

**National Institute of Diabetes and Digestive and Kidney Diseases  
Diabetes Centers 2005 Directors Meeting**

**November 16–17, 2005  
DoubleTree Hotel and Conference Center  
Rockville, Maryland**

*SUMMARY*

**Welcome/Opening Remarks**

*Allen Spiegel, M.D., National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), Bethesda, MD; Judith E. Fradkin, M.D., NIDDK, NIH*

Dr. Spiegel thanked members who had organized the meeting. He stated that the House and Senate Conference Committee had met recently and had not approved the 50/50 budget split for the NIDDK, which means that the 2006 budget will increase by only 0.5 percent. The macroeconomic situation also is difficult; across-the-board cuts of 1.5 percent are expected at most government agencies, including the NIH. Dr. Spiegel commented that elements had been put in place to try to mitigate budget cuts, particularly for pay lines, new investigators, first-time renewals, and R01s.

Approximately 5 years ago, Dr. Fradkin spearheaded a process of examining what the Diabetes Centers' mission and goals were and how the Centers could best accomplish their objectives. Dr. Spiegel noted that at the time there were far fewer budgetary constraints. During this time, caps were raised on the Diabetes Research Training Centers (DRTCs), and Diabetes Endocrinology Research Centers (DERCs) were revamped. These translational secondary "bedside-to-practice" projects, some of which have been well funded, have been critical in disseminating the message of the Diabetes Prevention Program into a real-world setting.

In the difficult times ahead, Dr. Spiegel indicated that the Centers' goals have to be revised. Although competition is valuable, stimulating, and necessary, there also is a need for cooperation to realize larger goals, such as the prevention and cure of type 1 and type 2 diabetes. For these goals, Dr. Spiegel suggested that there are economies of scale and other ways for Centers to collaborate, which was the primary focus of the meeting.

The Digestive Disease Centers annual meetings have been compelling because of the way these Centers interact. At the meetings, the host Center showcases its best talent, and all of the Centers share best practices at their core facilities and pool resources. Many of these components could be considered and emulated by the Diabetes Centers.

Dr. Fradkin welcomed participants. She emphasized that the theme of this meeting would be different than the theme of the meeting that was held in 2000 when additional resources were available. Today's focus must be on maximizing available resources.

Dr. Fradkin commented that she expected some meaningful developments to arise from the meeting, especially regarding working more cooperatively and effectively and sharing resources. She suggested that the Centers be used as a bulwark against the difficult budgetary times ahead to help recruit young investigators and to ensure that diabetes research continues to prosper at Center institutions. Dr. Fradkin encouraged Center directors to consider annual meetings and noted that 5 years between meetings was too long.

### **Meeting Goals**

*Kristin Abraham, Ph.D., NIDDK, NIH; Aldo Rossini, M.D., University of Massachusetts Medical School, Worcester, MA*

Dr. Abraham stated that there had been many changes at the Centers and in the program since the meeting 5 years ago. She thanked Drs. Rossini, Daryl Granner (Vanderbilt University, Nashville, TN), and Domenico Accili (Columbia University, New York) for spearheading the meeting. She introduced Dr. Rossini to discuss the meeting goals.

Dr. Rossini stated that the participants at the meeting represented the institutions that currently perform the most important work in diabetes research. The challenge and the focus of the meeting were to take the Diabetes Centers to the next level in the following ways:

- Devise creative solutions with limited funds;
- Work in partnership with each other;
- Assure a long-term commitment to attracting and nurturing scientific talent to secure the future of diabetes research.

A blueprint for transforming the diabetes program includes additional funding, collaboration, translation, communication, recruitment, and education. Each of these areas must be integrated and collaborative.

*Funding:* Additional funding should be sought from a variety of institutions and corporations and not solely from the NIH.

*Collaboration:* Together, Centers must develop ways to save money while at the same time using available money to grow.

*Translation:* Research goals, particularly DERCS, must be translational.

*Communication:* Centers must find ways to inform the public about diabetes. Centers have not marketed diabetes research effectively, and ways must be found to communicate diabetes information not only to patients but to all general populations.

*Recruitment:* The best scientists must be recruited aggressively to continue and advance diabetes research. It has been difficult to attract and retain outstanding young investigators.

*Education:* Education should involve not only patients but also young researchers who are considering the field of diabetes research.

Each of these areas is critical to the Centers' transformation. Concentrating on a few programs, however, would be more beneficial in transforming how the Centers operate than being involved in many programs. Centers must begin to operate under the assumption that the "sum is greater than the individual parts."

## **The Diabetes Center Program of Today**

*Dr. Kristin Abraham*

The overarching mission of the Diabetes Centers is to operate as an integral part of the national research effort to improve prevention and treatment of diabetes and related diseases. Currently the Diabetes Centers comprise 16 centers across the United States and include 11 DERs, which are located primarily on the East and West Coasts, and five DRTCs, centered in the Midwest. Four new Centers have been added since the last Center meeting. Each institution has a strong investigator base and a robust training support system in diabetes research. Approximately a quarter of R01 awards are allocated to Center institutions, with distribution of funds within the program fairly even among institutions. Approximately 40 percent of the NIDDK T32, fellowship (F), and career development (K) awards are distributed to the Diabetes Centers. This funding demonstrates continued support for the research and training currently underway at the Centers.

The Diabetes Centers often are recognized by their core facilities. The cores are diverse, though several Centers have similar cores, such as islet isolation facilities and transgenic/knock-out cores. Some cores are unique to the Centers that house them, including cores that are moving toward proteomics, metabolomics, and lipidomics.

Dr. Abraham strongly encouraged regular updating of core facility information so that the information could be included on a Diabetes Centers' website, which would enable Centers to disseminate the capacities and capabilities of the program.

Approximately 70 percent of the Pilot and Feasibility (P&F) program awards are junior faculty awards, which support young investigators in innovative, high-impact research. Currently, 80 percent of these awards support basic research and 20 percent support clinical awards, although this proportionality may need to be reevaluated. Within 2 years, 67 percent of P&F awards transition to R-support awards, which, if used as a metric, translates to a very successful program. Participants were encouraged, however, to consider whether transition to R-support should be the sole measure of success.

Dr. Abraham noted that the Division of Clinical and Treatment Research awards approximately \$3 million in P&F funds to the Diabetes Centers every year.

Although the Centers have enrichment activities, including seminar programs and symposia, the main focus of the Centers is on high-impact research. The goal of the Centers is to facilitate and advance diabetes research in the most efficient, effective way. High-impact research that is currently underway includes:

- Model organisms (*C. elegans*)
- Developmental biology
- Hypothalamus
- Fat cell biology
- Imaging
- Inflammation
- Autoimmunity
- Clinical research
- Second-phase translation

Although the Centers' programs have many strengths, such as core facilities, P&Fs, enrichment activities, investigator base, and publications, the 16 Centers operate as silos with little integration. Each Center supports cutting-edge research within its area of expertise, which is the model on which the Diabetes Center program was built. It may be time, however, to integrate Centers' programs to increase the strength of the diabetes program. Ultimately, the Centers could create a network of support that would be interactive across and between Centers. This network would facilitate and enhance the trainee experience and draw additional investigators into the diabetes research program.

Partnerships also would facilitate the mission of the Diabetes Center program. Two specific partners that would strengthen and stabilize the network are the Obesity Centers and the Clinical Nutritional Research Units. Both are DK-funded Centers that have overlapping missions within diabetes research. Future periodic joint meetings with the Obesity Centers in particular could be an important component of the diabetes research program.

### **Historical Perspective: A Brief History of NIDDK-Sponsored Diabetes Centers**

*Daryl Granner, M.D., Vanderbilt University Medical Center, Nashville, TN*

Dr. Robert H. Williams, Professor and Chairman of the Department of Medicine at the University of Washington in Seattle, had as a friend and patient Warren G. Magnuson, the senior senator from the state of Washington. Senator Magnuson was Chairman of the Senate committee that controlled health related legislation and was a powerful political figure. In the early 1970s Dr. Williams convinced Senator Magnuson that diabetes research should be pursued on a multidisciplinary basis and suggested that the Congress establish a network of Diabetes Research Centers. The idea was that physicians and basic scientists working together in coordinated laboratories would be the most efficient way to find the fundamental cause and eventually the cure for diabetes. It was an innovative and politically attractive idea, which garnered the support of both the American Diabetes Association (ADA), and the Juvenile Diabetes Foundation (JDF). The Diabetes Research Centers were to be administered by the National Institute of Arthritis and Metabolic Diseases (NIAMD), one of the institutes of the National Institutes of Health (NIH), and a predecessor of NIDDK. The NIAMD Director at that time was Dr. Donald Whedon. He, and others in NIAMD leadership, decided to launch a program in support of Diabetes Research Centers. The program was announced and \$200,000 was set aside to fund a group of Diabetes/Endocrinology Centers (DEC) selected by the competitive review of applications. The emphasis was to be on diabetes, and the principal

selection criteria were the quality and quantity of basic research already ongoing and funded at the application institution.

The center concept was novel at this time, and investigators at various institutions had to be convinced that: a) their basic research might, in fact, be related to a disease; b) that membership in a center would not corrupt their research efforts; and c) that the public, and their elected representatives, might need to know how tax money was spent, and that, over time, public understanding (interest) of research would be critical for continued support. Parenthetically, in most recent surveys, biomedical research is the one thing the public has said it would be willing to support with more tax dollars.

Convincing arguments must have been made as 38 schools of medicine submitted letters of intent to apply, 21 formal applications were submitted and 4 were approved for funding. These were from the University of Washington in Seattle, Washington University in St. Louis, the Joslin Clinic in Boston and Vanderbilt. When the budgets were examined, the \$200,000 allocation was sufficient to fund only one center for a period of 6 months, with the promise of another \$200,000 to follow. The application with the best priority score was selected. Vanderbilt University School of Medicine thus became the first nationally recognized and federally funded center for diabetes research (as a P17 grant). Oscar Crofford was the Principal Investigator of the grant and Director of the Center, which was funded to start in September 1973. The Center at Vanderbilt has been funded continuously since then. The following year 3 more DEC's were funded at the University of Washington (Bob Williams), Joslin (George Cahill) and Washington University (David Kipnis).

The American Diabetes Association (ADA) felt that more emphasis should be given to diabetes education and treatment and that the program should not be restricted to research. The Government Relations Committee of the ADA was led by Dr. John Davidson, a diabetes specialist from Emory University in Atlanta. Davidson was among the first physicians to realize the importance of teaching patients with diabetes how to care for themselves. He realized that patient education was a long process and that it was best carried out in an outpatient setting rather than with the patient in a hospital. Davidson's position, and that of the ADA, was that the DEC program should be expanded to include a component related to the demonstration of the best model for outpatient patient education and treatment. Legislation was introduced in both the Senate and in the House of Representatives to mandate the establishment of a group of federally funded Diabetes Research and Training Centers (DRTC). Congressional hearings on the legislative initiatives were scheduled:

*Hearings before the Subcommittee on Health of the Committee on Labor and Public Welfare, United States Senate, 93<sup>rd</sup> Congress, 1<sup>st</sup> Session on S. 17, National Diabetes Research and Education Act, and on S. 648, National Diabetes Act of 1973, February 26, 1973.*

The Chairman of the ADA Research Committee was Dr. Rachmiel Levine, a noted scientist and clinician in the diabetes field. He, along with the President and Chairman of the Board of the ADA, the chairman of the Government Relations Committee and a few others, were to testify in support of the legislation before a Senate Committee chaired by Senator Edward Kennedy. Dr.

Levine got sick so Oscar Crofford, as vice-chairman of the ADA Research Committee, had to present the ADA testimony. He was to bring a written statement of about 10 pages and give an oral summary not to exceed 3 minutes, and then answer questions. The group had little experience in such matters, so met for coaching by an ADA-hired attorney in a room in the basement of the Mayflower Hotel the evening (2-25-73) before the hearing. Sen. Edward Kennedy was chairman of the committee, but the ranking Republican, and chief sponsor of the bill, Senator Richard Sweiker from Pennsylvania, actually conducted most of the hearing. The Chairman of the House committee was William Natcher, the long-tenured Representative from the 1<sup>st</sup> congressional district of Kentucky.

The House and Senate versions of the bills were reconciled after many hearings and much testimony. The bill passed easily, on July 23, 1974. “The National Diabetes Research and Education Act,” Public Law 93-354, was one of the last laws signed by Nixon. One provision was the establishment of a National Commission on Diabetes, to develop a long-range plan to combat diabetes. The Commission consisted of 17 members – six nongovernmental scientists or physicians; four persons from the general public, at least two of whom had diabetes or children with diabetes; and the Directors of seven of the National Institutes of Health. The Commission met for the first time in March 1975, elected Dr. Crofford as its chairman, and initiated a series of deliberations aimed at preparing a report for submission to the Congress on December 10, 1975. Committees and workgroups of the Commission intensively researched and reported on specialized topics related to diabetes.

As noted in the preface to the report, “The Long-Range Plan was developed on the basis of information collected in a comprehensive survey of the epidemiology and nature of diabetes and its economic and social consequences. The Commission evaluated the most recent scientific information, consulted with nearly 300 experts in diabetes and diabetes-related disciplines from the United States and Western Europe, and heard extensive public testimony in cities throughout the nation. The result was the formulation of a plan that represented the express needs of an interacting social system – the patient, the health care deliverer, the medical researchers, and the public.” The Commission formulated a Long-Range Plan comprising four components:

1. Diabetes Research Programs – general support
2. Diabetes Research and Training Centers
3. Diabetes Health Care, Education and Control Program Activities
4. The National Diabetes Advisory Board

As part of the “National Diabetes Mellitus Research and Education Act,” Congress authorized Diabetes Research and Training Centers. The guidelines for these DRTCs were written by a committee established by the Commission. The members of this committee included: Philip Felts (Chairman), Bill Daughaday, John Davidson, John Fain, Steve Fajans, Jim Field, Joe Larner, Mort Lipsett, Leona Miller, Jesse Roth, Arthur Rubenstein, Don Steiner, Howard Tager and Bob Williams. Philip Felts and Bill Daughaday wrote most of the report. These Centers were to be located throughout the country, would conduct 1) basic and clinical research in diabetes and related conditions, 2) have training programs for physicians and allied health personnel, and 3) provide professional information programs for primary care physicians and other health professionals (translation).

Crofford delivered the Commission report to the Senate and House on December 10, 1975. The vast majority of the recommendations of the Commission were accepted, and significant funding for DRTCs was approved and provided. The Commission guidelines were adopted almost verbatim by NIDDK. The early Diabetes-Endocrinology Centers were renamed Diabetes-Endocrinology Research Centers (DERCs; P30) to distinguish them from the new Diabetes Research and Training Centers (DRTCs; P60). Vanderbilt subsequently converted to a DRTC, as did Washington University. The others remain as DERCs to this day.

### **Core Resources**

Both types of centers were founded on a strong base of science relevant to diabetes (appropriately, often quite liberally interpreted), and this research base was to be supported by cores. The cores were defined as shared resources that would enhance the ability of the research base achieve the stated goals of each Center. It was properly realized that these cores would, in some cases, be replicated in several Centers, whereas others would likely be unique to the needs of a given Center. No part of the DERCs and DRTCs has evolved more than the core concept. In the 1970s cores often provided services that were not only not available at the home university – they were not available anywhere. The few commercial organizations in existence had yet to get into the “kit” business, which blossomed in the late 1980s and 1990s. Cores provided services and were expected to provide training in specialized techniques (e.g., DNA sequencing) as well. Services were typically done at the entire expense of the Center – the investigator paid nothing. This feature combined with the uniqueness of the services offered, made membership in a center (and thus eligibility for core services) a highly desirable thing. With time, at least in the older Centers, this has changed in remarkable ways, largely owing to the fixed budget. Services considered novel in the 1970s became “routine/boring” and had to be dropped from the official roster of center-supported cores in order to escape the vigilant eyes of reviewers. Institutions often kept these services intact, as small service centers, on a fee-for-service basis. As cores became more complex, and thus more expensive, two things happened. First, the Center would no longer provide the service at no cost to the Center member; the latter had to pay part of the cost. Second, consortia of various centers at an institution began to collaborate to provide complex, costly services (example: transgenic and k/o mice).

### **Pilot and Feasibility Studies (P/F)**

The P/F concept has been a bedrock of the Centers from the beginning. At first \$100-150K was devoted to these from each annual budget. Since 2001 this number has been \$250-300K per year. The awards, originally in the \$20K range each year for up to two years, are now up to \$50K per year for two years. These were designed to: 1) entice young investigators into a career in diabetes research; 2) encourage senior investigators in other fields to engage in diabetes research; and 3) allow established investigators in diabetes research to try a new, novel approach. In practice, it seems most Centers have favored options 1 and 2. The P/F concept has proven to be amazingly successful. Many (? most) Centers report at least a 50% success rate in converting P/F awards into nationally awarded, peer-reviewed grants. Some Centers have exceeded a 70% success rate for their entire history as a Center (in some cases for over 25 years). This Program has also served as a very effective faculty recruiting vehicle for the Centers.

## **Enrichment Programs**

The Center budget includes funds for seminar speakers, visiting professors, retreats and administrative costs. These funds have been invaluable as a means of achieving local and national visibility for the Centers. This program has also served as a recruiting vehicle for the Centers. Most RFAs have asked the applicant to include a request for travel to an annual meeting of Center directors at the NIH. The directors were to provide a statement that they were willing to make this trip.

## **Demonstration-Education (D&E) Component**

The Commission report recognized a serious deficiency in the translation of research advances into improved clinical care of the diabetic, which as described above, is the reason the hearings were held, bill 93-354 was passed by Congress, and the Commission was established. DRTCs were to specifically address this problem through the D&E component, which was mandated to receive at least 30% of the budget, which for DRTCs was set at \$1.25 MM (as compared to ~\$750K for the 4 DERCs). The D&E components were to: 1) perform research into the translation of outcomes from biomedical and behavioral research into clinical care; and 2) develop, test and evaluate innovative methods for accomplishing item #1. Each D&E component had a Model Demonstration Unit (MDU), which served as a sort of core for the translational research. The MDUs were designed to provide the best, transportable care for diabetes. The budget for the D&E component was much like a component of a PPG. It was used to directly perform research. By contrast, the biomedical cores were to support research that had been peer-reviewed for support independently. The D&E component of the DRTCs operated in this manner for almost 25 years.

## **Control and Prevention Component (circa 2001)**

A fundamental change in DRTCs occurred as a result of the 2/01 RFA. The D&E component, each with an MDU, was dropped, as was the direct funding of translational and outcomes research. A core to support existing, funded research in the translation of research in prevention and control of diabetes was now required for all DRTCs. This core, like all the others supported by a Center, could be structured to best suit the needs of the funded investigators in this component of the research base. This core component is expected to use a significant portion of the budget. Also included in the 2/01 RFA was the suggestion that at least one P/F be awarded for translational research. A supplement for subcontracts that foster collaborations, with access to core services, with faculty at historically black colleges and universities could also be requested for the first time. This is in recognition of the serious disparity in the incidence and severity of diabetes in minority population groups. The supplement is intended to examine outcomes and behaviors in these populations, and can be supported by a separate core.

## **Diabetes Center Awards**

There are now 5 DRTCs and 11 DERCs. AECOM, Chicago and Michigan have been DRTCs from the beginning. Washington University and Vanderbilt started as DERCs (actually, as



DECs) and converted to DRTCs in the late 1970s. There have been no new DRTCs since then. The other Centers have existed as DERCs for their entire history.

With the recent cycle of approvals, the Centers have finally reached the geographic distribution envisioned in the “National Diabetes Mellitus Research and Education Act.” This geographic distribution may provide a logical basis for having a rotation of annual Center Directors meetings. A rotation could be set up whereby a region hosted the annual meeting. Thus, every 16 years a given center would serve as the regional host.

### **Budget**

The DRTCs have had a flat-line budget for years—almost since their inception. The DERCs enjoyed a raise in the cap from \$750K to \$1MM with the last cycle of review. This is in the face of a general increase of the NIH total budget, and NIDDK budgets for grants or total funds of about 200% between 1998 and 2003 (the latest figures available as of this writing).

More specifically, the NIH-wide allocations for RO1, P30 and awards have shown slight increases over the 1998 to 2003 period (from +6 to +21%). By contrast, the P60 awards have decreased by 17% (in constant 1998 dollars) over that same period. The challenges faced by the older Centers, over time, as illustrated in a comparison of the Consumer Price Index from 1978 to 2005. Simply stated, a dollar purchase in 1978 requires \$3.05 in 2005. Stated another way, \$1.25 MM buys one third of the goods and services today as compared to 1978 – when the DRTCs got going. The implications of this to the day-to-day functioning of Centers in their local and national environments cannot be over-stated.

### **NIDDK Staff**

A series of Directors of NIDDK, including Don Whedon, Mort Lipsett, Phil Gorden and Alan Spiegel have understood the importance of the Diabetes Centers. The Diabetes Centers program has been substantially enhanced by the very capable leadership provided by a series of Center Program Directors, including: Keitha Krueger, Sandy Garfield, Judy Fradkin, Tom Eggerman and Kristin Abraham.

### **Summary**

This NIDDK-sponsored diabetes centers represent an evolution from a primordial ancestor into the current, vigorous and productive 16-cell organism. This all began through the interaction of an enlightened scholar (Dr. Williams) and Congressman (Sen. Magnuson) 35 years ago. The ADA and JDF, voluntary health organizations, and their constituents, played a major role through their interactions with Congress, which was very receptive and forward-looking. The current epidemic of diabetes was not on the radar screen in 1973, when Congress was first approached. As much as we need additional support for the conquest of this disease now, imagine where we would be had our predecessors not been so visionary.

## **Report From Breakout Group #1—Diabetes Center Mission**

*Jerrold Olefsky, M.D., UCSD*

Dr. Olefsky thanked members of the breakout group. He provided the mission statement the group had developed and said that possible metrics to measure performance would be discussed.

### *Mission Statement*

The prevalence of diabetes mellitus in the United States is reaching epidemic proportions and accounts for a huge national burden of morbidity, mortality, and health care expenditures. The mission of the Diabetes Centers is to serve as a key component of the overall NIH approach to improve the health of Americans with diabetes and related endocrine and metabolic disorders. The Centers support cutting-edge basic and clinical research related to the etiology and complications of diabetes in order to generate knowledge that can be translated into novel prevention and treatment strategies. The Diabetes Centers provide funding for core laboratories to support biomedical and translational research, patient and physician education activities, and pilot and feasibility grants to support new investigators and novel ideas.

To accomplish this mission, the Diabetes Centers should:

- Create an environment that supports important and innovative research;
- Raise awareness and interest in diabetes research and clinical care at their institutions and locally, regionally, and nationally;
- Enhance diabetes education and training opportunities for patients, students, scientists, and clinicians;
- Attract and retain new and young investigators;
- Provide core services that leverage funding and unique expertise;
- Foster interdisciplinary collaborations, especially in the emerging areas of research, to catalyze new ideas and scientific approaches;
- Promote the translation of scientific discoveries from bench to bedside to community.

Group members discussed the meaning of “translation,” because it can be interpreted broadly. The broadest definition of the word was used. Translation begins with discovery and has a long path before it can be applied to the bedside and eventually to the community.

### *Metrics*

From a discovery's beginning to bedside use can be a circuitous course, and measurable outputs or metrics can help the process. Metrics provide a way to assess Centers against the goals that have been developed. The group developed metrics for each goal.

1. The metrics to create an environment that supports important and innovative research include: (a) publications from Centers; (b) research grant support; and (c) the number of investigators involved.

A participant asked how an "investigator" is defined and whether Centers define an investigator as either a critical person doing diabetes research or a person who is, for example, an adjunct, wanting to do research but not currently doing so. The investigator may be involved in research that currently is not diabetes research but may eventually lead to work in the diabetes field. Should this person be considered an investigator and be included in a metric? A participant recommended that criteria of this metric should be how many investigators the Centers have attracted and retained as meaningful diabetes researchers. It also was suggested that to increase visibility of the Centers and the diabetes field, it is better to be inclusive rather than exclusive about who is considered a diabetes investigator. A broader base of investigators could facilitate obtaining more resources.

2. The metrics to raise awareness and interest in diabetes research and clinical care at Center institutions, and locally, regionally, and nationally include: (a) websites; (b) seminars and symposia; (c) regional and national presentations; and (d) collaborations with other DERCs, institutions, and Centers.

One participant suggested videoconferencing seminars as a way to increase communication and minimize travel expenses. A central website was suggested as a way to provide highlights of core facility successes and feasibility grants. Dr. Joseph Avruch (Massachusetts General Hospital, Boston) said that the coordination breakout group would discuss the idea of a central website.

Better public relations were suggested as a way to publicize and promote publications such as "hot papers." These publications are not being transmitted to the media in a regular organized process.

3. The metrics to enhance diabetes education and training opportunities for patients, students, scientists, and clinicians include: (a) training (Ts) and F and K awards; (b) small research grants; and (c) seminars for patient outreach.

Patient outreach seminars and patient education could be developed and coordinated through a central format. These would include programs that encourage patient participation while also raising public awareness of diabetes programs. Developing more DERC-sponsored continuing medical education services also could improve patient education and diabetes training.

4. The metrics to attract and retain new and young investigators include (a) P&Fs, conversion to R grants, and other types of funding; (b) use of cores; and (c) growth in Center membership.

Dr. Olefsky commented that this goal might be the most important one his group discussed. Attracting new researchers is a major mission, not only of the Diabetes Centers but also of the NIH and the NIDDK; Centers can assist in attracting and retaining new investigators. Currently, an entire generation is missing from the field diabetes research. One participant remarked that this was another reason to be inclusive rather than exclusive when defining who the investigators are or which new researchers should benefit from training and education. There is a much greater chance that individuals will retain interest and attachment to a resource, such as a Diabetes Center if they have the benefit of that resource early in their careers. Mentored fellowships could be included as a metric and could assist with tracking how many junior investigators stay in the field of diabetes research.

Besides providing services to young investigators, the cores can be used to assist junior investigators find early employment and facilitate the careers of new researchers. One possible position is that of an associate core director, who would help support career development for junior researchers. Some participants felt, however, that this suggestion—although a valuable idea—would be difficult to use as a metric.

5. The metrics to provide core services that leverage funding and expertise include: (a) users and (b) utilization.

Dr. Olefsky commented that this was one of the easiest goals to measure by tracking how many people use the cores.

6. The metrics to foster interdisciplinary collaborations, especially in emerging areas of research, to catalyze new ideas and scientific approaches include: (a) a research base extended to other investigators in publications and grants; (b) P&Fs targeted to interdisciplinary studies; (c) publications, grants, seminars, presentations, and posters shared between Center programs and within or between institutions; (d) core labs that serve multiple disciplines; and (e) interaction with other disease-specific centers.

Dr. Willa Hsueh (UCLA) asked how the Centers could retain their specialties while also increasing collaboration and developing partnerships. What new developmental activities and techniques should cores facilitate? Dr. Luciano Rossetti (Albert Einstein College of Medicine, Bronx, NY) stated that the Diabetes Centers need more specialties to have greater impact and national visibility; more centers also should be included in the programs. Collaborations with Cancer Centers and other disciplines, for example, would be valuable for studying the impact of metabolism, nutrition, and the like.

7. The metrics to promote the translation of scientific discoveries from bench to bedside to community include: (a) continuum for type 1 (discovery to bedside research) and type 2 (bedside to community/patient-oriented research) translational research (type 2 is measured by DRTC prevention and control [P&C] output; type 1 could be measured as a continuum with examples needed along the continuum) and (b) program level analysis.

Type 2 research, from the bedside to the community, although not easy to do, is easy to understand. From a fundamental discovery to clinical application in a patient, however, is much more difficult to understand, define, and accomplish. Furthermore, the process of pushing a new development from bench to bedside may be an unrealistic goal for an individual Center. A more realistic goal is evidence that the Center is supporting a continuum of research that involves fundamental translational work and actual patient application efforts.

Dr. David Nathan (Massachusetts General Hospital) noted that the metrics all involve “process”; no single metric states that the health of people with diabetes has improved because of work done by the Centers. Should the Diabetes Centers have a metric that demonstrates that they have had an impact on public health? Dr. Fradkin suggested looking retrospectively at developments from the Centers. Recording examples of research and techniques that have progressed across the continuum and the contributions of the Centers to that movement would provide a helpful guide for documenting the Centers’ importance.

Dr. Gordon Weir (Joslin Diabetes Center, Boston) suggested including “cure of diabetes” in the mission statement and as a goal and stated that Cancer Centers, for example, have as their underlying goal a cure for cancer and include cure of cancer in their mission statement. Participants decided to include in the mission statement the words “promote the cure” of diabetes. Several participants suggested deleting the last sentence of the present mission statement. No decision was made on this suggestion. Dr. Abraham explained that a consensus document would be created so that everyone would have the opportunity to make suggestions and comments.

### **Report From Breakout Group #2—Roadblocks to Progress**

*Louis Philipson, M.D., Ph.D., University of Chicago, Chicago*

Dr. Philipson said that this group focused on identifying major roadblocks and devising possible solutions. The breakout group began by envisioning the Diabetes Centers approximately 10 years in the future. The effect of roadblocks on all facets of diabetes research, including cure, was explored. As a specific challenge, the group was not allowed to consider new money. The focus was on training, faculty and young investigator retention, and career development.

Several roadblocks were identified. These included the inability to recruit new and additional people, clinical roadblocks, core facilities that need updating, a shortage of regional or national cores, and lack of communication among Centers.

*Recruiting New and Additional People*—Vertical training could facilitate recruitment with training that begins at the undergraduate level. Because DRTCs do not have training in their mission, however, faculty leverage and cores can be used to start this process. The Vanderbilt program, for example, has used summer student training as a short initiative to introduce students to the program. This could be done regionally with retreats based on a rotation of regional summer activity and could include students at the undergraduate level; students would have the option of working with different Centers. The M.D./Ph.D. training is more difficult because of NIH funding rules, but it may be possible to provide a “reach-through” to support and attract

students, particularly through postfellowship. One idea is to pool T32 and K awards, link them both to the DRTCs and obtain training awards.

The group felt that 2 years of fellowship training is insufficient to generate R-level grants. The Centers should consider contributing to a long-range training program, possibly up to 7 years; the training program would have to show institutional commitment.

Dr. Philipson commented that training lasts for many years, is difficult, and there are no career guarantees at the end of training. This is an area that the Diabetes Program, in particular, and academic medicine, in general, must address to encourage greater numbers of researchers to remain in clinical research.

*Overcoming Clinical Roadblocks*—To overcome clinical roadblocks, new technologies can be coupled with P&Fs for research and development. The Einstein program has a strong connection between basic science and clinical investigation. The goal is to earmark P&F money for a specific purpose and to team a basic scientist with a clinical investigator.

*Core Facilities Need Updating*—Many core facilities suffer from obsolescence. Older facilities may not renew equipment in a timely manner. At the initiation of the last cycle, however, money for new equipment was made available. Shared instrument grants and other partnerships could be leveraged by the Centers and translated into new facilities.

*Shortage of Regional or National Cores*—The group discussed whether the costs of regionalization may outweigh the efficiencies of regional or national cores. Regional transgenomic cores, for example, would not be cost-effective because they must be located near research centers. These cores also often are overbooked, and excessive workloads could destroy existing efficient cores. Dr. Philipson commented that a regional stem cell core that required a great deal of infrastructure, however, might be useful. Developing regional imaging cores also may provide effective integration of Centers and increase translational ability.

*Lack of Communication Among Centers*—Lack of communication among the Centers has created opportunity gaps; there may be many potential advantages to better communication and integration. Stronger unification of Centers could result in more efficient trading of technology, information, and data. Mutual databases could be established to speed information transmission. Dr. Philipson suggested using access grids—used for the bioterrorism networks—to create “virtual reality” rooms, which would allow for virtual meetings, real-time web casting, and delayed web casting. Data, such as PowerPoints and other high-density information and file transfers, can be exchanged in real-time. Such grids are efficient and cost-effective and many institutions have developed these capabilities.

Dr. Alan Permutt (Washington University School of Medicine, St. Louis) commented that genome science cannot be done without many diabetic patients that are well phenotyped. He suggested that collaboration in this area would be very helpful.

A proposal to consolidate and coordinate the T32 activities involving both pre- and postdoctoral investigators has been made to coordinate the diabetes-related training activities within Center

institutions. The K30 grants leading to diabetes research also should be fully integrated into the Diabetes Centers. Investigators would benefit from Center activities such as enrichment, cores, and leadership, and this integration would facilitate monitoring the success of T32 and K awards. This type of integration also would offer the program greater clout and leverage within an institution and would assist in developing a training continuum for investigators. The challenge is to develop or find a mechanism by which coordination within the institution for training and Center grants is possible.

Coordination of T32s would result in tightly coordinated grant activities if the grants were integrated. This would enhance the training programs. Center support grants and T32s would not be the same grant, but could share common enrichment and decision-making activity. If a Diabetes Center is involved in recruiting, training, and mentoring trainees within a diabetes training grant, there will be greater success in retaining new investigators. Because some training grants are very specific regarding who can be appointed as a trainee or trainer, some project investigators (PIs) may find the language in integrated grants too restrictive.

Two other NIDDK programs have not been used as effectively as possible by Centers. One is a T35 grant, a mechanism used specifically for short-term training; it usually provides 3 months of summer training for medical students. Currently, none of the T35s are linked directly to a Diabetes Center.

The other program is a medical student research-training program that the NIDDK instituted 2 years ago that is linked to universities with a T32 and a Center from each of the three NIDDK divisions. This program offers a medical student a full year away from medical school to work with a mentor on a specific project with an existing T32.

Too many applications are needed for grants, and too much bureaucracy is involved in providing training money to investigators; this creates substantial roadblocks. The process should be simplified by granting funds directly to Centers. Also, the system currently has reviewers who often are not familiar with Center problems or processes. The challenge is for funding to go directly to the Centers so that they can evaluate the best individuals who are entering the diabetes research field. This would empower the Centers to move the training spectrum forward.

It has been difficult to attract minority investigators. Participants suggested that there were too few training instruments to attract new researchers, particularly members of underserved populations. Shortly after becoming director of the NIDDK, Dr. Spiegel created the Office of Minority Health Research Coordination. The office developed the Diabetes Education in Tribal School program. This program has partnered with the Indian Health Service, Centers for Disease Control and Prevention (CDC), and others to enlist tribal colleges and universities to develop curricula (K-12) for diabetes-focused health education. The program also attempts to inspire students to pursue science and medicine as a career.

Two other programs that may help with recruiting minority investigators are a minority high school and an undergraduate program. These summer training programs have existed for several years but currently are being redesigned to be more DK-focused. The Diabetes Centers could serve as venues for these programs.

Regarding metrics in health outcomes, Dr. Spiegel commented that the CDC does a good job with viral and bacterial diseases but not with chronic diseases, diabetes in particular. End-stage renal disease (ESRD), however, is an exception. For several years, the NIDDK has partnered with the Centers for Medicare and Medicaid Services and operated the U.S. Renal Data System, a highly detailed measure of both transplant and dialysis data. There has been a plateau and, in some cases, a decrease in ESRD in Caucasians with diabetes suggesting not only the expected health disparities but also that the decrease may be attributable to a type 1 versus type 2 diabetes difference. It appears, however, that lower rates of ESRD in Caucasians with diabetes are attributable to the Diabetes Control and Complication Trial message of tight control and to ACE inhibitors reaching some segments of the public.

The NIDDK also created the National Kidney Disease Educational Program to address health care disparities. The program, which targeted four largely African-American cities, has been successful in presenting straightforward information to patients.

#### **Report From Breakout Group #4—Coordination, Integration, and Collaboration**

*Dr. Joseph Avruch, Massachusetts General Hospital, Boston*

This breakout group developed five areas that would improve coordination, integration, and collaboration among the Centers.

*Annual Meetings*—There are many developments and activities at each Center, but the information is not disseminated well. An annual face-to-face meeting would provide a method for sharing information and staying current with Center developments. Four Centers within a particular region could organize the meeting; one Center from the designated region would host the meeting.

The annual meeting should be devoted primarily to the Centers' activities to inform the goals of the program, although this should not exclude other meetings and other venues. The group suggested that the meetings should focus on science-centered strategic issues and one or two themes based on core activities, e.g., technologies, program areas, transCenter communications, outreach, etc.

Participants discussed whether the annual meeting should be used for educational purposes with new investigators; opinion was mixed and the question unresolved. Could the annual meeting be a part of another ongoing meeting such as an ADA meeting? Many participants felt that the annual meeting was not an optimal place for science, but a science-based regional meeting would be an alternative.

*Central Website and Biannual Newsletter*—The website would be the primary mechanism that integrates and centralizes Center information. The website could describe, for example, core activities and services, availability of those services, reagent and P&F reviewer databases, training opportunities, and job openings at all levels. The website would be accessible to the public. The newsletter would provide information from the annual meeting and could include job and training openings and information on core developments.



*Coordinating Center*—A coordinating center should be recruited from among the existing Diabetes Centers. Because there are differences in the sophistication of information technology among Centers, the initial function of the coordinating center would be to organize and develop the central website using existing IT resources.

One participant suggested having individual Center websites as well as the central website. This would decrease the risk of duplicating research efforts. Although it would be possible to use links in the individual sites, making a centralized website unnecessary, many participants opposed the inconvenience of complicated searches using multiple links as the sole resource; a central website would provide the most accessible public face.

*Cost Saving Consortium*—Currently, individual Diabetes Centers spend money on many of the same goods and services. If the Centers were to act collectively, they could develop leverage for more cost-effective services, which ultimately would benefit the research base.

Some institutions prevent Centers from developing their own purchasing agreements with vendors; the NIH might assist Centers that have institutional conflicts or restrictions. This is an area that could be developed and coordinated by a central coordinating center.

*Reagent Repository*—Centers should devise a process to share reagents. This could be done most effectively through a reagent repository.

### **Report From Breakout Group #5—Promoting Clinical and Translational Research**

*Norman Fleischer, M.D., Albert Einstein College of Medicine, Bronx, NY*

Translational research was defined as the application of science to the pathophysiology and treatment of disease and the maintenance of health. It involves the translation of basic science knowledge to the understanding of clinical disease and advances in patient care and population health. It also includes the study of cellular and animal models of human disease. About 30 percent of research currently underway at the Centers is clinical, suggesting that significant translational research occurs in the Diabetes Centers.

The breakout group suggested that the following actions be taken to promote clinical and translational research:

*Enhance communication among Centers to identify clinical research activities*—Opportunities for complementary programs and technologies are available because of similar populations and projects. A representative in each Center could be appointed who would identify, within the Center, existing clinical research areas that need more visibility. Representatives also could survey the Centers for other clinical translation opportunities.

*Develop a category for P&F studies*—Currently, the primary applicant for a P&F study is a new investigator. A P&F study that supports clinical and basic partnerships would be a useful category for Centers. Also, the level of support from non-Center resources should be increased.

*Enhanced training in clinical research among Centers*—A formal program could be developed to provide training opportunities among Centers, particularly relating to translational research. The group proposed that a mechanism be created for acquiring expertise from other Centers for investigators with a translational goal.

*Increased interaction between general clinical research centers (GCRCs) or future Clinical Translational Science Awards (CTSAs) and cores and enhanced support from the Centers' institutions*—Support within the institutions for regulatory hurdles should be strengthened. Regulatory obstacles change continually and can hamper small trials or experiments. Institutions can assist with regulations and facilitate Center activities.

*Increased interaction between DERCs and DRTCs and existing clinical trials*—This also includes increased potential for ancillary studies. A participant commented that the Cancer Centers cores have a successful clinical trials office that facilitates early trials and wondered how the Diabetes Centers could integrate a similar type of approach to enhance translational research. Several Center institutions have clinical trials units that perform NIH-related trials, which could be expanded. The CTSAs were designed with an integration (not a silo) framework goal to better coordinate clinical and translational research.

The Diabetes Centers can motivate translational research by informing the U.S. Food and Drug Administration, for example, about new and alternate markers for people with well-controlled diabetes. Centers can enhance research by offering investigators the ability to file under the Centers' investigational new drug program as new reagents become available for trials. A central coordinating center could serve as coordinator for these tasks.

Dr. Fradkin noted that the NIDDK has created a repository that includes biosample, genetics, and data components. All large multicenter clinical trials will use the repository to provide information on specific trials.

### **Report From Breakout Group #3—Marketing the Diabetes Centers**

*Dr. Aldo Rossini*

In the field of diabetes, there is overwhelming agreement on two points. First, the program must support and retain new young investigators and second, the diabetes program has not done a good job of marketing itself. The following are ways to better market the diabetes program: (1) Transform the Centers around the new mission; (2) Better address the challenges of the diabetes epidemic; (3) Attract and retain new talent, faculty, and students; (4) Encourage clinical researchers to combat the paucity of investigators; (5) Encourage collaboration among Centers and external organizations; (6) Gain access to new technologies and resources; and (7) Modernize existing diabetes programs.

Currently, a major challenge for the Diabetes Centers is the lack of additional funding from the NIH. One large untapped funding resource is philanthropic giving. A component of philanthropy that the diabetes program has not understood well is that many affluent people are willing to donate money to medical causes such as diabetes research but are unfamiliar with the

process. The Centers also have not worked closely with corporate-sponsored research, another resource that can be explored. Governments at all levels also should be considered for funding purposes.

The program must continue to be involved in faculty and student recruitment and must attract collaborators to leverage research and explore areas outside of the fields the program has historically been involved in. More collaboration also is needed between Centers.

The audience for the diabetes program should be considered when exploring marketing options. The audiences that the program most often works with include the biomedical research community including diabetes research in other disciplines; the Diabetes Centers' research community, philanthropists, industry collaborators and supporters, and prospective faculty and students. A clearly defined audience base would assist young researchers understand how they might fit into the diabetes research program.

The program also should improve outreach to patients and their families by offering educational information and opportunities. Historically, the Centers have operated largely in a void, with limited patient contact.

The group discussed two specific communication strategies. One strategy would create a unified identity with a central core while maintaining independence within each institution. A second strategy is to promote the diabetes program mission whenever possible, with a focus on energizing people internally and externally.

#### *Unified Identity*

A unified identity includes the central website and other relevant websites and brochures, the Diabetes Centers' individual websites, profiles, research highlights and discoveries, publications, information on donors, and information and resources for industry. A Diabetes Centers' communication should promote Centers' expertise and accomplishments and encourage collaboration. Individual Centers could use the central website to announce specific missions and goals, news and events, publication information, and available research centers. The site would interface with all Centers; details of major highlights and research at each Center would be included as well as investigative profiles.

#### *Promoting the Mission*

The Diabetes Centers' mission and message must be reinforced in the public arena. The group suggested that the Centers host a national diabetes research event that could be coordinated regionally and locally or jointly with the ADA. Research addenda meetings also could be organized to define key future research areas so that the Centers could influence research programs and industry needs. The Diabetes Centers' message should be published on websites, in brochures, and via media outlets. The new mission must be effectively communicated, and stakeholders must be enrolled for the diabetes program to advance and become more effective.

Channels should be established to accept philanthropic contributions and corporate support. Special events could be created for donors, prospects, and patients to meet leading diabetes researchers. This would partner patients and donors with the Centers with the common goal of

increasing funding. An industry liaison also could be established to encourage corporate support of basic research and to facilitate industry interaction with the Centers. Centers also could consider hosting a series of roundtable meetings with PIs and industry leaders.

(At this point in the meeting, a short video of a public service announcement featuring Patti LaBelle was shown.)

Concerning funding, Dr. Spiegel commented that \$150 million is available annually as special type 1 diabetes funding. A strategic plan including long-range activities has been developed through 2008 using this funding.

The national vision of the coordinated Diabetes Centers is similar to the umbrella organizations for sports, such as the National Football League and the National Basketball Association. A central diabetes entity is envisioned with its own identity while the individual Centers operate with an integrated but distinct identity. Participants were urged to consider if other diabetes research institutions besides the 16 funded NIDDK Diabetes Centers should be included in the central entity.

The NIH has constraints regarding industry, cobranding with industry, and philanthropy; federal agencies cannot augment Federal dollars. The Centers must consider carefully how a coordinated, unified identity will be structured; a non-NIH facet may be an advantage to the program. The NIH currently is developing innovative and legitimate ways to engage industry. Dr. Spiegel said that any process must benefit public health.

## **Friday, November 17, 2006**

### **Lessons from the NCI Cancer Centers Program**

*Devi Vembu, Ph.D., National Cancer Institute (NCI), NIH*

Four program directors manage the existing Centers. There are many supplements to the Cancer Center support grant as well as several planning grants. The following seven areas were discussed:

- Purpose of the Cancer Centers Program and the Cancer Center Support Grant
- Types of Centers
- Eligibility Requirements
- The Six Essential Characteristics of the Centers
- Cancer Center Support Grant Components
- Comprehensiveness
- Review Process

### *Purpose of the Cancer Centers Program and the Cancer Center Support Grant (CCSG)*

The purpose of the NCI Cancer Centers is to foster excellence in research across a broad spectrum of scientific and medical concerns relevant to cancer and to extend the benefits of research to patients, their families, and the general public through clinical care, outreach, and

education. A model Center is a local, regional, and national resource that directly serves the immediate community.

The CCSG, also known as P30, funds Center infrastructure and development to (1) provide organizational focus and structure; (2) stimulate, organize, and coordinate the competitive cancer research base into interdisciplinary scientific research programs; and (3) provide access to quality and cost-effective technologies, services, and scientific consultation to facilitate interaction and enhance scientific productivity.

### *Types of Centers*

There are two categories of NCI-Designated Cancer Centers: a comprehensive Center and a noncomprehensive Center. There are 39 comprehensive Centers that include research in basic, clinical, and population sciences and a nonresearch component that includes outreach, education, and information. The other 21 Centers focus on basic, clinical, or population sciences or any two of the three components. A translational/clinical component is essential for each Center.

### *Eligibility Requirements*

For an organization or institution to be eligible for a Cancer Center support grant, a minimum of \$4 million in annual direct costs of peer-reviewed, cancer-relevant funding in the institutions is required.

### *The Six Essential Characteristics of the Centers*

The structure of the Cancer Centers concerning the six essential organizational and administrative characteristics include the following:

- Cancer focus concerns demonstration of a clearly defined scientific focus based on the grants, which should be relevant to cancer, program structure and objectives, and should promote interdisciplinary research at the Center. The area of research is flexible.

Reviewers normally look at NCI funding, which reflects the cancer focus. Peer-reviewers analyze many other cancer-relevant grants; decisions are based on the subject matter of the grants.

- Institutional commitment includes recognition of the Cancer Center as a formal organizational component. It should be equivalent in status to other areas of similar importance. Resources and space must be provided, and a plan should be in place for continuing support to the Cancer Center if a change in directorship occurs.

The NCI designation attracts patients, industry support, and philanthropy, and the CCSG contributes considerably to an institution's research infrastructure. Because the NCI invests heavily in Cancer Centers, the Institute expects similar commitment from the Center institution.

- ✧ Organizational capabilities include the maximum advantage of available institutional capabilities in cancer research, promotion of collaboration and interaction at the Center, processes in place for planning and evaluation, and fully developed processes for determining and maintaining Center membership.

The external advisory board consists of individuals with a variety of scientific expertise, including basic, clinical, epidemiology, cancer prevention and control, as well as biostatisticians and administrators. The board meets annually, and an internal advisory committee must be in place to advise on scientific research decisions. Each Center has its own criteria for membership, although members usually have peer-reviewed cancer grants.

- Adequate and appropriate facilities have been developed and are available.

Cancer Center facilities should be dedicated to research, shared resources, and to administrative activities. Center members need not be located in Center-controlled facilities, although there should be equal access to shared resources.

- Center directors should be highly qualified scientists and administrators with the appropriate authority to control membership appointments, space, and equipment. A Center director also must have full or shared authority over faculty appointments and access to in- and outpatient facilities.

Center directors should have demonstrated leadership skills and may have joint control with the department chair. A director has authority over the appointment and performance of individuals who are instrumental in linking oncology care to clinical research.

- Interdisciplinary coordination and collaboration are required of all Cancer Centers.

Interactions and collaborations among members should enhance the productivity and quality of research at the Centers and maximize the institution's potential to conduct transdisciplinary and translational science.

### *CCSG Components*

The main CCSG components are the scientific programs and the shared resources. The purpose of a Cancer Center is to exploit all of the institute's cancer research and dissemination capabilities. A Center with many laboratory, clinical, and population research programs must integrate these into a single interdisciplinary cancer research enterprise across departmental, school, and institutional boundaries. Colleges, such as nursing, pharmacy, dentistry, or public health that are involved in cancer research, are included in Cancer Centers.

The NCI support to Cancer Centers is intended to foster collaborative research; membership is based on scientific excellence and a commitment to work together. The minimum requirement for a cancer program is three peer-reviewed projects from three independent investigators.

The shared resources provide access to technologies, services, and scientific consultations that enhance scientific interaction and productivity. The support of shared resources provides stability, reliability, cost-effectiveness, quality control, and access to specialized technologies. Centers have flexibility in the types of shared resources they want to propose.

Central resources include biostatistics, informatics, clinical protocol, and data management. The biostatistic and informatic resources are central to the mission of most Centers, particularly those that perform clinical or population sciences. Cancer Center support is available for pilot projects, assisting investigators in developing research projects, analysis for publications, and development of methodology. Funding is not intended, however, to support independent investigative research.

Clinical protocol and data management resources provide central management and oversight functions for coordinating, facilitating, and reporting the institution's clinical trials. This resource also provides a central location for cancer protocols, a centralized database for protocol-specific data, and an updated list of currently active protocols.

The protocol review and monitoring system ensures that clinical resources are used wisely and that all cancer trials are reviewed. The system focuses on protecting human subjects and does not perform auditing functions. Scientific merit, priorities, and clinical protocols progress are analyzed. All clinical trials at the institution are evaluated under the protocol review system, which does not consider protocols for population sciences that include healthy human subjects.

Protocol-specific research support funding is dedicated to innovative proof-of-principle trials involving early phase testing of agents or devices. This funding also supports a core group of research nurses and data managers.

The developmental funds provide Cancer Centers with budgetary flexibility for research; they have no dollar amount or percent cap. This funding strengthens weak scientific areas and facilitates the exploration of innovative ideas. There are five categories of use, which include recruitment of faculty, interim salary research support, support of pilot projects, support of technology development projects, and development of other resources. These funds are monitored centrally by the Cancer Center director.

### *Comprehensiveness*

The NCI determines, in two phases, whether a Cancer Center is comprehensive or not. Peer reviewers are responsible for the first phase. They determine the breadth and depth of research activities in basic, clinical, and population sciences and also determine whether the research areas are interactive. The second phase involves nonresearch activities, such as service to the community, and includes education, outreach, and information. Comprehensiveness is based on research and nonresearch activities.

### *Review Process*

The predominant review criteria include the quality of science and the added value of the CCSG. The review focuses on science process and recognizes excellence in a variety of forms; the review process evaluates functions relative to research and rewards risk-taking.

### *Funding*

First time (T1) Cancer Center awards are capped at \$1 million for 3–5 years. Subsequent awards vary from \$2 million to \$10 million annually, for up to 5 years. Although these are not entitlement awards, they are difficult to lose. Five Cancer Centers, however, have been discontinued since 1995. Dr. Vembu also noted that only four or five Centers have received the \$10 million grants.

A Center is evaluated on institutional commitment, review criteria, expansion of the Center, and how well the Center operates; Centers with a strong institutional commitment have an advantage. Most Centers, however, are re-funded after the first year, although this may change in the future because of decreased NIH funding. Currently, the NCI receives approximately \$4.8 billion in funding, of which the Cancer Centers receive approximately \$240 million.

Metrics used to determine the success of a Center and its programs include accrual of patients, outreach to the community, and how well the Center is integrating with other programs. Cancer Centers Program operates as a very intrusive entity ensuring that institutions strongly engage in the outcomes and activities of the Centers.

For marketing purposes, a central website has been established, but much of the marketing is determined and carried out by individual Centers. The website, which was created externally, is managed by one individual and augmented by the program. It includes basic information on all Centers.

A participant asked if there was a formula for determining how much money is spent annually on administrative costs. Dr. Vembu replied that there is no specific formula, but reviewers try to contain administrative costs. She said that a Center with \$6 million in funding spends approximately \$400,000 on administrative costs.

### **Presentation and Discussion of the National Center for Research Resources (NCRR) Clinical Translational Science Awards Initiative**

*Robert Star, M.D., NIDDK*

The aim of the CTSA program is to create academic homes for clinical and translational science and to create a community of researchers who can influence the emerging discipline of clinical and translation science. The CTSA initiative seeks to facilitate interactions among researchers by lowering barriers between disciplines and encouraging creative approaches for solving complex medical problems. The CTSA is intended to provide an integrated, synergistic, innovative, and adaptable environment that builds on institutional strengths but remains flexible. Institutions are required to integrate on four levels: within the program itself, within the surrounding Centers, vertically into the nearby community, and horizontally across sites to create a national community.

The program seeks to:

- Captivate, advance, and nurture a new generation of clinical and translational researchers;
- Create an incubator for new research tools and methods; and



- Synergize multidisciplinary and interdisciplinary approaches to clinical and translational research.

The CTSA program allows institutions to start from ground zero and design their clinical and translational science program from scratch. A CTSA educational core, for example, could involve a curriculum or degree-granting mechanism that would provide training and education for new researchers and help them with career transitions. The program could include undergraduates and predoctoral students; mentors also could be trained in this new system. An education core would be infused within the entire CTSA program to provide training in, for example, regulatory affairs, conducting a clinical research project, biostatistics, or working with the community.

The NIH expects institutions to create a synergistic, integrated program that speeds translation from bench to bedside while training new investigators. Research teams must be fostered and new methodologies created to energize new and existing programs. CTSA components might include advanced education and training, biomedical informatics, and cores in the areas of design and development incubators, biostatistics, patient and community interactions, and P&F studies.

The CTSA initiative hopes to create a centralized department where basic scientists can present research ideas and plans. Several participants commented that although the overall goal of integration is an excellent idea, vertical integration should be more contained.

A participant asked how the GCRCs, which should be the heart of patient-oriented research (POR), would be integrated in the CTSA program. Dr. Star replied that the GCRCs would become the core upon which the CTSA program is based.

Funding for the CTSA program is awarded from NCRP and the NIH Roadmap Initiative using funds that have been precommitted. To construct a budget, each institution begins with a base of existing components that includes NCRP GCRCs, NCRP K12, NIH K30, and Roadmap K-12 and T32 programs, and can request up to an additional \$6 million dollars per year. Most of the CTSA money will be placed in a U54 budget. The predoctoral training slots will be funded by a T32 budget, and the postdoctoral slots via the K-12 budget.

The CTSA's are based on the belief that education is critical; many types and levels of people need to be educated. Involving the CTSA program with the Medical Scientist Training Program (MSTP) or running the programs in parallel is possible. Universities with more than one GCRC must create a highly integrated program.

Regarding metrics, Dr. Star said that institutions will develop their own metrics to track the programs. The CTSA program will be evaluated at the local and national levels.

### **Integrating Diabetes Centers Into the CTSA: A UCSD Model**

*Dr. Jerrold Olefsky*

A goal of the CTSA program is to transform programs and break down silos. The UCSD has started this process by combining a DERC with UCLA, which provides a model for Southern California collaboration. The program uses a broad definition of translational research, which is the operating principle the institution uses regarding CTSA. Training programs, such as the K30s and GCRCs, comprise the base of the research program and eventually may include integration of disease centers.

For approximately 4 years, UCSD has had an umbrella program known as the College of Integrated Life Sciences (COILS), which consists of the Clinical Investigation Institute, Institute for Molecular Medicine, Academy of Clinician Scholars, and a medical scholars program. Currently, UCSD is considering how best to align COILS with the CTSA program.

The Diabetes Centers must determine the most productive way to align a CTSA with already existing DERCs or DRTCs. Dr. Olefsky suggested three possibilities. One possibility would begin with several cores and integrate them with the CTSA. A separate core, one that is “upstream” of the CTSA clinical infrastructure, such as bioinformatics or animal models, integrates with the CTSA and assists in guiding design or implementing other activities. Another core, such as an assay core, which is “downstream” of the CTSA, also could be integrated into the CTSA. In this model, cores on different ends of the research continuum straddle the CTSA.

A second model for aligning CTSA with DERCs and DRTCs involves a CTSA with three separate cores, A, B, and C. If cores A and B are close conceptually, they could be integrated effectively. This integration could involve funding, which would enable the cores to expand and improve; this would be a cost-savings advantage. Geographical integration also is possible. Integrating two cores would create expanded services for a greater number of people. In this model, the diabetes-specific cores are outside of and not integrated into the CTSA.

The third model is the fully integrated model, in which not only cores but also DERCs are integrated and merged with a CTSA. In this model, the research programs are arrayed around the CTSA. This model would break down silos and be completely transforming.

Dr. Star presented an additional model for Centers to consider. This model includes a core that is completely integrated into the CTSA and could involve training a new investigator. Instead of training within a T32 attached to one of the DERCs, a Center could use a slot inside the CTSA, perhaps paying for that slot, but all training would be done within the confines of the CTSA, with oversight from the DERC.

Obstacles to integrating DERCs and DRTCs with CTSA include how best to merge money from two different sources and who determines what programs the money will support. Another challenge is determining how specific funding requirements are for DERCs. Dr. Olefsky commented, however, that he is optimistic that this type of integration is possible for the Diabetes Centers and that the Centers will benefit from it.

The design of the next RFA is critical to the success of CTSA integration with DERCs. For Centers that currently have DERCs, this integration will be an excellent way to convert DERCs into DRTCs.

Several participants said that a great deal of effort had gone into the Centers to create highly effective diabetes research organizations that have their own integration within the Center. If the goal is to break down all silos, it is possible that the diabetes research component and its mission could get lost. Dr. Olefsky acknowledged those concerns but emphasized that the NIH has created a matrix infrastructure. If the Diabetes Centers are going to participate within this infrastructure, the challenge will be to maintain a strong, separate diabetes identity while integrating with CTSAAs.

### **Ongoing and Upcoming NIH Roadmap Activities**

*Arthur Castle, Ph.D., NIDDK*

The NIH Roadmap Initiative was developed in 2002 after stakeholders identified major gaps and opportunities in biomedical research. The stakeholders discussed roadblocks and challenges to progress, how to overcome the roadblocks, and what initiatives could help improve biomedical research.

The three main areas of the Roadmap Initiative include the following:

- New pathways to discovery—the basic research, which focuses on developing new tools for researchers;
- Research teams of the future—to help improve training, especially in interdisciplinary areas;
- Re-engineering the clinic enterprise—whose main area includes the CTSAAs.

*New pathways to discovery.* This area of the Roadmap attempts to quantitatively understand the networks of molecules, cells, tissues, and proteins and how they interact in the pathway. The networks are analyzed in a temporal-spatial manner and tools, such as imaging probes and nanotechnology devices, are being developed to work at the cellular level. Computational infrastructure also is being developed to support biomedical informatics and bioinformatics across all extramural communities. The main areas in this component of the Roadmap are molecular libraries and imaging, developing improvements for all aspects of work with small molecules, and an informatics component that integrates these areas. There are seven national centers for biomedical computing, two of which include diabetes research components. These computational centers help develop the bioinformatics infrastructure and components necessary to integrate large volumes of research data.

Building blocks and biological pathways and networks for new pathways have two main components. One is the National Technology Centers for Networks and Pathways, which is a proteomic component that focuses on developing proteomic tools, not only to measure quantities of proteins but also the temporal-spatial interactions of proteins. The other component, metabolomics technology development, is a similar effort but involves R21 and R33 phase transition awards rather than centers because research focuses primarily on developing rather than integrating the basic technology needed. The NIH also has an interagency agreement with

the National Institute of Standards and Technology to help develop reference material for metabolomics technology development.

Thousands of points of data currently are generated for both proteomics and metabolomics studies, and developing the informatics of interconnecting and transferring data via the computer are necessary. Workshops were held to better enable this exchange of information.

*Research teams of the future.* This area of the Roadmap supports training programs and different ways of encouraging investigators who are moving out of traditional disciplines or who are crossing disciplines. The Director's Pioneer Award, a high-risk research initiative at the NIH, is one model that supports a specific researcher instead of a research project. Interdisciplinary research is at all levels of training, from very short courses to large training grants. Different mechanisms are applied to interdisciplinary rather than multidisciplinary training with many levels of funding involved; there is special emphasis on behavioral and social sciences. Currently, the NIH also is pursuing public and private partnerships to explore how industry can become more involved. This initiative includes a public and private liaison.

*Re-engineering the clinical enterprise.* Two areas are involved in this component of the Roadmap; one is to develop the new partnerships and the other is to promote better clinical research. These areas include CTSA's, patient-reported outcomes for chronic diseases, the cooperative agreement, and the NIH effort to provide access to basic needs for translational research.

Roadmap projects attempt to develop the tools and training necessary to create and accomplish many of the programs mentioned in the CTSA discussion. The goal is to progress from basic science to clinical outcomes. The Roadmap Initiatives provide flexibility for the NIH to adapt to the community more rapidly and provide funding for many of the efforts discussed at the current Diabetes Centers meeting.

Although there is an ongoing evaluation program, the programs are too new (the first year of funding was in 2004) to have significant feedback on the impact of specific activities. The intent of the Initiative is not to create ongoing projects, but rather to have the flexibility to phase out unsuccessful projects and try innovative strategies. Dr. Castle said that some of the activities currently underway are pilot and planning projects.

### **Summary of Discussion and Recommendations From the "Diabetes/Obesity Translational Research Program Workshop" November 14–15, 2005**

*William H. Herman, M.D., M.P.H., University of Michigan, Ann Arbor, MI*

Dr. Herman acknowledged Dr. Joe Selby (Kaiser Permanente), who summarized the 2-day meeting and from whose summary Dr. Herman borrowed. The meeting involved funded translational researchers, with either R34 or R18 grants, as well as representatives from the DRTCs.

The meeting had several purposes, which included:

- Fostering a sense of community among translational researchers
- Discussing translational research study design and analysis
- Reviewing selected ongoing R34 and R18 projects
- Describing DRTC P&C activities
- Discussing new ideas
- Providing guidance on future directions for the NIDDK translational efforts

*Fostering a sense of community among translational researchers.* The meeting fostered a good sense of community and interchange. It was the first meeting organized by the group, and there was a consensus that such a meeting was overdue and should be continued.

*Translational research study design and analysis.* This component of the meeting reviewed traditional randomized controlled clinical trials (RCTs) and their use in translational research. Translational research presents unique logistical and ethical problems. One of the challenges is that community partners in translational research often refuse to adopt RCT designs. Many of these partners feel it is unethical to withhold treatment to individuals who need it; they want to move forward quickly with interventions and are not patient enough to wait for RCT results. Group RCTs involve randomizing practices or communities to intervention and addressing some of the problems of individual randomization in RCTs. There is a great deal of focus on nonrandomized, quasi-experimental designs for translational research, which many agree are a viable option. Newer methods to evaluate and control for selection bias in observational studies also were discussed.

*Reviewing selected ongoing R34 and R18 projects.* Pilot data is crucial to the design of R34 and R18 research studies but often is hard to obtain. Preliminary qualitative research also often is necessary. Most of the projects presented were theory-driven, multifactorial interventions that targeted patients, families, providers, and health systems. The projects involved diverse populations because there is a clear recognition of health disparities in diabetes and diabetes care. A number of challenges were recognized, including: (1) recruitment, often related to the perceived ethics associated with RCTs; (2) system instability when community partners dissolve, lose funding, change or have major personnel changes; (3) partnership issues concerning the shared resources between academic centers and community organizations and the fact that funding often comes via the academic institutions, and it often is difficult getting the money into the community; and (4) sustainability of projects that have been successful. Incorporating these successes into ongoing clinical and community care is difficult.

*Describing DRTC P&C activities.* Many of the R34s and R18s have grown out of the DRTCs. The DRTCs serve large communities of researchers and have valuable expertise for translation and dissemination. The DRTCs enhance translation at both ends of the spectrum (bench to clinical research and clinical research to community practice). The expertise offered by DRTCs differs among the Centers; how support has been provided to the Centers also differs.

*New ideas.* Measurement instruments and intervention tools within the public domain must be shared and adapted to commercialize products for translational research. Many initiatives involve duplication, and there are measures, tools, and protocols available, but better information sharing is needed.

*Future directions for NIDDK translational efforts.* Participants at the meeting want more true pilot work before the R34 mechanism is in place. Many participants expressed frustration over the slow funding cycle and want rapid funding cycles similar to the Agency for Healthcare Research and Quality's ACTION Task Orders. Dr. Herman said that there was considerable focus on sustainability and dissemination.

There was considerable discussion of the review of the R34s and R18s. Review panels tend to be conservative and traditional, which creates problems for dissemination and sustainable programs. Open-mindedness to quasi-experimental design is limited. The NIDDK, however, has worked hard to train reviewers. The solution may be for current translational researchers and DRTC members to become reviewers and facilitate the transition away from low-risk, conservative designs to more cutting-edge, innovative research designs.

The second day of the meeting focused on examining challenges and barriers, specific strategies, and potential future directions for translational research, while recognizing that translational research involves the coordination of academic organizations, community partners, and funding agencies. An appropriate venue is needed to get these three organizational levels to communicate and work together.

*Challenges and barriers to academic organizations, community partners, and funding agencies working together.* There is insufficient attention to sustainable models for translation and dissemination. The models that were developed and tested did not fit into the existing health care delivery or community infrastructure. Test models should be developed and, if successful, could be slotted into existing systems.

Competing missions and tensions exist between academic institutions and community partners. Long lag times exist between problem identification at the academic level and implementation and evaluation at the community level. Lack of shared resources across studies and limited funding for P&F studies also are roadblocks to translational research. Participants agreed that strategies for both areas must be developed.

*Specific strategies.* Several strategies were suggested to address these issues and challenges. One strategy is to develop a resource center to support translational researchers. Another suggestion was to focus on more support for theoretical and empirical research on dissemination. Improving the speed of grant review and funding also was suggested. The last strategy, recognizing future limited NIH resources, was to expand the pool of research funding and explore cofunding with foundations, insurers, and other organizations.

*Future directions for translational research and suggestions to the NIDDK.* Dr. Herman commented that some of the suggestions to the NIDDK were subsumed in the CTSA initiative. Suggestions included:

- Fund academic and community translation centers for practice-based research networks;

- Create more community and academic partnerships through community-based participatory research grants;
- Develop career awards in translational research;
- Support research focused on training for community-based health care professionals;
- Support small pilot funding, which would be rapidly funded;
- Support research on patient, provider, and system barriers.

There was consensus that the NIDDK's translational research initiative has produced a diverse set of projects with fidelity to the RFPs. Participants also agreed that translational research remains a new discipline, but appreciation is growing for its methods and challenges. Although many key questions are being addressed in multiple projects, synthesis of findings across studies is needed. There also is a strong need and desire for resource sharing.

Dr. Herman was asked how this information could integrate with the DERCs. He replied that some DERCs are conducting translational research, and the R34 and R18 mechanism is available to investigators at those sites. Horizontal collaboration between DRTCs and DERCs also is possible to get specific projects started.

Dr. Fradkin said she was impressed with how many participants at the translational meeting had moved into the diabetes research area as a result of available R18s. The DRTCs could play a role in encouraging translational research talent from other institutions to enter diabetes research. The CTSA, in particular, focus on infrastructure more than many GCRCs. These infrastructures are designed to help researchers use parts of the CTSA at much lower costs than if they had to develop the infrastructure themselves.

A participant asked what percent of P&Fs involve community-based outcome research versus cell-based research. Dr. Herman replied that up to 40 percent of the P&F grant funding is awarded to translational research studies among the DRTCs.

### **Finalized Reports and Discussion Summaries From Each Working Group**

*Drs. Rossini, Granner, and Accili*

Dr. Rossini said that he thought the 2005 Diabetes Centers meeting had been extremely productive and complimented and thanked Dr. Abraham for organizing and coordinating the event. The following main points developed from the meeting:

- A medical and scientific evolution is underway, which includes the current funding crisis at the NIH. Those research areas that are well prepared will survive and thrive at all levels.
- A continuous goal, and the central mission of the diabetes program, must be prevention and cure of the disease.

- The Diabetes Centers should be united in their support of the diabetes research program and in their efforts to propel the Centers to the “next level.” Time should be taken to contemplate the ideas that were presented at the meeting.
- Participants agreed that better marketing of the Centers is needed. The central website is an important tool for this. Dr. Abraham announced that the Joslin Diabetes Center has offered to assist the Diabetes Centers in developing the website.
- Better communication in all areas between Centers is crucial to integrate and energize the program.
- A plan must be developed to attract and train the best young innovative investigators. The diabetes research program is losing too many young investigators.

Dr. Granner agreed with Dr. Rossini that several common themes had developed from the meeting, including the ones Dr. Rossini identified. He volunteered the Midwest region to coordinate and host the next Diabetes Centers meeting. Dr. Granner concurred that the next several years would be challenging. He reminded participants that the Center concept had been developed and used for many years and that the Centers had had many successes. Diabetes and obesity represent an enormous opponent; it will take the best of what the Centers can do to make headway. This meeting and the Centers mission promote progress.

Dr. Accili commented that he leaves the meeting with great respect for the program people who are caught between the organizations asking for increased funding and Congress, which is trying to decrease current funding. Prospects for the next few years will create challenges.

Dr. Accili reminded participants that the Diabetes Centers do make a difference. At Columbia University, the visibility of diabetes research within the institution has increased considerably. Young people are attracted to the diabetes research being done at the Center. The Center at Columbia is in an underserved area with a large population of minorities who have a considerable incidence of diabetes and poor clinical care. The Diabetes Center has made a difference in the way diabetes care is delivered in the neighborhood.

Dr. Accili agreed that the two points most strongly articulated at the meeting were the need for better training and education of new investigators and better communication in all areas of the diabetes program. He suggested that the training should be appealing and high profile. Instead of a single position attached to each Center for training purposes, several national, high visibility DERC professorships, similar to MacArthur Fellowships or American Cancer Society professorships, could be offered. These types of positions could generate considerable attention to the diabetes research base and trainee program.

Better communication among all members of the Centers is the first step toward successful collaboration. Collaboration must be the goal as resources are no longer available for the Diabetes Centers to individually sustain large and expensive cores and pilot grants. The central website can be the first step toward establishing a coordinating center. Diabetes research and



care can be carried out more effectively and efficiently if the Centers bargain as a whole instead of individually.

Dr. Accili recommended that participants be very involved with how their institutions establish the CTSA's. All DERC and DRTC directors should work closely with the institutions to keep abreast of CTSA applications. The success of the Centers will depend on how well the CTSA's are structured for diabetes research. It is up to the Centers and diabetes research participants to take advantage of these new funding opportunities in an effective, aggressive way.

Dr. Abraham said she welcomed suggestions, input, and ideas as the Centers move forward and begin structuring the next RFAs. The next RFA will be released in February 2006, with a receipt date of midsummer 2006. Another RFA will be released in the late spring of 2006, with a receipt date of late December 2006. Dr. Abraham encouraged participants to send her their thoughts and comments concerning these RFAs as soon as possible.

The meeting was adjourned at 11:00 a.m.