NATIONAL SCIENCE ADVISORY BOARD FOR BIOSECURITY

NIH RECOMBINANT DNA ADVISORY COMMITTEE (RAC)

AGENDA
Roundtable on Synthetic Biology
October 11, 2007

NIH Campus
9000 Rockville Pike, Bethesda, MD
Building 31, C Wing, 6th Floor, Conference Room 10

8:00 a.m. **Welcome and Opening Remarks**

Paul Keim, PhD
NSABB Member
Northern Arizona University

Howard Federoff, M.D., Ph.D.
Chair, NIH RAC
Georgetown University Medical Center

8:10 a.m. **Overview of Roundtable**

David Relman, M.D.
Chair, NSABB Working Group on Synthetic Genomics
Stanford University

8:20 a.m. **Session 1: State of the Science of Synthetic Biology**

This session will provide a broad understanding of the field of synthetic biology—the various research approaches, current capabilities, short and long-term goals. Questions to be addressed during the presentations and/or discussion period are listed below.

Moderators:

Harvey Rubin, M.D., Ph.D.
NSABB Member
Director, Institute for Strategic Threat Analysis and Response
Professor of Medicine, Microbiology, and Computer Science
University of Pennsylvania

Stephen Dewhurst, Ph.D.
RAC Member
Professor of Microbiology & Immunology and of Oncology
University of Rochester

Questions for Consideration:

- How would you define the field of work to which various parties refer under the rubric of "synthetic biology"? How is this field of scientific activity related to, and distinguished from other fields? What are the goals of synthetic biology?
- What are the principal lines of research in this area?
- What are the capabilities and applications associated with the field of synthetic biology at present? What capabilities do the approaches used in synthetic biology provide that are beyond those that can be achieved using recombinant DNA or other related technologies?
- What are some of the more important accomplishments to date by those that might be labeled as synthetic biologists? What are the current major hurdles or challenges in synthetic biology?
- Where do you see the field of synthetic biology headed in the near and long terms?
- How close are we to predicting the detailed behavior of a cell based upon its component parts? How close are we to designing biological systems and novel organisms with predictable functions?
- Does your research within the realm of synthetic biology routinely undergo any biosafety review? If so, please describe.

8:25 a.m. **A Bird's Eye View of Synthetic Biology**

Roger Brent, Ph.D.
Director and President
The Molecular Sciences Institute
Berkeley, CA

8:50 a.m. **Synthetic Biology As A Twenty Year Old Field**

Steven A. Benner, Ph.D.
Distinguished Fellow
Foundation for Applied Molecular Evolution
Gainesville, FL

9:15 a.m. **Synthetic Biology: From Bacteria to Stem Cells**

Ron Weiss, Ph.D.
Professor of Electrical Engineering
Princeton University

9:40 a.m. **Synthetic Organisms**

Steen Rasmussen, Ph.D.
Team Leader for Self-Organizing Systems
Los Alamos National Laboratory

10:05 a.m. ***Break***

10:20 a.m. **Discussion**

11:40 a.m. Break for Working Lunch

12:00 noon **Session 2: Predicting Function**

This session will address our current understanding of the relationship between biological properties and sequence and structure, our ability to predict biological function/properties, and the tools that are available or under development for predicting function. Questions to be addressed during the presentations and/or discussion period are listed below.

Moderators:

Claire Fraser-Liggett, Ph.D.
NSABB Member
Director, Institute of Genome Sciences
University of Maryland School of Medicine, Baltimore

Nikunj Somia, Ph.D.
RAC Member
Assistant Professor
University of Minnesota, Twin Cities

Questions for Consideration:

- To what degree are we able to explain virulence of the more common bacterial and viral pathogens, based on their genome sequences? How accurately can virulence or other pathogenic properties be predicted on the basis of sequence alone? Can the predictions be generalized or are they restricted to a particulare pathogen-host system?
- In general, what kinds of virulence factors (and how many, in relative terms) are sufficient in establishing virulence in a heterologous, avirulent organism?
- What kinds of factors determine the evolutionary distance across which virulence might be genetically transferred? How does our current understanding of lateral gene transfer (its prevalence and role) in nature help us predict the degree to which virulence and other relevant phenotypes can be deliberately manipulated or created *de novo*?
- What are the major challenges and unmet needs that hinder recognition and prediction of virulence? What would be the most effective strategies for addressing these challenges and needs?
- What are the considerations for predicting function within systems?
- What kinds of properties of a biological system are most successfully predicted from its genetic composition?
- To what degree, and in what ways do current scientific knowledge allow construction of entirely new systems or organisms with predictable behaviors? How will this capability change as continued efforts increase our understanding of the function of individual proteins and macromolecular complexes?
- What kinds of tools or approaches are currently most effective for predicting function from sequence? What are their capabilities? What are their limitations? How are they currently being used?
- What are the major challenges and goals for developing more accurate predictive tools?

12:05 p.m. **Form and Context in Predicting Biological Function**

William Goldman, Ph.D.
Professor of Molecular Microbiology
Washington University School of Medicine

12:25 p.m. **Genotype to Phenotype**

Jim Musser, M.D., Ph.D.
Co-Director and Executive Vice President
The Fondren Foundation Distinguished Endowed Chair
The Methodist Hospital Research Institute

12:45 p.m. **Design Considerations for Robustness and Vulnerability in Biological Systems**

Marc W. Kirschner, Ph.D.
Chair, Department of Systems Biology
Harvard Medical School

1:05 p.m. **Design and Use of Predictive Tools: State of the Art**

Owen White, Ph.D.
Director of Bioinformatics
Institute for Genome Sciences
University of Maryland School of Medicine

1:25 p.m. **Discussion**

2:45 p.m. ***Break***

3:00 p.m. **Session 3: Risk Assessment and Risk Management in a Context of Uncertainty**

This session will explore the challenges of assessing biosafety risks in synthetic biology research when there is uncertainty about the biological properties of an agent, how biosafety risk assessment might be approached in such circumstances, and principles and strategies for risk management. Discussion questions are listed below.

Moderators:

Claudia Mickelson, Ph.D.
RAC Biosafety WG Member
Biosafety Program Deputy Director, Environment, Health & Safety
Massachusetts Institute of Technology

Michael Imperiale, Ph.D.
NSABB Member
Professor
University of Michigan Medical School

Panelists:

Rocco Casagrande, Ph.D.
Managing Director
Gryphon Scientific

Lawrence McCray, Ph.D.
Research Associate, Program on Emerging Technologies
Massachusetts Institute of Technology

3:30 p.m. **Discussion**

- Are there novel or distinct biosafety risks or challenges associated with synthetic biology?
- In general, to what degree are the biosafety risks of synthetic biology currently being adequately addressed?
- For recombinant DNA research, the initial risk assessment is based on the risk group of the parental agent. However, for the more novel synthetic agents, a parental agent may not be obvious and/or the biological properties of the new organism may be largely unknown. How can risk assessment be conducted in such situations? What is the most appropriate risk management approach in such cases?
- What kinds of efforts have been, or are being taken to engineer biological containment into synthetic systems/organisms (e.g, use of unnatural genetic code or amino acids, self-destruct mechanisms, other safeguards)? Are there other biological containment practices that could be considered?
- Are there any existing risk assessment tools that would be applicable to the biosafety risk assessment process in the context of synthetic biology?
- Once the difficult and inherently imprecise process of risk assessment has been completed and a risk management plan has been defined, are there ways to assess the efficacy of the management plan as the project goes forward?

4:50 p.m. **Closing Remarks**

5:00 p.m. ***Adjourn***
