Final Report
National Heart, Lung, and Blood Institute
Level 1 Strategic Planning Working Group
July 24-25, 2006

Cardiovascular Program – Theme # 7: Emerging and Evolving Technologies

Introduction:

Although important strides have been made in reducing cardiovascular mortality, the incidence and prevalence of cardiovascular disease are at epidemic proportions in the U.S. The present tools of cardiovascular science are clearly insufficient to address this epidemic, which will require the development of new technologies to detect, treat, and prevent heart disease much earlier than is presently possible. History shows us that new technologies drive medical advances and often set the stage for quantum leaps in health care. Some of the critical problems that these evolving and emerging technologies (EET) will allow us to address are:

- Early detection and treatment of atherosclerosis at a stage well before it manifests as heart attacks and strokes, thus eliminating the top killers of adult American men and women.
- Early surgical correction of valvular and congenital heart defects through minimally invasive methods to prevent heart failure in children and adults.
- Regeneration of damaged cardiovascular tissues using cellular and molecular approaches to provide new functioning heart muscle and blood vessels.
- Selective delivery of drugs or imaging agents to specific tissues or cell types, vastly increasing their effectiveness and reducing side effects.

The power of EET to advance cardiovascular health and science will be realized fully only if the NHLBI supports and nurtures a robust discovery and implementation process, since industry is unlikely to pursue these ideas without a solid commercial justification.
The following **general principles** apply:

- EET requires an academic, trans-disciplinary approach that involves teams of physical scientists, engineers, biologists and clinicians. Supporting current developers of EET and training the next generation will require specialized mechanisms.
- The potentially transforming impact of EET on cardiovascular medicine will be blunted unless methods to translate these discoveries from the academic world to the clinic are developed. NHLBI must foster academic-industrial partnerships, set standards, design clinical trials, and take any and all measures required to facilitate adoption of groundbreaking technologies that will improve cardiovascular health.
- In the past, the focus has often been on structural or anatomic parameters. The NHLBI should exploit new knowledge in sensors, nanotechnology, biomarkers, and molecular/functional imaging to develop diagnostics that address non-anatomic targets such as metabolic, functional, and mechanical properties.

Recommendations:

The six recommendations below also will stimulate the economy through creation of new biotechnology companies, enhance training and education in interdisciplinary areas, assist in preserving America's leadership in science and technology and ultimately reduce the cost and improve the quality of healthcare in America.

1. Invest in concept development and basic discovery of novel biomarkers and therapeutic targets and methods for detection of cardiovascular disease initiation and progression, including clinical events. Biomarkers are defined broadly as any characteristic that is objectively measured and evaluated as an indicator of genotype, normal biological (including functional) processes, pathological processes, or responses to a therapeutic intervention.

- Develop technologies for robust, reproducible, rapid and inexpensive biomarker discovery including detection and monitoring of events at the single cell, organ and systems levels.
- Focus on the critical issue of identifying specific and high affinity protein- and cell-binding agents by creating a database of existing reagents.
- Encourage the discovery of new protein- and cell-binding molecules and their incorporation into novel sensors, drug-delivery devices, molecular imaging agents, and so forth.

2. Support the discovery of programmable, adaptable, self-sustaining, smart materials and devices.

- Technologies including, but not limited to, nanoparticles, surgical robotics, MEMs, bio-mimetic surfaces, self-assembling proteins and scaffolds, and new power sources for devices.
- Enhanced affinity reagents for molecular targeting.
- Cell- and gene-based therapy targeting, delivery and monitoring for cardiovascular repair.
- Biohybrid and cell-instructive scaffolds directing vessel and cardiovascular regeneration/repair.

3. Accelerate development of biomarkers and new technologies into clinically useful diagnostic tools for molecular and clinical phenotyping of cardiovascular disease.

- Support development of infrastructure including: open source coding, insertion of software/hardware access ("hooks") in existing devices, and high quality reagent availability through professionally curated databases.
- Establish and make readily available databases of large, highly phenotyped populations for genomics/proteomics, biomarker and molecular imaging.
- Create tools for application of molecular diagnostics in point-of-care (POC)/home settings.
- Promote concepts of new and emerging technologies to stakeholders to increase effectiveness and efficiency of development.

4. Accelerate the translation of molecular diagnostics and imaging technologies to the clinical setting through validation, refinement, and scale-up; and accelerate the application of diagnostic testing by promotion of routine community use and incorporation into standard of care.

- Develop clinical trials infrastructure including networks of investigators and core laboratories for evaluation of emerging diagnostic and therapeutic technologies.
- Develop and apply rigorous methodologies for evaluating clinical efficacy and cost effectiveness of diagnostic testing.
- Encourage the testing and validation of surrogate biomarkers in clinical trials.
- Institute mechanisms for rapid translation, including health services research and definition of methods for commercialization involving partnerships with industry.

5. Support integration of diagnostic and therapeutic technologies, especially imaging, for targeted cardiovascular treatments.

- Candidate technologies might include: sensors, molecular imaging agents, multi-modality imaging and motion adaptive imaging for surgical /therapeutic intervention.
- High priority clinical areas might include, but not be limited to: detection and treatment of high-risk atherosclerotic lesions and diffuse vascular disease, structural heart and blood vessel diseases, and functional electrophysiological derangements.
- Development of surrogate biomarkers for gauging the effectiveness of proposed cardiovascular therapies to assist in assessment of early efficacy.
- Development of virtual surgical planning/training tools.

6. Ensure multimodality/interdisciplinary focus at all discovery/translation levels in areas including, but not limited to:

- Data sharing across multiple platforms including multimodality displays of images.
- Linking and integrating diagnostic agents to interventions and therapeutics, and outcomes.
- Development of multi-platform computational methods and models.
- Creating funding mechanisms to foster collaborative research including multi-PI and multi-institution grants such as BRP grants.
- Supporting interdisciplinary training programs that link physical, biological and clinical sciences such as K25, and pre- and post-doctoral training programs.

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Business Operations
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Recommendations:

In order to facilitate the development, translation, and application of emerging and enabling technologies to cardiovascular diseases, the working group recommends that NHLBI consider implementing the following business operations suggestions:

1. Facilitate translation of technologies from discovery to practice by formulating and disseminating policy to encourage academic and industry/pharmaceutical collaborations. Stating where intellectual property and conflict of interest issues are relevant and not relevant would pave the way for junior and senior faculty to pursue the translation of novel technologies for clinical application.

2. Develop novel mechanisms to support joint academic/industry awards to encourage and ensure the translation of technologies to medicine. Open source technology, devices, and software should be encouraged in order to fully develop novel applications.

3. Encourage and support multi-disciplinary teams through novel or existing grant mechanisms. Multi-disciplinary teams are necessary to design, develop, and apply technologies to support novel diagnostic and therapeutic approaches. The Bioengineering Research Partnerships are an ideal mechanism to develop and sustain team science. In addition, a new mechanism to facilitate team building for junior investigators who are not yet ready to lead large programs would aid assembly of new teams that include broad based expertise in physical, biological, and medical sciences.

4. Create a special/standing NHLBI study for emerging and evolving technologies, similar to the standing NHLBI study section for multi-center Clinical Trials. The design-based (hypothesis-*enabling* rather than testing) nature of technology applications necessitates review of multi-disciplinary applications that feature bioengineering, physiology, and health/disease approaches in special study sections that include experts in technology and medical arenas. An accelerated review/funding cycle (6 months) is recommended in view of the rapid pace of technology change.

5. Support cross training of investigators in technology (nanotechnology, imaging, bioengineering, -omics) and physiology/pathophysiology. The use of mini-sabbaticals to cross-train established investigators would be an ideal way to increase interdisciplinary approaches to the development of novel diagnostics and therapeutics.

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