Dual Use Research

PIBS 503

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Dual Use Research

- **Dual use research includes life sciences research:**
  - **with legitimate scientific purpose**
  - **that may be misused to pose a biologic threat to public health and/or national security**

Group A streptococcus "flesh-eating bacteria"

- interesting finding:
  - one never finds penicillin-resistant strains
- implications for undertanding resistance in other bacteria

- an experiment:
  - determine why this is so

Science Policy in the US

- Bush Report, post-World War II
- "Science the Endless Frontier"
  - universities should be the primary infrastructure for basic research
  - research should be funded by federal dollars
  - grants should be awarded on competitive merit
  - establish NSF

U.S. Commission on National Security in the 21st Century

- **Hart-Rudman report, March 2001**
  - **terrorist attack likely within quarter century**
  - **second only to WMD**
  - **nothing more dangerous than failure to manage properly science and technology, and education**

Immediate Response to 9/11

- executive orders
- USA PATRIOT Act
  - Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism
- select agent rules

Publication of Research Results

- **NSDD 189 – Reagan**
  - **“It is the policy of this Administration that, to the maximum extent possible, the products of fundamental research remain unrestricted.”**
  - **re-affirmed by C. Rice after 9/11**

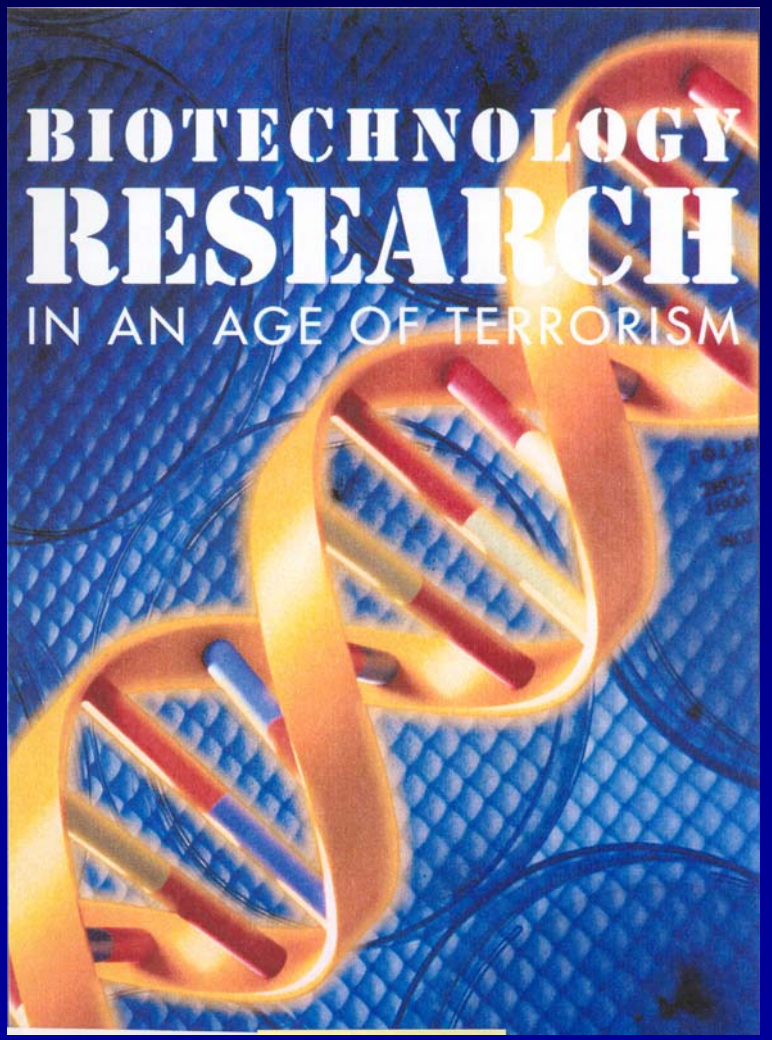
Biosecurity

- **“Dual use” potential of certain life sciences research requires consideration of new biosecurity measures**
  - **Biosecurity refers to processes and procedures designed to minimize the likelihood that biological research will be misused for production and enhancement of biological weapons**
- **Goal (*and* challenge) is to enhance biosecurity protections for life sciences research while ensuring that any impact to the free flow of scientific inquiry is minimized**

NRC Report on Dual Use Research

Report of the National Research Council of the National Academies:

"Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma" (October 2003)



National Science Advisory Board for Biosecurity (NSABB)

- Advisory to the Secretary of Health and Human Services, Director of National Institutes of Health, and heads of all US federal departments and agencies that conduct or support life science research
- Will recommend specific strategies for efficient and effective oversight of US federally conducted or supported dual use biological research

NSABB Charges

Recommend:

- Criteria for identifying dual use research of concern
- National guidelines for oversight of dual use research at both local and federal levels, including
  - Local review and approval processes, perhaps similar to Institutional Biosafety Committees (IBCs)
  - Criteria/processes for referral of issues to NSABB
- Strategies for oversight of new classes of experiments and technologies

NSABB Charges

Advise on:

- Program for biosecurity education and training for all scientists and laboratory workers at federally funded institutions
- A code of conduct for scientists and laboratory workers in life sciences research
- National guidelines on communication and dissemination of dual use research methodology and research results
- Strategies for promoting international dialogue on dual use research issue

NSABB Structure

- 25 voting members appointed by Secretary, HHS, after consultation with other federal agencies

NSABB Expertise

- Molecular/genomics
- Microbiology
- Clin. ID/diagnostics
- Lab biosafety/security
- PH/epidemiology
- Health physics
- Pharm. production
- Veterinary medicine
- Plant health
- Food production

- Bioethics
- National security
- Intelligence
- Biodefense
- IBCs
- Export controls
- Law, law enforcement
- Scientific publishing
- Perspectives from academia, industry, public, RAC

Ex officio members of NSABB

- Exec. Office of the President
- Department of Health and Human Services
- Department of Energy
- Department of Homeland Security
- Department of Veteran's Affairs
- Department of Defense
- Environmental Protection Agency
- United States Department of Agriculture
- Department of Interior
- National Science Foundation
- Department of Justice
- Department of State
- Department of Commerce
- National Aeronautics and Space Administration
- Intelligence community

What is Dual Use?

THE CIVILIAN PASSENGER SEDAN IS AN EFFECTIVE WEAPON OF WAR IN IRAQ

Is This a Weapon?

Saccharomyces cerevisiae

JOURNAL OF CLINICAL MICROBIOLOGY, June 2004, p. 2840–2842 Vol. 42, No. 6
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.6.2840–2842.2004
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Use of Paraffin-Embedded Tissue for Identification of *Saccharomyces cerevisiae* in a Baker's Lung Nodule by Fungal PCR and Nucleotide Sequencing

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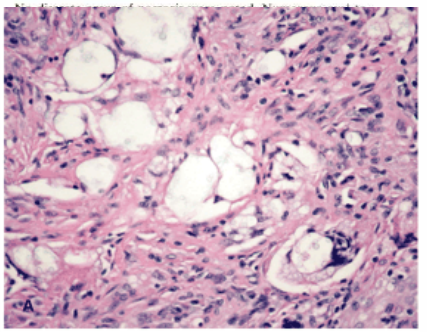
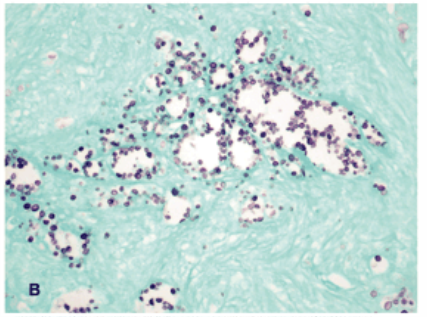
A 40-year-old healthy male employed in a bakery presented with a single lung nodule and underwent investigations to rule out pulmonary carcinoma. Biopsy was positive for yeast cells, which did not match common fungal pathogens. PCR assay of paraffin-embedded tissue and nucleotide sequencing with ribosomal *ITS1-ITS2* universal primers revealed the presence of *Saccharomyces cerevisiae*.

Identification of fungal pathogens in histological sections frequently requires application of specialized stains (6). Many pathogenic yeasts appear as budding, rounded cells without any characteristic tissue forms (9). This situation is alleviated in instances in which the incriminating fungus can be isolated in culture. However, tissue specimens are not always available for culture. Recently, the application of PCR and nucleotide sequencing has been extended for identification of pathogenic fungi in histological sections. The paraffin-embedded tissue is used as a source of template DNA for a PCR assay with universal fungal ribosomal gene primers and/or a nested PCR assay with pathogen-specific primers, and the amplicons are then analyzed by restriction fragment length polymorphism and/or nucleotide sequencing for confirmation of fungal identity (2–5, 8, 11, 13). This approach is very promising in diagnostics, as it could lead to conclusive identification of the causal pathogen independently of histological or culture observations. We describe a case of a lung nodule in a healthy male that proved to be histologically negative for suspected lung carcinoma and instead revealed budding yeast cells, which were confirmed as *Saccharomyces cerevisiae* by PCR and nucleotide sequencing.

A 40-year-old healthy male was referred to the surgeon at Coney Island Hospital for a lung nodule discovered during a routine chest X-ray done as part of an annual physical examination. The patient was a nonsmoker with no history of any medical illness. A wedge resection of the lung was performed. A 0.7-cm-diameter solid grey-tan nodule was present in the lung parenchyma. The edges of the lesion were sharply demarcated from the surrounding normal lung parenchyma without any calcification. Histopathologic examination revealed an inflammatory mass composed of a background of fibrotic tissue with a moderately dense population of inflammatory cells composed of an equal admixture of histiocytes and lymphocytes.





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Is yogurt a weapon?

June 2001, Volume 21, Number 4, Pages 258-260

Clinical Perinatal/Neonatal Case Presentation

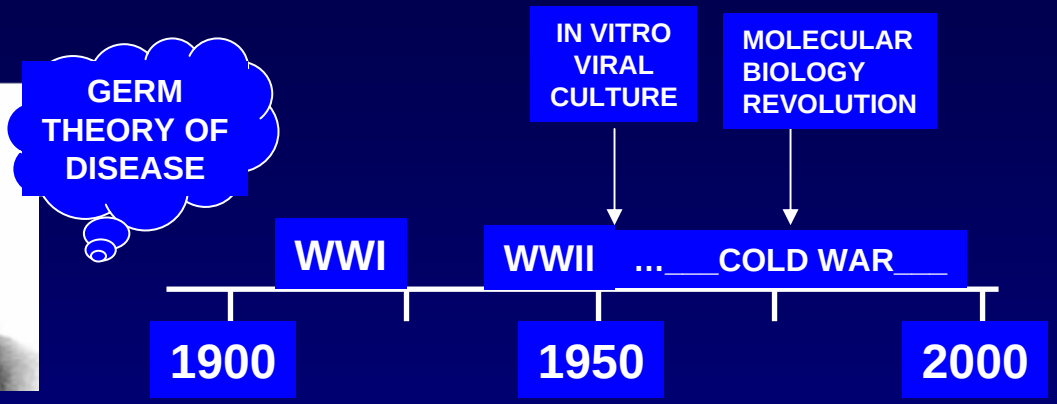
***Lactobacillus acidophilus* Sepsis in a**

Charles Thompson MD[1], Yvette S McCarter PhD[2], Peter J Krause MD[3] and Victor C Herson

L. acidophilus
FOOD?
MICROBE?
COMMENSAL?
OPPORTUNIST?
PATHOGEN?
WEAPON?

DELIVERABILITY AND IMMUNITY CHANGE WEAPON POTENTIAL OF MICROBE OVER TIME

PASTEUR & KOCH c1890



CLASS A AGENT	1890	1945	2004	2020
Bacillus anthracis	NO	YES	YES	?
Yersinia pestis	YES	YES	YES	?
Variola major	YES	NO	YES	?
Francisella spp.	NO	NO	YES	?
Hemorrhagic fever viruses	NO	NO	YES	?
Coxiella spp.	NO	YES	YES	?
POLIO VIRUS	NO	YES	NO	YES?*
MEASLES VIRUS	NO	YES	NO	YES?*

*ASSUMING GLOBAL ERADICATION AND DISCONTINUATION OF VACCINATION

Identifying Dual Use Research

- **Criteria are needed to identify research which should be considered "of concern" because of the likelihood that it could produce knowledge, products or technologies that could be misapplied to pose a threat to national security**
  - **The criteria will require periodic review and modification in response to scientific advances**

Key Concept: National Security

- **Term not understood same way by all**
  - **Solution: Identify and use the relevant component elements of national security**
    - **Public health**
    - **Agriculture**
    - **Plants**
    - **Animals**
    - **Non-biological resources (materiel)**
    - **Environment**

Draft Criteria for Identifying Dual Use Research of Concern

- Research that, based on current understanding, can be reasonably anticipated to provide knowledge, products, or technologies that could be directly misapplied by others to pose a threat to:
  - Public health
  - Agriculture
  - Plants
  - Animals
  - Environment
  - Materiel

Research Areas of Special Concern

- **Enhance the harmful consequences of a biological agent or toxin**
- **Disrupt immunity or the effectiveness of an immunization without a clinical and/or agricultural justification**
- **Confer to a biological agent or toxin, resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin, or facilitate their ability to evade detection methodologies**

Research Areas of Special Concern

- **Increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin**
- **Alter the host range or tropism of a biological agent or toxin**
- **Enhance the susceptibility of a host population**
- **Generate a novel pathogenic agent or toxin, or reconstitute an eradicated or extinct biological agent**

Publications

- **Should certain results not be published?**
  - **poisoning the milk supply with Botulinum toxin**
  - **sequence of the 1918 influenza virus**

Controversial Manuscripts:
1918 Pandemic Influenza Virus

LETTERS

Characterization of the 1918 influenza virus polymerase genes

RESEARCH ARTICLE

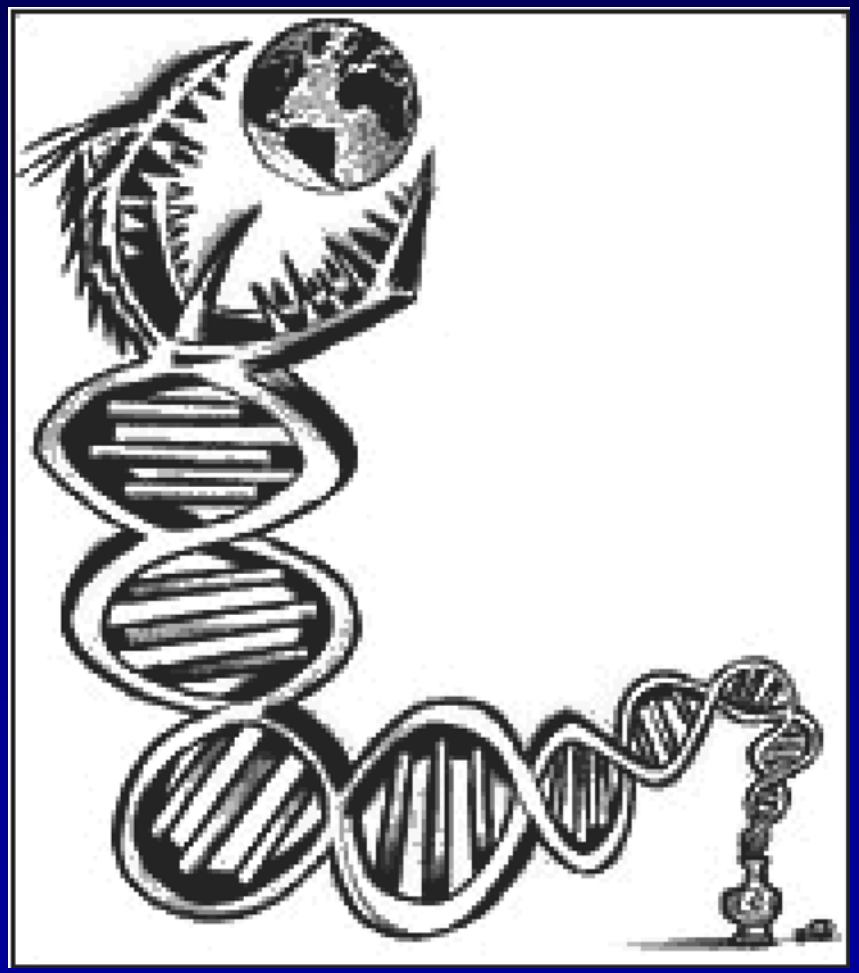
Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus

“1918 Flu and Responsible Science”

“I firmly believe that allowing the publication of this information was the correct decision in terms of both national security and public health.”

***Science* Editorial**
Vol. 310, 7 October 2005
Philip A. Sharp

“The 1918 flu genome: Recipe for Destruction”



“This is extremely foolish. The genome is essentially the design of a weapon of mass destruction.”

New York Times Op-Ed
October 17, 2005
Ray Kurzweil and Bill Joy
contributors

How would you have voted? Why?

International Cooperation

- “the world is flat”
  - internet, travel, satellites
  - instant access to information
- any unilateral efforts will be futile

Emerging technologies

- should purchase of certain types of equipment or supplies be regulated?
  - precedent: nuclear technologies
  - problem: can buy lots of stuff at Home Depot
- what about synthetic genomics?
- synthetic biology?

Recombinant DNA

- when DNA cloning was first proposed, there was a lot of concern
- moratorium
- Asilomar Conference, 1975
- led to development of NIH Guidelines

“Some bacteria are so dangerous, scientists call them ‘wild type’.”

- Anon. UM faculty member

Is Too Much Money Being Spent on Bioterrorism Research?

- 1/3 of NIAID budget goes towards bioterrorism-related research
  - (1/3 to AIDS, 1/3 to everything else)
- letter to Director of NIH, signed by >700 microbiologists, saying priorities are wrong

The number of NIAID's grants for six potential “bioweapon diseases” that kill relatively few people in the United States each year, anthrax, plague, tularemia, brucellosis, glanders, and melioidosis, has increased 1500% since the late nineties

Benefits of Directed Research

- During 1980's, a lot of money was set aside for HIV
  - mRNA transport
  - recombination
  - immune evasion
  - innate immunity
  - vaccine development
  - signal transduction

NSABB Website

http://www.biosecurityboard.gov