WISCONSIN
CITIZEN ACTION

February 15`, 2005

Members of the Wisconsin United for Health Foundation
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Introduction

ABC for Health and Wisconsin Citizen Action have previously articulated strong apprehensions regarding the application and oversight of Blue Cross/Blue Shield conversion funds distributed to the University of Wisconsin Medical School and the Medical College of Wisconsin. Review of the allocations made by MCW for use of the 65% of funds designated for research and health care provider education demonstrates just cause for concern. Having conducted a limited investigation of two of the projects funded by MCW in fiscal year 2004, we arrive at the following conclusions:

1. That many of the projects and acquisitions funded with conversion proceeds appear to be items which could, in the absence of BCBS funds, be funded through the normal operational budget of MCW;
2. That objective and impartial oversight of the proposal review and funds allocation process has not been effectively applied; and,
3. That Supplant Determination Criteria required by the Order of the Commissioner of Insurance have not been conscientiously observed by the bodies entrusted with accountability for management of conversion funds.

We propose that an appropriate test of supplanting is whether a given project or piece of equipment is one which, in the absence of conversion funds, President Bolger and MCW would have otherwise funded from the institution's operating budget. Where an acquisition is of a species that one would normally expect to be an element of an advancing medical college it is an inappropriate diversion from the purpose of these public health funds.

Our investigation, though relatively superficial, also raises issues concerning flowback to MCW of conversion funds dedicated to equipment acquisitions. Certain approved proposals request funding for the purchase of instrumentation which is to be operated on a fee-for-use basis. We maintain that any proceeds resulting from equipment purchased by way of conversion funds, excepting nominal maintenance and operational costs, should be distinguished from the normal operational budget of MCW and returned to the fund balance.

Further, we are concerned that the Board of Directors of WUHF in failing to rigorously apply their power of oversight over decisions of allocation of conversion funds have also failed in their fiduciary duty as administrators of the public trust, wherein all the individual citizens of Wisconsin stand as beneficiaries.

Discussion of Analysis

ABC for Health and Wisconsin Citizen Action are concerned about the allocation of vital public health resources generated by the Blue Cross Blue Shield conversion proceeds to the Medical College of Wisconsin (MCW).

We have previously expressed our strong concerns that the public's resources in the form of conversion proceeds could become so commingled with pre-existing program budgets as to be diverted from their vital role of promotion of public health and public health initiatives. Moreover we maintain that your public meeting of February 3rd, 2005, OAC member Terry Brandenberg articulated the wrong supplanting analysis as he described the process of grant review and oversight. The essence of Mr. Brandenberg's statement indicated that MCW considered supplanting to mean only the replacement of funds already in place for a given project.

MCW asserts that coordination of conversion funds into its annual budget process "will assure a comprehensive evaluation of the initiatives proposed for funding, a determination of whether it is supplanting existing funding, and whether other resources exist to support the initiative."[1] However, as conversion funds are rolled into the operating budget of an institution posting an annual net profit of 34 million dollars, the likelihood of comprehensive review of allocations diminishes substantially. Those funds designated for the purpose of promoting public health initiatives risk becoming indistinguishable from those funds associated with the normal operational expenditures of the Medical College.

Former Commissioner of Insurance O'Connell recognized the potential for conflict between the institutional goals of the medical schools and the stated commitment of conversion funds for promotion of public health. "The BCBSUW plan represents, and creates the expectation, that the conversion funds will be applied for this purpose (promotion of public health initiatives). However the missions of the medical schools, while they may include or relate to the conversion funds purpose, do not coincide with it."[2] While Commissioner O'Connell envisioned the medical schools as efficient

administrators of the funds, she also intended to establish a system of transparency, accountability, and public oversight of their expenditure.[3] However, under the administrative structure devised by MCW for management of the funds designated for education and research initiatives, their use is governed by the input and decisions of the MCW Consortium, subordinate to the Research and Education Advisory Committee (comprised of the senior academic officers of the Medical College), subordinate to the MCW Budget Committee. Given the affiliations of those charged with review of the use of conversion funds, it is easy to envision how the goal of the promotion of public health initiatives might be co-opted into the goals of MCW as an institution.

Further, while MCW has established a framework of criteria for evaluation of supplanting of resources, we have yet to see an example of the practical application of these criteria. Indeed, in the summary of funded projects made available for public inspection, there exists a noteworthy omission of supplanting analyses.

A limited analysis of proposals funded under the heading of Health Improvement through Research and Education serves only to deepen our prior concerns, yet ABC for Health and Wisconsin Citizen Action lack the dedicated resources to conduct a thorough investigation into the application of non-supplanting criteria to projects funded by conversion funds designated for education and research. However, a review of just two of the proposals funded in the first year of disbursements reveals Commissioner O'Connell's concerns to have been well-founded regarding the divergence of interests of the medical schools and the public who may benefit from the application of conversion funds. Our brief review illuminates numerous apparent conflicts with Supplant Determination Criteria established, in general terms, by the Order of the Commissioner of Insurance, and in more specific terms by MCW's own Five Year Plan. While by no means comprehensive, our examination may serve as an indicator of the standard of review that *should be applied* in determining appropriate use of conversion funds, and suggest that the current review process has fallen well short of these standards.

ABC for Health and Wisconsin Citizen Action ask the Wisconsin United for Health Foundation and the Office of the Commissioner of Insurance to investigate our specific concerns:

1. That Supplant Determination Criteria have not been appropriately and comprehensively observed or applied, as required by the Order of the Commissioner of Insurance, in determination of proposal funding by MCW.
2. That many of the funded proposals appear to be of a nature that one would expect to be included in the normal operating budget of a successful medical college, and, as such, may be more appropriately funded by MCW's net $34 million profit than by BCBS conversion funds.
3. That oversight of the proposal review and funding process by disinterested third parties appears lacking.

Supplanting Analysis of Two Approved Proposals

1. High-throughput Crystallization Robotics

A. Project Overview

The stated purpose of this project is "…to facilitate the development of structural biology…by developing a robotic facility for high-throughput crystallization trials", in order to "…generate protein crystals suitable for X-ray diffraction." *Project Narrative,* Joseph T. Barbieri, Principal Investigator, ¶1. The instrument would be sited at the **Protein and Nucleic Acid Facility** "as a service to the MCW faculty." Id.

The project proposal requests $225,000. $150,000 is designated for the purchase of a Gilson 925 PC Workstation, intended to "automate the preparation of high-throughput protein crystallography" and "significantly reduce time and expense…" http://www.gilson.com/Products/products.asp?pID=15. The remainder of requested funding is designated for personnel costs at $25,000 per year for each of three years.

B: Recently Funded Similar Projects

NIH granted funds to project co-investigator Jung-Ja Kim in FY 2003. (Grant #1S10RR017929-01). Kim requested the funds through an abstract entitled *High-throughput HomeLab System – R-AXIS++Option*. "This application proposes that our current unreliable (protein crystallography) instrumentation be updated to 21st century standards." Jung-Ja Kim, Abstract: *High-throughput HomeLab System: R-AXIS++Option.*
"Participants in this shared instrumentation come from the department of Biochemistry…Microbiology and the University of Wisconsin at Milwaukee." Id.
"On going projects that will benefit from continued X-Ray diffraction here at the Medical College include…Structural Analysis of the Mannose 6-Phosphate Receptors." Id.

Mannose 6-Phosphate Receptors are specifically identified as a target for the instrumentation requested in the proposal for *High-throughput Crystallization Robotics.*

C: Related Projects/Uses

1. Center for Eukaryotic Structural Genomics:

"CESG is a collaborative effort aimed at developing the critical technologies needed for economical high-throughput structural determination of…proteins." http://www.uwstructuralgenomics.org. CESG instrumentation and staff are "primarily located in the Department of Biochemistry at the University of Wisconsin-Madison and the Medical College of Wisconsin…" Id. The X-Ray Crystallography Team currently lists among its research assets six different instruments, including the

Gilson Cyberlab C-250, which appears to have several of the same features and capacities as the Gilson 925 PC Workstation requested by the Protein and Nucleic Acid facility:

Gilson Cyberlab C-250

- Pipette liquids using a 96-channel, 8-channel, or single channel pipettor
- Deliver amounts as low as 1µl
- Automatically changes disposable tips to prevent sample carryover
- Stated Applications: Plate replication, ELISA, DNA/RNA preparation, Plasmid preparation, PCR Plate preparation, filling applications.

http://www.johnmorris.com.au/html/Gilson/JMSprod_gilson_c250.htm

Gilson 925 PC Workstation

- Pipette liquids using a 96-channel or 8-channel pipettor
- Deliver amounts as low as 0.5 µl
- Automatically changes disposable tips to prevent sample carryover
- Stated Applications: High-throughput crystallography, screening large numbers of different proteins**.**

http://www.gilson.com/Products/products.asp?pID=15

D: <u>Current Funding Sources</u>

CESG is funded by a *Pilot Projects for the Protein Structure Initiative* grant administered by the NIGMS division of NIH. (Grant P50 GM64598 (JLM)) The stated purpose/objective of the PSI grant is "…support for research centers in the…field of structural genomics…that will lead to...large scale research networks in…high throughput structural determination of proteins by X-ray crystallography and NMR methods." http://grants.nih.gov/grants/guide/rfa-files/RFA-GM-00-006.html, p. 2.

"Emphasis should be placed on protein structural determinations in a high throughput mode." Id., p. 4.

Administration: NIGMS
Funding Cycle: 5 Years beginning Sept., 2001
Funds Available: Up to $3M in year 1, Total received unknown
Intended Use of Funds: The establishment of described research centers; Specific uses of funds not described in RFA, but presumably includes equipment, personnel, and necessary infrastructure.

E. Alternate Funding Sources Available

The second phase of PSI funding, the production phase, begins July, 2005. Two grants are available for continuation of the projects begun under the first phase of PSI.

Large-Scale Centers for the Protein Structure Initiative (RFA-GM-05-001)

The stated objective of the *Large-Scale Centers for the PSI* grant program is "…to support large-scale centers for the high-throughput production of unique protein structures", http://grants2.nih.gov/grants/guide/rfa-files/RFA-GM-05-001.html, p. 4, and "to make the three dimensional atomic level structures of most proteins easily obtainable…" through systematic sampling processes utilizing "structural studies by X-Ray crystallography…in a high throughput mode…" Id., p. 2.

Administration: NIGMS
Funding Cycle: 5 Years beginning July, 2005.
Funds Available: Up to $12M in year 1, Up to 3% COLA each year thereafter. Up to 5% of the total annual budget may be designated as Center Development Funds. These funds allow flexibility to "make major changes and move in new directions. The primary use of these funds must be to support staff and purchase equipment and supplies…" Id., p. 17.
Intended Use of Funds: Personnel, infrastructure, equipment and indirect costs of sub-projects

Summary: This grant program intends to build upon successful PSI research centers established through the *Pilot Program* grants. The RFA evidences that intent in stating that large-scale centers, "should contain all of the constituent tasks of structural genomics...", and "…the ability to accomplish these in a high-throughput operation." Id., p. 4. "Applicants will be expected to demonstrate the capability for high-throughput (operation)." Id., p. 5. "Applicants…are expected to demonstrate their access to state-of-the-art synchrotron and/or NMR facilities." Id.

The CERG NMR Spectroscopy team "…takes advantage of the facilities available at the National Magnetic Resonance Facility at Madison (NMRFAM) and the Medical

College of Wisconsin (MCW)." http://www.uwstructuralgenomics.org/nmr.htm. CERG likely has developed the experience necessary to meet the goals of high-throughput operation stated in the RFA. CERG appears eligible for the funding provided in this RFA. If eligible, CERG could use the funding from this grant to purchase the high-throughput robotic crystallization equipment requested by the Protein and Nucleic Acid Facility.

Specialized Centers for the Protein Structure Initiative (RFA-GM-05-002)

The objective of the *Specialized Centers for the PSI* grant is to "…support specialized centers for methodology and technology development for classes of challenging proteins." http://grants2.nih.gov/grants/guide/rfa-files/RFA-GM-05-002.html, p. 4. "These centers will be expected to at least approach high-throughput operation…by the end of the project." Id. "The specialized centers must have the capability for all components of structural genomics…but not necessarily in a high-throughput operation." Id., p. 6.

Administration: NIGMS/NCRR
Funding Cycle: Up to 5 Years beginning July, 2005.
Funds Available: Up to $4.5 M in year 1, variable each year thereafter. Up to 5% designated as Center Development Funds.
Intended Use of Funds: Personnel, infrastructure, equipment and indirect costs of sub-projects

Summary: The Specialized Centers represent the second tier of the PSI research center hierarchy. This grant is targeted at centers which have not yet demonstrated a capability to move to high-throughput operation, and its standards for grant approval are accordingly lower than those for the Large-Scale Centers. It is very likely that CERG qualifies for this grant. If CERG received only $3M of the possible $4.5M award in any grant year, the 5% allowance for Center Development Funds would be enough to purchase the equipment requested by PNA.

Unannounced PSI Third-tier Grant

The RFAs for the Large-Scale and Specialized Research Centers grant programs describe a third tier of the PSI program. Funding has not yet been allocated for this grant cycle, but is anticipated. "The third component…will consist of specialized centers that determine protein structures from microorganisms, tissues, or organ systems related to diseases. This…is being considered as an activity of the NIH Structural Biology Roadmap initiative." http://grants2.nih.gov/grants/guide/rfa-files/RFA-GM-05-002.html, p. 4.

Doris Duke Charitable Foundation CIAP Grant

Administration: Doris Duke Charitable Foundation
Funding Cycle: 5 Years
Funds Available: Up to $2.25M over 5 years. 3 full grants will be awarded in 2005.
Intended Use of Funds: Support of inter-disciplinary, collaborative clinical research.

Summary: DDCF *Clinical Interfaces Award Program* grants are intended to promote collaborative efforts between medical researchers and other scientific disciplines such as biology, chemistry, computer sciences, and engineering. This appears an appropriate avenue of funding for the High-throughput Crystallization Robotics program. "A long term goal is to establish an attractive infrastructure for all faculty and enhance recruitment efforts for faculty with interests in structural-functional biology." *Project Narrative,* ¶ 1. "This technology will provide a platform on which to establish collaborative research efforts between investigators involved in the disciplines of molecular genetics and structural biology at MCW." Id., ¶ 4.

See Appendices A., B. for grant description and example of similar funded project.

Shared Instrumentation Grant (RFA-RR-03-002)

The purpose of the *Shared Instrumentation Grant* (SIG) is "…to provide for the acquisition or updating of expensive shared-use instrumentation not generally available through other NIH mechanisms, such as…center grant programs. Proposals for advancing the design or for the development of new instrumentation will not be considered." http://grants.nih.gov/grants/guide/rfa-files/RFA-RR-03-002.html, p. 1. "The program does not provide facilities and administrative costs…" Id., p. 3.

SIG funded 149 applicants in each of FY 2003 and FY 2004 from an annual budget of $48,957,000. The same budget amount is anticipated for FY 2005.

Administration: NCRR
Funding Cycle: Annual
Funds Available: $100,000 minimum to $500,000 maximum
Intended Use of Funds: Purchase price of equipment/instrumentation.

Summary: SIG funds have been available annually since at least 2003, and are specifically intended for the purchase of research instrumentation.

F. Conclusion

Funding for this project appears to conflict with non-supplanting criteria identified in both the Commissioner's Order and the Addendum to MCW's Five Year Plan.

a. Funds for High-throughput X-Ray Crystallography instrumentation were received from NIH in FY 2003, within the three year period identified in the Five Year Plan.
b. A project with a similar purpose, CERG, exists at MCW and "in the community" by way of collaboration with UW-Madison.
c. Funding exists for CERG to purchase the equipment requested by PNA.
d. Funding appears likely to exist, by which PNA could purchase the requested instrumentation, through the third-tier PSI grant program.
e. Alternate funding exists through the Doris Duke CIAP grant program.
f. Alternate funding exists through the NIH Shared Instrumentation grant program.

2. Advanced Nanospray Mass Spectrometer for Proteomic Applications

A: Project Overview

The purpose of this proposal is "…to purchase a new Agilent Technologies XTC (sic) Plus Liquid Chromatograph/Mass Spectrometer." *Project Narrative,* Bassam T. Wakim, Principal Investigator, ¶ 2. The instrument would be sited at the **Protein and Nucleic Acid Facility** of the department of Biochemistry. Funds are designated exclusively for instrumentation purchase at $311,414.

The instrument, Model 1100 XCT Plus, is the analytical (Mass Spec.) component of a conjunctive sample delivery/analysis system collectively referred to as "Nanospray Mass Spectrometer". The XCT Plus is the flagship model of Agilent's spectrometry product line, and offers four times the sensitivity of its predecessor. http://www.americanpharmaceuticalreview.com/news.asp?newsid=68. It "will increase the sensitivity of detection a minimum of 1000-fold…" over the ABI Voyager-Pro MALDI spectrometer currently in use for protein sequencing at PNA. *Project Narrative*, ¶2.

B: Recently Funded Similar Projects

NIH granted funds in FY 2004 to Professor William Campbell of the Department of Pharmacology and Toxicology. (Grant #1S10RR017824-01A1). An abstract entitled *LC-MS/MS for Biomedical Research* requested funding to purchase a Waters Quattro Liquid Chromatograph/Mass Spectrometer to be sited at the Mass Spectrometry Shared Facility of the department of Pharmacology and Toxicology.

C: Related Projects/Uses

"The PNA is the only such facility in Southeast Wisconsin and the requested instrument represents a…technology not widely available to MCW investigators." *Project Narrative*, § 6 ("Significance and Innovation"). However, "Comparable instruments are owned by individuals (sic) investigators or groups…" and are available for use on an as-available basis. Id. No mention is made of fees associated with the use of these "comparable instruments", whereas the requested instrument would be "used by all investigators at MCW on a fee-for-use basis…" *Project Narrative*, § 6 ("Fit with the Principles of Stewardship").

The Proteomics and Functional Genomics Core Facility at UW-Oshkosh currently operates an Agilent 1100 series Liquid Chromatograph for protein separation. Protein analysis is accomplished using a Bruker Reflex IV MALDI-TOF mass spectrometer. This mass spectrometer compares with the existing Applied Biosystems Voyager-DE PRO MALDI-TOF instrument operated at PNA, but is further enhanced by a sample delivery system allowing for high-throughput operation. A stated goal of the UW-Oshkosh facility is "to provide access to this instrumentation not only for UW Oshkosh students and faculty, but also for area student and faculty researchers from area institutions."
http://www.uwosh.edu/faculty_staff/sandrin/proteomics/prot_index.php.

The Biotechnology Center at UW-Madison operates an Agilent 1100 series LC/MSD Trap SL for proteomics and peptide sequencing.
http://www.biotech.wisc.edu/ServicesResearch/MassSpec/agilent.htm.

This facility is available for use by other institutions in the UW system.
http://www.biotech.wisc.edu/PDF/Biotech_72f.pdf, p. 3.

D: Alternate Funding Sources Available

American Diabetes Association Research Award

"These awards provide grant support to both new and established investigators. Applications will be considered in any area that is relevant to the etiology or pathophysiology of diabetes and its complications."
http://www.diabetes.org/diabetes-research/research-grant-application-forms/nationwide-research-awards.jsp#research.

Administration: American Diabetes Association
Funding Cycle: Two award cycles: July 15, 2005 and January 1, 2006.
Funds Available: $20,000 - $100,000 per year for up to three years

Summary: The research to be conducted by investigators associated with this proposal will be "directed towards chronic diseases such as…diabetes, and cancer among others." *Project Narrative*, § 6 ("Fit with Healthiest Wisconsin 2010). This grant may provide partial funding for the requested instrumentation.

American Cancer Society Research Scholar Grants

"Support investigator-initiated research projects in basic, preclinical, clinical and epidemiologic research."
http://www.cancer.org/docroot/RES/content/RES_5_2x_Research_Scholar_Grants_for_Beginning_Investigators.asp?sitearea=RES.

Administration: American Cancer Society
Funding Cycle: Up to four years
Funds Available: Up to $200,000 per year direct costs, plus up to 20% additional for indirect costs.

Summary: This grant may provide partial funding for the requested instrumentation.

Shared Instrumentation Grant (RFA-RR-03-002)

Funding from the SIG grant program helped establish the PNA facility in 1986, and is a regular source of funding for equipment acquisition. "Equipment acquisition for the PNA does not come from central financial resources but rather from investigator-initiated external grants; however, acquisition of other mass spectrometers on campus precludes using our *usual mechanism of a Shared Instrumentation Grant* in the present case." *Project Narrative*, ¶ 2. *Emphasis added.*

It is unclear if and why the PNA could not receive SIG funds in FY 2004, or could not apply for those funds in any future fiscal year. The "unprecedented service" of PNA "has provided MCW investigators with the competitive edge in…grant applications." Id., ¶ 1.

Doris Duke Charitable Foundation CIAP Grant

Identification of three Principal Investigators from different disciplinary fields would qualify this proposal for CIAP funding consideration.

E: Conclusion

Funding for this project appears to conflict with non-supplanting criteria identified in both the Commissioner's Order and the Addendum to MCW's Five Year Plan.

a. Funds for similar instrumentation were received from NIH in FY 2004, within the three year period identified in the Five Year Plan
b. Comparable instrumentation exists and is available for use by MCW students and faculty at UW-Oshkosh and at UW-Madison.
c. Alternate funding exists through the NIH SIG program.
d. Alternate funding exists through the Doris Duke CIAP grant program.
e. Alternate funding likely exists through American Diabetes Association and American Cancer Society grant programs.

Other Issues

ABC for Health and Wisconsin Citizen Action understand that the Order of Commissioner of Insurance mandates collaborative participation of a medical school faculty member in each of the partnerships funded under the 35% of conversion funds designated for public health projects. MCW has elected to compensate faculty members who participate in projects under this mandate on the premise that compensation promotes active and willing involvement. We are concerned by the fact that compensation for these faculty collaborators is drawn from the 35% pool of public health funds. We question whether it was the intent of the commissioner that the conversion funds, directed for use in promotion of public health initiatives, provide for faculty salaries at the medical colleges. If it is appropriate in any way that these funds be so directed, it is then rational that, whereas these partnerships will undoubtedly enhance the professional experience and qualifications of participant faculty members, the more appropriate source of compensation for their involvements is the 65% funding pool designated for health professional education and research, and not the 35% allocated to community partnership initiatives.

Conclusion

The responsibility of assuring that these precious public assets are dedicated to appropriate use is entrusted to the Wisconsin United for Health Foundation. We ask you to exercise leadership and vigilance in your oversight that these funds may yield a benefit to the people of our state which sounds beyond the halls of the Medical College of Wisconsin.

Endnotes:

[1] Addendum to the Medical College of Wisconsin Five-Year Plan, Advancing a Healthier Wisconsin, § IV(B.), p. 6.
[2] Final Order of the Commissioner of Insurance, Case No.99-C26038, ¶ 5, p. 15.
[3] Id., ¶ 1, p. 16.

APPENDIX A.

Doris Duke Charitable Foundation

Purpose

Established in 2003, the Doris Duke Clinical Interfaces Award Program seeks to catalyze activity at the interface of clinical and other research disciplines by:

- Supporting the formation of new collaborations and strengthening existing collaborations of outstanding scientists across disciplines;
- Demonstrating successful models for clinical research at the interface of multiple disciplines; and
- Supporting interdisciplinary and inter-institutional endeavors that go beyond the program project mindset.

Rationale

Historically, most research into human disease has involved single disciplines or at most two closely related disciplines. However, we are now on the cusp of a new era in biomedicine where technologies have opened a vast frontier that should take us to the next level of knowledge and understanding of human health and disease, and then to improved prevention, treatment and cures. The exploration, and indeed exploitation, of this frontier requires research at the interface of clinical and other sciences, including the biological, physical, chemical, social and population sciences, mathematics, computer sciences and engineering.

Grant Details

Full grants of up to $2.25 million over 5 years are awarded to established teams with key investigators from at least three disciplines. Up to 3 full grants will be awarded in the 2005 competition.

Planning grants of $80,000 are awarded to new teams for the development of full proposals over 18 months. Teams receiving planning grants will be able to compete for full grants during the next award competition. Planning grants will not be awarded as part of the 2005 competition.

Criteria

Teams of at least three key investigators whose primary expertise lie in different disciplines are eligible to apply. Key investigators must have advanced degrees (M.D., Ph.D., M.D./Ph.D., or the equivalent), and one of the key investigators must be a clinical researcher.

The team leader must work in a U.S. nonprofit institution, such as an academic medical center. The team may include investigators at other institutions in the United States and overseas.

Process

The Clinical Interfaces Award competition is structured in three phases:

1. The Medical Research Program issues a Request for Pre-Proposals, which are reviewed and ranked by an Advisory Panel.
2. The Medical Research Program invites applicant teams of the top-ranked pre-proposals to submit a proposal for either a full grant or a planning grant.
3. An Advisory Panel reviews full grant and planning grant proposals, and recommends teams for funding. Site visits are conducted for finalist teams applying for a full grant.

APPENDIX B.

DORIS DUKE CIAP FULL GRANT AWARDED 2003

Genomics-based Approaches to New Pathogen Discovery in Chronic Human Diseases

Team Leader:
Donald E. Ganem, M.D., Howard Hughes Medical Institute/ University of California, San Francisco

Key Investigators:
Joseph R. DeRisi, Ph.D., University of California, San Francisco; Homer A. Boushey, M.D., University of California, San Francisco

Team Disciplines:
Virology, Infectious Diseases, Genomics/ Informatics, Pulmonology

Abstract

In the past 2 decades, great strides have been made in identifying infectious agents that cause human disease. Particularly important has been the recognition that many chronic diseases once thought to be genetic, metabolic or degenerative in origin are in fact precipitated by infection. (Examples: peptic ulcer disease, Lyme arthritis and cervical cancer). Suspicion is now growing that other disease processes - chronic inflammatory states, autoimmune diseases, and some degenerative disorders - may likewise have infectious precipitants or cofactors. However, our ability to identify new pathogens has been strongly impaired by the inadequacy of currently available techniques for identifying infectious agents. The emerging science of genomics provides new opportunities to advance this area of research. Rather than attempting to identify new pathogens by their growth properties in culture, genomic methods allow pathogens to be sought by directly attempting to detect their DNA in a clinical specimen. We have developed a new, genomics-based method for the detection of viral genomes in such specimens, using DNA microarrays bearing the conserved sequences of all known viruses. Several short fragments of DNA from each known virus are deposited on a glass slide; the DNA or RNA from the patient sample is biochemically labelled and then tested for its ability to recognize the spots of known viral DNA that are on this lside. The subsequent pattern of reactions is analyzed by computer to yield the identity of the pathogen present in the sample. In this way, in a single test we can search for nearly 1000 known viruses; in addition, the test has the potential to identify new viruses that are only partially related to presently known agents. Using this test, we are searching for new agents implicated in asthma, pneumonitis, hepatitis and other chronic diseases.

APPENDIX C.

Non-Supplanting Criteria

"…the application of the funds will not supplant other resources that may be available to accomplish the same purpose…" Final Order of the Commissioner of Insurance, Case No. 99-C26038, ¶ 16, p. 30.

"A related project or use includes (i) a project or use with a similar or related purpose conducted by the college or within the community and (ii) all projects, research activities and education activities conducted by the faculty member and/or community partner within the three-year period immediately prior to the application or submission." Addendum to the Medical College of Wisconsin Five-Year Plan, ¶1 , p. 15.

"Financial support provided by a governmental source for a project or use within the three year period prior to the date of the application…should be identified and considered. Financial support…other than a governmental source…within the (prior) two year period…should be identified and considered." Id., ¶ 2, p. 15.

"Consideration should be made whether Federal funding is available, including grants awarded for the project or use, announced available funding for the project or use and eligibility to apply for the available funding." Id., ¶ 3, p. 15.

"Supplant means to replace." Id., ¶ 2, p. 14.

"By way of contrast, supplement means to add to. Use of the funds to supplement other financial resources is not prohibited under the order. Matching funding and opportunities to leverage the funds to obtain other sources of financial support are to be encouraged." Id., ¶ 3, p. 14.