



The NIH Roadmap for Structural Biology

TCNP All Hands Meeting, March 1, 2007

**John Norvell, Ph.D., NIGMS, NIH, DHHS
Division of Cell Biology & Biophysics
Branch Chief
Structural Genomics & Proteomics Technology Branch**

**Jean Chin, Ph.D., NIGMS, NIH, DHHS
Division of Cell Biology & Biophysics
Program Director, Cell Biology Branch**



The NIH Roadmap for Structural Biology

The Process

- Planning Committee of NIH Staff with Outside Advisers
 - Planning Document in December 2002
- Structural Biology Working Group
 - Project Matrix of Risk vs. Time
 - Grand Challenges
 - FY2004-FY2007 Activities



The NIH Roadmap for Structural Biology

- **Structural Biology Working Group**

Jeremy Berg, Director

John Norvell, Principal Leader

Jean Chin, Program Director

- NIGMS, NIDDK, NHGRI, NCRR, NIMH, NIAID, NLM, CSR, NIDCR, NIAMS, NEI
- NIH Intramural & Extramural Programs



The NIH Roadmap for Structural Biology **Grand Challenges**

- Determination of the structures of many large assemblies of proteins
- Determination of the atomic level structures of most proteins by experimental studies and computational modeling from their DNA sequences
- Improve expression of membrane proteins



The NIH Roadmap for Structural Biology

Roadmap Activities

- FY04: \$5M for Centers for Innovation in Membrane Protein Production
- FY05: \$5M for research grant programs for membrane proteins (P01, R01, R21)
- FY06: Conference on the “Structural Analysis of Large Macromolecular Assemblies”
- FY07: \$1.6M for research grant programs for membrane proteins (3-year R01)



The NIH Roadmap for Structural Biology

Improving Membrane Protein Expression

- Three initiatives to request applications for developing innovative approaches to membrane protein production, stabilization, solubilization, purification, reconstitution, and preparation for structural determination
 - RFA-RM-07-003 for R01s only and \$1.6M
 - RFA-RM-04-026 for P01, R01, R21 and \$5M
 - RFA-RM-04-009 for P50 Centers and \$5M



The NIH Roadmap for Structural Biology

Number of Awards and Mechanisms

2 Centers - P50

1 Program Project - P01

10 Research Projects - R01

~4-5 Pending R01 applications

(May 2007 Council)

8 High Impact-High Risk Projects - R21



The NIH Roadmap for Structural Biology

- Diversity in Approaches
 - Crystal Production, IMP Stabilization with Ligand or Lipid or Hybrid Domains, Vector Design, Chemical Synthesis of Membrane Proteins
- Diversity in Biological Systems
 - Bacteria, Yeast, Pichia, Sf9 Insect Cells, HEK Cells, Chlamydomonas chloroplasts, Chorella
- Diversity in Resources to the Community
 - Publications, Reagents, Equipment, Protocols, Websites, High Throughput Screens, Collaborations
- Diversity in Methods
 - XRC, Solution and Solid-State NMR, CryoEM, EPR, Microfluidics



The NIH Roadmap on Structural Biology

- Principal Investigators (21)

- Senior PIs (18)

- New PIs (3)

- Distribution of Awards

- CA (7), IL (5), MA (1), NY (2), PA (1), VA (1)

- Canada (1) and Ireland (1)

Common Interests & TCNP Interactions

■ Common Interests

- Probes for Assessing Membrane Protein Structural Dynamics and Interactions
 - Intramembrane Interactions: P-P, L-L, P-L
 - Interfacial Interactions: Extra- & Intra-cellular Milieu
- EM Capability to Determine in Situ Structures of Membrane Proteins in Lipid Bilayer

■ Potential Interactions

- Research Collaborations with Roadmap Investigators
- Possible, Future All-Hands and Open Meeting for Roadmap Structural Biology