TENTH

ANNUAL

REPORT

WORK IN PROGRESS

THE PATRICK AND CATHERINE

WELDON DONAGHUE MEDICAL

RESEARCH FOUNDATION

2001

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

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

LETTER FROM THE TRUSTEES

Annual report letters are a welcome occasion for the Donaghue Trustees to reflect — on the year just ended and also on large issues facing the Foundation we oversee. Each letter offers an opportunity for comment on the annual report it introduces and, in doing so, for conveying a sense of our philosophy and vision and our commitment to carrying out Ethel Donaghue's beneficent purpose: promoting practical benefit to human life through the disciplined study of health questions. The exercise of sitting down to compose the letter is a welcome respite from the routine and a chance to put things in perspective.

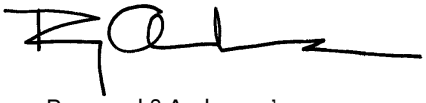
We were all forced to put things in perspective on one infamous day in 2001 — the unforgettable September 11th — which cast a lingering dark shadow over all of our lives — over everything we believe in. The shocking news caught us at the Foundation in the midst of finalist interviews for our Donaghue Investigator awards. Like so many others who were hit so much harder, we pressed on, believing that, in the words of one indignant observer, the September 11th terrorists "hit the buildings but missed America."

We have been blessed by the capable assistance of a cadre of policy and science advisers who have always stepped forward to lend a willing hand.

In recent months we've had occasion to revisit this thought of purposeful perseverance, as the stock markets reversed a dizzying upward trend we had become accustomed to for several years. Though recession undermined our portfolio, we pressed on with our mission while also gearing ourselves for a disciplined assessment of our policies. We completed successful cycles of investigator-initiated research in 2001, launched two important Practical Benefit Initiatives, and actually ended the year with our highest level of research grant-making ever — well over $8 million - more than 10% of our year-end assets.

In the realm of reversals and responses, there's an old folk saying, "Many hands make light work," that focused us on our imagery for this report on Donaghue's eventful 2001. Since our first days, we have been blessed by the capable assistance of a cadre of policy and science advisers who have always stepped forward to lend a willing hand. So we'll take this opportunity to give them a hand and express our deep appreciation for their service to Miss Donaghue's purpose. While all the advisers listed in this report deserve great credit, surely one stands out for particular recognition. Howard Bailit, DMD, PhD, has been a linchpin of our Foundation work since 1994, stepping up repeatedly not only to participate but to lead – and, further, to bridge skillfully the divide between science and those of us outside science. Our most sincere thanks go out to Dr. Bailit for his countless key contributions.

"Hands" is a timely focus in view of recent news about patient care and research errors. James Conway, chief operating officer of Dana-Farber Cancer Institute and a veritable crusader for patient safety, said of the circumstances at his hospital when a patient died from a chemotherapy dosing error several years ago, "We were all working *hard*, but we weren't working *together*." A recent Institute of Medicine report, Bridging the Quality Chasm, targeted our fragmented health care system as a cause of lapses in quality; the report strongly advocated working toward a seamless, integrated system. Donaghue believes strongly in bridging gaps, in collaborating, in gripping hands with others in a cause that is common to all who work to improve human health. And, as this year's report suggests, we see ourselves and our efforts as a patient, determined work in progress.



Raymond S. Andrews, Jr.
Trustee

Sheilah B. Rostow
Senior Vice President, Fleet Bank
Trustee

Donaghue believes strongly in bridging gaps, in collaborating, in gripping hands with others in a cause that is common to all who work to improve human health.

HANDS-ON

Sheilah B. Rostow, Senior Vice President, Fleet Bank, Trustee and Raymond S. Andrews, Jr., Trustee

PURPOSE AND PROLOGUE

A Working Document

The theme of the Patrick and Catherine Weldon Donaghue Medical Research Foundation's 10th annual report — "Work in Progress" — is especially appropriate for two reasons. First, the report is about the extraordinary work being done by teams of talented researchers carrying out the stipulations in Ethel F. Donaghue's will, which devotes nearly all of her family's wealth to the search for useful knowledge about human health. Second, it also is about a work in progress, the Donaghue Foundation itself, which, despite its accomplishments to date, continues to "redesign" itself to maximize its effectiveness in health research grantmaking.

To carry out the search for useful knowledge of "practical benefit to … human life," Miss Donaghue, who died in 1989, created a charitable trust of more than $50 million in honor of her parents, Patrick and Catherine Weldon Donaghue. Her will was to be a working document that addresses human needs by providing a helping hand — in the form of generous financial resources — for people (including those featured in this report) who have the expertise and dedication to achieve that practical benefit.

As we work and rework assumptions as to what is being done and what more we need to do, we are confident that the body of work the Foundation has supported over the last decade would earn a "thumbs up" from Miss Donaghue.

As a working woman — and one of Connecticut's first woman lawyers — Ethel Donaghue undoubtedly appreciated how difficult the process of carrying out her wishes might — perhaps should — be. When she put her fortune in our hands, she wanted those involved in carrying out her vision to work at it — to evaluate and re-evaluate what should be done to benefit the people who needed it most. As we work and rework assumptions as to what is being done and what more we need to do, we are confident that the body of work the Foundation has supported over the last decade would earn a "thumbs up" from Miss Donaghue.

There is, of course, a lot more on our agenda. Miss Donaghue's will permits the spending of trust principal for "unusual" and "non-standard" activities, enabling — and challenging — her trustees to "do whatever they deem necessary or desirable" to further her purpose. While we appreciate the trust she has placed in us, it would have been far easier if she had just told us what to do.

But "easy" is not what meaningful work is all about. As you will see in this report, the challenges facing Donaghue Investigators, Clinical and

Community Health Program grantees, and recipients of Practical Benefit Initiative grants are daunting, particularly in today's economic and health care environment. Yet, every one of them shares a drive and an optimism about what their hard work can do to get a better grip on some of our most pressing medical and social problems, particularly those close to home.

The work most recently funded by the Donaghue Foundation is taking place in various venues, including research laboratories in Connecticut's leading hospitals and universities, independent research institutes in Connecticut and New York, and senior housing complexes in Hartford. While these settings are very different from one another, the goals of Foundation researchers are very much consistent with our determination that the work benefit disadvantaged or understudied populations. This year, those populations include people with schizophrenia or obsessive-compulsive disorder, older people dealing with osteoporosis and the loss of driving privileges, African Americans with certain types of cancer, adults with ADHD, and others.

As we look ahead, we know that while the medical community is making great strides in many important areas, there always is more work to do. We are not bowed by this prospect for we have seen that Ethel Donaghue's own handiwork — her last will and testament — is making a difference in the lives of the many people for whom the Foundation's support is reaping practical, hands-on benefits.

Since the Donaghue Foundation began its grantmaking, almost $43 million have been put to work in important health research projects — a number that is beginning to approach the total amount Miss Donaghue initially gave us to carry out her vision in 1989.

That's work — and progress.

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2001

THE YEAR IN REVIEW

The Donaghue Foundation began 2001 with a lot of internal work to do as a result of the "circling back" assessment we had conducted during 2000. A lot of new Foundation knowledge needed to be translated into structure and process improvements, and we tackled the job right away.

We developed a strategic communications plan to support the translation of research results into practice and connect the Foundation itself more closely to its various constituencies. We strengthened our staff by the creation of a new position: Director of Program Development and Evaluation. Staffers Maggie Willard and Jacque Watson were joined in September by Lynne Garner, PhD, who promises to bolster the Foundation's program capabilities as we proceed in our second decade of grantmaking.

We developed a strategic communications plan to support the translation of research results into practice and connect the Foundation itself more closely to its various constituencies.

After examining the workings of our advisory mechanisms, we refined them in several ways, looking to a flexible and productive future. We created a new Program Advisory Committee, which we're confident will serve two important purposes: it will give meaningful support to Dr. Garner in her program work and at the same time provide our policy advisers a clearer window into program matters. The Policy Advisory Committee continues to be tuned by the blending of more science expertise into the mix; we envision an eventual ongoing conversation across the gap between science and the community, a conversation that will keep Donaghue alert and opportunistic in our work. Finally, we shuffled the line-up of advisory leadership, both to bring more scientists into closer proximity to the Foundation and to facilitate assigning Dr. Howard Bailit to yet another pioneering role, that of chairing the new Program Advisory Committee.

As the Foundation's internal remodeling went on through 2001, we pressed forward with our Practical Benefit Initiatives program, making two key PBI grants. We progressed in our fashioning of an emphasis on ethics by launching a bold inquiry by Thomas Murray, PhD, and The Hastings Center into the troubling national problem of financial conflicts of interest in health research. The credibility of research reports, the trust the public has in science, the willingness of people to continue playing the role of human research subject — all of these are critical to the long-term success of the research enterprise we count on for medical advances. The Hastings Center project seeks to identify ways to advance both science and the public interest in these changing, challenging times.

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A second PBI grant was made to a collaboration of researchers headed by the local Institute for Community Research.The project,led by Jay Schensul,PhD, focuses on a very real, very serious, very practical issue:clinical depression among older citizens that goes undiagnosed and untreated because of access barriers confronting them.An important aspect of the project is its attention to learning about how diverse ethnic groups differently experience and deal with similar health problems.

The Donaghue Investigator program continued to assemble an impressive cadre of research talent — across Connecticut and in an increasingly diverse pattern of studies.The addition of three 2001 Donaghue Investigators examining osteoporosis, safety of older motorists,and brain function brings the Foundation's complement to seventeen Investigators and our annual investment in the program to more than $2 million.A roughly comparable amount — $1.7 million — was invested in 2001 in the work of Clinical and Community Health Issues researchers hard at work on a wide variety of studies.

Even as the Foundation's investments were buffeted by recessionary market trends during 2001,our program investments — largely driven by continuing commitments to multi-year projects but also fueled by an abiding determination to put Donaghue money to productive work in research — continued apace, and we finished the year with an aggressive $8.7 million in expenditures.As our funded research projects went on around the state, we in the office continued to explore several interesting topics: research opportunities in patient safety, further ways to align ethical analysis with scientific progress,and techniques for concentrating research resources and effort on public health issues.While we were comfortable with our work in 2001, we weren't satisfied.

We never will be, and that attitude propels the Donaghue Foundation into the work of 2002.

As our funded research projects went on around the state, we in the office continued to explore several interesting topics: research opportunities in patient safety, further ways to align ethical analysis with scientific progress, and techniques for concentrating research resources and effort on public health issues.

"My passions are cars and history, which my research interest combines nicely."

Richard Marottoli,MD, MPH

DONAGHUE INVESTIGATOR

Richard Marottoli,MD, MPH

Richard Marottoli,MD, MPH,Associate Professor of Internal Medicine at Yale School of Medicine, is conducting research that he hopes will enhance the safety and mobility of older drivers — an issue that will affect virtually everyone. "It is clear that the number of injuries and fatalities from motor vehicle crashes involving older drivers is on the rise," says Marottoli,"due in large part to their increasing population and inherent frailty in response to trauma."

Whether older drivers are more likely to be involved in accidents depends on how the data is interpreted.There is no question,however, that driving is critical to maintaining independence for older people — an important quality of life issue. As one of Marottoli's patients said when told he should not drive anymore, "You might as well hang a rope around my neck."

Marottoli's body of research will help define which drivers are at greater risk for safety problems, what interventions can be implemented to enhance the safety of those identified,and in cases where interventions are not possible, how to make the transition to driving less — or not driving at all — more successful.

"There are a number of exciting challenges in the work we are doing," says Marottoli."Can we eventually effect change in societal attitudes toward older drivers,especially when preliminary evidence suggests that it is not the entire population of older drivers that may be at increased risk, but rather a smaller segment with certain conditions or impairments? Given time constraints on practicing clinicians,can sufficiently simple and effective tests to gauge risks be developed that are likely to lead toward successful strategies to enhance safety? And can we identify approaches — including alternative transportation sources — for helping to maintain mobility and activity levels for older people who need to limit or stop driving?"

Marottoli is confident that over the next five years his work will go a long way toward addressing those challenges.

From left to right: **Robert Reenan,PhD, Richard Marottoli,MD, MPH,Carol Pilbeam,PhD, MD**

WORKING WONDERS

DONAGHUE INVESTIGATOR

Carol Pilbeam,PhD, MD

Osteoporosis — decreased bone mass leading to fragile bones and increased risk for fracture — is a major cause of disability in older people. With her Donaghue Foundation grant,Carol Pilbeam,PhD, MD, Assistant Professor of Internal Medicine at UConn Health Center, expects to "improve our understanding of the mechanisms underlying this disease" — which contributes to 1.3 million hip and spine fractures in the U.S.each year.

"Throughout life, bone is undergoing cycles of resorption (removal of mineralized bone) followed by formation of new bone," says Pilbeam."The net balance of these cycles determines bone mass." Maintenance of bone mass is dependent on the ability of bone-forming cells (osteoblasts) to proliferate and differentiate into cells that can secrete new bone matrix.

"Menopause in women and aging in general are characterized by increased bone turnover in which more bone is removed than formed," says Pilbeam."Current medical therapies inhibit bone resorption,but have limited ability to replace lost bone, which can be up to 50% of peak bone mass in the very old. My research is aimed at gaining a better understanding of factors regulating osteoblastic differentiation,proliferation and apoptosis (programmed cell death) so that we will be able to increase bone formation more than resorption." Pilbeam's research will also address whether certain anti-inflammatory drugs used to treat pain secondary to osteoarthritis and rheumatoid arthritis might actually increase bone loss.

Pilbeam notes that osteoporosis has yet to be "cured" because "we have limited ability to replace bone once it has been lost from the skeleton." While osteoporosis is most prevalent in postmenopausal white women,it is now recognized as a significant problem in older men and aging Orientals and Hispanics. "As a geriatrician,one of my major goals is to improve the quality of life of the elderly. I hope that my research will ultimately contribute to the development of new, more effective therapies for this debilitating disease."

"I like to cook, read mystery books and travel,but 'who I am' is probably best described by my desire to see older patients get appropriate care."

Carol Pilbeam,PhD, MD

The Donaghue investigators featured here are working on very different bodies of research with one important goal in common: they all hope to work wonders.

"What I do outside the lab pretty much involves the outdoors: hiking with my collie Gregor (named after Gregor Mendel,of course),mountain biking (in which I have this tendency to plummet…) and watching hawks."

Robert Reenan,PhD

DONAGHUE INVESTIGATOR

Robert Reenan,PhD

With his Donaghue Foundation grant, Robert Reenan,PhD, Assistant Professor of Genetics and Developmental Biology at UConn Health Center, is studying how normal and diseased brains function by looking at the electrical signaling process."Rapid, reliable and efficient electrical signaling is an absolute necessity for normal human function," stresses Reenan."It also is taken for granted until something goes wrong with signaling in ourselves or someone we know."

Because certain processes involved in proper brain function are common in humans and fruit flies,Reenan's research will focus on behavior and brain function in this ubiquitous insect."Our research addresses basic questions in the fly," says Reenan,"using mutations that essentially cause neurological disorders."

Reenan's preliminary work shows that adult flies lacking a particular enzyme (dADAR) exhibit a neurological disorder that causes poor coordination,tremors and seizures."We have shown that when the enzyme is supplied to adults who suffer from this defect…they essentially recover much of their normal function," says Reenan."In a very real sense, we have found a way to 'treat' a disorder in flies by adding back an enzyme function that humans also possess,but for which no human disease has yet been identified.Thus, we have preemptory data on how to treat a disease in a model organism,and this data may be extremely beneficial in treating human diseases arising from a genetic defect in the same process."

Reenan believes his findings could have a positive impact on how the human nervous system functions with aging."Since the research my lab is doing is not aimed at any specific disease but rather a better understanding of how normal and diseased brains function in general,the potential for enhancing the quality of life is substantial.Can we extend the quality of life in terms of how our nervous systems function with advancing age, without necessarily extending life itself? I think there is a compelling need to find this out."

CLINICAL AND COMMUNITY HEALTH ISSUES PROGRAM

From left to right:
David F. Tolin, PhD
Quing Zhu, PhD
Deepak D'Souza, MD
Beth A. Jones, PhD, MPH
Leighton Y. Huey, MD
Tandy Miller, PhD

D-Serine Treatment of Negative Symptoms in Schizophrenia

Over the next three years, Deepak D'Souza, MD, Associate Professor at the Yale School of Medicine, will use his Clinical and Community Health Program grant to test his belief that the amino acid D-serine can correct reduction in brain NMDA receptor function (a specific chemical messengering system) and, as a result, reduce negative and cognitive symptoms of schizophrenia.

"Existing drug treatments have proven to be effective against positive symptoms of schizophrenia like hallucinations, delusions and disorganized thinking," says D'Souza, "but have limited efficacy against negative symptoms (such as decreased motivation and drive and social withdrawal) and cognitive symptoms (which include deficits in learning, memory, abstraction and intelligence)" — symptoms that can have a devastating impact on patients and their families.

"Work at our center has shown that the same principles that apply to rehabilitating patients who undergo brain injuries such as stroke may be applied to retrain fundamental cognitive processes in patients with schizophrenia," adds D'Souza. He believes that D-serine, by increasing NMDA receptor function in the brain, will enable schizophrenic patients to derive greater and sustained benefit from cognitive retraining.

Treatment with D-serine is a relatively new strategy for addressing some of the symptoms of schizophrenia. "If our approach proves to be beneficial, it may allow patients with schizophrenia to lead more productive lives," says D'Souza, "which, in turn, will significantly impact the socioeconomic burden of schizophrenia on the community at large."

HELPING HANDS

This year's Clinical and Community Health Program grant recipients are helping to address major medical conditions and social problems in Connecticut with a hands-on approach to their research.

"We hope to confirm that there is abnormal activity in brain regions known to be important to attention and behavior regulation."

Leighton Y. Huey, MD

Event-related Functional MRI of Adult ADHD

Leighton Y. Huey, MD, Professor and Chairman of the Department of Psychiatry at UConn Health Center, will undertake the first study of its kind to systematically use functional neuroimaging (fMRI) and neuropsychological and behavioral data to determine whether brain-imaging data can help in diagnosing attention deficit hyperactivity disorder (ADHD) in adults.

Until recently it was thought that children and adolescents with ADHD outgrew it when they became young adults. According to Huey, "the field now believes that a significant percentage of adolescents (1-3%) will continue to have some or all of the same kinds of problems in adulthood, affecting achievement, performance, and social interactions."

Currently, little is known about how the brains of people with ADHD function differently from persons without the disorder. In addition, because ADHD symptoms are common to other psychiatric conditions (such as depression and anxiety), diagnosis is often difficult. "We hope to confirm that there is abnormal activity in brain regions known to be important to attention and behavior regulation," says Huey. "Ideally, we believe that brain function patterns will have logical relationships with the symptoms of ADHD. It is equally likely that we will discover abnormalities in brain areas we have not previously considered important to ADHD.

"Understanding ADHD brain function will ultimately lead to better and more targeted treatment approaches for the nearly 100,000 adults in Connecticut who are estimated to suffer from the disorder," Huey concludes.

Chemotherapy, Race and Cancer Survival

Beth A. Jones, PhD, MPH, Assistant Professor of Epidemiology and Public Health at the Yale School of Medicine, is studying four common cancers whose outcomes are generally worse for African Americans than for whites. "Learning more about the role of genetic polymorphisms and survival from cancer might help explain why some patients, even when diagnosed at the same stage, don't fare as well as others," says Jones.

Specifically, Jones and her collaborator, John Wise, PhD, aim to determine if certain Glutathione-S-transferases (GSTs), a family of genes that some people lack (and which are involved in the metabolism of chemicals), are associated with survival in breast, uterine, colorectal and prostate cancer, and whether these genetic polymorphisms "modulate the association between chemotherapy and survival…and occur with the same frequency in African American and white patients."

While Jones notes that epidemiologists often focus on a specific disease or exposure (such as

HELPING HANDS

nutrition,lifestyle and psychosocial factors),her research is broad-based and problem focused."I am trying to understand the factors that contribute to the observed race/ethnic differences in cancer. As such, my research addresses race-specific factors that impact adherence to cancer screening guidelines,breast density, and a wide-ranging set of factors — from sociodemographic and psychosocial factors to tumor characteristics and genetic alterations that impact survival. My hope is that the project will contribute to our growing understanding of the observed race disparities in survival from some cancers."

Screen Development to Detect the Schizophrenic Prodrome

According to Tandy Miller, PhD, Assistant Clinical Professor at the Yale School of Medicine's Psychiatric Institute, a prodromal, or symptomatic pre-psychotic, phase of schizophrenia has been recognized for more than a century. Yet,in spite of the fact that early intervention may significantly improve the natural course of psychosis,no practical and comprehensive screen has been developed to identify people in the prodromal phase of schizophrenia. Miller and her co-researchers propose to do exactly that with their two-year Clinical and Community Health Program grant.

Miller believes that identification of patients in a prodromal state may be important for two reasons. "First, early identification can enable anti-psychotic treatment to be given at the onset of schizophrenic psychosis.Second,as one yet-to-be published study suggests,identifying and treating patients in the prodromal phase appear to prevent or delay the onset of psychosis in a significant proportion of patients."

Miller and her collaborators at Yale hope to develop a powerful screening tool that eventually could be used throughout the country. "Our growing data on young people evaluated as being prodromal for psychosis will facilitate the development of this screen.Further, our working relationships with the Connecticut school system, the juvenile justice system and local pediatric practices place us in a unique position to ensure a high rate of screen returns and accomplish this next important step in the early detection of schizophrenia."

Behavior Therapy for Medication Nonresponders with OCD

Obsessive-compulsive disorder (OCD) is a common and debilitating psychiatric illness.While psychiatric medication is the most common treatment for OCD, David F. Tolin,PhD, Director of the Anxiety Disorders Center at the Institute of Living/Hartford Hospital,believes medication may not be the best treatment option."Behavior therapy

"Learning more about the role of genetic polymorphisms and survival from cancer might help explain why some patients, even when diagnosed at the same stage, don't fare as well as others."

Beth A. Jones,PhD, MPH

appears to be at least as effective as medications, perhaps more so," says Tolin, "and costs much less in the long run. Our research aims to address two specific questions: First, is behavior therapy effective for people with OCD who have failed to respond to medication? Second, to what extent can people with OCD be taught to carry out their own behavior therapy programs?"

To date, Tolin's research has shown that behavior therapy is effective for a broad range of anxiety-related disorders. "I am particularly interested in developing ways to integrate behavior therapy into healthcare networks so that they are readily available and cost-effective," stresses Tolin. "To do this, I am developing a series of studies that will answer 'real-world' kinds of questions about behavior therapy for anxiety disorders."

In the next few years, Tolin's team hopes to have developed a behavior therapy program that can be integrated with the existing healthcare system. "To accomplish this, we will need to be able to answer questions about what type of treatment (such as therapist-administered or self-administered behavior therapy) works best under which circumstances."

"The most promising aspect of our dual-modality imaging is the significant reduction we expect to achieve in the total number of false breast biopsies among a large pool of cancer patients."

Quing Jhu, PhD

3-D Ultrasound and NIR Imaging for Breast Cancer Reduction

Quing Zhu, PhD, Associate Professor of Bioengineering at the University of Connecticut in Storrs, is working with three co-investigators to improve breast cancer detection and diagnosis through the use of simultaneous ultrasound and near infrared (NIR) diffusive light. Zhu's research project is being funded under a three-year Clinical and Community Health Program grant of approximately $180,000.

Today, ultrasound is commonly used in conjunction with mammography to differentiate simple cysts from solid lesions. When the criteria for a simple cyst are strictly adhered to, the accuracy of ultrasound is 96%-100%. However, with ultrasound, certain features of benign and malignant lesions overlap, prompting many radiologists to recommend biopsies on most solid nodules. "This results in a large number of biopsies yielding normal or benign breast tissue," says Zhu, who adds that currently 70% to 80% of biopsies are normal.

According to Zhu, NIR imaging is extremely sensitive to functional parameter changes of early breast tumors. "Simultaneous imaging will add optical parameters to ultrasonically detected lesions," he says. "Our hybrid imaging system is designed to combine the high sensitivity of NIR imaging in distinguishing between benign and malignant lesions with the high spatial imaging resolution inherent in ultrasound. The most promising aspect of our dual-modality imaging is the significant reduction we expect to achieve in the total number of false breast biopsies among a large pool of cancer patients."

PRACTICAL BENEFIT INITIATIVES

Through its Practical Benefit Initiatives program, the Donaghue Foundation helps to initiate integrative research projects showing particular promise for producing practical benefit to human health.

Improving Access to Mental Health Services for Older Hartford Residents

The Hartford-based Institute for Community Research (ICR) is partnering with the North Central Area Agency on Aging, the Hartford Housing Authority, and the Braceland Center for Mental Health and Aging at the Institute of Living on a three-year study of depression in older adults living in senior housing in Hartford. The study will assess the prevalence of depression and anxiety among these residents, refer those with diagnosed conditions to appropriate clinical care, and follow them to identify factors that may facilitate or impede their care.

"Our study will provide new information on the mental health status of a large group of older adults from diverse ethnic backgrounds and experiences," says Principal Investigator Jay Schensul, PhD, "particularly information on anxiety, depression, and somatic symptoms. This information will be useful for clinicians and others in our network, including clinicians planning to deliver services in the buildings in which we conduct our research. It also will add to scientific knowledge about mental health in minority and low-income older adults."

Left to right: **William B. Disch, Ph.D, Senior Research Analyst, Sonia Gaztambide, M.P.H, Community Researcher, Jay Schensul, Ph.D, Principal Investigator, Kenneth Brockman, Community Researcher, Carmen Y. Reyes, M.S.M., Site Principal Investigator, and Julie Robison, Ph.D., Site Principal Investigator.**

The ICR study also aims to better understand barriers to mental health services for older adults who don't speak English, whose literacy levels are low, and who have experienced challenges in seeking quality health and mental health care. "It also will add to our understanding of how older adults of diverse ethnic backgrounds conceptualize, describe and report sadness, depression and associated losses," says Schensul. "Understanding local or indigenous definitions of depression and anxiety will add to the scientific literature on these topics — and enhance clinical treatment of older adults in Hartford."

"Our mission is to support the use of research in the identification and solution of human problems in marginalized, poor, or underserved communities."

Jay Schensul, PhD

AN INTERACTIVE PROCESS

THE HASTINGS CENTER

Over the last few years, the Donaghue Foundation has awarded Practical Benefit Initiative grants to The Hastings Center, an independent research institute based in Garrison, New York, that addresses fundamental ethical issues in the areas of health, medicine and the environment.

Ethical Issues in the Management of Financial Conflicts of Interest in Research in Health, Medicine and the Biomedical Sciences

According to Hastings Center President Thomas Murray, PhD, dramatic changes in the structure and financing of biomedical research have brought opportunities for financial gain to investigators, universities, medical centers and others in the biomedical research world. Those changes also have enhanced the potential for financial conflicts of interest.

What are the potential effects of new financial arrangements on the safety of research subjects, the process of obtaining informed consent, and the integrity of the research? What will be the impact on the traditions of scientific cooperation, the free flow of information and educational process as universities become increasingly entrepreneurial? How will the practice of medicine be affected as research moves away from traditional academic settings?

From left to right:
Sheilah B. Rostow, Senior Vice President, Fleet Bank, Trustee, Raymond S. Andrews, Jr., Trustee and Thomas H. Murray, PhD, President of The Hastings Center

AN INTERACTIVE PROCESS. . .

PRACTICAL BENEFIT INITIATIVES

INGS CENTER

With a two-year, $400,000 grant from the Donaghue Foundation, the Hastings Center seeks to clarify these and other ethical issues arising from financial conflicts of interest in research in health, medicine, and the biomedical sciences. "The Hastings Center project differs from other comparable efforts in several ways," says Murray. "It is comprehensive and non-partisan, considering relationships among the different stakeholders without taking sides. It also seeks insights about conflict management from an interdisciplinary group of experts. Finally, it will anticipate future challenges and develop proactive approaches."

Project findings will be broadly disseminated to ensure that the many stakeholders in research can make constructive use of the Center's insights and recommendations.

Promoting Patient Safety: An Ethical Basis for Policy Deliberation

Nearly two years ago, the Donaghue Foundation awarded the Hastings Center a $205,000 Practical Benefit Initiative grant to help undertake a comprehensive patient safety project. According to the Center's Deputy Director Nancy Berlinger, PhD, the project, which got underway early last year, is exploring the ethical basis of patient safety proposals, many of which came out of *To Err is Human*, the Institute of Medicine's report on medical errors in the U.S. "Our project aims to promote ethically informed policy decisions on the federal, state and institutional levels," says Berlinger. Although Virginia Ashby Sharpe, PhD, the initial principal investigator, recently left the Hastings Center, she continues to work closely with Berlinger on the project.

The first project meeting addressed the economics of patient safety, the sociology of medical error, the ethics of how different kinds of errors are handled within healthcare institutions, and questions of moral and legal responsibility. The core group of experts convened for the project has since focused on issues related to disclosure and provider accountability. "Both meetings featured presentations by individuals who became advocates for patient safety following the deaths of family members as the result of medical error," says Berlinger.

In 2002, project participants will address compensation for injured patients, alternatives to malpractice litigation, and quality improvement within healthcare systems.

"Our project aims to promote ethically informed policy decisions on the federal, state and institutional levels."

Nancy Berlinger
Deputy Director
Hastings Center

. . . AN ONGOING INITIATIVE

FOUNDATION PROGRAMS

The Donaghue Foundation conducts several programs and initiatives in support of Connecticut-focused research and related work. Interested persons should contact the Director of Administration and Operations 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, about 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.



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Stanislav Kasl, PhD
Judith Kunisch,RN,MBA
TV Rajan,MD, PhD



AWARDS

RESEARCH IN CLINICAL AND COMMUNITY HEALTH ISSUES

Deepak D'Souza,MD
Yale School of Medicine
D-serine treatment of negative symptoms in Schizophrenia

Leighton Huey, MD
University of Connecticut Health Center
Event-related functional MRI of adult ADHD

Beth Anne Jones, PhD, MPH
Yale School of Medicine
Chemotherapy, race & cancer survival

Tandy Miller, PhD
Yale School of Medicine
Screen development to detect the schizophrenia prodome

David Tolin, PhD
Institute of Living/Hartford Hospital
Behavior therapy for medical nonresponders with OCD

Quing Zhu, PhD
University of Connecticut
3-D ultrasound and NIR imaging for breast cancer detection

DONAGHUE INVESTIGATOR PROGRAM

Richard Marottoli,MD, MPH
Yale School of Medicine
Enhancing older driver safety and mobility

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

PRACTICAL BENEFIT INITIATIVES

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

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 on 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

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

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

RESEARCH IN CLINICAL AND COMMUNITY HEALTH ISSUES

Cheryl Tatano Beck,DNSc
University of Connecticut School of Nursing
Screening hispanic mothers for postpartum depression

Sandra Bellantonio, MD
University of Connecticut Health Center
Quality care for assisted living persons living with dementia

Janet Brandsma, PhD
Yale University School of Medicine
Novel HPV probes to improve cervical cancer

Thomas Carpenter, MD
Yale University School of Medicine
Effects of magnesium nutrition on bone health

Jonathan Covault, MD, PhD
University of Connecticut Health Center
Markers of biological risk in schizophrenia

Anne Delany, PhD
St. Francis Hospital and Medical Center
Association of osteonectin mutations with osteoporosis

Peter DeLuca,MD
Sylvia Ounpuu, MSc
Connecticut Children's Medical Center
10-year follow-up of orthopedic surgery in Cerebral Palsy



AWARDS

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

Thomas Gill,MD
Yale University School of Medicine
Intervening events and functional decline in older persons

Gloria Gronowicz, PhD
University of Connecticut Health Center
Effect of aging on human bone cell/implant interactions

Ralph Hoffman,MD
Yale School of Medicine
Transcranial magenetic stimulation and hallucinated voices

Beth Anne Jones, PhD, MPH
Yale University School of Medicine
Mammographic patterns in African American & White Women in CT

Song Lai, PhD
University of Connecticut Health Center
Improved stroke outcome using quantitative functional MRI

Gerald Leonard, MD
University of Connecticut Health Center
Non-invasive measures of auditory integrity in infants

Robert Malison,MD
Yale University School of Medicine
Ketoconazole antagonism of cocaine-induced euphoria

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

Gerald Sanacora,MD, PhD
Yale University School of Medicine
Cortical GABA concentrations in depression

Eva Sapi, PhD
Yale University School of Medicine
A novel model system for the development of ovarian carcinoma

Victoria Seitz, PhD
Yale School of Medicine
Effects of a mentoring program on maternal & child health

Francisco Sylvester, MD
St. Francis Hospital & Medical Center
Crohn's disease and osteopenia

Pamela Taxel,MD
University of Connecticut Health Center
Effect of estrogen therapy on men with prostate cancer

Paul Thompson,MD
Hartford Hospital
Effect of E Genotype on lipid response to exercise

Marietta Vazquez,MD
Yale University School of Medicine
Efficacy of lyme vaccine in clinical practice

William White, MD
University of Connecticut Health Center
Blood pressure measurement during pregnancy

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

Therese Kosten, PhD
Yale School of Medicine
Early Life Stress and Cocaine Abuse in Male and Female Rats

Virginia Ashby Sharpe, PhD
The Hastings Center
Promoting Patient Safety: An Ethical Basis for Policy Determination

Geraldine Pellecchia, PhD
University of Hartford
Influence of Cognitive Activity on Coordination Dynamics

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



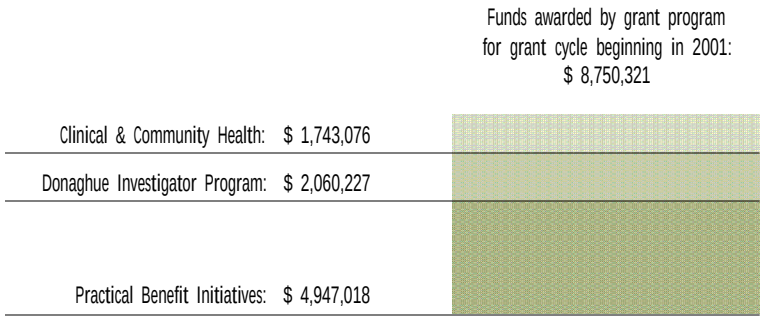
GRANTS

GRANTS IN 2001

Institution	New	Continuation	Total
Connecticut Children's Medical Center	0	1	1
Hartford Hospital	1	2	3
The Hastings Center	1	1	2
Institute for Community Research	1	0	1
St.Francis Hospital & Medical Center	0	2	2
University of Connecticut Health Center	3	15	18
University of Connecticut/Storrs	1	0	1
University of CT School of Nursing	0	1	1
University of Hartford	0	1	1
Wesleyan University	0	2	2
Yale University	0	1	1
Yale School of Medicine	4	21	25
Yale School of Nursing	0	2	2
Total	**11**	**49**	**60**

FUNDS AWARDED BY GRANT PROGRAM FOR GRANT CYCLE BEGINNING IN 2001

Research in Clinical & Community Health Issues	**Total**
New (6)	$ 445,818
Continuing (26)	$ 1,297,258
Donaghue Investigator Program	**Total**
New (3)	$ 330,000
Renewal (14)	$ 1,730,227
Practical Benefit Initiatives	**Total**
New (2)	$ 517,866
Continuing (9)	$ 4,429,152
Total	**$ 8,750,321**



FINANCIAL INFORMATION

2001 FINANCIAL INFORMATION

Statement of assets and fund balance as of December 31,2001

Investment in marketable securities	$ 67,222,994
Cash and cash equivalents	$ 8,043,366
Other assets	$ 52,384
Total assets and fund balance	**$75,318,744**

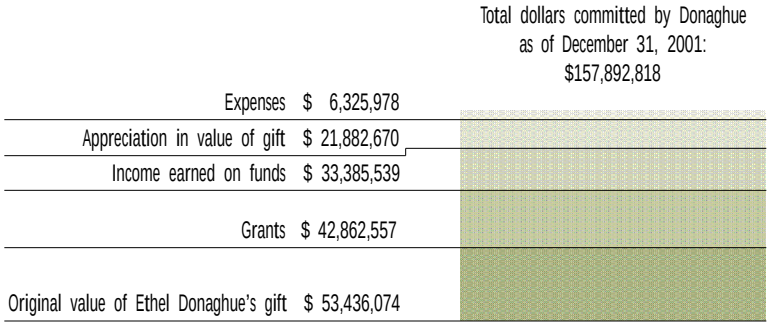
Statement of income and expenditures for the twelve months ended December 31,2001

Income (interest, dividends)		**$ 2,978,902**
Expenditures		
Program:		
Grants		
Clinical and Community Health Issues	$ 1,743,076[1]	
Donaghue Investigator	$ 2,060,227	
Practical Benefit Initiatives	$ 4,947,018	
Subtotal		$ 8,750,321
Program Support		$ 224,629
Management and General		$ 368,061
Investment Management		$ 115,919
Total Expenditures		**$ 9,458,930**[2]

Note 1:Included in this figure is $86,617 the Foundation facilitated in grants to medical research from other foundations or philanthropic sources.

Note 2:In addition to these expenditures,an estimated amount of up to $10,103,444 has been earmarked for future spending in support of ongoing grants.

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



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 does not seek additional funds itself unless 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.

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2001

THE PATRICK AND CATHERINE

WELDON DONAGHUE MEDICAL

RESEARCH FOUNDATION

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