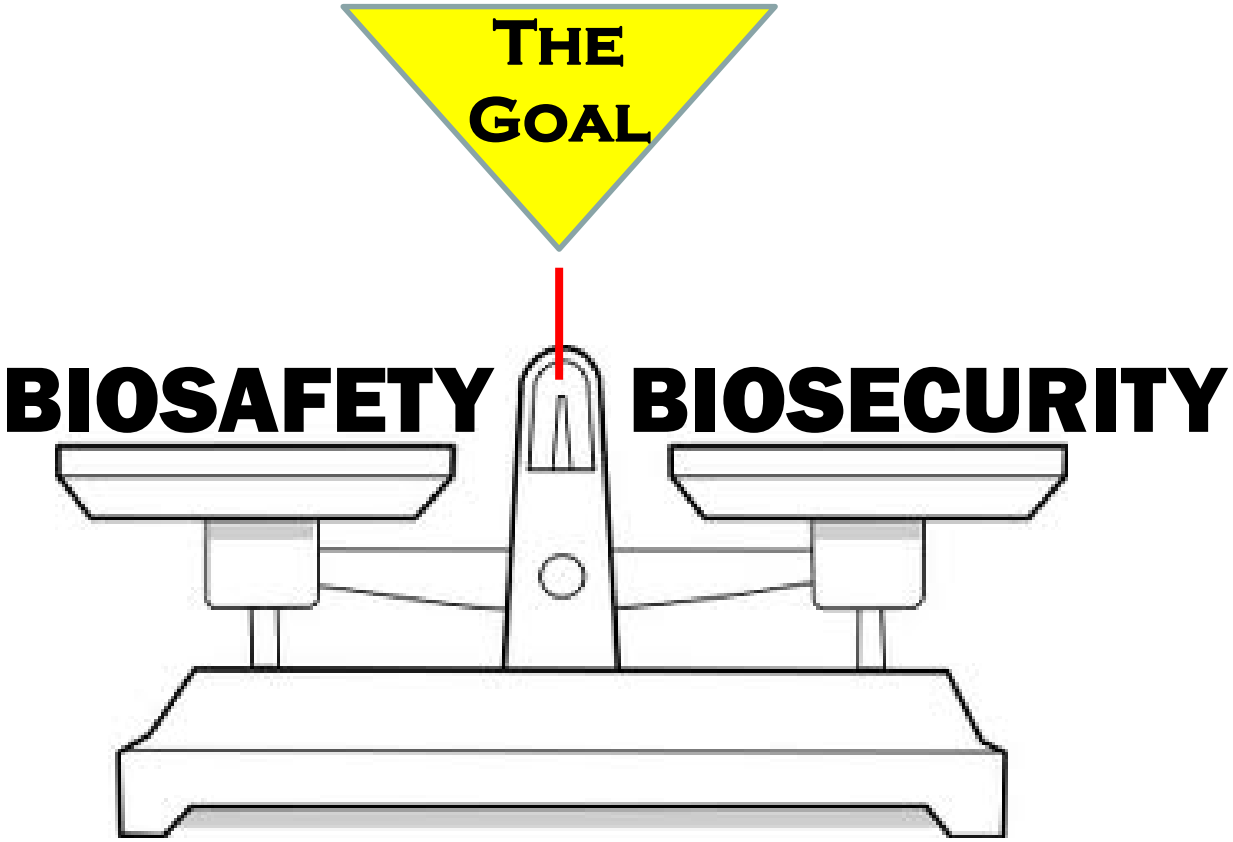
This Guy Does NOT Exist



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

- <u>Minimization of Risk</u>

Striking the Proper Balance



Threats: Actors and Consequences

Actors

- Non-state Actors/ Extremist Groups
- Insiders
- Criminal Organizations
- Cyber
  - Hacktivists
  - Competitors
- State Actors

Consequences

- Bioterror Event
- Disruption of Services
- Economic Loss
- Loss of Trust
- Excessive Regulations
- Disruption of Research
- $$$

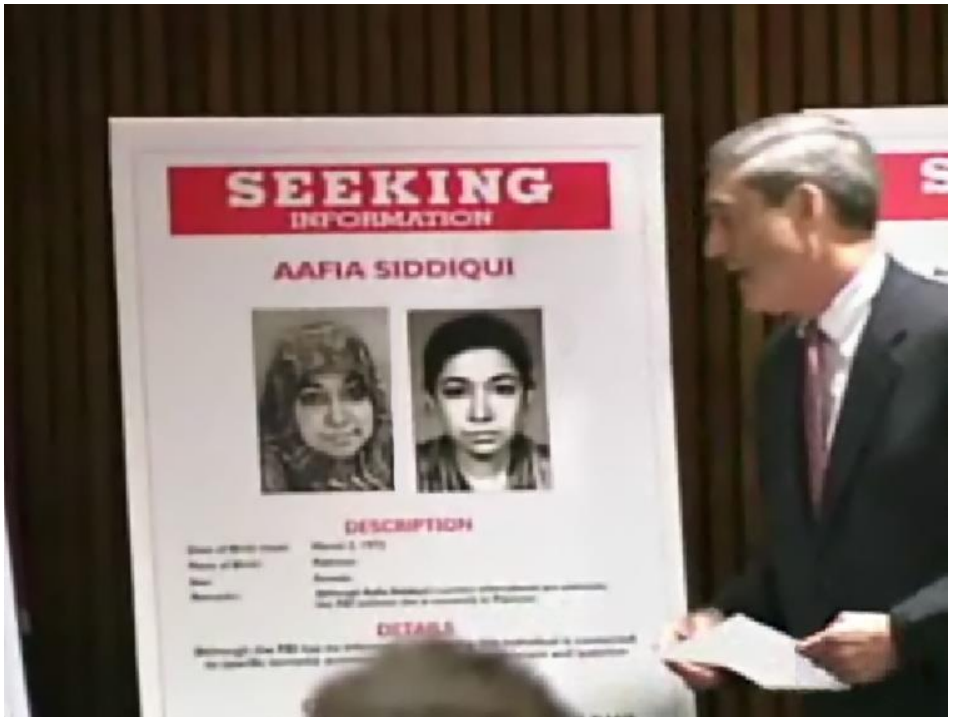
Al Qa'ida Linked Subject

Aafia Siddiqui sought by FBI for questioning since 2004

MIT & Brandeis educated neuroscientist arrested in Afghanistan on 17 July 2008.

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

Non-State Actors Continual Efforts

EXCLUSIVE

Found: The Islamic State's Terror Laptop of Doom

Buried in a Dell computer captured in Syria are lessons for making bubonic plague bombs and missives on using weapons of mass destruction.

BY HARALD DOORNBOS , JENAN MOUSSA | AUGUST 28, 2014

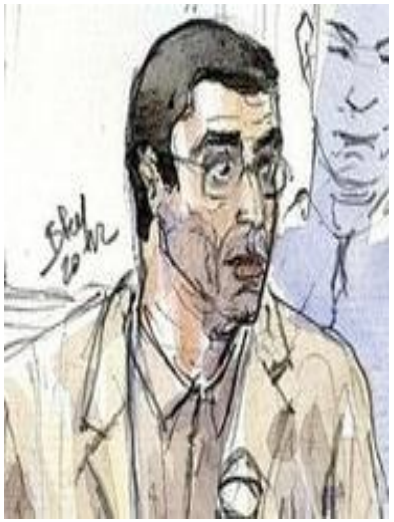
And any jihadi organization contemplating a bioterrorist attack will face many difficulties: Al Qaeda tried unsuccessfully for years to get its hands on such weapons, and the United States has devoted massive resources to preventing terrorists from making just this sort of breakthrough. **The material 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.**

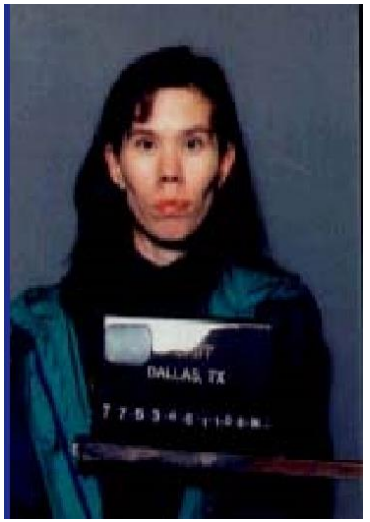
http://www.foreignpolicy.com/articles/2014/08/28/found_the_islamic_state_terror_laptop_of_doom_bubonic_plague_weapons_of_mass_destruction_exclusive

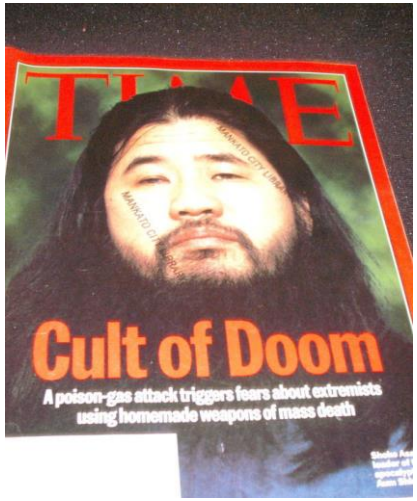
Chemical Weapons Use – OPCW FFM

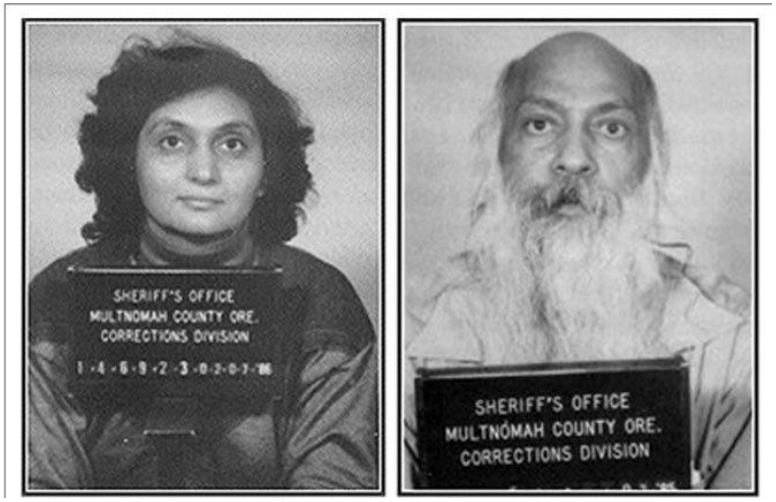
That incident prompted the brokering of a deal by major powers that dismantled much of Syria's chemical weapons stockpiles, but attacks using chlorine have since continued in the country. Moreover, Islamic State has also deployed chlorine and mustard agent in attacks on opposition and anti-Isis fighters.

Insider Threats









Flu Researcher Alleged Illegally Activities

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.”

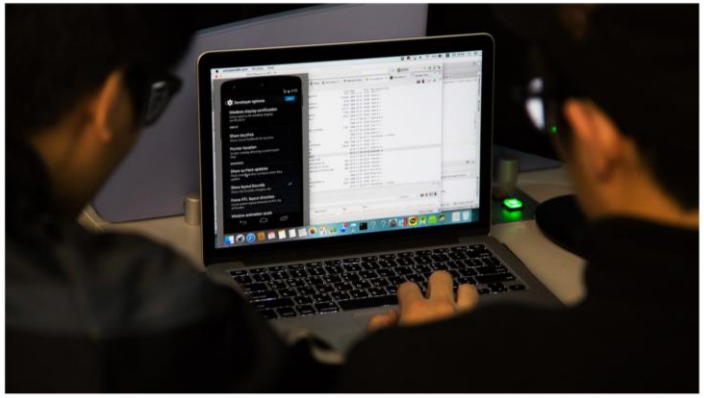
Science 5 September 2014:
Vol. 345 no. 6201 pp. 1105-1106
DOI: 10.1126/science.345.6201.1105
Italy

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.

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



Learn what you need to know about WannaCry, the vicious strain of ransomware that has affected roughly 200,000 computers in over 150 countries. Seong Joon Cho/Bloomberg/Getty

Get your stuff back – Just $300 in Bitcoins

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

Unfortunate Cyber Issue – Round 2

Petya author releases master decryption key for all versions of the ransomware

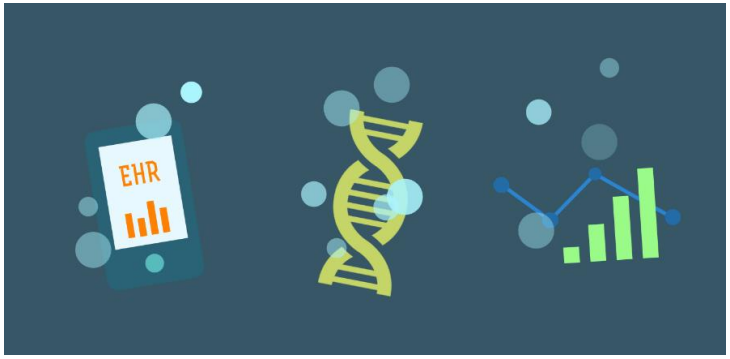
By Mark Wyciślik-Wilson | Published 2 days ago | Follow @MarkWilsonWords

9 Comments | Like 84 | Share 29 | G+1 7 | Tweet

- 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

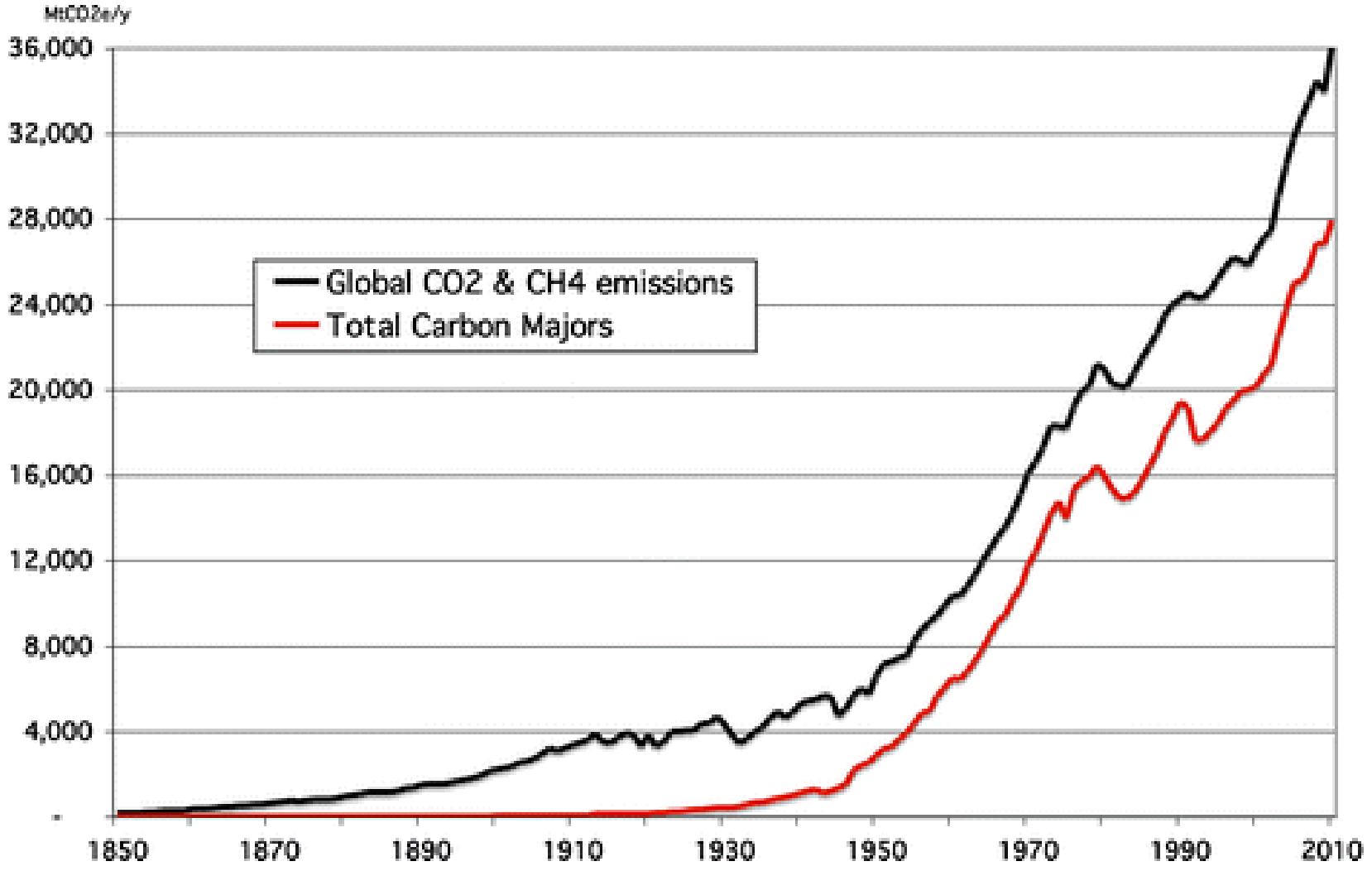
U.S. Healthcare Data Losses

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

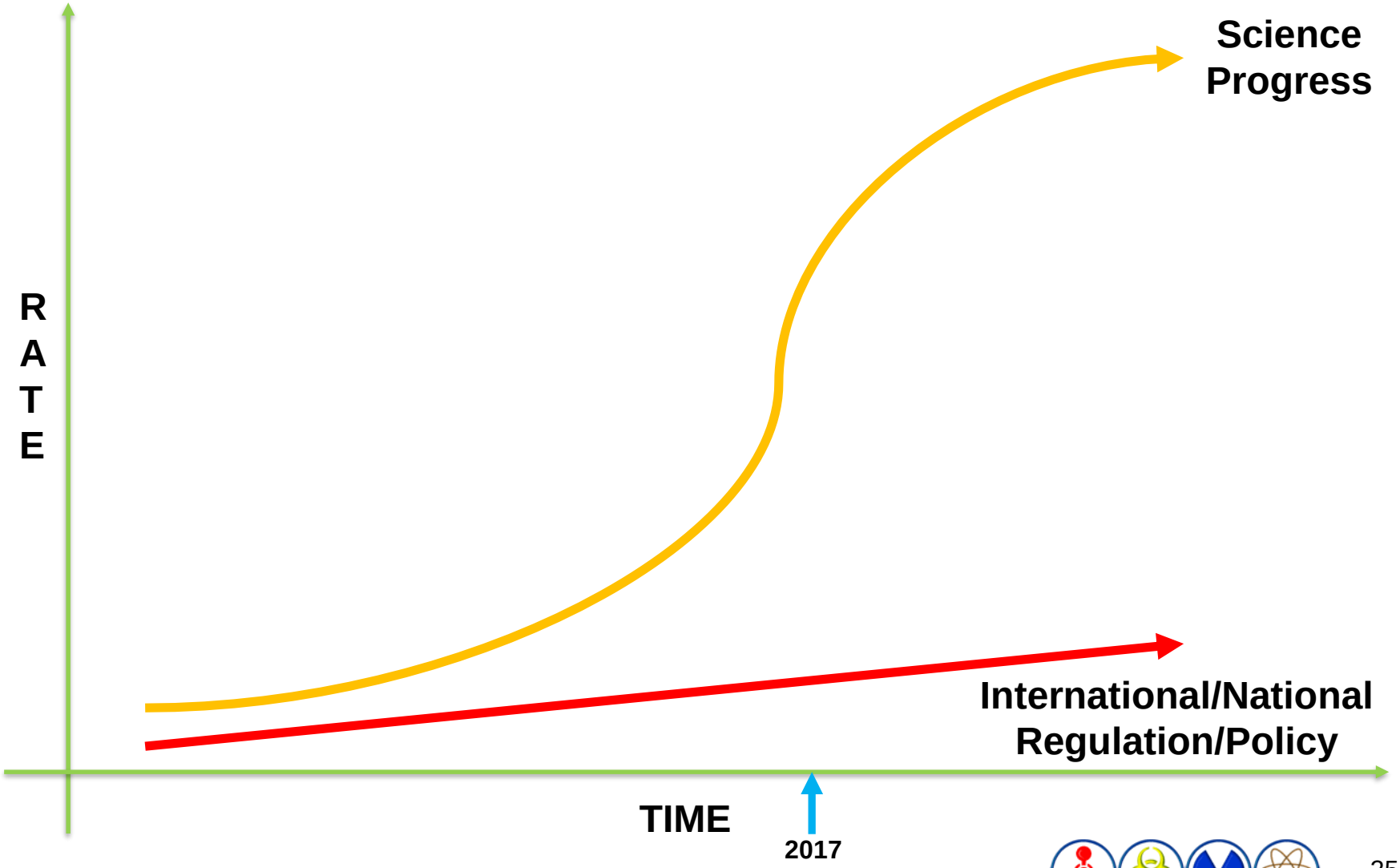


- Anthem Blue Cross Blue Shield,
  80 million patient records (Jan. 2015)
- Premera Blue Cross Blue Shield, 11 million patient records (Mar. 2015)*
- UCLA Health System, 4.5 million patient records (Jul. 2015)*
- **Quest Diagnostics, 34,000 patient records (Dec 2016)****
- **~ 7 million health records lost in 2017**
  http://www.healthcareitnews.com/slideshow/biggest-healthcare-breaches-2017-so-far?page=1

The Challenge of Progress

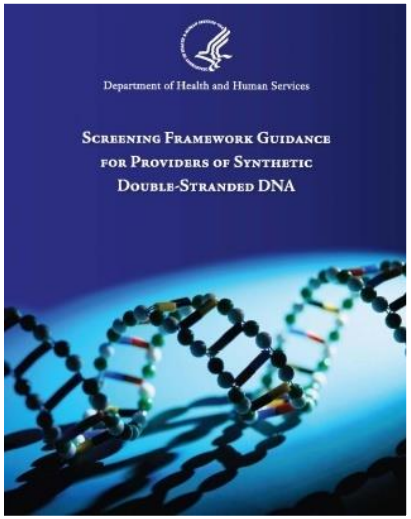


What About Scientific Progress

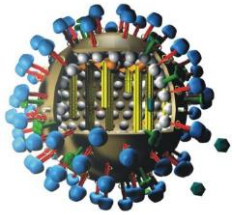


Lower Cost

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



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



2010	2017
$7965	$945

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,[1,2*] ALISTAIR J. RAMSAY,[2†] CARINA D. CHRISTENSEN,[2] SANDRA BEATON,[1] DIANA F. HALL,[1‡] AND IAN A. RAMSHAW[2]

Pest Animal Control Cooperative Research Centre, CSIRO Sustainable Ecosystems,[1] and Division of Immunology and Cell Biology, John Curtin School of Medical Research, Australian National University,[2] 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 fulminant 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 biowarfare 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

MNT medicalnewstoday.com

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.

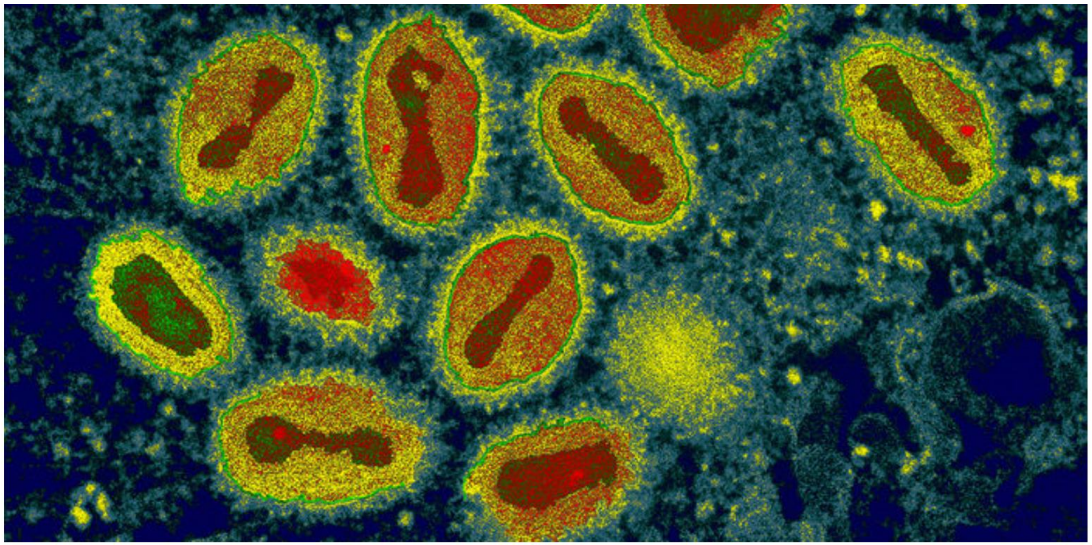
The H5N1 virus that is circulating at present has an extremely high mortality rate, killing approximately 60% of the more than 500 confirmed human incidents, but in comparison to seasonal flu, this strain has not has not spread easily amongst humans. Two research teams, who bear no relationship with 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*



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

Eye of Science/Science Source

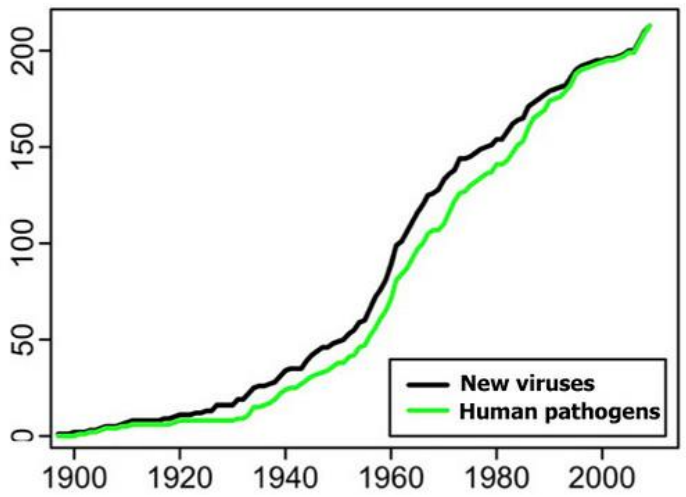
- 212,000 bp (~ 30X poliovirus)
- 6 months
- Team of scientists

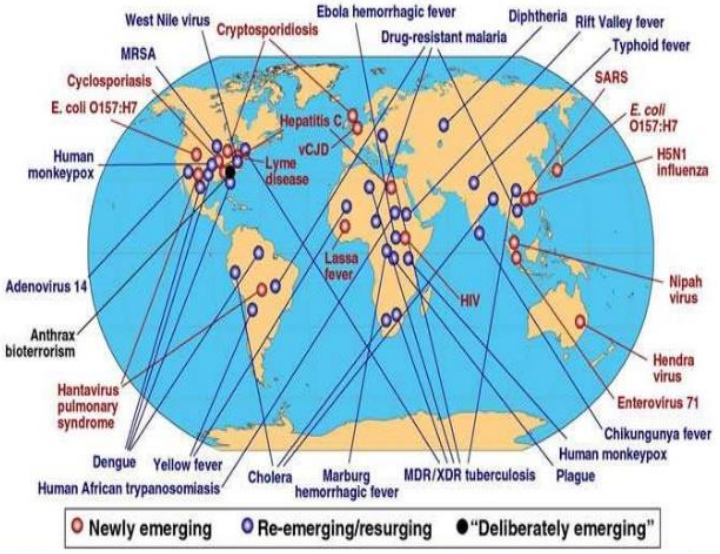
http://www.sciencemag.org/news/2017/07/how-canadian-researchers-built-poxvirus-100000-using-mail-order-dna

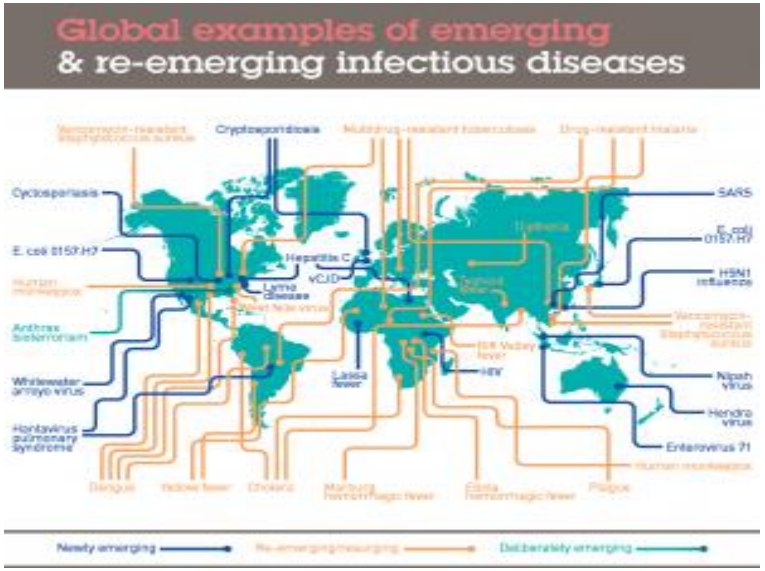
How Canadian researchers reconstituted an extinct poxvirus for $100,000 using mail-order DNA

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

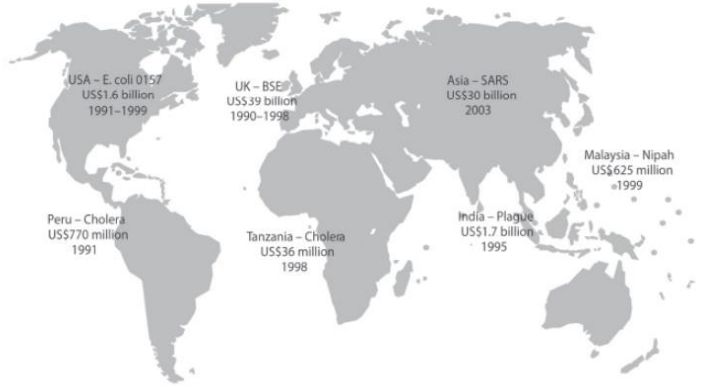
More Science is Needed for Better Defense







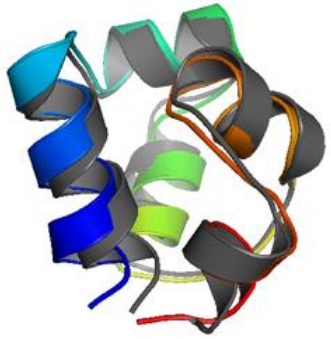
Direct economic impact of selected infectious disease

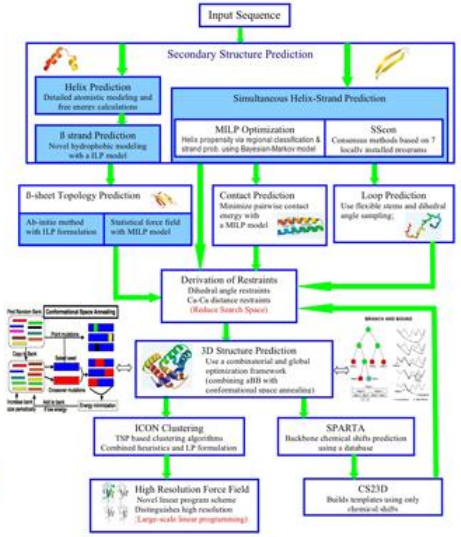


[a] Excludes economic impact of human sickness and death.

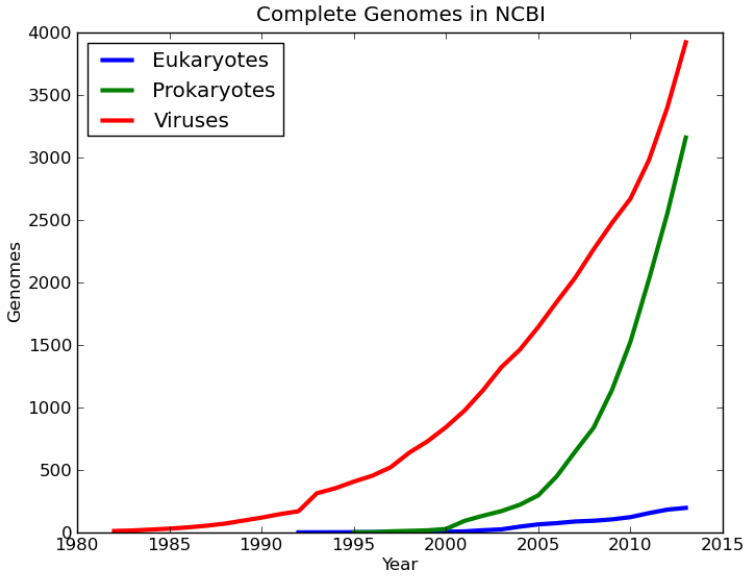
Heymann DL. Emerging and re-emerging infections. In *Oxford Textbook of Public Health*, 5th ed, 2009, p1267.

Leveraging Bioinformatics





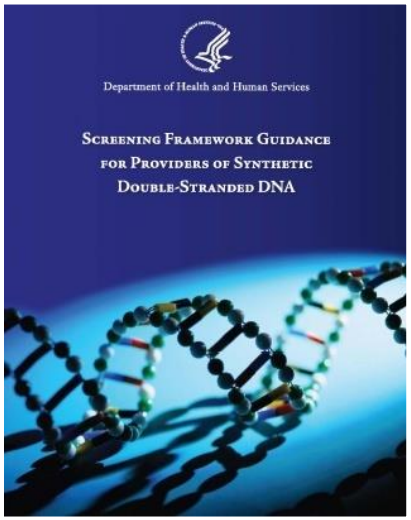
ASTRO-FOLD: first principles-based protein structure prediction



Computer Aided Design

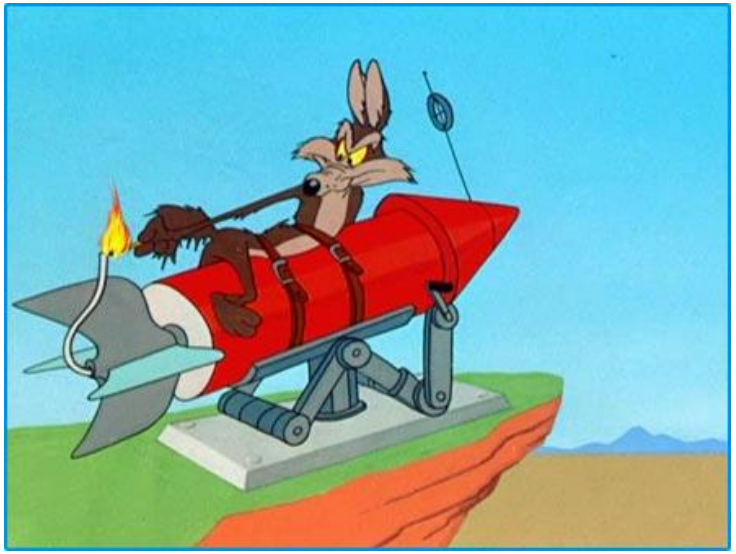
Archetype®

Sequence Orders – Sequence → Function



2010 Screening Guidance

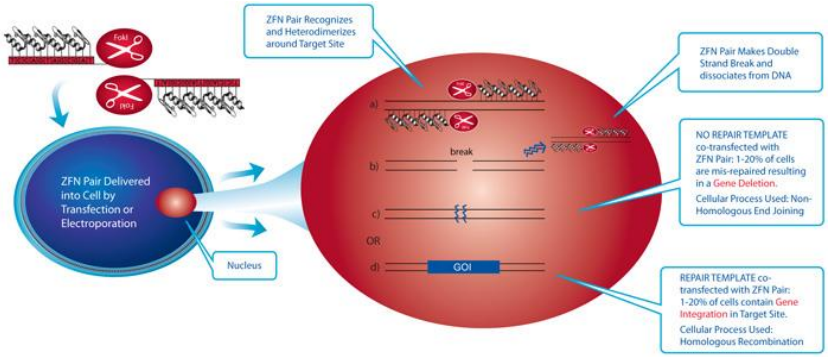
- Screens against genome databases
- Flags raised if hit against list of Biological Select Agents and Toxins



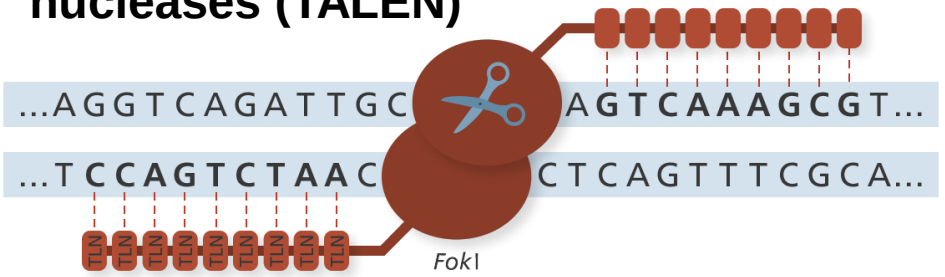
There is **no** 2017 Screening Guidance

Better Tools – Gene Editing Technologies

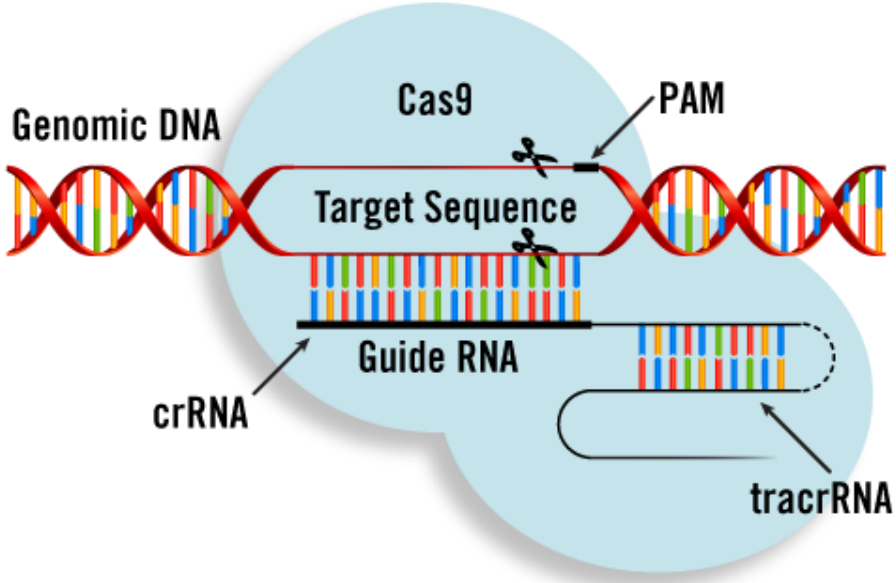
Zinc Finger Nuclease (ZFN)



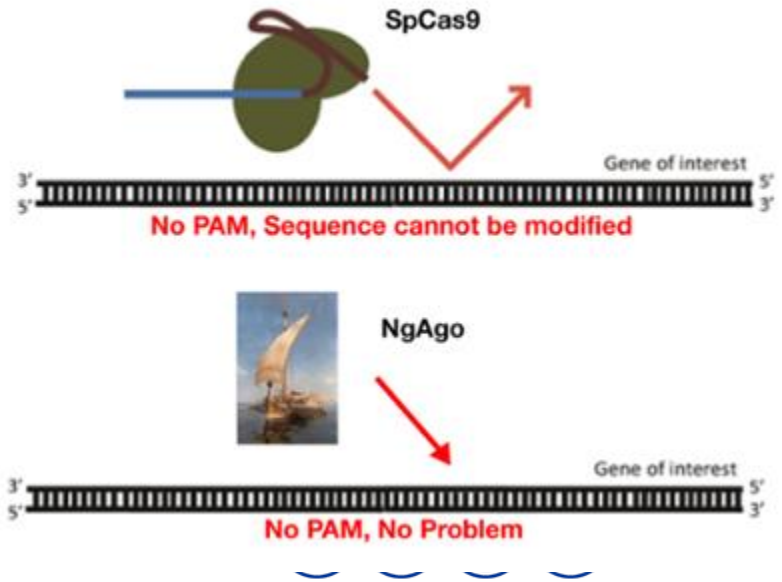
Transcription activator-like effector nucleases (TALEN)



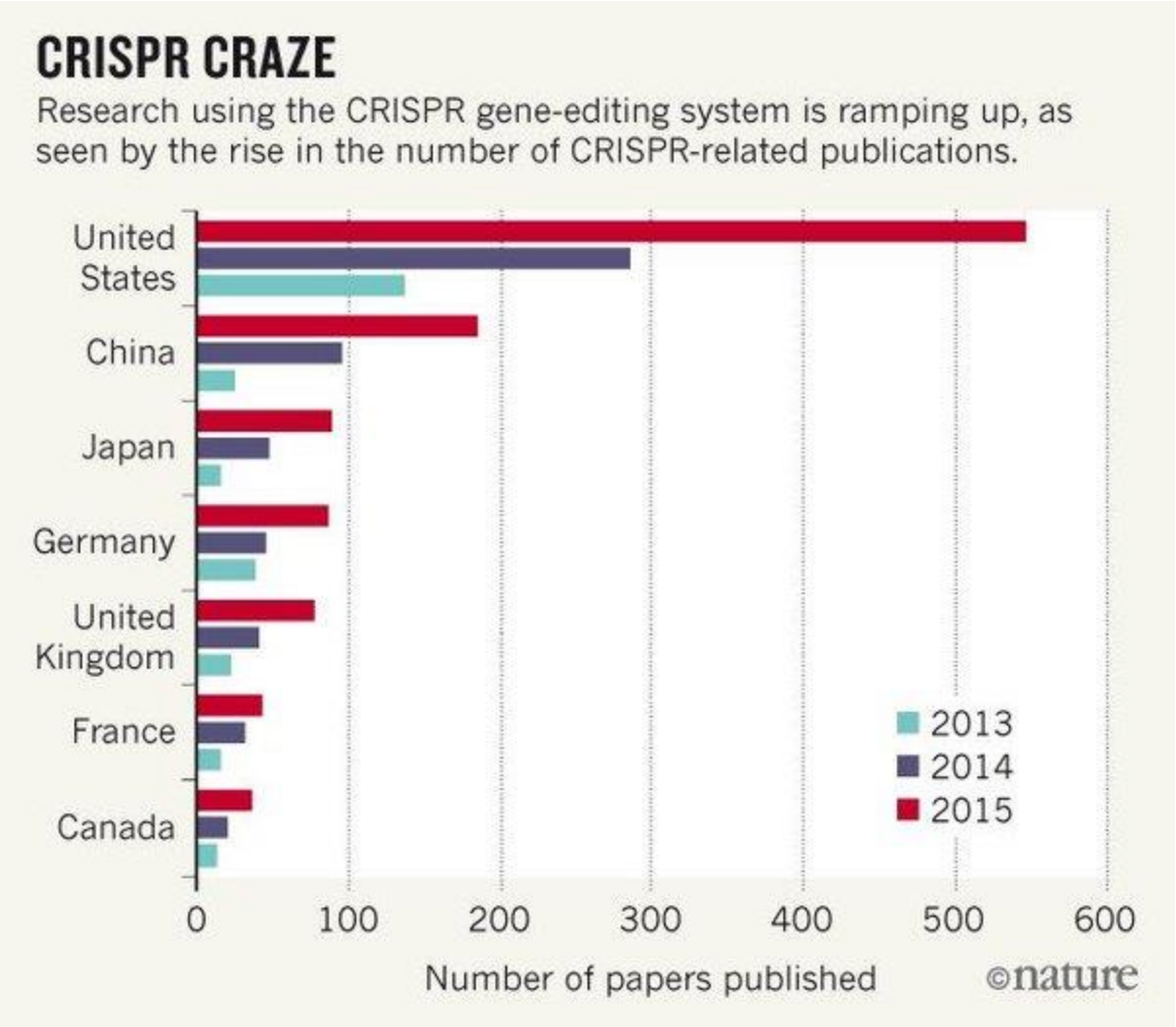
Clusters of regularly interspaced short palindromic repeats (CRISPR)



NgAgo (Argonaute endonuclease)



More Information Available



Graphic attributed to Francois Houllier, President of the French National Institute for Agricultural Research

Security Concerns of Gene Editing

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**.

https://www.trunews.com/dni-chief-calls-gene-editing-a-wmd-mit-suggests-use-for-zika/#8SEyadecyzm0aipd.99

Science…Entertainment…Reality

The Washington Post

New gene-editing trick discovered just in time for J-Lo's "CRISPR" TV series

By Joel Achenbach October 26

Zachary Quinto Is Returning to TV for a Biohacker Drama

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

The Concern over DIYbio

I played God with The Odin's DIY CRISPR Kit

And lo, it was glorious.

Andrew Tarantola, @terrortola
06.30.16 in DIY

Comments

2862
Shares

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.

International Attention

MAKERY media for labs FR

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.

EN FR

Bavarian Government found Contaminants

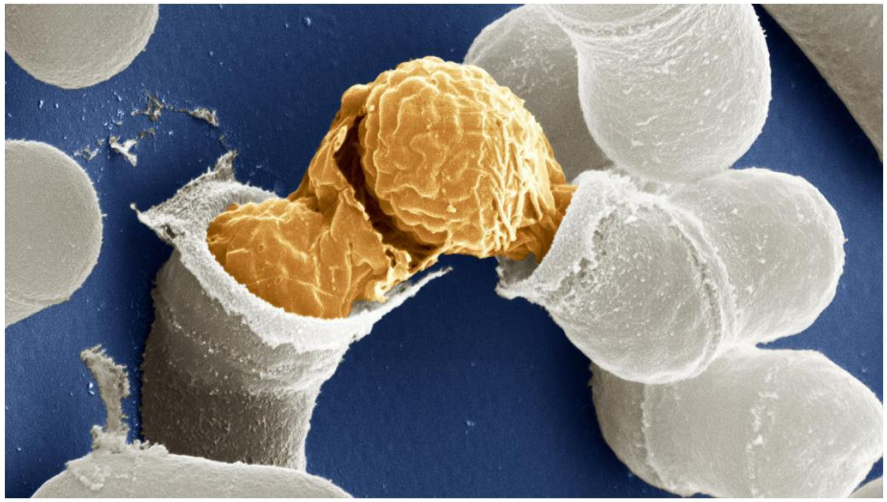
	dissolved lyophilisate (17-0042151-001-01)	open, but not dissolved lyophilisate (17-0042151-002-01)	originally sealed aliquot (17-0042151-003-01)
isolate 1	*Kluyvera intermedia* (Ampicillin resistant)	*Klebsiella pneumoniae* (phenotypically Extended- β-lactamase-formers = ESBL)	*Klebsiella pneumoniae* (phenotypically Extended- β-lactamase-formers = ESBL)
isolate 2	*Kluyvera intermedia* (Ampicillin resistant)	*Klebsiella pneumoniae* (phenotypically Extended- β-lactamase-formers = ESBL)	*Enterococcus faecalis*
isolate 3	*Enterobacter* spp.	Representatives of *Enterobacter cloacae*-group (phenotypically Extended- β-lactamase-formers = ESBL)	*Klebsiella pneumoniae* (phenotypically Extended- β-lactamase-formers = ESBL)
isolate 4	*Klebsiella pneumoniae*		*Klebsiella pneumoniae* (phenotypically Extended- β-lactamase-formers = ESBL)
isolate 7		*Klebsiella pneumoniae* (phenotypically Extended- β-lactamase-formers = ESBL)	Bacteria of the *B. cereus* group (no formability for human medically relevant toxins Cereulide, NHE, HBL and cytotoxin K)
isolate 8		*Klebsiella pneumoniae* (phenotypically Extended- β-lactamase-formers = ESBL)	
isolate 9		Bacteria of the *B. cereus* group (no formability for human medically relevant toxins Cereulide, NHE, HBL and cytotoxin K)	
isolate 10			

The Buzz About Gene Drives

IN THE LAB

College students try to hack a gene drive — and set a science fair abuzz

IKE SWETLITZ @IKESWETLITZ / DECEMBER 14, 2016

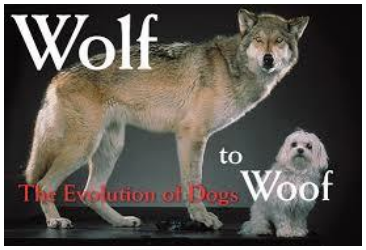


College students worked with yeast cells like these, attempting to insert a "gene drive."

"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]."

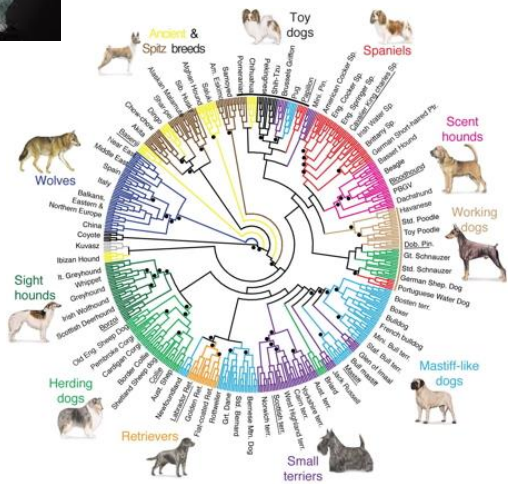
Meanwhile, sophomore Ajinkya Limkar said that the controversy inspired by their project has only motivated him further.

Directing Evolution



33k+ years

NOT
33k+ years



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.

TYPE	STRINGENT CONFINEMENT STRATEGY	EXAMPLES
Molecular	Separate components required for genetic drive	sgRNA and Cas9 in separate loci (*8*)
	Target synthetic sequences absent from wild organisms	Drive targets a sequence unique to laboratory organisms (*3*,*4*,*8*)
Ecological	Perform experiments outside the habitable range of the organism	*Anopheles* mosquitoes in Boston
	Perform experiments in areas without potential wild mates	*Anopheles* mosquitoes in Los Angeles
Reproductive	Use a laboratory strain that cannot reproduce with wild organisms	*Drosophila* with compound autosomes*
Barrier	Physical barriers between organisms and the environment	Triply nested containers, >3 doors (*6*)
	•Remove barriers only when organisms are inactive	Anesthetize before opening (*6*)
	•Impose environmental constraints	Low-temperature room, air-blast fans
	•Take precautions to minimize breaches due to human error	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*

The Economist

Biotechnology

A new opium pipe

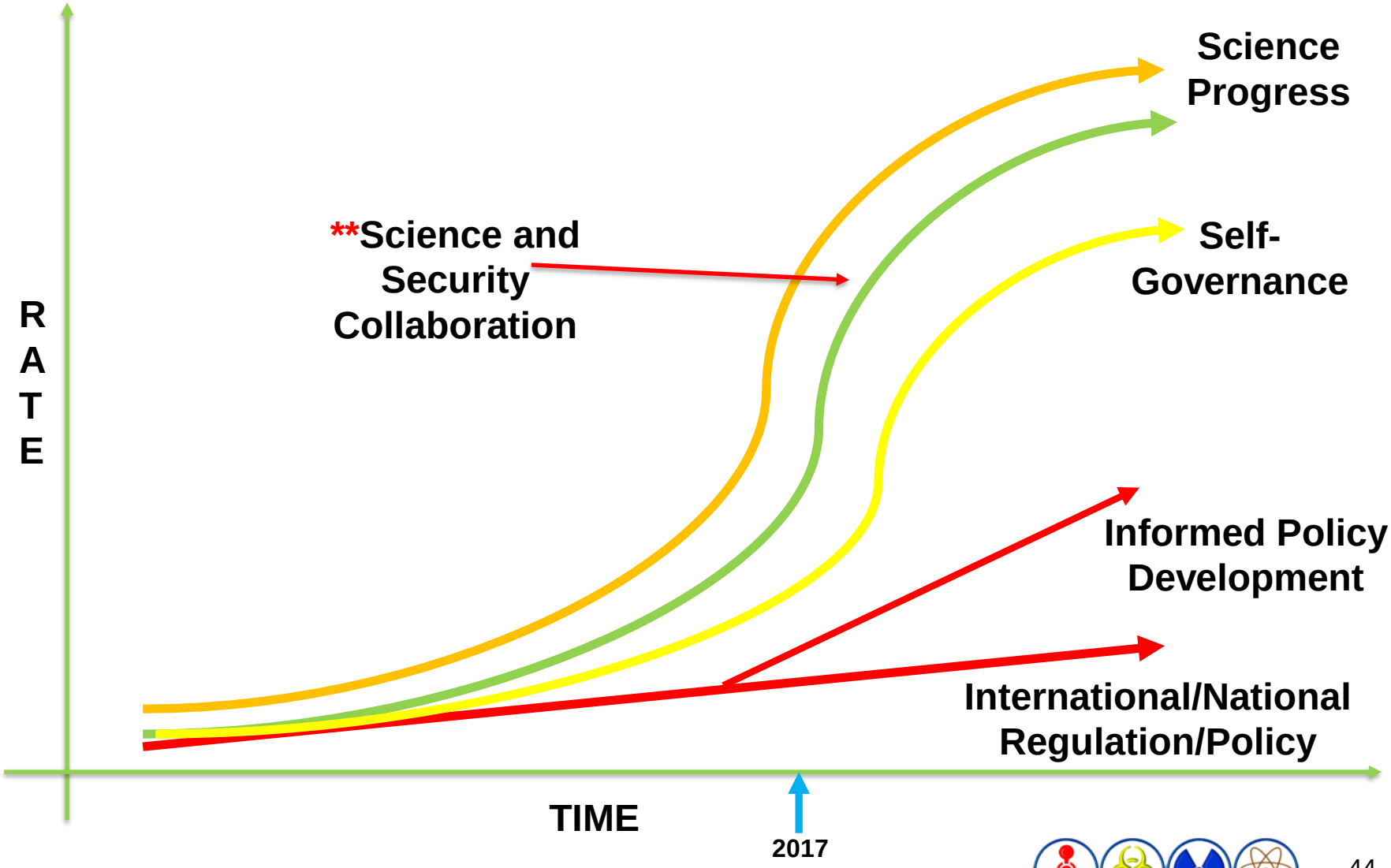
Aug 30th 2014

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.

http://www.economist.com/news/science-and-technology/21614093-narcotic-drugs-could-soon-be-manufactured-yeast-new-opium-pipe

Importance of Partnerships

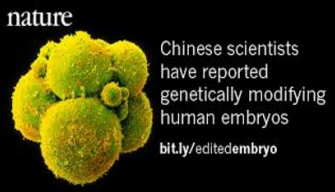


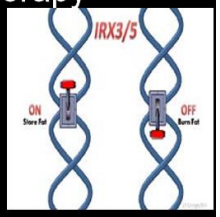
Emerging Applications

AGRICULTURE — GM Crops and Livestock N Fixation, Glowing Plants, Aquabounty

INDUSTRY — Synthesis of Organic Materials — Fuel, Flavors, Drugs

MEDICINE — Regenerative Medicine, Somatic and Germline Cell Therapy





ENVIRONMENT — Remediation; Control Vector Borne Disease and Invasive Species

Slide curtesy 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

THANK YOU