Harnessing Academia, Government, and Industry

Santa J. Tumminia

One of the goals of the recent workshop, “An Eye on Glaucoma: New Opportunities for Treatment,” was to highlight areas of glaucoma research that, with appropriate funding, are ripe for major advancement for prevention, diagnosis, and treatment. Another goal was the exploration of collaborative partnership and the process for facilitating translation of these areas, not just for glaucoma but for all diseases affecting visual function. In this article, I address the second of the two goals. Since the National Eye Institute (NEI) was established in 1968, its mission has been to conduct and support research, training, health information dissemination, and other programs with respect to blinding eye diseases, visual disorders, mechanisms of visual function, preservation of sight, and the special health problems and requirements of the blind in all areas of vision research. As part of the federal government, the NEI has distinct guidelines and rules that govern how it can foster vision science along the continuum from basic research, to clinical application, to acceptance and adoption by the medical community as the standard of care. Vision research is a collaborative process shown to be successful through engaged scientific discussion, investigator-driven hypotheses, and responsible program management and support.

How does the vision research community best interact with the NEI to foster successful vision research? Most members of the community are familiar with the more traditional mechanisms of interaction (i.e., grants and contracts), but the topic “Harnessing Academia, Government, and Industry” gives us the opportunity to discuss other, perhaps less well-known partnership mechanisms. The purpose of this article is to explore the NEI toolbox and the various support mechanisms available for fostering research in eye disease, through partnerships between NEI, academia, and industry.

NEI and the Vision Community: Support Mechanisms

The NEI conducts and supports laboratory and patient-oriented research through both intramural and extramural programs. The intramural program encompasses strong basic, translational, and clinical programs in molecular genetics, retinal degenerations, retinal circuits, neuroprotection, angiogenesis, immunology, and visual processing. The extramural program supports a diverse portfolio of vision research on retina; cornea; lens and cataract; glaucoma; strabismus, amblyopia, and visual processing; low vision and its rehabilitation; oculomotor systems and neuro-ophthalmology; myopia and refractive error; ocular genetics; ocular inflammation; infections; and immunology. The most well-known mechanism of partnership between the federal government and its respective research communities is through the Office of Extramural Research’s contracts and grants programs. The NEI’s Division of Extramural Research (http://www.nei.nih.gov/funding/) supports approximately 1600 research grants and training awards made to scientists at more than 250 medical centers, hospitals, universities, and other institutions across the country and around the world. In fiscal year 2011, the NEI had a budget of $700.8 million. More than 86% of the total NEI budget was spent extramurally on grants, contracts, and cooperative agreements with the vision research community (Fig. 1). Given that the focus of the workshop was glaucoma, it is worth noting that approximately 10% of the extramural budget was directly spent on glaucoma and the optic neuropathies.

Other Mechanisms for Collaboration

There are other mechanisms, perhaps less well known than the extramurally supported grants, collaborative agreements, and contracts that can be used to partner academia, industry, and government. They include the Material Transfer Agreement (MTA), the Collaborative Research and Development Agreement (CRADA), the Clinical Trials Agreement (CTA), and the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs.

Agreements. The MTA is used for the exchange of materials with outside organizations for research purposes. In 2003, the NEI had ~20 MTAs with outside organizations; in 2010, the number was more than 100. This mechanism—although technically a type of partnership—is not necessarily the best mechanism to use in the spirit of a “true” research partnership, since an MTA is generally used when any proprietary material is exchanged, when the receiving party intends to use it for his or her own research purposes, and more important, when no research collaboration among scientists is planned. The CRADA, on the other hand, facilitates public–private partnerships by allowing federally employed scientists to collaborate with industry and academia to leverage research resources and facilitate the development and commercialization of health care pharmaceuticals and products. A CRADA is authorized only for collaborators who will make significant intellectual contributions to the research project undertaken or will contribute essential research materials or technical resources not otherwise reasonably available to the National Institutes of Health (NIH). Under the Public Health Service, the NIH laboratory can provide personnel, services, facilities, equipment, or other resources, but not funds, to nonfederal parties, with or without reimbursement; the other party can provide funds, personnel, services, facilities, equipment, or other material, and/or technical resources. The CRADA provides the nonfederal party with the important option of negotiating an exclusive license for the resultant CRADA subject invention(s). The primary difference between the standard CRADA and the MTA is the level of NIH collaborative involvement with the nonfederal party. In 2010, the NEI had 12 signed CRADAs. Clearly, this partnership area is ripe for growth.

From the National Eye Institute, National Institutes of Health, Bethesda, Maryland.

Submitted for publication January 17, 2012; revised April 11, 2012; accepted April 19, 2012.

Disclosure: S.J. Tumminia, None.

Corresponding author: Santa J. Tumminia, Office of the Director, National Eye Institute, 31 Center Drive, MSC 2510, Building 6, Room 6A03, Bethesda, MD 20892; tumminias@nei.nih.gov.

DOI:10.1167/iovs.12-9483q

Copyright 2012 The Association for Research in Vision and Ophthalmology, Inc.
The CTA is used between an NIH institute and an outside party for studies conducted to determine the safety and efficacy of new agents and devices in humans. It defines the terms and conditions associated with the conduct of the clinical trial. A protocol describing how patients will be treated is normally included in the agreement. The CTA describes responsibilities specific to clinical trials, such as protocol drafting, regulatory filings, interactions with regulatory agencies, and use of data.

For more in-depth information on all these mechanisms, see the NIH Office of Technology Transfer website at http://www.ott.nih.gov/index.aspx.

**Small Business Programs.** The SBIR and STTR programs resulted from the Small Business Innovation Development Act of 1982 and the Small Business Research and Development Enhancement Act of 1992. Congress prioritized four major goals for these programs: (1) to stimulate technological innovation, (2) to use small business to meet federal research and development (R&D) needs, (3) to foster and encourage participation by minorities and disadvantaged persons in technological innovation, and (4) to increase private-sector commercialization of those innovations derived from federally supported R&D. Federal agencies with extramural R&D budgets in excess of $100 million are required to administer these programs. Since both of these programs are set-asides—that is, an agency must spend a certain percentage of its extramural budget on them—it is important that it receive high-quality applications. The SBIR program issues grants to small businesses to engage them—it is important that it receive high-quality applications. The SBIR program issues grants to small businesses to engage in federal R&D with a potential for commercialization and public health benefit. The current set-aside for the SBIR program is 2.6% and is scheduled to increase to 3.2% by 2017. The STTR program issues grants to facilitate cooperative R&D between small businesses and U.S. research institutions. Its current set-aside is 0.35% and will increase to 0.45% by 2017.

Both programs increase the participation of small businesses in federal R&D and increase private sector commercialization of technology developed through such R&D. The two programs differ in that one (SBIR) relates to the principal investigator (PI) and the other (STTR) to a research partner. For the SBIR, the PI must be primarily employed with the small business concern (SBC) at the time of the award and for the duration of the project period, unless a waiver is granted by the NIH. For the STTR, primary employment is not stipulated, and so the PI may be from the small business or the collaborating nonprofit research institution. The unique feature of the STTR program is the requirement for the SBC applicant organization to formally collaborate with a research institution in phases I and II. There are also regulations as to how much work the SBC must perform with respect to its research partner(s). The NEI SBIR/STTR program is very active and currently has more than 65 active SBIR/STTR grants, with 7 being specific to glaucoma in the R&D areas of ophthalmic instruments for detecting glaucoma, drugs to treat glaucoma, and drug delivery devices. NEI-supported SBIR/STTR awards have led to the development and commercialization of several technologies, including a touchpad and audio viewer for the visually impaired and a pediatric optical coherence tomography device.

Both the SBIR and STTR programs are structured in three phases. The phase I objective is a feasibility study. The PI must establish the technical merit and potential for commercialization of the proposed R&D efforts. Phase II continues the R&D efforts initiated in Phase I. In Phase III, the SBC is expected to pursue—with non-SBIR/STTR funds—the commercialization of the product or service resulting from its Phase I/II R&D activities. During this phase, many of the SBCs are developing drugs or medical devices that require regulatory approval from the U.S. Food and Drug Administration (FDA). This hurdle is a major one for small companies, most of which do not have any experience in navigating the FDA approval process. To improve the success rate of the companies funded through the small business grant programs, the NEI initiated a new SBIR/STTR Regulatory Assistance Program (http://www.nei.nih.gov/funding/sbir_sttr_awardees.asp) to improve the commercialization success of companies funded through the small business grant program. Small business grant recipients selected for this program receive 30 hours of high-quality regulatory consulting, provided by an experienced regulatory consulting firm, to assist them in developing a step-by-step plan for FDA approval. The program is modeled on a pilot established by the National Cancer Institute. The NEI has just completed its first round of reviews for this program, and nine awards were issued: three in the area of drugs and drug development and six in the area of devices. The NEI is optimistic that this program will speed the regulatory approval process and improve the success rate of small companies that are developing ophthalmic drugs and devices to treat the blind and visually impaired.


As an entry portal into the next stage of development (i.e., post-SBIR/STTR), the NIH created the Pipeline to Partnerships...
(P2P), a virtual space for NIH licensees and SBIR/STTR awardees to highlight developing technology and product development for any potential investors. Although listing on the P2P site does not constitute an endorsement or recommendation by the NEI or the NIH, the site functions as an initial meeting space for the developers of new technologies and interested potential investors. It can be searched by disease or application category and highlights the position on the development timeline for a specific project. An example of one technology that was highlighted on the P2P site was an instrument for early detection and monitoring of glaucoma. Synabridge Corporation (Veri\v{s}ci; Raritan, NJ) received SBIR phase I and phase II support for the Neucodula electronic instrument, which uses patented isolated-check (ic)VEP technology to detect and quantify neural deficits that are caused by glaucoma. The SBIR support provided seed and early-stage development funds for business growth. Clinical trials showed a 90% and higher accuracy in detecting early-stage glaucoma.1 The technology was patented in several countries, including the United States, and the company received 510k FDA clearance in 2009.

THE NIH AND PUBLIC–PRIVATE PARTNERSHIPS

The NIH Public–Private Partnership (PPP) program was established in 2005 as an end product of the NIH Roadmap. Its mission is to “facilitate collaborations to improve public health.” NIH PPPs involve the NIH in collaboration with a wide range of organizations, including patient advocacy groups, professional societies, charitable foundations, industry members, trade organizations, and academic institutions. NIH PPPs are, first and foremost, science driven. They “aim to improve the health of the American people and are structured to uphold the principles of transparency, fairness, scientific rigor, and compliance with federal laws and NIH policy.” PPPs vary in size and scope and center on the shared goals of the partners, leveraging knowledge, skills, resources, and services.

Unlike other Roadmap programs, the PPP does not have an end date, as developing a mutually beneficial PPP takes patience and commitment. To develop a meaningful PPP with the NIH, one should identify a scientific or clinical problem that can be better answered through a partnership than by a sole entity. PPPs can be established directly between the NIH, either as a whole or through one of its institutes or centers, and one or more outside entities. A partnership is based on agreements between the partners regarding the goals of the partnership, the roles of the partners, and governance. Other issues such as the management of intellectual property, data access and data sharing, and human subject concerns require careful consideration and planning. The NIH Manual Chapter 1167 (http://www1.od.nih.gov/oma/manual chapters/management/1167/main.html) provides further guidance regarding when and how to consider PPPs. Given today’s tight budgets, PPPs should be further explored as opportunities for scientific growth. For more information, see http://ppp.od.nih.gov/.

THE FOUNDATION FOR THE NIH

Congress established the Foundation for the NIH (FNIH) as a 501(c)(3) charitable organization to support the mission of the NIH and advance PPP collaborations. As a nongovernmental entity, the FNIH is not subject to a variety of policies and regulations that the NIH, as an agency of the U.S. government, is bound by, thus allowing it to have a unique role in PPPs. Its purposes range from fundraising to support of NIH initiatives and activities; meeting sponsorship to encourage scientific dialog; and hands-on management of projects including the publication of funding initiatives, scientific review, and award management. The staff includes developmental specialists, science and project managers, and individuals devoted to partnership development and implementation. The foundation works closely with NIH to ensure that PPPs promote the public health and serve the mission of the NIH. Its role varies with the needs of each partnership. The NEI has facilitated collaborations to improve public health through biomedical research supported through the NIH PPP program. In 2006, Dr. Jane Sayer, an NIH research scientist at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), established the Sayer Vision Research Lecture and Award at the FNIH in partnership with the NEI, to provide an opportunity for honorees to explore areas of interdisciplinary collaboration that may lead to advances in diverse medical specialties with relevance to vision research. Topics for this award series have included stem cells, G protein-coupled receptor signaling in phototransduction, basic and clinical applications of vascular endothelial growth factor, and the use of fluorescent proteins to visualize synaptic circuits and glial cells. The NEI also actively collaborates with the FNIH to partner with several pharmaceutical companies to support postdoctoral fellows as well as research through this mechanism. The NEI encourages potential partners to contact the foundation for more information at http://www.fnih.org/.

NEI PARTNERSHIPS WITH GOVERNMENT AND NONGOVERNMENT AGENCIES

The NEI has forged alliances and working relationships with other government agencies to advance its vision mission. One of its strongest partnerships is with the FDA. Both agencies often partner with nongovernmental agencies to support meetings that further their respective missions. The NEI has initiated a series of meetings with the FDA to discuss evaluating endpoints for clinical trials. These meetings are held in conjunction with the Association for Research in Vision and Ophthalmology (ARVO) and provide a forum to explore new clinical metrics as study outcomes for clinical trials.

Examples of these NEI–FDA joint meetings include Ophthalmic Clinical Trial Design and AMD Endpoints, Use of Patient-Reported Outcomes in Medical Product Development, Glaucoma Clinical Trial Design and Endpoints Symposium: Measures of Structural Change and Visual Function, and Use of Functional Vision Endpoints in Visual Prostheses Product Development. These symposia have helped guide outcome considerations for future clinical research.

The two glaucomatocentric meetings were fruitful in that the FDA informed glaucoma researchers of its willingness to consider additional outcome measures beyond intraocular pressure, especially related to optic nerve and retinal nerve fiber layer structure and function, in the approval process for new glaucoma drugs. The second glaucoma-themed meeting focused on measures of structural change as it relates to visual function. Researchers and clinicians discussed the latest technologies for identifying clinically significant structural changes related to glaucoma progression that are greater than expected during normal aging and are associated with future visual function changes. The FDA clarified its position, stating that the research community bears responsibility for demonstrating that structural measures correlate with clinically relevant functional measures for the different stages of glaucoma (i.e., early, middle, and late). This step is necessary before the FDA can consider accepting a structural parameter as the basis for approval of a drug or device for glaucoma treatment. The meetings are a major boon for the field of clinical vision testing in the context of clinical trials, and they demonstrate the emphasis that the NEI places on interagency collaboration.
The NEI frequently collaborates scientifically with other government agencies—specifically, with the Veteran’s Administration on its diabetic retinopathy study, the Centers for Disease Control and Prevention on the Age-Related Eye Disease Study (AREDS and AREDS2) and a study of childhood retinopathy, and the National Center for Health Statistics in multiple iterations of the National Health and Nutrition Examination Survey. Other federal collaborators include the Department of Energy, the Department of Defense, the National Aeronautics and Space Administration, and the Center for Medicare Services (CMS).

The NEI has responsibilities for representation of several constituencies besides its sister federal agencies, including professional societies, advocacy groups, other nonfederal institutions, and the U.S. Congress. Each of these groups has a particular set of interests and needs, and it is important for the NEI to remain aware of mutual and common interests, to maximize partnerships, and to report goals, opportunities, and successes to Congress. The NEI regards each advocacy organization as an important part in its mission to preserve sight and treat and cure low vision and blindness. A primary and important means of interaction with these communities is through the National Advisory Eye Council (NAEC). The advice and recommendations of the NAEC are critical to NEI staff in setting research priorities and in assuring that the wide variety of interests has a voice. The membership of the NAEC typically consists of one or more optometrists, ophthalmologists, and research scientists from different vision disciplines and members of the public who often represent various advocacy groups.

Most NEI grantees are members of ARVO, whose purpose is “to encourage and assist research, training, publication, and dissemination of knowledge in vision and ophthalmology.” ARVO has in excess of 10,000 members in more than 70 countries. A significant number of those members are not funded by the NEI, but are actively engaged in vision research. The ARVO membership is multidisciplinary and includes both clinical and basic researchers. The NEI maintains close ties with the ARVO executive leadership and board of trustees, to ensure that national and international researchers are connected with its priorities and funding opportunities. Over the past 10 years, the NEI and ARVO have initiated a pattern of jointly sponsoring scientific and administrative workshops and educational events, and input into the NEI strategic planning process has been formally organized and submitted on behalf of the ARVO membership. This input is valuable, and it guarantees that relevant expertise is solicited and continues to be considered in NEI planning documents. Other partnerships include working with nonprofit advocacy groups to promote vision research, often through meetings on specific research topics.

The NEI and Community Engagement

The NEI is working to strengthen its partnerships through a variety of mechanisms and activities.

National Eye Health Education Program

The National Eye Health Education Program (NEHEP) is an NEI partnership established at the request of Congress. It works with more than 65 public and private organizations that have an interest in eye health education or that represent populations at higher risk of eye disease. NEHEP is the final step in the research continuum with the dissemination of results to health professionals, patients, and the public in the form of public education. There are five NEHEP program areas that provide information and resources, in both English and Spanish, to audiences at higher risk for eye disease and to the health professionals who serve these populations. These programs include Glaucoma, Diabetic Eye Disease, Low Vision, ¡Ojo Con Su Visión! (Watch out for your vision, the Spanish language program), and Vision and Aging.

NEHEP’s advisory structure is composed of a planning committee and a formal partnership. Its current working groups address low vision, glaucoma, diabetic eye disease, health disparities, community activity, and outcomes. The role of the NEHEP Planning Committee is to advise the NEI on the overall development, implementation, and evaluation of NEHEP programs. The professional organizations participating in this partnership include civic organizations, voluntary organizations, nonprofit organizations, and other government agencies. A list of current NEHEP partnership organizations may be found at http://www.nei.nih.gov/NEHEP/about/directory.asp.

The purpose of the NEHEP partnership is to establish ongoing, interactive, mutually beneficial relationships with the NEI and other organizations, to achieve NEHEP goals and objectives. The NEHEP website gives information on planning eye health education activities and provides access to educational resources and materials. NEHEP develops a wide variety of educational materials (e.g., e-cards, publications, Web resources, public service announcements, stickers and magnets, posters, fact sheets, and teaching toolkits) to support its program areas and reach people at higher risk for eye disease with specific eye health messages. There is also a Healthy Eyes website considered to be the consumer website. All NEHEP materials and resources point the public to this page to find more information about eye health.

The NEI recognizes the importance of strengthening the capabilities of community-based organizations to develop innovative eye health education and promote community vision projects. The Healthy Vision Community Awards Program is supported by the NEHEP budget and provides awards of up to $10,000 each. It is intended to stimulate collaborative initiatives that address eye health topics, including age-related macular degeneration, diabetic eye disease, glaucoma, occupational eye safety, and vision rehabilitation. The awards are limited to health education programs conducted within the United States and its territories. Since the program was established in 2003, the NEI has funded 366 programs in almost every U.S. state and territory. All programs are kept in a searchable database that is open to the public, to help people gain ideas and information about projects in their states. The NEI is the first NIH institute to establish such a program; other NIH institutes are in the process of establishing programs using the Healthy Vision Community Awards as a model.

Fortieth Anniversary Events

The NEI began a year-long celebration of its 40-year history with NIH-wide scientific symposia and other commemorative events in 2009. Commemorative events included a showing at National Geographic's “Blindlight,” an award-winning documentary about Erik Weihenmayer, a blind mountain climber who embarked on an expedition up the north face of Mount Everest with six blind Tibetan students. Weihenmayer worked with NEI-supported vision researchers at the University of Wisconsin, who developed the BrainPort, a device that presents a tactile visual image to the tongue from a head-mounted camera. Weihenmayer is the first blind person to scale Mount Everest.

Subsequently, several scientific symposia were held on the following topics: Genetics and Genomics in Vision, Advances in Optical Imaging and Biomedical Science, Neuroscience and Vision, Stem Cell Therapies, From Degeneration to Regeneration, Focus on Glaucoma, The Fourth Sayer Vision Research Lecture, and Translational Research and...
Vision (http://www.nei.nih.gov/anniversary/). Glaucoma topics included control of axon growth by retinal ganglion cells, mechanisms of neurodegeneration, genetic defects and the biological bases that predispose to inherited glaucoma and computational methods supporting this research, imaging, translational medicine for glaucoma, the exploration of novel treatment strategies, and clinical trials.

**Program-Planning Activities**

The NEI is also actively engaged in program-planning activities and has held several planning meetings in each of its main program areas. In 2011, the Glaucoma and Optic Neuropathies planning group met to discuss the progress, goals, needs, and opportunities of the field. Its review of the field will be part of the NEI’s ongoing strategic initiatives. In March 2012, the NEI posted the draft of the National Eye Institute’s “Vision Research: Needs, Gaps, and Opportunities,” which includes the Glaucoma and Optic Neuropathies Panel Report, for public comment. This first step is critical for a thorough analysis of the field and for the identification of vision research priorities. Its publication will be followed by the next phase of the planning process which will expand the NEI’s efforts to obtain broad and diverse input from academia, industry, foundations, and other agencies worldwide. For more information on NEI planning process, go to http://www.nei.nih.gov/strategicplanning/.

**NEI Alignment with NIH and National Opportunities**

When Francis Collins, MD, PhD, became NIH director in 2009, he articulated five opportunity areas for NIH science; NEI programs and priorities mesh well with these goals. The five priorities are as follows.

**Genomics and High-Throughput Technologies for Uncovering the Causes of Diseases**

The NEI has fully embraced the phenomenal opportunities of human genetics to elucidate causes and mechanisms of disease. In 2010, a new position, NEI Associate Director for Ophthalmic Genetics, was created. As a result, large collaborative networks have been organized for the major eye disease areas. The NEI created the NEI Glaucoma Human Genetics Collaboration (NEIGHBOR), the International AMD (Age-Related Macular Degeneration) Genetics Consortium, the Fuchs’ Endothelial Corneal Dystrophy Genetics Consortium, the International Consortium on Genetics of Refractive Error, and the Diabetic Retinopathy Genetics Consortium. These collaborative groups have ascertained substantial numbers of cases and controls that no single individual could accomplish—for example, 7,000 advanced cases and nearly 50,000 controls for the AMD network—leading to identification of new genetic loci. NEIGHBOR and the Glaucoma Genes and Environment Network, both glaucoma-specific networks, have incorporated state-of-the-art exome sequencing and whole-genome sequencing, with more than 3000 well-characterized cases and more than 3000 controls, and are beginning to make great strides in the identification of genetic variation predisposing to primary open-angle glaucoma. Collaboration is key for most successful scientific research, but the real value of consortia such as these is severalfold. It begins with data sharing and continues with using complementary expertise to analyze the vast amount of data. Finally, pooling research resources enables the collaborating investigators to carry out large-scale genetic and genomic studies that are not possible for the individual investigator alone and yet are so critical for understanding the nature of complex eye diseases.

**Translational Research**

The NEI has a record of supporting all aspects of translational research, from basic to clinical studies. The vision community has made great strides in disease treatment studies in gene therapy, drug delivery, device development, and adult limbal stem cell use in corneal transplants. Last year, NEI-supported investigators demonstrated that adult stem cells can be used to generate normal functioning retinal pigment epithelial cells to replace damaged ones. Induced pluripotent stem cell transplants are being studied as potential treatment modalities for Stargardt macular degeneration and atrophic AMD. These examples build on the foundation of basic scientific discovery over many decades. The work involves hypothesis-driven applied clinical research.

The NEI is using the R24 grant mechanism to foster translational research. The mechanism allows partnering of individuals with complementary scientific and clinical expertise at different locations to move vision science from the bench to the bedside. One major success of this program mechanism, the phase I RPE65 gene therapy for the childhood blinding disease Leber’s congenital amaurosis (LCA), is a prime example of successful gene therapy for a nonlethal condition. Three LCA trials have established the safety profile of gene therapy and demonstrated restoration of some visual function in trial participants.

The NEI also partnered with the Department of Energy and Second Sight Medical Products, Inc. (Sylmar, CA) to develop the first vision prosthetic device to receive marketing approval. The Argus II Retinal Prosthesis System has received marketing approval in the European Economic Area. The device has been implanted safely in 50 blind patients, who have acquired some

Monogenic diseases are preeminent as identifiable translational opportunities, and vision is rich in single-gene disorders. In 2006, the NEI launched the National Ophthalmic Disease Genotyping Network (eyeGENE). eyeGENE is a partnership of the federal government, eye health care providers, CLIA (Clinical Laboratory Improvements Amendments)-approved molecular diagnostic laboratories (http://www.cms.gov/CLIA/01_Overview.aspx#TopOfPage), more than 250 clinical and research organizations in more than 40 states, private industry, and extramural scientists who support a broad research constituency. The mission of the network is to facilitate research into the genetic causes of ophthalmic disease by broadening patient accessibility to diagnostic genetic testing. To date, more than 3500 DNA samples from individuals with medical phenotype information have been processed and entered into the research repository; new cases are arriving at a rate of 800 to 1000 per year. The network tests more than 65 genes for more than 30 inherited eye diseases and offers diagnostic testing for the glaucoma genes CYP1B1, OPTN, and MYOC.

The eyeGENE partnership benefits three groups of individuals. First, community-based ocular health care providers submit a patient’s blood sample and receive a DNA molecular evaluation for diagnosis and genetic counseling. The cost of the diagnostic testing is free to the patient and provider. Second, patients contribute blood samples and clinical information to a de-identified registry. The results may make them eligible for clinical trials or for participation in a research study. Third, researchers have access to de-identified DNA samples and clinical information to investigate genotype-phenotype relationships and the causes of eye disease. The eyeGENE Network has begun to change the standard of care in private practice, and ophthalmologists and optometrists are now asking questions about genetics and disease mechanisms in their practices consequent to the expanding participation in this network.
visual function. This remarkable engineering project has also provided a wealth of information about retinal neural organization and of the central visual system. Continued development should lead to improved design and better vision in newer generation devices. An intriguing question is how to build on these successes for other vision disorders.

Putting Science to Work for the Benefit of Health Care Reform

Long before the descriptor “comparative effectiveness research” came into common usage, the NEI conducted studies comparing clinical outcomes, effectiveness, and appropriateness of items, services, and procedures for diagnosis, prevention, or treatment of eye and vision conditions and diseases. Examples during the past 10 years include the Standard Care versus Corticosteroid for Retinal Vein Occlusion (SCORE) study and the Randomized Trial of Atropine versus Patching for Treatment of Moderate Amblyopia in Children, to name just two examples. Last May, investigators conducting the Comparison of AMD Treatments Trials (CATT) published results showing that two anti-vascular endothelial growth factor drugs, Avastin (bevacizumab) and Lucentis (ranibizumab; both from Genentech, South San Francisco, CA), are equivalent in treating wet AMD. Avastin (~$50 per treatment) has been used off label by ophthalmologists since 2006. The derivative antibody fragment Lucentis (~$2000 per treatment) was approved for wet AMD in 2007 and currently is used in approximately 40% of AMD treatments of Medicare patients. The NEI broke new ground in collaborating with the CMS to pay for these expensive trials. The huge cost differential led to changes in CMS regulations for determining the comparative effectiveness of research trials.

Global Health

Eye disorders are responsible for 3.1% of the global burden of disease, according to the 2003 World Health Report of the World Health Organization. The NEI mission naturally extends to vision and vision research on a global scale. There is a long history of NEI support for international research and of collaboration between individual NEI-supported scientists and their international counterparts. In 2005, building on two decades of scientific exchanges with vision scientists and clinicians in India, the NEI orchestrated a new bilateral government-level agreement to facilitate research. The Indo-U.S. Collaboration on Expansion of Vision Research was established by a joint statement of intent between the Ministry of Science and Technology of the government of India and the U.S. Secretary of Health and Human Services (http://www.nei.nih.gov/indo-uscollaboration/index.asp). This agreement supports collaborative research projects that will result in new or refined approaches to preventing and treating visual disability and blindness in India, the United States, and globally. The program’s processes are overseen by a joint working group consisting of Indian and U.S. scientists with expertise spanning a wide programmatic range of vision research. This agreement has made possible enhanced joint funding of collaborative research in areas of ophthalmic genetics, disease biology, and clinical treatment. One application specific to the glaucoma field, Identification of Primary Open-Angle Glaucoma Biomarkers, is supported through this program.

The NEI has also promoted the development of collaborative research partnerships through the Civilian Research and Development Foundation, a nonprofit organization authorized by Congress in 1992 to support international collaborations in science and technology. Projects funded include studies on perception in the aging visual system, topical drug delivery, glaucoma, and genetic risk factors in AMD.

An example of NEI extramural-supported international research is the medical treatment of trachoma that became possible in the 1990s with the discovery that the antibiotic azithromycin can be used against the infectious agent Chlamydia trachomatis. Since then, NEI-funded research has played a critical role in assessing the effectiveness of administering this antibiotic to entire communities. The NEI-funded STAR (Surgery for Trichiasis, Antibiotics to Prevent Recurrence) clinical trial showed that a single oral dose of azithromycin after surgery reduces recurrence by 30%.

Empowering the Biomedical Research Community

The NEI believes that individual investigator-initiated research is one of the most crucial and creative drivers of new ideas and insights in biomedical research. The collective wisdom and scientific perspectives of the extramural research community has demonstrated time and again that it is well positioned to identify both needs and opportunities to carry out cutting-edge research. Accordingly, most extramural research funding goes to support these applications. Biomedical vision research is also enhanced by careful selection of opportunities for support. The NEI is committed to developing the next generation of vision researchers and has expanded its institutional training grants by instituting programs in ocular statistical genetics at several universities. Such programs will foster the partnership of young research trainees in all areas of vision science with experts in mathematics, modeling, and computation—fields that are not usually affiliated with ocular research—to provide state-of-the art training for a new breed of investigators. This need was identified by the 2009 NEI Workshop to Identify Gaps, Needs and Opportunities for Ophthalmic Genetics. The NEI created a new Intramural Physician–Scientist Development Program for early career support for MDs desiring to embark on a research career. The NEI was only the second NIH institute to develop such a career opportunity at the time of the program’s initiation.

SUMMARY

Partnership takes many forms. In answering the original question of how to partner academia, government, and industry to promote good vision science, we have explored the many NIH mechanisms that can be used to advance vision science, in addition to the more well-known traditional mechanisms. CRADAs, CTAs, SBIR/STRTR, and the PPG program of the FNIH can all be more fully used. Networks and consortia are already yielding dividends to the field and show that they can be successful. The glaucoma field has much to offer in the way of discovery, development, design, and implementation. Science is evolving rapidly, and new translational opportunities are now available. In a difficult budgetary climate, we must determine how best to augment resources to maximize our investments and capitalize on scientific opportunities. The way to achieve this goal is through partnerships, but partnerships are not always easy. They take strong commitment from all parties. One must identify from the outset how to balance the strengths of the partners. All participants must remain actively involved, and everyone should be aware of and agree on the expected results of the partnership. A partnership should have structure. A well-developed business plan, contract, or memorandum of understanding clearly describing the roles and responsibilities of each partner is vital. Ongoing monitoring of the performance of the partnership is important in ensuring its success. The frequency of monitoring should be defined in the plan, as should a clearly defined method of dispute resolution.
The partnership should delineate clearly defined long-term goals.

It is also important to keep in mind that more people are affected by a partnership than just the participants. The American people—particularly, their vision health, eye health care providers, other interested private sector businesses, and relevant interest groups—may be affected by the partnership. It is important to have good and open communication about the goals and successes of the partnership. PPPs are all about relationships, and it is vital to nurture them the same as any other relationship. For more information on keys to a successful partnership, see the National Council for Public–Private Partnerships (http://ncppp.org/).

The past decade has witnessed revolutionary advances in biology in deciphering the human genome, gene therapy for monogenic eye and vision diseases, the discovery and application of induced pluripotent stem cells, small molecule therapies, and drug development and delivery. There is no reason to believe that the pace of opportunities and advances will slow down over the current decade. With increasing budgetary constraints, using innovative methods to create successful partnerships between academia, government, and industry can enable the vision community to leverage resources and maximize the opportunities for success.

References