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

Cardiovascular Program – Theme # 4: Vascular Diseases and Hypertension

Introduction:

The following three recommendations seek to guide efforts to improve the diagnosis, prevention, and treatment of hypertension and vascular diseases for the coming decade. The terms "vascular diseases and hypertension" should be understood to broadly include all arterial and venous diseases, not only hypertension, kidney diseases, cerebrovascular disease and peripheral arterial disease and aneurysms, or solely atherosclerotic diseases. Vascular diseases and hypertension are collectively responsible for the greatest morbidity and mortality in our nation. Despite enormous and powerful advances in basic and clinical research, there remains an alarming deficit in our society's awareness, prevention, treatment, and control of the leading causes of vascular disease, including hypertension, diabetes, dyslipidemia, and chronic kidney disease. Aging of the population and the epidemic of obesity threaten to further increase the prevalence of these conditions, with disastrous consequences for the health of Americans. An underlying premise for these recommendations is that the NHLBI should continue to strongly support basic scientific discovery to achieve a deeper understanding of the etiology, development, progression, and clinical manifestations of vascular diseases and hypertension. It will be impossible to advance our understanding of etiology, prevention, and intervention for vascular diseases and hypertension without far more effective bridging between the many disciplines and methodologies that can address these diseases. Also critical to the recommendations that follow is a substantive focus on preclinical disease and the continuum of risk across the life course, and attention to population diversity, especially where population differences and health disparities are recognized. It is also critical to better understand and flexibly address the various maladaptations that are occurring in an ongoing way in our populations due to societal changes and lifestyle trends.

Recommendations:

1. NHLBI should provide resources to increase access of researchers to novel technologies and emerging approaches to phenotype refinement for vascular disease and hypertension. Despite major technological advances in the biomedical sciences, access to and application of emerging technologies has been confined to far too few investigators. NHLBI should focus on approaches that make critical technologies available to more investigators to develop novel and refined phenotypes for vascular diseases and hypertension. Such approaches and technologies should be carefully standardized and validated, and centralized resources should be distributed geographically with open access to all NHLBI investigators. These centralized resources and technologies should strongly encourage multidisciplinary and inter-institutional network interactions to facilitate investigator-initiated projects and provide multiple training opportunities. Facilities should both encourage new research on technologies for phenotypic refinement and provide service functions to all NHLBI investigators in vascular diseases and hypertension research. Critical areas for focus include but are not limited to: phenotypic refinement of biomarkers for diseases and outcomes, metabolomic/proteomic phenotyping, core laboratories for critical, complex analyses; new imaging techniques for animals and humans; new and improved

murine and other experimental models, bionanotechnology; new analytical tools/approaches of 'systems biology'; computational biology/genomics; new analytical tools for social and behavioral sciences; and mathematical modeling of vascular physiology and disease.

2. NHLBI should develop a comprehensive, integrated approach to optimize the translation of information for vascular diseases and hypertension to public health and practice. The approach to optimizing translation should focus on detecting vascular diseases and hypertension earlier and guiding preventive interventions more effectively, with the ultimate goal being to improve our rates of control and outcomes. This approach should be broad, should be directed at validating risk stratification approaches and treatment, and should include clinical trials to evaluate the efficacy and effectiveness of treatments, with a focus on underserved and understudied populations. Better methods should be developed to evaluate beneficial behavioral changes and to evaluate ongoing community-based methods that provide surveillance of clinical approaches to vascular disease. Bench research should be better translated by facilitating access to current and emerging resources, such as small molecule libraries and expertise in molecular and structural modeling. In addition, creation of novel partnerships between basic science and industry should be emphasized to better bridge basic science and therapeutic development. Flexible partnerships or networks of investigators should be evolved to evaluate new surrogates and therapies expeditiously, study ways to improve adherence to prevention and treatment efforts, and develop better methods of implementing our findings and evaluating cost/effectiveness throughout the life course. For example, comparative genomics information should be better integrated at all levels (gene association, haplotype analyses, animal model studies, large population datasets, pharmacogenomic data, large clinical studies, etc) to realize the potential of this research to improve diagnostic and preventive strategies, as well as clinical outcomes.

3. NHLBI should Support the creation and designation of specialized, highly flexible, multidisciplinary, multi-institutional NHLBI centers or networks for the study of vascular diseases and hypertension. These should be newly created regional or national collaborative partnerships or networks that excel at fostering and accelerating productive academic interactions. The term "Center" has historical connotations that these recommendations seek specifically to avoid. *The committee wishes to emphasize that creative and flexible ways of partnering are the essence of the centers or networks envisioned and recommended.* These new centers or networks should also emphasize recruitment and nurturing of trainees at all levels skilled in the new, multidisciplinary study of hypertension and vascular diseases. These entities should be boldly structured, investigator-designed teams that can follow a variety of partnering structures. The structure should in each case be proposed and justified by the team of collaborating investigators. These centers should include a broad and diverse mixture of a critical mass of investigators in proximity to one another, and should also create multiple partnerships with numerous constituencies off site, such as but not limited to academicians from diverse disciplines, other government agencies, industry, the community, foundations, not-for-profit organizations, and providers of care. These centers should have specific leadership personnel dedicated to facilitating interactions between all constituencies, should be distributed geographically across the U.S., and should focus thematically on key and emerging areas central to vascular disease and hypertension. It is expected that rigorous internal and external reviews of these networks at all levels will be regularly undertaken, and that the networks will be required to propose self-evaluation methods. These facilities should foster novel, multisystem, integrative approaches to exploring vascular diseases and hypertension. Critical areas for focus include but are not limited to genomic, proteomic,

metabolomic, molecular and translational studies; inflammatory mechanisms and the adaptive immune response; neural mechanisms, obesity and metabolic diseases, the biology of the vasculature across the life course, social and behavioral sciences, gene-environment and lifestyle-environmental interactions, and modeling of vascular systems. For example, optimizing the prevention, early detection, diagnosis, and treatment of atherosclerotic plaque progression requires a broad and integrated set of investigators and approaches, such as (but not limited to) genomics, proteomics, and bioinformatics to characterize populations at risk, novel imaging techniques and biomarkers, medicinal chemistry, and effective partnering with industry, primary care providers and patient advocacy groups to implement and disseminate the knowledge. The centers or networks envisioned would facilitate and optimize such interactions.

09/29/06

Business Operations
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Recommendations:

There was minimal discussion of the business practices. Those who did not prioritize the seven business practices before the meeting were asked to do so as well as provide comments. Three of the business practices were felt to be very important: (1) funding and award mechanisms, (2) create incentives and mechanisms for cross-institute and interagency funding of large projects, and (3) issues related to CSR. Three were ranked of lesser importance: (1) create streamlined procedures for renewing grants for established investigators, (2) review the NHLBI pre-approval process for investigator-initiated grants with direct cost > $500 K, and (3) dissemination and communication of advances and discoveries by NHLBI supported investigators.

The working group provided few written comments of the seven business practices; however, many focused on review and the need to help the young investigator.

1. For grant review, it was suggested that incentives should be provided to solicit the best people to participate on study sections; the chair should assist the SRA in choosing reviewers; with electronic submission, the turn around time for application should be reduced; and all grantees should be required to participate in review.

2. For the young investigators, it was suggested that the process of fostering clinician-scientists needs further development, especially in the current environment of fiscal austerity; senior co-investigators should have protected mentoring time, without developing a new mechanism; and help junior investigators make the K to R transition.

3. Others suggested that the established investigator should not be given special advantages.

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