

Connections

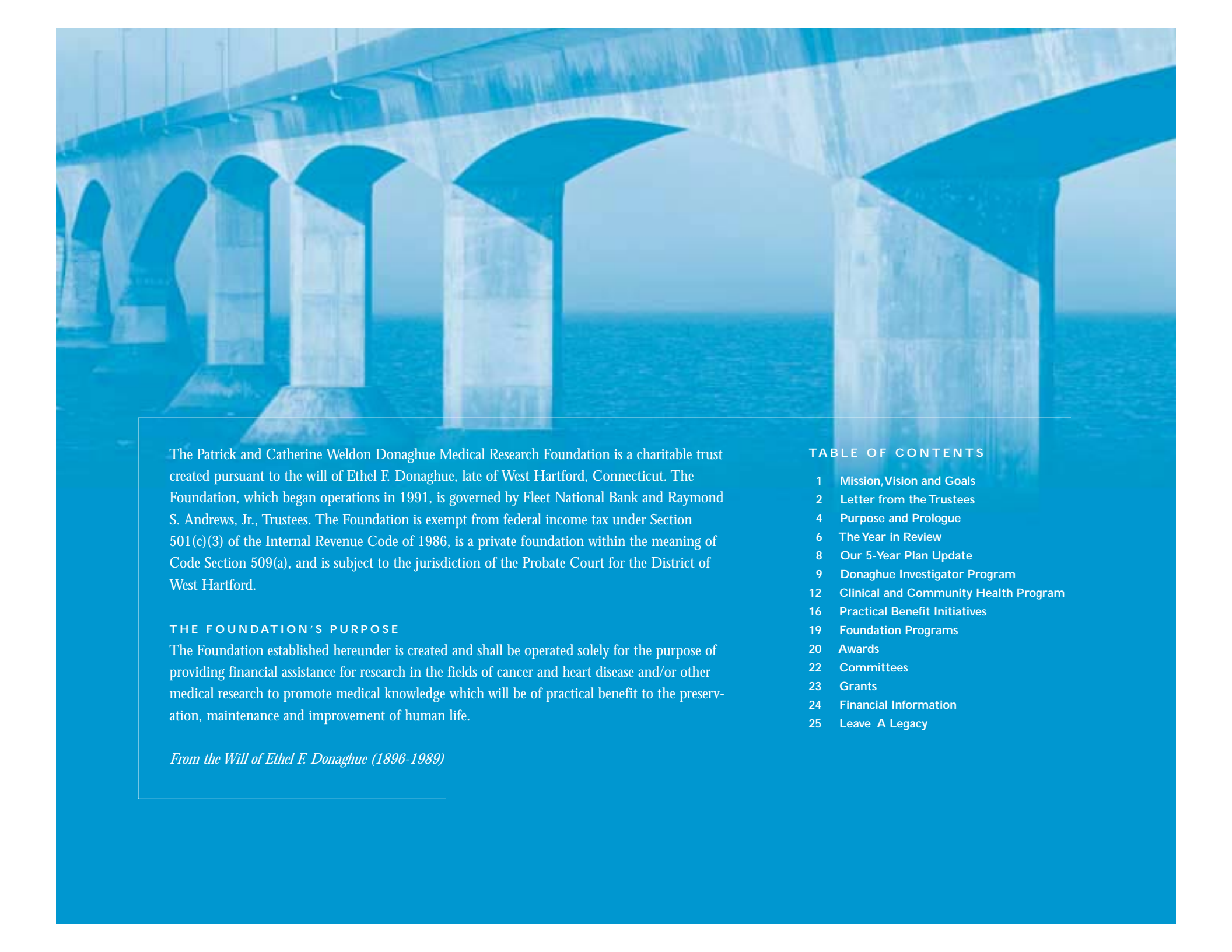
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The Patrick and Catherine Weldon Donaghue

Medical Research Foundation

Eleventh Annual Report





The Patrick and Catherine Weldon Donaghue Medical Research Foundation is a charitable trust created pursuant to the will of Ethel F. Donaghue, late of West Hartford, Connecticut. The Foundation, which began operations in 1991, is governed by Fleet National Bank and Raymond S. Andrews, Jr., Trustees. The Foundation is exempt from federal income tax under Section 501(c)(3) of the Internal Revenue Code of 1986, is a private foundation within the meaning of Code Section 509(a), and is subject to the jurisdiction of the Probate Court for the District of West Hartford.

THE FOUNDATION'S PURPOSE

The Foundation established hereunder is created and shall be operated solely for the purpose of providing financial assistance for research in the fields of cancer and heart disease and/or other medical research to promote medical knowledge which will be of practical benefit to the preservation, maintenance and improvement of human life.

From the Will of Ethel F. Donaghue (1896-1989)

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STATEMENTS OF VISION, MISSION & GOALS

As updated by the Trustees August 29, 2000

OUR VISION

We will be an exemplary participant in the ongoing conduct and continuing advancement of useful health research in Connecticut and beyond.

OUR MISSION

We will benefit human life and the individual lives of people as an active, imaginative, and collaborative supporter of useful health research, primarily in Connecticut, and we will thereby honor the memory of Ethel Donaghue and her family.

OUR GOALS

Fidelity to Purpose

We will faithfully carry out the charitable intentions of Ethel Donaghue as expressed in her will, being careful to give her words their proper meaning and best expression in a context of changing facts and conditions.

Grantmaking

We will develop and manage a flexible and well-rounded program of grantmaking initiatives. In so doing:

- (1) We will reflect our Connecticut roots, the Hartford derivation of the Donaghue fortune, and the current health needs of the people of Hartford, Greater Hartford, and Connecticut, with appropriate regard for the underserved, understudied, and disadvantaged.
- (2) We will use and help to develop Connecticut talent in health research, fostering teamwork between investigators and clinicians and among individual researchers, disciplines, and institutions throughout Connecticut's complement of research resources.
- (3) We will be alert to opportunities and needs for responsive and imaginative focusing of our resources upon targets of importance, with particular thought to those which, but for our involvement, might find inadequate financial support.
- (4) We will strive for a balance between the pursuit of new knowledge and its translation into useful forms, between scientific exploration and thoughtful reflection upon the implications of discovery, and between the gaining of knowledge and the pursuit of wisdom to temper our use of it for practical benefit to human life;
- (5) We will make full use of our skills and our independence of judgment in seeking out, evaluating, and taking on challenges, being always willing to effect beneficial change through our research funding.

- (6) We will promote public awareness of research activities and accomplishments and an appreciation of the value of steady and continued support of skilled inquiry into problems affecting human health.

Community Responsibility

We will work actively and collaboratively within the community of philanthropic organizations in Connecticut to promote responsible service of the public interest, particularly in the field of health research, and we will work to build a strong and enduring bond of understanding, respect and teamwork among those in Connecticut who engage in health research and those who finance their efforts.

OUR VALUES

Purpose, Principle, Practicality, Prudence



The Patrick and Catherine Weldon Donaghue Medical Research Foundation was founded by Ethel Donaghue in loving memory of her parents.

The year 2002 was a very different one for us, one laden with change and the prospect of further change. Accustomed to the gas pedal, in 2002 we had to apply the brakes and think hard about the nature and the future of the Donaghue Foundation. The confluence of a crumbling economy and our prior “put our money to work in research” practices, replete with sizable multi-year commitments, threatened to shrink our assets and our potency as a supporter of important research. With “subtraction” on our minds for the first time in our short history, we tightened up our policy on spending. While our ongoing programs proceeded apace and just under \$6 million in grants flowed from our coffers for several promising projects, we launched a planning process to connect our future programs to our past learning, and our budget to our new, disheartening reality. Revisiting our values of purpose, principle, practicality and prudence, we concentrated this time on prudence.

Since “connections” is our theme for this 2002 annual report — portraying not only the year’s work but also our ongoing philosophy — perhaps it’s fitting to link up a bit of imagery from our past to illustrate our approach to the future. *Two Boxes, Three Trusts*, the 1995 history of the Donaghue family, included a passage about the precocious Ethel as a teenage schoolgirl in 1912, writing an essay about the sinking of the “unsinkable” Titanic. The ill-fated ocean liner has become a symbol of great expectations shattered, of how pride goeth before a fall. Miss Donaghue insightfully assessed the factors that brought about the Titanic disaster, including the fact that overconfident people didn’t think it could happen. We’re not overconfident. Our steering corrections today will ensure the continuation of the Foundation’s voyage as an ongoing, long-haul research resource — and a suitable memorial to the Donaghue family. One connection the Donaghue Trustees are determined *not* to make is a collision with the iceberg of economic reversal.

**Our steering corrections today will ensure
the continuation of the Foundation’s voyage as an ongoing,
long-haul research resource — and a suitable memorial
to the Donaghue family.**

We've often characterized ourselves as a tugboat, nimble and rugged and meant for work. In 2002, we realized that we also have some of the attributes of the huge ocean liner: it's not easy to change our financial course quickly when we have so many ongoing commitments to honor. Nor do we want to make abrupt, perhaps disruptive course changes (though we *may* rock the boat a bit). We are beginning to focus more narrowly on a few priorities, spend more frugally, devote a lot of time and effort to developing our course correction, and do a lot of program evaluation to base our correction on. Ethel Donaghue made many ocean voyages in her day, no doubt encountering heavy weather at times. Her legacy will weather the current storm and journey on with optimism and perseverance.

Having said that, we must close on a somber note. Even as we were preparing this letter, the Foundation — and we, personally, as well — lost an important connection to Ethel Donaghue. Joe Flood, MSW, a much-valued charter member of our Policy Advisory Committee, died on March 21st. Joe was a kind and compassionate professional, who served as Miss Donaghue's personal conservator for the last six years of her life. He brought to us not only his good humor and insights but also a helpful window into the person whose trust we carry out. We will miss Joe greatly — maybe now, as *we* work to connect Miss Donaghue's trust to practical benefit, *he'll* re-connect with Miss Donaghue.



Raymond S. Andrews, Jr.
Trustee



Sheilah B. Rostow
Senior Vice President, Fleet Bank
Trustee



The Donaghue Foundation is a living connection to the beneficent vision of Ethel F. Donaghue (1896-1989) that the wealth accumulated through her family's enterprise and prudence could work indefinitely to benefit her fellows and bring enduring honor to her family. When Miss Donaghue died without immediate family surviving her, her will placed over \$50 million in a charitable trust in memory of her parents, a trust devoted to The Patrick and Catherine Weldon Donaghue Medical Research Foundation.

The Foundation Trustees feel a strong connection to Miss Donaghue as we carry out our duty of interpreting and effectuating her intent against a changing and challenging backdrop of needs and opportunities. Understanding the Foundation and its ways is aided by a grasp of Miss Donaghue herself, one of Connecticut's first woman lawyers, trained in admiralty law and deeply committed to the advancement of women. From her childhood she gave evidence not only of a brilliant and searching mind but also of an intensely logical and practical bent. Blessed with great family wealth, she was able to enjoy the broadening experience of many years of global travel, but she always kept a quiet connection to her "neighborhood" in West Hartford.

We did not have the privilege of a real and personal connection with Ethel Donaghue. The picture we have of her is gleaned from her will and from our own research. Our annual report of five years ago described her as "a brilliant, strong-willed, stubbornly practical woman who co-existed with convention and challenged others to keep up with her spirited and colorful — but also eminently commonsensical — ways," a woman who lived with "a paradoxically confining affluence sabotaged by the pains of illnesses and afflictions within her own family and by the loneliness of three decades alone after they were all gone."

Surely the illnesses and afflictions prompted Ethel Donaghue's interest in medical research; she established research-related trusts during her lifetime. When she died, she devoted virtually all of her fortune to the search for medical knowledge of practical benefit to human life. Her design was predictably practical: an enduring (but not necessarily perpetual) mechanism with the independence, flexibility, imagination and — if we look to her as a model — the audacity to have a meaningful impact on research and health. The Donaghue Foundation is that mechanism, and the Trustees regularly address decisions by reflecting on "what Miss

...Miss Donaghue would have counseled us,
"If you think *somebody* should be doing something,
remember that *you're somebody*."

Donaghue would do if she were here today armed with the facts we have before us.” We also imagine that Miss Donaghue would have counseled us, “If you think *somebody* should be doing something, remember that *you’re* somebody.”

In its decade of existence, the Donaghue Foundation has built its grantmaking upon some undergirding principles:

- (1) make the most of our independence and flexibility;
- (2) focus on Connecticut to strengthen research and improve health in Miss Donaghue’s home state;
- (3) make a deliberate effort to confer benefits on Greater Hartford, from which the Donaghue fortune derived;
- (4) resolve to benefit the understudied and the underserved, because Miss Donaghue crafted her mechanism as a charity;
- (5) refuse to be a caboose, satisfied with tagging along behind others; and
- (6) make and maintain connections, whether they be among researchers or research institutions, between researchers and funders or between funders themselves, between science and humanity, between knowledge and understanding or knowledge and behavior, or — of paramount importance — between our resources and the ultimate desideratum of practical benefit to human life.

In giving her Trustees great latitude in administering her trust, Miss Donaghue embraced the creative side of medical research — creativity that enables investigators and Trustees alike to make connections that hold great promise for the people in Miss Donaghue’s beloved home state. This annual report is itself an important connection the Donaghue Foundation makes. We hope it serves as an effective way to link us to our many constituencies, whether governmental, institutional or public. We hope that after reviewing our report for 2002 you may feel moved to initiate or strengthen your connection to the Foundation.

2002

2002 was a productive and successful year for the Donaghue Foundation, in spite of a need to impose new funding discipline on ourselves. As always, our established grant programs went as planned, with three new Donaghue Investigators joining our diverse and growing complement and five Clinical and Community Health Issues studies being funded. Program evaluation emerged as an active and illuminating element of our work and provided some important insights for a planning process we began so we could adapt to a changing climate. Two important Practical Benefit Initiatives were funded after long negotiation, and a third took shape over the year and was funded just after year end. All are described more fully later in this report.

A few years ago, in the belief that Donaghue money should promote connecting health care to the social surroundings of our people, we began discussions with Saint Francis Hospital about a study that would examine the value of weight control education for African American women in the structural and spiritual setting of their churches. In August, we made a \$665,000, three-year grant to the Hospital to support Sister Talk Hartford, a collaboration with twelve Hartford churches using an adaptation of a previously proven video technique to seek health improvements. A new Donaghue practice, incorporated in this grant to learn about the conduct of such research, was the earmarking of an additional amount for a concurrent qualitative study of the study itself.

Over the past few years, the Foundation has increased its interest in mental health research, and during 2002 we worked with the Department of Psychiatry of the Yale School of Medicine on a proposal to study the early — or prodromal — stages of schizophrenia. The disease takes a heavy toll once it emerges as psychosis, and the Yale team wishes to find ways to detect its developing grip on a patient before full-blown symptoms show themselves. In December, after we reached agreement on a plan that featured collaboration with the Institute of Living to focus the powerful talent of both institutions on the problem, we made a \$1.6 million, five-year grant to support the project.

Since deciding to make ethics an abiding theme of our work a few years ago, we have actively encouraged projects that connect research and ethics so each can constructively inform the other. Having developed a concern about patient safety, we observed serious issues in the safety of research subjects as well, and we began discussions with the leadership of the Yale University Interdisciplinary Bioethics Project, an impressive array of academic talent and initiative. Throughout 2002 we molded a partnership to bolster the Project's efforts to study research ethics and also extend the fruits of those efforts across the state, all in the interest of achieving the highest levels of ethics in research and safeguarding those people who volunteer to participate in studies. At the end of 2002 it was all over but the signing, and in early 2003 we made a \$2.1 million, five-year grant to Yale to establish the Donaghue Initiative in Biomedical and Behavioral Research Ethics.

While the grantmaking proceeded, the Trustees began in earnest a serious examination of the Foundation's options in light of the decline in the economy and in our asset value. Tapping the talents of Foundation advisers, we hammered out a principle-based spending policy to take effect in 2003 and, in a measured fashion, reduce our annual spending so that our assets will in short order level out — and thereafter remain — at no less than \$60 million. We based the new policy on a commitment to maintain indefinitely a suitable memorial to the Donaghue family without reliance on outside money, adopting for the next few years a more cautious reading of Miss Donaghue's permission for us to spend trust principal.

The spending policy needed — and indeed required - the context of a careful repositioning of the Foundation. Since we could no longer indulge ourselves in several directions of research support at once, we began work on a five-year plan to establish priorities. We undertook a systematic review of options, a review that featured our first planning retreat in October. Many useful insights emerged from the all-day session. A snapshot of the status of our five-year plan is contained in this report.

Our interest in promoting patient safety in Connecticut prompted us to connect with another funder during 2002 in a way that was new for us. We provided grant money for a National Patient Safety Foundation grant for a project to be conducted in the state.

The departure of long-time staffer Maggie Willard late in the year was the occasion for an assessment of the Foundation's staff structure. The result was a redesign that would lead in early 2003 to the redeployment of Lynne Garner and Jacque Daniel to the new positions of Executive Director and Program Administrator, respectively.

As 2002 ended, staff were busy working on one of the Foundation priorities for the next five years that had emerged from the Trustee's planning: active dissemination of health knowledge developed through our research grants. A patient safety conference for Connecticut hospital leaders, built upon the Donaghue-funded Hastings Center project on patient safety, was in preparation, as was a University of Connecticut Health Center public lecture series featuring Donaghue-supported scientists and studies. In these undertakings, as in all else the Foundation does, we will work to make healthy connections.

**Tapping the talents of Foundation advisers,
we hammered out a principle-based spending
policy to take effect in 2003...**

five UPDATE

Planning for 2003-2007 is ongoing. What follows is a snapshot of the plan to date.

- (1) **Less spending.** Decrease grant making for 2003-2007, following a spending policy designed to maintain at least \$60 million in Foundation assets, an amount essential for a suitable memorial to the Donaghue family. Consistent with honoring commitments, avoid spending trust principal. Undertake fewer and more focused initiatives, looking for targets in public health, quality improvement, patient safety and ethics.
- (2) **New staff structure.** Establish office of executive director, responsible for conducting all routine operations, for making program evaluation a priority for 2003 and 2004, and for assisting Trustees in ongoing planning. Establish office of program administrator, responsible for grant and office administration.
- (3) **Keep planning and learning.** During 2003 and 2004, incorporate program evaluation into ongoing re-assessment of all existing programs. Redesign or replace programs to achieve alignment with priority directions.
- (4) **Priority directions.** Placing greater emphasis on the perspective of the patient, connect work increasingly to two priorities, while honoring pre-existing commitments and avoiding disruptive course changes.
 - 1) Connect knowledge to behavior, narrowing the gap between what the knowledge we already have tells us and what we actually do — or don't do — about it. Support research in human relationships and behavior and in how to use knowledge to change behavior for improved health. Go not only beyond research but also beyond knowledge to achieve practical benefit to human life.
 - 2) Transform our Knowledge at Work program to make dissemination of knowledge a fully integrated element of mission. Assume greater direct responsibility for connecting our resources to ultimate practical benefit.

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Elizabeth H. Bradley, PhD

With her Donaghue Investigator grant, Elizabeth H. Bradley, PhD, Associate Professor of Epidemiology and Public Health at Yale University, is examining why clinical care is often disconnected from clinical guidelines widely supported by scientific evidence. “Despite evidence of inconsistent adherence to accepted standards for quality of care, we know little about how to ensure that such guidelines and standards are implemented,” says Bradley, a health services researcher with a focus on quality improvement in the care of older adults.

According to Bradley, quality improvement strategies used in industry have limited relevance to the complex systems and processes of medical care, and are rarely evaluated scientifically. “My career goal is to identify best strategies for enhancing adherence to evidence-based standards for care,” says Bradley, the first Donaghue Investigator from Yale’s School of Epidemiology and Public Health. “Quality issues are particularly critical for older adults, whose increasing numbers and health care needs challenge the health care system to deliver high-quality and cost-effective care — often for life-threatening diseases.”

Bradley’s early work has identified specific quality improvement efforts — such as clinical pathways and standing orders — as possible factors in improving care, as well as the possibility that the organizational environment in which such efforts take place might hold particular promise for improving care. “We find that facets related to organizational culture regarding quality, clinician leadership, and administrative support may distinguish the performance of hospitals. While difficult to measure, they remind us that clinical care takes place in a larger system, which may be malleable to improve clinical performance and ultimately patient outcomes.”

Bradley’s objectives for the next five years are two-fold: to build a base of scientific knowledge about effective strategies for promoting adherence to clinical guidelines in the hospital setting; and to disseminate that knowledge to hospital-based administrative and clinical staff. “Scientific evidence is lacking when it comes to identifying the critical elements of quality improvement initiatives that are most associated with improved adherence to clinical guidelines or standards,” she says. “I plan to examine these issues in a targeted way for beta-blocker use for patients after acute myocardial infarction (AMI), although the research also will generate insights for quality improvement strategies for other clinical conditions.”

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whose increasing numbers and health care needs challenge
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care — often for life-threatening diseases.”**




Kevin P. Claffey, PhD

Kevin P. Claffey, PhD, Assistant Professor of Physiology at the Center for Vascular Biology at the University of Connecticut Health Center, is studying molecular mechanisms related to tumor growth and metastasis in order to develop patient-specific diagnostic tests for cancer. “We expect that these tests will help determine the specific nature of a patient’s cancer mechanism,” says Claffey, “and enable physicians to apply the most effective therapeutic regimen for that patient’s individual profile.”

Through his research, Claffey has discovered that low oxygen conditions – hypoxia – can promote the growth of tumors by inducing new blood vessels, which, in turn, can activate cancer cells. These observations suggest that there may be a primary connection between sedentary behavior and low tissue oxygenation, a possible risk factor with regard to the potential for a primary tumor to expand and spread. “The goal of our research is to understand how these mechanisms may be operating in each patient, and to translate this information into preventive actions or specific therapies for at-risk individuals. We are increasingly finding that selective and specific therapies work on select sub-classes of patients. As a result, it is critical to diagnostically define which subclass each patient falls into, and to customize therapeutic treatments for significantly improved prognosis and outcome.”

According to Claffey, the most promising aspect of his work is the possibility of developing novel diagnostic technologies and therapeutic approaches for individual patients. “Although the technical challenges are significant, these are the types of problems that are very rewarding to work out, especially when there is the potential for diverting the progressive nature of cancer, particularly metastatic breast cancer.”

Over the next five years, Claffey hopes to be able to view the cancer paradigm as an evolution from therapeutic intervention based upon the location of the cancer (breast, colon, prostate, etc.) to where the therapeutic regimens are designed for each patient. “This will enable individuals to get the therapy or therapies they need based on their specific cancer profile, not necessarily the profiles observed most often with a certain type of type of cancer. It is very exciting.”



“We expect that these tests will help determine the specific nature of a patient’s cancer mechanism and enable physicians to apply the most effective therapeutic regimen for that patient’s individual profile.”

TUMOR GROWTH & METASTASIS

Barbara Kazmierczak, MD, PhD

In her body of research, Barbara Kazmierczak, MD, PhD, Assistant Professor of Medicine & Microbial Pathogenesis at Yale School of Medicine, hopes to discover how the human body recognizes potential disease-causing agents and organizes an immediate immune response that protects against illness. “We are particularly interested in opportunistic pathogens that we can fight off successfully under normal circumstances, but that can make us very ill when our local defenses are compromised by trauma or certain types of medical procedures. Understanding how these pathogens establish an infection shows us what features of normal tissue are indispensable for successfully resisting infections.”

Kazmierczak says she is excited about translating her team’s laboratory findings into clinically useful tools for physicians. “For example, we have some data about what makes a particular opportunistic pathogen very virulent in model systems in the lab,” she says. “We’d like to see whether we can use this information to help physicians predict whether the bacteria that they isolate from a given patient in the hospital has a high potential for causing serious illness, or whether the isolate is unlikely to lead to disease.”

Kazmierczak hopes that her research will eventually improve the way in which care is provided to patients whose immune systems are compromised by “modern” medical procedures and treatments, such as chemotherapy. “We don’t really understand why certain patients who undergo immunosuppressive chemotherapy succumb to infections in the hospital, while others survive,” she says. “We think the difference may partly lie in how their immediate immune systems fight infection. For a long time, we’ve thought that this immediate response was pretty much the same from individual to individual, but we are becoming increasingly aware that there is variability built into this system.”

As an infectious disease physician, Kazmierczak looks forward to the day she will be able to admit patients to the hospital for chemotherapy knowing, for example, that they have a particular variant of a TLR (a receptor that is part of the innate immune response) that makes them highly susceptible to a fungal infection. “In situations like these, I could give them protective antifungals – and ultimately improve their chances of surviving chemotherapy.”

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undergo immunosuppressive chemotherapy succumb
to infections in the hospital, while others survive.”**



Nicotine Antagonistic Augmentation of SSRI Antidepressants

With his Clinical and Community Health Issues Program grant, **Tony P. George, MD**, Assistant Professor of Psychiatry at Yale University School of Medicine, will examine the effects of a novel medication treatment strategy for persons with major depressive disorder (MDD), a condition that affects approximately 15-20% of the U.S. population. “Most people with MDD now take the SSRI class of antidepressants, such as Prozac, Zoloft and Paxil,” says George. “Unfortunately, many of them do not respond completely to SSRI therapy, and they continue to suffer from the symptoms and psychosocial impairment associated with depression.”

George notes that about half of all MDD sufferers are tobacco users, and that smoking has been suggested to have antidepressant effects. “It has been discovered recently that SSRIs and several other classes of antidepressants bind to the brain receptor that is responsible for the addictive properties of nicotine,” George says. “This may suggest that drugs which block the nicotine receptor might have antidepressant effects. Our study will use a classical blocker of the nicotine receptor, mecamylamine, (along with a placebo) to ‘boost’ the effects of SSRI antidepressants in people who are not responding completely to SSRI therapy.”

According to George, positive results from his team’s trial study would suggest that the blockade of nicotine receptors is responsible for some of the antidepressant effects of SSRIs, and that the use of nicotine receptor-blocking drugs may be a useful treatment for people who respond poorly to antidepressant medications. “There is evidence from animal and early human studies that this treatment strategy has significant potential,” he says. “Hopefully, data from our study will lead to the funding of larger studies by the National Institutes of Health. If it does, ultimately our findings could lead to a whole new class of medications for the treatment of depression — and provide much needed help for the millions of people in Connecticut, the nation and the world who suffer from this disorder.”

Urinary Incontinence in the Elderly: A Translational Approach

Approximately 25 percent of older individuals living at home and more than one-half of those residing in nursing homes suffer from urinary incontinence. “Incontinence can have a significant impact on one’s independence and quality of life,” says **George A. Kuchel, MD**, Director of the UConn Center on Aging and Chief of the Division of Geriatric Medicine at the UConn Health Center. “Yet, it is commonly neglected in the elderly, since many patients and even health professionals believe that little can be done to help incontinent individuals, particularly if they are older.” As a result, medications — which often produce side effects — are often stopped within days. Moreover, because bladder medications have not been designed to influence the processes which cause abnormal bladder function, symptoms and incontinence commonly continue.



Tony P. George, MD

ANTIDEPRESSANTS, INCONTINENCE...

With their Clinical and Community Health Issues Program grant, Kuchel and his colleagues hope to develop an understanding of the cellular mechanisms that lead to an important type of bladder dysfunction in incontinent, older individuals — a pattern known as detrusor hyperactivity with impaired contractility. “This pattern causes the bladder to develop involuntary spasms that are too weak to enable the bladder to empty properly,” Kuchel says. “Not only is this pattern common, but current approaches to treating the problem are generally ineffective and lack any clear scientific rationale.”

According to Kuchel, bladder spasms and weakened bladder contractions appear to develop through entirely distinct mechanisms, most likely representing the presence of two common, yet distinct conditions in the same older individual. “Current studies from our laboratory indicate that prolonged estrogen depletion, like the type seen in many post-menopausal women, can contribute to the development of specific degenerative changes and weakened bladder muscle contractions. We are now studying a number of proteins that appear to be involved in this process, and we believe that such studies will lead to better ways of diagnosing, preventing and treating this common condition.”

Dietary Protein Impact on Calcium and Bone Metabolism

Karl L. Insogna, MD, Professor of Medicine at Yale University School of Medicine, is using his Clinical and Community Health Issues Program grant to examine the effect of dietary protein — particularly from soy sources - on calcium metabolism and skeletal health. “Individuals are increasingly turning to specialized diets to improve their health and stave off chronic illness and osteoporosis,” says Insogna, noting that osteoporosis affects more than 30 million Americans, primarily women. “Of special relevance to our proposal is the contention that soy-based diets improve skeletal health. Our work systematically addresses the influence of these soy-based diets on the skeleton.”

Insogna emphasizes that the results of his work should have a direct practical benefit for Connecticut citizens. “We believe that our studies will provide quantitative information upon which informed guidelines can be based to better guide women and men in Connecticut on how to use soy products in their diets. Informed recommendations require more than qualitative information about whether a given food is ‘good’ or ‘bad.’ We hope to be able to precisely quantify the magnitude of any effect, so that recommendations to address or ameliorate that effect can be equally quantitative.”

Insogna notes that he is excited about the multi-disciplinary nature of his work. “Our



George A. Kuchel, MD



Karl L. Insogna, MD

...AND DIETARY PROTEIN

research brings together a team of nutritionists from UConn, a group of investigators interested in mineral metabolism from Yale and Johns Hopkins, and a group of scientists from industry, all with different expertise. We are working closely together to solve an important problem."

According to Insogna, his team's preliminary data indicate that soy-based diets may alter the body's calcium balance in a way that is deleterious to skeletal health. "In the next few years we hope to acquire precise information about the quantitative effect of the phytate component of soy on calcium absorption. These data should enable us to develop recommendations about dietary modifications or changes in soy products to optimize skeletal health."

Epidemiological Investigation of Human Respiratory Viruses

Jeffrey S. Kahn, MD, PhD, Assistant Professor in the Department of Pediatrics at Yale University School of Medicine, will use his Clinical and Community Health Issues Program grant to study two human respiratory viruses that are a major cause of death worldwide: human metapneumovirus (hMPV) — which was discovered in the Netherlands just two years ago — and respiratory syncytial virus (RSV).

"Preliminary data suggested that hMPV was associated with severe lower respiratory tract infection in infants and children," says Kahn. "Using the tools of molecular biology, we have detected hMPV in infants and children in Connecticut - an exciting finding, as the discovery of the virus in the United States had not yet been reported. To date, we have identified nearly 50 infected individuals. With our Donaghue grant, we will continue to develop methods to screen for and test exposure to hMPV. Ultimately, this project will define the clinical manifestations and epidemiology of this newly identified pathogen."

According to Kahn, RSV — the major respiratory pathogen of infants and children — is responsible for nearly 100,000 hospitalizations per year in the U.S. "Although RSV was discovered nearly 50 years ago, the mechanism by which it causes severe disease remains poorly understood," he says. "As a result, there are no specific therapies to treat RSV disease, nor are there any available vaccines to prevent RSV infection. We are attempting to identify virulent strains of RSV by studying virus obtained from infected children." Kahn hopes that his findings may lead to specific therapies for RSV disease. "Our initial studies suggested that certain strains are associated with greater severity of illness. By firmly establishing this association, we will gain insight into the genes responsible for viral virulence.

Jeffrey S. Kahn, MD, PhD



R E S P I R A T O R Y V I R U S E S

"Together, our studies will provide invaluable insight into the genetic factors responsible for severe respiratory disease," concludes Kahn. "We expect our findings will launch further investigations as to how these viral genes cause respiratory disease and what might be done to prevent its progression."

A Regional Database to Study Outcomes in Premature Babies

Despite medical advances, the incidence of premature births is rising. With his Clinical and Community Health Issues Program grant, **Naveed Hussain, MBBS**, Assistant Professor in the Department of Pediatrics at UConn Health Center, will establish a regional database of infant admissions to neonatal units in the Greater Hartford area in order to study the various factors that are responsible for premature births and variables that determine the ultimate outcomes of premature babies. Projects that will be undertaken to illustrate the efficacy of the database include: a study of "best practice parameters" used in specific neonatal units to improve such outcomes as infection rates and length of stay; an epidemiological surveillance study of the unusually high rates of penile birth defect in the region; a study of hearing and visual problems in these premature infants; and a study of rare but important problems, such as food allergies in premature babies.

"The development of a regional database with common definitions and protocols in the four major neonatal centers in the Hartford area is a challenge," says Hussain. "With the use of modern communication technology, the time has come for the establishment of such a database, not only for the region but for the entire country. Our project is a promising step in that direction."

Hussain believes the regional database he and his research collaborators are developing will be functional within six months. "The data we gather over the next several months will soon have an impact on best-care practices relating to hospital-acquired infections," he says. Over the next two years, Hussain hopes to gain valuable insights into conditions like food allergies in premature infants, the reason for increased genital birth defects in the Hartford area, and factors associated with hearing problems in infants discharged from neonatal intensive care units. "I expect this project to lead to the implementation of a statewide database that will help address significantly more global issues in the future."



Naveed Hussain, MBBS

NEONATAL OUTCOMES

Hospitals and Churches: A Partnership to Improve Health

As part of its 2002 Practical Benefit Initiatives program, the Donaghue Foundation awarded the St. Francis Hospital and Medical Center a \$665,000 grant to undertake a three-year study to assess the feasibility, acceptability and efficacy of delivering an existing weight control program in a church setting. The project, known as SisterTalk Hartford, will be conducted in twelve Hartford churches with predominantly African American congregations. “Our grant focuses on the translation of an existing Boston-based weight control program for ownership and delivery by members of the African American church in the Hartford area,” says **Judith Fifield, PhD**, Director of Research in Family Medicine at St. Francis, who heads up the project.

According to Fifield, SisterTalk Hartford was designed to include elements that transcend common barriers to translational work, such as “boundary spanning” personnel and participatory planning. “For instance, the health educator position will be filled with educators who are close to, if not members of, the African American culture and church. In addition, one ministerial representative from each church will have a central role in developing the spiritual material for the video series and the SisterTalk sessions.”

At the onset of the study, approximately 400 women from a dozen churches will participate. “SisterTalk Hartford is designed be self-sustaining in the long-term,” says Fifield. “It is being translated for delivery in collaboration with both leaders and members of each church, and the church will retain both the tools and the training to continue the program independently.”

While SisterTalk Hartford is in its early stages, Fifield reports that the research team already has established a successful collaboration with the leaders and members of the participating churches. “This collaboration promises to result in a unique and powerful weight control program that will be for – and by – the sisters of the church,” she says. “We have already seen the wonderful synergy of how relationships have been created and deepened by the collaborative and spiritual climate participants bring to their work.

“We expect that SisterTalk Hartford will have both immediate and long-term practical benefit for human health, in particular through weight loss and control, which, in turn, will improve other aspects of physical and mental health.”



From left to right:
Carmen Strachan, MSW,
Marcus McKinney, DMin,
Judith Fifield, PhD,
Adwoa Dadzie, and
Melanie Peele, MA.

Donaghue Initiative in Biomedical and Behavioral Research Ethics

In 1997, the Yale University Interdisciplinary Bioethics Project (IBP) was established to coordinate, facilitate and support the work of Yale faculty and students in the area of bioethics — a field, in the words of the project's mission statement, "that addresses questions of life and death, vulnerability and possibility, in human existence and the whole of nature." A \$2.1 million Practical Benefit Initiatives grant from the Donaghue Foundation will be used to create a Donaghue Initiative in Biomedical and Behavioral Research Ethics within the Yale IBP, with the specific purpose of supporting work on the ethical dimension of medical research — a new element that will strengthen the overall project and importantly promote the development of ethical practices in medicine and research.

"Research involving human subjects is essential to improve the ability of the health care delivery system to provide prevention and treatment for diseases," says **Robert J. Levine, MD**, Professor of Medicine, who co-chairs the Yale IBP with **Margaret A. Farley, PhD**, the Gilbert L. Stark Professor of Ethics at the Yale Divinity School. "Clearly, it is essential that this research be carried out in compliance with ethical and legal standards designed to protect the rights and welfare of the research subjects."

According to Levine, different contributions can be expected of each of the essential components of the Donaghue Initiative. "For example, new knowledge about the nature of research ethics will emerge from our sponsorship of individual researchers in the small grants program and through our support of visiting scholars and bioethicists-in-residence. In addition, new and existing knowledge will be shared through the development of a program to engage members of institutional review boards (IRBs) throughout Connecticut in a network designed to exchange experiences and to present and discuss the results of scholarship and policy development in the field."

Levine notes that experts in the field of ethics will be available to help scientific researchers and IRB members carry out the ethical analysis of the problems they face. "This blend of expertise is likely to produce valuable insights into problem-solving in the practical world. The practical benefit, then, will be the enhanced protection of human subjects and, by increasing public confidence in the adequacy of such protection, increased support for the conduct of the scientific research."



From left to right:
Robert J. Levine, MD,
Margaret A. Farley, PhD,
and Julius Landwirth, MD, JD

Early Schizophrenia Initiative

Scott Woods, MD, Associate Professor of Psychiatry at Yale University School of Medicine, is the recipient of a five-year, \$1.6 million Practical Benefit Initiatives program grant that will enable Woods and his research team to continue their study of early schizophrenia. Woods hopes to develop increasingly successful methods of identifying people who have symptoms of the early — prodromal — phase of schizophrenia. “Current treatment guidelines for schizophrenia apply only to the phase of illness after patients have become frankly psychotic,” says Woods. “Most studies with anti-psychotic medication suggest that treatment beginning shortly after patients have become frankly psychotic may be associated with better long-term outcomes than delayed application of the same treatment. These results suggest that earlier intervention yet may be associated with even better long-term outcomes.”

According to Woods, little information is available regarding the pathophysiology of the prodromal phase of schizophrenia and, as yet, there is no standard of care to guide treatment for patients. “Our investigators at Yale are among the world leaders in this area. The Donaghue Foundation grant will help keep Connecticut at the forefront of efforts to prevent chronicity in schizophrenia.”

Specifically, Donaghue funds will support the PRIME Research Clinic at Yale, where studies will be undertaken in the areas of early detection, identification, monitoring, and intervention. The Donaghue grant also will enable the early schizophrenia research program to be expanded to the Institute of Living in Hartford. “To date, our work suggests that schizophrenia can be identified before frank psychosis with excellent reliability and good validity,” says Woods. “The Donaghue Early Schizophrenia Initiative research is designed to improve further the overall accuracy with which these patients can be diagnosed. The most exciting aspect of the work is seeing that patients diagnosed early can have an unusually complete response to treatment and that many of them enter a very high quality remission. These excellent results can usually be achieved without the social damage that often occurs when treatment initiation is delayed.”

“The most exciting aspect of the work is seeing that patients diagnosed early can have an unusually complete response to treatment and that many of them enter a very high quality remission.”

programs

The Donaghue Foundation conducts several programs and initiatives in support of Connecticut-focused research and related work. Interested persons should contact the Executive Director for detailed program information and application forms.

Investigator-Initiated Research:

(1) The Clinical and Community Health Issues Program is for health-related research projects that address major medical conditions and social problems affecting the health of individuals, groups and communities. Of particular interest are studies focusing on more effective methods of preventing, diagnosing, and treating illnesses and conditions that have a major impact on health in Connecticut. C&CH grants are up to \$240,000 over periods of one to three years. Applications are invited after scientific and policy review of statements of intent.

(2) The Donaghue Investigator Program supports particularly promising medical researchers holding faculty appointments at Connecticut institutions. The program emphasis is upon the researcher rather than upon a specific research project. Annually, up to four awards of \$100,000 per year, for up to five years, are made.

Practical Benefit Initiatives:

The PBI program has no specific timeline for applications and no pre-determined award amounts. The Foundation itself initiates research projects in an interactive process with prospective investigators. Funding is based upon promise of practical benefit to human life and a likelihood that but for the Foundation's support, the research might not be done.

(1) Targets of Research Opportunity: The Foundation actively seeks funding opportunities for timely and needed research projects outside the parameters of Investigator-Initiated Research programs.

(2) Focused Centers of Research: The Foundation invites discussion of proposed programs of coordinated research effort. The Foundation prefers collaborative, multidisciplinary, integrative programs that are patient-oriented and/or community-focused and that target understudied fields or populations.

(3) Knowledge at Work: The Foundation supports research focused specifically on improving the ways new discoveries are translated into useful knowledge and disseminated to the point of actual use.

(4) Trustee Initiatives: In addition to the programs above, the Trustees are prepared to spend a small percentage of each year's grant funds on exploratory undertakings that further Foundation purposes.

NEW AWARDS

RESEARCH IN CLINICAL & COMMUNITY HEALTH ISSUES

Tony George, MD

Yale School of Medicine

*Nicotinic antagonist augmentation of SSRI antidepressants***Karl Insogna, MD**

Yale School of Medicine

*Dietary protein impacts calcium and bone metabolism***George Kuchel, MD**

University of CT Health Center

*Urinary incontinence in the elderly: A Translational Approach***Jeffrey Kahn, MD, PhD**

Yale School of Medicine

*Epidemiological investigation of human respiratory viruses***Naveed Hussain, MBBS**

University of CT Health Center

Regional database to study outcomes in premature babies

DONAGHUE INVESTIGATOR

Elizabeth Bradley, PhD

Yale School of Medicine

*Quality improvement efforts in the care of older adults***Barbara Kazmierczak, MD, PhD**

Yale School of Medicine

*The role of epithelial cells in host defense against pathogens***Kevin Claffey, PhD**

University of CT Health Center

Mechanisms of MT1-MMP-dependent breast cancer metastasis

PRACTICAL BENEFIT INITIATIVES

Judith Fifield, PhD

St. Francis Hospital & Medical Center

*Hospitals and Churches: Partnership to Improve Health***National Patient Safety Foundation**

James Judge, MD

*Clinical decision support to reduce adverse drug events in high risk home care patients***Scott Woods, MD**

Yale School of Medicine

Donaghue Early Schizophrenia Initiative

CONTINUATION AWARDS

DONAGHUE INVESTIGATOR PROGRAM

Stephen Devoto, PhD

Wesleyan University

*Developmental Biology: Study of muscle cell development in vertebrates using zebra fish***Mark B. Gerstein, PhD**

Yale University

*Genetics: Analysis of gene sequences and protein structures***Carlos Grilo, PhD**

Yale University School of Medicine

*Psychiatry: Treatment of binge eating and obesity***Stephen Helfand, MD**

University of Connecticut Health Center

*Geriatrics: Molecular genetics of aging***Sandra Hewett, PhD**

University of Connecticut Health Center

*Neuroscience: Mechanisms of inflammatory central nervous system injury***Sharon K. Inouye, MD, MPH**

Yale University School of Medicine

*Geriatrics: Delirium and functional decline in hospitalized older persons***Zeev Kain, MD**

Yale University School of Medicine

*Pediatrics: Anxiety in children undergoing surgery***Stephen King, PhD**

University of Connecticut Health Center

*Biochemistry: Intracellular transport and the regulation of molecular motor-cargo interactions***Richard Marottoli, MD, MPH**

Yale School of Medicine

*Enhancing older driver safety and mobility***Ishita Mukerji, PhD**

Wesleyan University

*Molecular Biology & Biochemistry: Structural studies of sickle cell hemoglobin fibers***Nancy Petry, PhD**

University of Connecticut Health Center

*Psychiatry: Brief interventions for problem gamblers***Carol Pilbeam, MD, PhD**

University of Connecticut Health Center

*Development of new therapies for increasing bone formation and treating osteoporosis***Robert Reenan, PhD**

University of Connecticut Health Center

*Changes in ion channel and receptor function in brains of adults***David Rimm, MD, PhD**

Yale University School of Medicine

*Cancer: Adhesion protein expression as mechanism to predict metastasis***Scott Rivkees, MD**

Yale University School of Medicine

*Pediatrics: Prevention of brain injury in premature infants***Stephen Strittmatter, MD, PhD**

Yale University School of Medicine

*Neurology: Axonal regeneration after spinal cord injury***Joann Sweasy, PhD**

Yale University School of Medicine

Genetics: Understanding how mutations occur during meiosis

awards

RESEARCH IN CLINICAL AND COMMUNITY
HEALTH ISSUES**Deepak D'Souza, MD**

Yale School of Medicine

*D-serine treatment of negative symptoms in Schizophrenia***Ellen Dornelas, PhD**

Hartford Hospital

*Comprehensive treatment for low-income pregnant smokers***Caroline Easton, PhD**

Yale School of Medicine

*Substance Abuse/Domestic Violence treatment outcome study***Leighton Huey, MD**

University of Connecticut Health Center

*Event-related functional MRI of adult ADHD***Ralph Hoffman, MD**

Yale School of Medicine

*Transcranial magnetic stimulation and hallucinated voices***Beth Anne Jones, PhD, MPH**

Yale School of Medicine

*Chemotherapy, race & cancer survival***Gerald Leonard, MD**

University of Connecticut Health Center

*Non-invasive measures of auditory integrity in infants***Tandy Miller, PhD**

Yale School of Medicine

*Screen development to detect the schizophrenia prodrome***Cheryl Oncken, MD, MPH**

University of Connecticut Health Center

*Effects of nicotine on bone turnover in older women***Lois Sadler, RN, PhD**

Yale School of Nursing

*Intensive care for teens with negative pregnancy tests***Juan Salazar, MD**

Connecticut Children's Medical Center

*Erythema migrans-window to Lyme Disease pathogenesis***Victoria Seitz, PhD**

Yale School of Medicine

*Effects of a mentoring program on maternal & child health***David Tolin, PhD**

Institute of Living/Hartford Hospital

*Behavior therapy for medical nonresponders with OCD***William White, MD**

University of Connecticut Health Center

*Blood pressure measurement during pregnancy***Quing Zhu, PhD**

University of Connecticut

3-D ultrasound and NIR imaging for breast cancer detection

PRACTICAL BENEFIT INITIATIVES

Howard Bailit, DMD, PhD

University of Connecticut Health Center

Michelle Cloutier, MD

Connecticut Children's Medical Center

Public-Private Alliance Study: Easy Breathing (Asthma Study)**Howard Bailit, DMD, PhD**

University of Connecticut Health Center

Thomas Babor, PhD, MPH

University of Connecticut Health Center

Public-Private Alliance Study: Vital Signs (Substance Abuse)**Howard Bailit, DMD, PhD**

University of Connecticut Health Center

Mary Duncan, PhD

University of Connecticut Health Center

Public-Private Alliance Study: Domestic Violence**Virginia Ashby Sharpe, PhD**

The Hastings Center

Promoting Patient Safety: An Ethical Basis for Policy Determination**Jean Schensul, PhD**

Institute for Community Research

Improving Access to Mental Health Services for Older Adults in Hartford**Thomas Murray, PhD**

The Hastings Center

Ethical Issues in the Management of Financial Conflicts of Interest in Biomedical Research**Mary Tinetti, MD**

Yale School of Medicine

Dorothy Baker, PhD

Yale School of Medicine

CT Collaborative Fall Prevention Project**Sally Cohen, RN, PhD**

Yale School of Nursing

Judith Krauss, RN, MSN

Yale School of Nursing

Regina Cusson, RN, PhD

University of Connecticut School of Nursing

Program for the Study of Health Care Relationships**Carolyn Mazure, PhD**

Yale University School of Medicine

Ethel Donaghue Women's Health Investigator Program**Theresa Kosten, PhD**

Yale University School of Medicine

Early Life Stress and Cocaine Abuse in Male and Female Rats**Geraldine Pellecchia, PhD**

University of Hartford

Influence of Cognitive Activity on Coordination Dynamics

committees

CLINICAL & COMMUNITY HEALTH ISSUES
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Honorable Alvin W. Thompson

Windsor
Judge, US District Court, Hartford

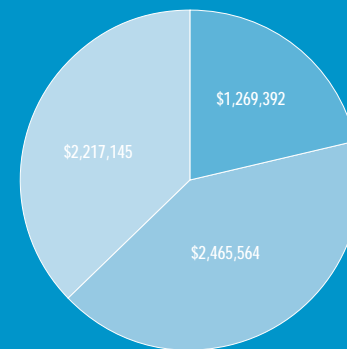
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grants

Institution	New	Continuation	Total
Connecticut Children's Medical Center	0	1	1
Hartford Hospital	0	2	2
The Hastings Center	0	2	2
Institute for Community Research	0	1	1
National Patient Safety Foundation	1	0	1
St. Francis Hospital & Medical Center	1	0	1
University of Connecticut Health Center	3	12	15
University of Connecticut-Storrs	0	1	1
University of Hartford	0	1	1
Wesleyan University	0	2	2
Yale University	0	1	1
Yale School of Medicine	6	16	22
Yale School of Nursing	0	1	1
Total	11	40	51

FUNDS AWARDED BY GRANT PROGRAM FOR GRANT CYCLE BEGINNING IN 2002

Research in Clinical & Community Health Issues	Total
New (5)	\$ 481,944
Continuing (12)	\$ 787,448
Donaghue Investigator Program	Total
New (3)	\$ 330,000
Renewal (17)	\$2,135,564
Practical Benefit Initiatives	Total
New (3)	\$ 482,800
Continuing (11)	\$1,734,345
Total	\$5,952,101



FUNDS AWARDED BY GRANT PROGRAM FOR GRANT CYCLE BEGINNING IN 2002: \$ 5,952,101

- Clinical and Community Health: \$1,269,392
- Donaghue Investigator Program: \$2,465,564
- Practical Benefit Initiatives: \$2,217,145

2002 Financial Information

Statement of assets and fund balance as of December 31, 2002

Investment in marketable securities	\$ 60,704,241
Cash and cash equivalent	\$ 3,642,902
Other assets	\$ 41,751
Total assets and fund balance	\$ 64,388,894

Statement of income and expenditures for the twelve months ended December 31, 2002

Income \$ 2,251,844

Expenditures

Program:

Grants	
Clinical and Community Health	\$1,454,762
Donaghue Investigator	\$2,465,564
Practical Benefit Initiatives	\$2,217,145
Subtotal	\$ 6,137,471 ¹
Program Support	\$ 194,243
Management and General	\$ 456,073
Investment Management	\$ 104,441

Total Expenditures \$ 6,892,228 ²

Note 1: Included in this figure is \$185,370 the Foundation facilitated in grants for medical research from other foundations or philanthropic sources.

Note 2: In addition to these expenditures, an estimated amount of up to \$10,575,777 has been earmarked for future spending in support of ongoing grants.

The figures listed above are unaudited. Fair market values are approximate.

	\$7,080,735
	\$13,408,940
	\$35,637,383
	\$49,000,028
	\$53,436,074

TOTAL DOLLARS COMMITTED BY DONAGHUE AS OF DECEMBER 31, 2002: \$158,563,160

Expenses	\$ 7,080,735
Appreciation in value of gift	\$ 13,408,940
Income earned on funds	\$ 35,637,383
Grants	\$ 49,000,028
Original value of Ethel Donaghue's gift	\$ 53,436,074



LEAVE A LEGACY CONNECTICUT

Ethel Donaghue's legacy would be even more meaningful if her Foundation's efforts prompted others to support health research as a part of their own philanthropic planning. The Donaghue Foundation supports the work of Leave a Legacy Connecticut and encourages people to include charitable bequests for health research purposes in their wills. While the Foundation will accept additional funds itself only if they are solely and expressly for Miss Donaghue's own testamentary purpose, we do believe strongly in the public value of committing private sector resources to the ongoing cause of health research.

The Patrick and Catherine Weldon Donaghue
Medical Research Foundation
Eleventh Annual Report
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