

# Hereditary Disease

## F O U N D A T I O N



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## HDF Gala Raises \$1 Million Toward A Cure!

On November 1, 2005, people came from around the globe to New York's Waldorf-Astoria Hotel to celebrate and support the critical work of the HDF. Founding trustees, new trustees, Scientific Advisory Board members, scientists, loyal supporters and friends from everywhere flew in to make this a joyous occasion!!!! Thanks to the support of so many, the evening was spectacularly successful!!! We raised over \$1 million to advance research for the Huntington's disease cure!!!

The master of ceremonies, organizer, facilitator and guru of the evening - who deserves the most special thanks - is trustee **Herb Pardes**!!! It was Herb's idea and Herb's genius that made it happen!!!! Herb's "Variations on a Theme of Hugging"- featuring Nancy and numerous Venezuelan children - rivals Bach's and brought tears to our eyes! HATS OFF and THANKS!!

NBC's science correspondent **Robert Bazell** was our fabulous emcee for the evening. He announced the launch of our new **Milton Wexler Award**, named for the visionary, charismatic, imaginative, creative, tenacious man who

*Article continued on page 2,  
\$1 Million Toward A Cure!*



*Trustees Carrie Fisher, Berta and Frank Gebry with Peter Arnell*

"If one looks back in the development of human genetics in our current form, I think the Hereditary Disease Foundation played really the same role that the Rockefeller



Foundation played in the 30s and 40s, when it permitted the development of molecular biology. It was a small group of people who weren't waiting around, but were giving money to the right people, with the thought that it was sensible."

*— Excerpted from Dr. James D. Watson speech at the HDF Gala. Dr. Watson is the winner of the Nobel Prize in Physiology or Medicine in 1962, co-discoverer of the structure of the DNA molecule with Dr. Francis Crick, and Chancellor of Cold Spring Harbor Laboratory, Cold Spring Harbor, New York*



*Princess Firyal of Jordan, Lionel Pincus, Katherine Farley, and Jerry Speyer*

*More Gala Photo Highlights on page 3*

# \$1 Million Toward A Cure!

*continued from page 1*

founded the Hereditary Disease Foundation in 1968. The Milton Wexler Award honors those who follow in his footsteps. The scientists receiving this inaugural award have donated as much as three decades of their lives to innovative, revolutionary science, pushing the boundaries of the known. They are:

**Kenneth (Kurt) H. Fischbeck, M.D.**, Chief of the Neurogenetics Branch at the National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health (NIH)

**Susan Hockfield, Ph.D.**, President of the Massachusetts Institute of Technology

**H. Robert Horvitz, Ph.D.**, David H. Koch Professor of Biology, Massachusetts Institute of Technology, Member of the McGovern Institute for Brain Research, Investigator of the Howard Hughes Medical Institute, and recipient of the Nobel Prize in Physiology or Medicine in 2002

**David Housman, Ph.D.**, Ludwig Professor of Biology at the Massachusetts Institute of Technology

**Carl Johnson, Ph.D.**, Executive Director for Science of the Hereditary Disease Foundation

**Richard C. Mulligan, Ph.D.**, Mallinckrodt Professor of Genetics at Harvard Medical School and Director of the Harvard Gene Therapy Initiative



*Milton Wexler Award recipient and Scientific Advisory Board member David Housman, Nancy Wexler, and HD Researcher Jim Gusella*



*Howard McGillin, the Phantom in Broadway's "Phantom of the Opera" sings "Nancy With the Laughing Face"*

**Anne B. Young, M.D., Ph.D.**, Julieanne Dorn Professor of Neurology at Harvard Medical School and Chief, Neurology Service at Massachusetts General Hospital

Those giving the Awards to the honorees deserve honors in their own right - **Christopher O'Brien, Alice O'Brien Ross, and Meghan O'Brien Donaldson**, whose brother, **Michael O'Brien**, lost his life on Mt. Everest, climbing to raise funds for the HDF and awareness of the cause. **Carlos Urrutia**, a special friend of the HDF family, also presented an award.

Honored guest **James Watson**, the father of modern genetics who identified the structure of DNA, gave a spontaneous tribute to the Hereditary Disease Foundation and its scientific visionary leadership, comparing us to the Rockefeller Foundation. What an honor! We were deeply touched by his remarks. (See text box on page 1 for his tribute.)

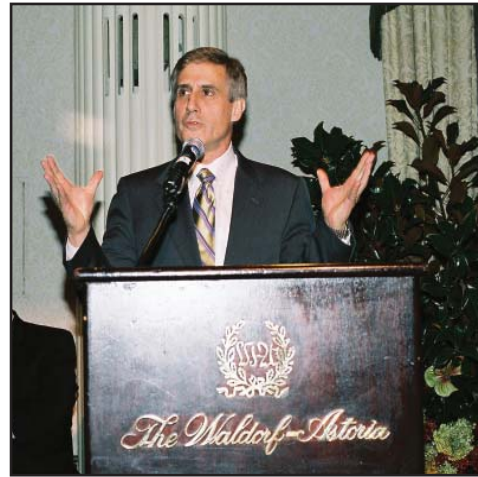
**Howard McGillin** took a night off from starring on Broadway as the Phantom in "Phantom of the Opera" and serenaded Nancy with "Nancy With the Laughing Face" with extra lyrics created by Howard and **Richard Samson**. Thank you, cousins!!

And another very special thanks to HDF trustees **Carrie Fisher** and **Frank Gehry**, who had everyone roaring with laughter during the live auction that featured items contributed by them. Trustees **Carol Burnett, Peter Falk** and **Claes Oldenburg** contributed other items to the auction. **Many, many thanks to the fantastic donors and purchasers who raised MORE FUNDS FOR SCIENCE and made for AN EXTREMELY FUN EVENING!!!!** ■

# Gala Highlights



*Trustees Frank Gebry and Carrie Fisher auctioning profiterole statue by Claes Oldenburg*



*Robert Bazell, NBC News' Chief Science and Health Correspondent, our emcee for the evening*



*Trustee Carrie Fisher with Richard Axel, Nobel Laureate*



*Trustee Herb Pardes*



*Trustees Arthur and Dewanna Golding*



*Trustees Harry and Evelyn Lieberman with Jay Tolson*

*Please see more Gala Photo Highlights on pages 4-7*



*This bowl, made by HD researchers Jim Olson and Sally Ditzler, was presented by Anne Young to Nancy Wexler at the HDF Gala. To learn more about it, please visit [www.hdfoundation.org](http://www.hdfoundation.org). You can also find the invitation and program book online.*



*The Fox sisters - Tacie, Liza and Sarah*



*Alice O'Brien Ross (left) and Meghan O'Brien Donaldson (right), sisters of Christopher and the late Michael O'Brien, with Carl Johnson (middle), Executive Director for Science of the Hereditary Disease Foundation and Milton Wexler Award recipient*



*Trustees Kelly Posner Gerstenhaber and David Gerstenhaber*



*Trustee Shelby Modell*



*Trustee Mary Carol Rudin (center) with Phyllis Parvin and Sheldon Slaten*



*Nancy and Herb sharing a laugh*



*Nancy Wexler flanked by Nobel Laureates Bob Horvitz and James Watson*



*Trustees Max Palevsky and Jodie Evans, with Nancy Wexler, Trustee Carrie Fisher, and Jill Ginsberg*



*Trustees Elaine May, Frank and Berta Gebry*



*Trustees Nancy and Alice Wexler with Bob Horvitz, Nobel Laureate, Scientific Advisory Board member and Milton Wexler Award recipient; drawing auctioned off by Trustee Peter Falk in background.*



*Rafe and Kerry (Blethen) Quinn, Trustee Debbie Blethen, Rebecca Stodola, Liz Nizick, and Courtney Blethen*



*Scientific Advisory Board member Robert Hughes and Lisa Ellerby, both HD Researchers*



*Trustees Harry and Evelyn Lieberman with Lieberman Award recipient and HD Researcher Steven Finkbeiner*



*Lieberman Award recipient Leslie Thompson (left) and Marie-Francoise Chesselet (right), HD Researchers and Scientific Advisory Board members, with Liliana Menalled (center), HD Researcher*



*HD Researchers Daniela Brunner and Ai Yamamoto*



*Two-time Lieberman Award recipient Gillian Bates and William Yang, both Scientific Advisory Board members and HD Researchers*



*Trustees Bob and Kiyo Higashi*



*Trustees Marjorie Fasman and Kiyo Higashi*



*Carlos Urrutia gives Milton Wexler Award to Anne Young, Scientific Advisory Board member; William Yang, Scientific Advisory Board member (foreground) and Michael Lorimer (background)*



*Stetson Ames, Anne Young, Nancy Wexler, and Carl Johnson, Executive Director for Science of the Hereditary Disease Foundation*



*HD Researcher Ed Stern, Scientific Advisory Board member and HD Researcher Michael Levine, Illene Tonick, and HD Researcher Ilya Bezprozvanny*



*Doris and Norman Tipograph*

# Hereditary Disease Foundation Benefit Celebration

November 1, 2005

This success of this evening is due in large part to the extraordinary generosity of

Berta & Frank Gehry  
Harry & Evelyn Lieberman  
Herbert Pardes, M.D.  
Lionel Pincus & H.R.H. Princess Firyal of Jordan  
Katherine Farley & Jerry I. Speyer

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Dr. Ralph Wharton  
Margrette & Hans Wold  
Ai Yamamoto

\*Nobel laureate

*The Hereditary Disease Foundation has supported groundbreaking research at MIT and Harvard Medical School. This research was reported in the March 14, 2006 issue of the Proceedings of the National Academy of Sciences.*

*Professor David Housman is a longstanding member of the Hereditary Disease Foundation's Scientific Advisory Board. Ruth Bodner is a post-doctoral fellow whose research is supported by the Hereditary Disease Foundation.*

*The following is the press release recently issued by MIT about this exciting new research:*

## RESEARCH GOOD NEWS!!!!

- ▶ Tetrabenazine Works to Treat Chorea! A highly significant study proves tetrabenazine works. (Huntington Study Group, *Neurology* 2006; 66; 366-372)
- ▶ Neural transplants help motor and cognitive problems for HD patients. (Bachoud-Lévi AC, Gaura V Lefaucheur JP, et. al., *Lancet Neurology* - Vol. 5, Issue 4, April 2006, Pages 303-309)

Read all about it on the HDF website – [www.hdfoundation.org](http://www.hdfoundation.org)!

## Research holds promise for Huntington's treatment

*Anne Trafton, Massachusetts Institute of Technology News Office  
March 6, 2006*

Researchers at MIT and Harvard Medical School have identified a compound that interferes with the pathogenic effects of Huntington's disease, a discovery that could lead to development of a new treatment for the disease.

There is no cure for Huntington's, a neurodegenerative disorder that now afflicts 30,000 Americans, with another 150,000 at risk. The fatal disease, which is genetically inherited, usually strikes in midlife and causes uncontrolled movements, loss of cognitive function and emotional disturbance.

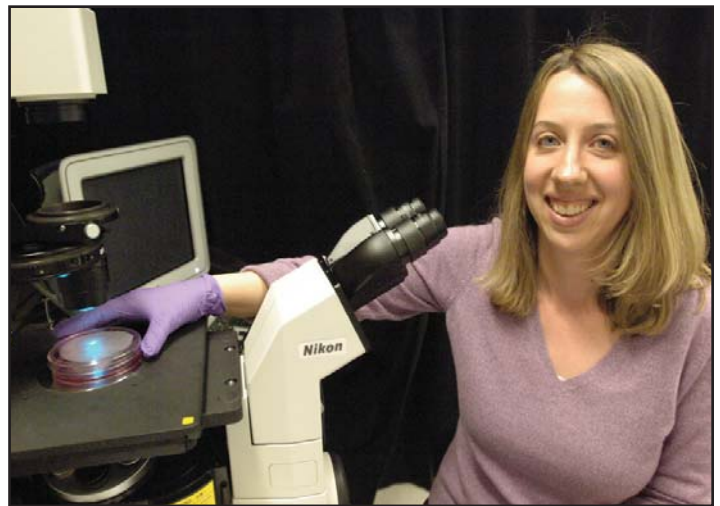
"There are now some drugs that can help with the symptoms, but we can't stop the course of the disease or its onset," said Ruth Bodner, lead author on a paper that appears this week in the online edition of the Proceedings of the National Academy of Sciences and which will appear in the print edition March 14. Bodner is a postdoctoral fellow in MIT's Center for Cancer Research.

The compound developed by Bodner and others in the laboratories of MIT Professor of Biology David Housman, Harvard Medical School Assistant Professor Aleksey Kazantsev and Harvard Medical School Professor Bradley Hyman might lead to a drug that could help stop the deadly sequence of cellular events that Huntington's unleashes.

"Depending on its target, any one compound will probably block only a subset of the pathogenic effects," Bodner said. Huntington's disease is caused by misfolded proteins, called huntingtin proteins, that aggregate and eventually form large clump-like "inclusions." The disease is characterized by degeneration in the striatum, an area associated with motor and learning functions, and the cortex. The proteins may disrupt the function of cellular structures known as proteasomes, which perform a "trash can" function for the cell – disposing of cellular proteins that are misfolded or no longer needed, said Bodner.

Without a functional proteasome, those cellular proteins accumulate, poisoning brain cells and impairing patients' motor and cognitive function.

Until now, most researchers looking for Huntington's treatments have focused on compounds that prevent or reverse the aggregation of huntingtin proteins. However, recent evidence suggests that the largest inclusions may not necessarily be harmful and could in fact be protective, said Bodner. So, the MIT and Harvard scientists decided to look for compounds that actually promote the formation of large inclusions.



*Ruth Bodner, a postdoctoral fellow in MIT's Center for Cancer Research, has discovered a compound that could lead to the development of a new treatment for Huntington's disease, a fatal neurodegenerative disorder. (Photograph by Donna Coveney/MIT)*

The highest concentration of protein inclusions was found when the researchers applied a compound they called B2 to cells cultivated in the laboratory. The compound also had a strong protective effect against proteasome disruption, thus blocking one of the toxic effects of the huntingtin protein.

The B2 compound also promoted large inclusions and showed a protective effect in a cellular model of Parkinson's disease, another neurodegenerative disorder caused by misfolded proteins.

In Parkinson's disease, the mutant proteins destroy dopamine-producing cells in the substantia nigra. Normally, the dopamine transmits signals to the corpus striatum, allowing muscles to make smooth, controlled movements. When those dopamine-producing cells die, Parkinson's patients exhibit the tremors that are characteristic of the disease.

The researchers are now working on finding a more potent version of the compound that could be tested in mice. This work was funded by the Hereditary Disease Foundation, Massachusetts Biotechnology Research Council, National Institutes of Health, American Parkinson's Disease Association and the MassGeneral Institute for Neurodegenerative Disease. ■

# HDF Names Lieberman Award and Milton Wexler Fellowship Winners



**S**heng Zhang of Harvard Medical School, working in the laboratory of Norbert Perrimone, has been named the 2006 recipient of the prestigious **Lieberman Award**. Named in honor of long-time HDF trustee, benefactor, and friend, Harry Lieberman, the Lieberman Award provides \$150,000 in research funding over two years to an investigator who is conducting particularly innovative and important research that advances the search for a cure for Huntington's disease.

Dr. Zhang's efforts are focused on using a new technology known as "genome-wide siRNA" in fruit flies as a way to discover new, potential targets for HD therapies. This approach turns off one gene at a time to figure out what each gene does. ■



**A**nat Ben-Zvi of Northwestern University, a postdoctoral fellow in the laboratory of Richard Morimoto, has been awarded the prestigious **Milton Wexler Fellowship**. The Milton Wexler Fellowship was created in 1998 to honor the visionary leadership of HDF founder Dr. Milton Wexler on his 90th birthday and to celebrate the Foundation's 30th anniversary.

Dr. Ben-Zvi received this award for a project utilizing a tiny worm to determine whether mutant huntingtin causes a disruption in the natural protein folding within cells and to examine the interaction of these effects with biochemical mechanisms that control longevity.

Her work is expected to clarify how extending life suppresses the mutant huntingtin protein from collecting - leading to possible new HD treatments. ■

## Science Funding

**H**ereditary Disease Foundation grants, postdoctoral fellowships and research contracts are helping identify routes to the development of treatments and a cure for HD. With your support and the expertise of the HDF's Scientific Advisory Board - comprised of world renowned experts in genetics, neurology, neuroscience and therapy development - HDF funds groundbreaking research. Projects funded following the November 2005 and January 2006 Scientific Advisory Board meetings include:

### **Research Grant:**

**Emmanuel Mignot**, Stanford University (Stanford, CA)  
Sleep disruption and hypocretin deficiency in HD and HD mice.

### **Postdoctoral Fellowships:**

**Justin Legleiter**,  
The Gladstone Institute at UCSF (San Francisco, CA)  
Mentor: Paul Muchowski  
Analyzing mutant huntingtin oligomers using atomic force microscopy.

**Geraldine Liot**, The Burnham Institute (La Jolla, CA)  
Mentor: Ella Bossy-Wetzel  
The role of mitochondrial fission in the pathogenesis of HD.

**Sebastien Marion**, Duke University (Durham, CA)  
Mentor: Marc Caron  
Neuroprotection from polyglutamine toxicity by arrestin 2 in HD mice.

**Brigit Riley**, Stanford University (Stanford, CA)  
Mentor: Ron Kopito  
The regulation of autophagic degradation of huntingtin inclusions. ■

*O'Brien family and friends pass \$100,000 goal, raising over \$120,000 for the HDF! See <http://hdfoundation.org/news/O'Brien.html> for more details. Congratulations! We're so proud!*

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## Donor Profile: Harry A. Lieberman



Long-time trustee and friend of the Hereditary Disease Foundation, **Harry A. Lieberman**, credits his involvement with HDF to the groundbreaking work HDF scientists are doing to stop the horrific progression of Huntington's disease and rapidly find a cure.

When first learning of Huntington's disease and the effect that it would have on his family, Harry joined the board of Huntington's Disease Society of America, an organization seeking to provide care to families with HD. In the early eighties, Harry's focus turned to supporting research and he became a trustee of HDF.

Following the HDF-supported discovery of the Huntington's disease gene in 1993, Harry created the **Lieberman Award**, the most prestigious award given by the Hereditary Disease Foundation and in HD research internationally. It is awarded annually to one scientist to ignite phenomenally innovative, fast-track research towards the treatment and cure of HD.

Harry has made countless generous contributions over the years to fund the innovative research of HDF's scientists because the organization "continues to support scientists who are extremely committed to curing Huntington's disease. I put my family's lives in their hands and trust them to do the necessary work."

"Harry's push to see immediate results drives us and HDF-funded researchers to move faster towards treatments and cures. His personal story speaks movingly to researchers, keeping all of us aware of how crucial our work is both in the lab and in the world. He is an inspiration to us all! We thank him for his fantastic gift of the Lieberman Award and we love him!" says Nancy Wexler, HDF President. ■

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## In Memoriam: Alden "Buster" Blethen



The Hereditary Disease Foundation family mourns the loss of Alden "Buster" Blethen. Buster and Debbie - trustees of the HDF - and their daughters, Kerry and Courtney, have been close friends for many years. Buster was an extraordinary human being! He used to visit scientists around

the country to learn about their work. And Buster always motivated them to do even more and work even faster!! Seeing Buster come into a room was like watching sunshine bloom across the sky.

Buster was diagnosed with Huntington's disease when he was in his mid-thirties. He worked at the Seattle Times from 1973 to 1989, rising to the position of national advertising manager, until his illness forced his retirement. We offer our most heartfelt condolences to the Blethen family. We all miss him deeply. Please visit [www.hdfoundation.org](http://www.hdfoundation.org) to read more about Buster. ■

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## Welcome, Davey! Thank You, Edy!

We're excited to welcome to the HDF family, Davey Mitchell, our new Science Administrator! Davey will be coordinating the workshop and grants programs. He can be reached at [DaveyMitchell@hdfoundation.org](mailto:DaveyMitchell@hdfoundation.org) or by phone at 212.928.2121.

HDF would also like to thank Edy Shackell for over 18 years with the Hereditary Disease Foundation. Through her work with our donors, scientists and on the Venezuela Collaborative Research Project, Edy has been an invaluable partner. She will be missed by the entire HDF family, and we wish her all the luck in her future adventures! THANK YOU, EDY!!! ■

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## Recent and Upcoming Events

October 1-2, 2005  
Workshop: "Autophagy in the pathogenesis and treatment of Huntington's disease"  
New York, NY

November 19-20, 2005  
Workshop: "Stem cells in the treatment of HD"  
Los Angeles, CA

January 7-8, 2006  
Workshop: "The HD therapeutic pipeline" (see Workshop Update, page 12)  
Los Angeles, CA

August 11-13, 2006  
Biennial Symposium: HD2006: Changes, Advances, and Good News (CAG)n  
Cambridge, MA

## A Note from the Board



Dear Friends,

*We are a part of the Hereditary Disease Foundation family because we know that by continuing and expanding the ground-breaking*

*work of this incredible organization, we are playing a role in not only stopping the progression of Huntington's disease, but helping HDF to uncover valuable truths applicable to all science.*

*As part of the HDF family, your partnership is essential as we move full speed ahead towards a treatment and cure for this devastating disease. Join us, and together our contributions will fund the work of researchers around the globe who are seeking answers to treating and curing Huntington's disease. Join us in changing the future of the many hundreds of thousands of people worldwide who now are suffering from Huntington's disease or are awaiting their cruel fate.*

*Let's change their future together and thank you for being a part of our mission,*

*Berta Gebry      Frank Gebry*  
*Treasurer      Vice President*

## Your Legacy Today Advances the Science of Tomorrow

Your gift of cash or appreciated securities will help the HDF meet our critical mission today. Including the HDF in your estate planning can help ensure that the progress of today will lead to a cure. You can make a bequest to HDF simply by asking your attorney to include HDF in your will or codicil.

If you are affiliated with one of the many matching gift companies, you can double or even triple the dollar value of your annual gift. Please take a moment to check with your company's Department of Human Resources.

For more information about making a donation or how your legacy gift today can fund the discoveries of tomorrow, call Karen Dean at 212.928.0420 or e-mail her at [karendean@hdfoundation.org](mailto:karendean@hdfoundation.org). ■

## Workshop Update

For additional workshop reports, go to [www.bdfoundation.org/workshop.htm](http://www.bdfoundation.org/workshop.htm)

"The HD Therapeutic Pipeline" sponsored by the HDF and the Albert Parvin Foundation  
January 7-8, 2006  
Santa Monica, CA

The HD therapeutic pipeline boasts a rapidly growing number of therapeutic candidates ranging from compounds in the initial phases of experimental testing to drugs being evaluated in human clinical trials. Workshop participants discussed the status of these candidates, highlighting promising approaches, identifying potential limitations, and providing ideas for future directions.

Participants agreed that these are exciting times for HD research, with several promising therapeutic candidates on the horizon. ■

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