

## **Cardiovascular Program – Theme # 11: Bioinformatics and Computational Biology**

### **Introduction:**

The lives of 20 million Americans and the economic well being of our nation are affected dramatically by heart, lung, blood, and sleep diseases and disorders. Advances in science have brought us to a watershed moment where our ability to understand and improve human health and to develop integrative personalized approaches to medicine is no longer limited by our ability to conduct experiments. Rather, it is limited by our ability to integrate and model data at levels of organization ranging from the molecular to the organism to the population.

Achieving this integrative, model-based understanding of disease will require new methods from the quantitative sciences. It will involve extracting knowledge from diverse existing and future data sources by an interdisciplinary workforce, trained in the computational and biomedical sciences, with unencumbered sharing of data and knowledge.

Accomplishing this goal is critical to enable the efficient use of existing funds, to capitalize on previous advances, and to avoid duplication of effort. It depends on the immediate and successful implementation of the following recommendations:

### **Recommendations:**

#### **1. Develop and support an information infrastructure that embodies comprehensive standards for biomedical information**

- NHLBI should adopt or develop controlled vocabularies, ontologies, data models, and data representation formats for data types important to the NHLBI research mission. These resources should describe relevant metadata such as experimental protocols, instruments and parameters and should explicitly bridge the gap from the molecular and genomic to the clinical data types measured routinely in healthcare. NHLBI should assure community involvement in the sustenance and growth of these ontologies to meet emerging research needs.
- NHLBI should support the development of software that leverages these shared vocabularies and data models to assure long-term interoperability of data sources
- NHLBI should encourage efficient use of existing resources and avoid duplication by creating a universally searchable inventory of existing public datasets related to HLBS.

#### **2. Facilitate the development of models that integrate data from molecules to organisms in health and disease**

- NHLBI should encourage new proposals supporting comprehensive study of cardiovascular disease at the systems level. NHLBI should identify focus areas for this systems approach (e.g. arrhythmogenesis, cardiomyogenesis etc).
- NHLBI should provide incentives for new team approaches that support the development of mechanistic cell- and disease-specific computational models and

should assess the impact of these approaches and models on understanding and treatment of heart, lung, blood and sleep (HLBS) disease.

- NHLBI should define grand challenge problems that require the integration of data types (sequence, phenotypes, genotypes, clinical, animal models, expression arrays, etc), with the ultimate goal being to enhance clinical decisions about the disease(s).
- NHLBI should encourage joint projects between clinical and molecular/cellular researchers, the aim being to establish connections between clinical phenotypes and cellular pathways that define pathology in cardiac systems.
- NHLBI should encourage the development and validation of new mathematical and computational methods and should support scalable software development and verification as an integral research activity that will enable the implementation of predictive large-scale computational models of complex heart, lung and blood diseases,
- NHLBI should develop mechanisms to permit the use of non-anonymized clinical data to support patient-specific computational modeling research, advancing the use of multi-scale modeling and global biological systems approaches in drug-discovery and clinical trial design..

### **3. Develop Disease Oriented Portals as gateways to information and tools for research and therapy.**

- **Disease-centric portals** will be an essential resource for integrative understanding of HLBS disease and community-wide collaborations. These portals must be interoperable with other federated, distributed data and information resources to allow a comprehensive understanding of HLBS diseases, particularly those that are multi-system and multi-organ. Portals will enable:
  - i. Sharing, linking of disparate data types: sequence, SNPs, phenotypes, disease mechanisms
  - ii. Development of tools, analysis strategies, and data visualization approaches to manage the disparate data sets.
- Disease-centric portals will also be used to support the establishment and curation of a federated public repository of computational models and systematic context-specific multi-scale data on cardiovascular structure and function in humans and key model organisms needed for model formulation and validation.

### **4. Encourage and enable broad sharing and use of research data while respecting privacy and minimizing risk to individuals**

- NHLBI should develop criteria to be used to assess the Investigator's commitment to disseminate workflow, protocols and meta and raw data in projects that will generate large data. NHLBI should ensure, in competing renewal applications, that the Investigator has fulfilled these commitments.
- NHLBI should pro-actively develop policies and procedures to ensure maximum yield of research data and benefits to the individual. Furthermore, NHLBI should shorten the loop between discovery and translation to health care of the individuals studied and society.

### **5. Develop an interdisciplinary NHLBI research community fluent in quantitative approaches and experimental methods and catalyze change in NHLBI training programs to emphasize the centrality of computational methods.**

- Establish flexible interdisciplinary graduate and post-doctoral training programs to train scientists at the interface between experimental and computational biomedical

science that: a) emphasize the close interaction of experimental and computational research; b) support the development of interdisciplinary curricula; and c) provide training in software development, maintenance, documentation and validation.

- NHLBI should support supplements to existing graduate and post-doctoral training grants for training of medical students and fellows in quantitative approaches to biomedical research.

09/29/06

Business Operations  
National Heart, Lung, and Blood Institute  
Level 1 Strategic Planning Working Group  
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**Recommendations:**

After a full roll-call vote on high, medium and low priorities on the seven business practices that were provided by program staff, the Bioinformatics and Computational Biology committee identified the following areas of business practice that were not captured in the voted upon items.

In rough order of expressed interest, these areas included:

- 1. NHLBI should develop policies and procedures that can be used as close guidance by investigators and institutions to pursue data acquisition, analysis and management methods that are protective of patients' confidentiality and respectful of the nature of the consents with which the data were acquired.** The NHLBI is urged to consider novel methods of institutionalizing these procedures.
- 2. The review of grants that are database construction/maintenance grant proposals.** Estimating the quality and likelihood of sustainable success of these proposals requires a mechanism other than the standard 25 page written proposal. Support was expressed for alternate mechanisms such as "reverse" site visits, on-line inspections, reviews of the software and preliminary studies that might be more predictive of the quality of the database proposals.
- 3. Mechanisms should be developed to enhance partnership with industry which minimize risk to intellectual property and maximize the integrity of research.**
- 4. The real cost of software development, even when it is of a prototype, is often under-appreciated and under-funded in a wide range of non-informatics grants.** Mechanisms for providing support for such meritorious software development should be developed.

	High	Medium	Low	Priority Rank
1. Create streamlined procedures for renewing grants for established investigators, including a briefer application and greater emphasis on prior productivity	1	5	10	
2. Funding and Award Mechanisms	12	4	1	<b>1</b>
3. Create incentives and mechanisms for cross- Institute and interagency funding of large projects	7	6	1	<b>3</b>
4. Review the NHLBI pre-approval process for investigator-initiated grants with direct costs >\$500K in any year and the process for Institute-initiated programs (RFAs, RFPs):	0	0	16	
5. Create a mechanism to provide infrastructure support for large observational studies to facilitate addition of ancillary studies. Create mechanisms to assure that the data and samples from the core studies are made available to the wider scientific community as a resource for further research	4	10	3	<b>4</b>
6. Issues related to CSR and study sections	8	8	1	<b>2</b>
7. Dissemination and communication of advances and discoveries and resources made by NHLBI Supported Investigators	1	2	13	

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