

Your Donation Goes Even Farther!

Thanks to the generous support of the Greene and Lusk families, your donation this season will go even farther!

Sunny Greene and the Lusk family have challenged us. They will match all contributions of \$100 or more that we receive by December 31, 2005, up to a total of \$20,000. Please help us earn these wonderful donations!

In addition, first-time donations in any amount received by December 31 will be matched by an anonymous donor, up to \$1000. Please help spread the word!

We're offering you something you can't buy at any price -- life-saving information to help you stay healthy with VHL, and targeted research projects working for a cure for VHL.

Gifts of the Artists: Several talented members of our community have donated CDs and books. For a donation of \$150 or more, you can choose one of these wonderful performances as your free gift.

Thank you!

**** Write in the item number on your donation form.**

1. *New York Times* Best-Selling book, "How Full is Your Bucket" by Donald O. Clifton and Tom Rath, Gallup Press
2. CD, Bach, "Goldberg Variations" for Piano, by Pierre Jacomet
3. Music CD, "Forever In His Care," by Deb Hogan
4. Music CD, "Wayfaring Stranger," by Clenton Winford II

Remember VHLFA in Your Will

You can give hope to millions of people worldwide with VHL, kidney cancer, and other tumors by extending your support of VHL Family Alliance programs beyond your lifetime. Whether your legacy is large or small, you can support our research and education programs by remembering VHLFA in your will.

To make a bequest of cash or other property to VHLFA, please set up a meeting with your attorney and provide him or her with the following information:

VHL Family Alliance, Inc., a non-profit corporation organized under the laws of Massachusetts
 171 Clinton Road, Brookline MA 02445
 Federal tax ID 04-3180414

A bequest to VHLFA is fully deductible for estate tax purposes. In addition, remembering VHLFA in your will is an important and personal way of providing hope to people with von Hippel-Lindau disease for generations to come. You may wish to learn about other gift opportunities by consulting with advisors, or simply write to Director of Development, development@vhl.org, 617-277-5667 ext. 4



Mail to: VHLFA, 171 Clinton Road, Brookline, MA 02445

Enclosed is my tax-deductible gift to support: VHLFA Research only

- \$25 \$50 \$100 \$150 \$500 \$1000 \$_____
- My employer will match my donation. I have enclosed the necessary forms.
- First-time donor! My gift will be matched.
- Gifts of \$100 or more will be matched by the Greene and Lusk families.
- With my gift of \$150 or more, please send me item # _____ above **

(Please make checks payable to VHL Family Alliance)

Name: _____
 Address: _____
 City: _____ State: _____
 Zip/Postcode: _____ Country if not U.S.: _____
 Tel: _____ Fax: _____
 E-mail: _____

U.S. IRS Tax ID 04-3180414
 Canada Charity No. 887961423 RR0001
 UK Charitable Organisation
 2005 Federal CFC # 9710
 or write us in on your
 United Way campaign

- Send newsletter
 Audio version needed
 I would like to receive occasional alerts via e-mail from VHLFA only
 Please send me **___ wristbands**
 (minimum donation \$5 each)

I am a Person with VHL Family member Friend Sponsor Health professional _____ (specialty)

Please charge my Visa MasterCard Amex Discover Card number _____

Name as it appears on the card _____ Exp Date _____

One-time payment of \$ _____ or Budget Plan: Twelve monthly payments of \$ _____ each

VHLFA is a non-profit corporation in the U.S. and a registered Charity in Canada

My donation is In Honor of ... In Memory of ... _____

Please send an acknowledgment card to ... Name: _____

Address: _____

Challenge! Your Gift Goes Farther!

Two families have challenged you to make a special pledge to VHLFA this season. Special thanks go to Sunny Greene and the Lusk Family for their generous Challenge Grants! See how you can help us earn these challenge gifts ... and choose a special thank-you gift for yourself.

On the Line . . . When You Call

When you call our telephone number, 800-767-4VHL or 617-277-5667, you hear a menu in the resonant tones of **Bruce Weinberg**, a certified Talking Book reader and member of our Board of Directors.

As Bruce will tell you, you can press 1 for the English-language hotline, press 2 for service in Spanish, or press 5 for service in French.

Our menu routes calls to the home of the volunteer most suited to answer your questions. These very special people all have VHL themselves, and have experience in their own families and with hundreds of callers over many years. If they can't answer your question themselves, they will help you find a good answer.

During the recent hurricane, they helped people who had been treated in New Orleans find alternative sources of health care for VHL.

Altheada Johnson [1] in New York chairs the Hotline committee, and is in her tenth year of service on our Board of Directors.

Audrey Clifton [2] in North Carolina is a grandmother with a very big heart.

Alexandra Morais [3] in New Jersey comes from Colombia and answers calls in Spanish



Your Hotline Team

language from literally all over the world.

Emily Stevens [4] also from New Jersey, is new to the hotline team. She has been dealing with VHL in four generations of her family. She has also been an active participant in the online list.

Paul Bonneau [5] from Quebec, Canada, is a long-time leader and participant in the Canadian VHLFA and in the French language online support group. He answers calls in French on extension 5.

Evelyn Werner [6] from New York joins the hotline team this season, bringing her rich experience with VHL. She and her husband Bob have attended nearly every VHLFA meeting since 1994. **Lois Erickson** [7] from Minnesota is an alternate, filling in when needed. Her story was one of the first we ran in the newsletter, sharing five generations of VHL in her own family. Lois, her sister Audrey, and her niece Kelly Heselton have all served as leaders in VHLFA.

Christina Doyle [8] from California is a college student with VHL, studying to be a genetic counselor. She does special projects for Joyce and is glad to speak with you about DNA testing.

We are grateful to each of these very special people. Collectively, they have more than 325 years of personal experience with VHL, and more than 50 years of service to the VHL Family Alliance.

Volunteers of the Year

Gale Lugo (Florida) and Rachael Morgenstern (Massachusetts) were honored this year as Volunteers of the Year. **Gale** [left] has been chairman for Florida since 1994. She is one of the moderators of the English-language Online Support group, and is Acting Chair for the Southeastern Region. **Rachael** [right] has been our volunteer Clerk and Office Coordinator since 1993. She opens the mail, records the donations, sends thank-you notes, and maintains the database. She has been our steadfast friend through many operations, and is enjoying having Robin Cochrane in the office as well.



Four new grants

-- Joseph M. Verdi, Ph.D.,
Director of Research

We received 16 applications this year from all over the world, from as far away as Switzerland, the Netherlands and Canada. Ten of these grants were outstanding. This is a huge improvement over last year.

Each grant will have a significant impact on VHL science and our understanding of the disease process. Major breakthroughs have occurred in the last few years, leading us to explore new questions that will result in new therapies in the not too distant future.

The Board voted in June to award four grants, for a total of \$120,000 in new grants this year. Because we are still paying second-year funding to Dr. Judith Frydman of Stanford, we will pay out a total of \$160,000 in grant money between now and June 2006.

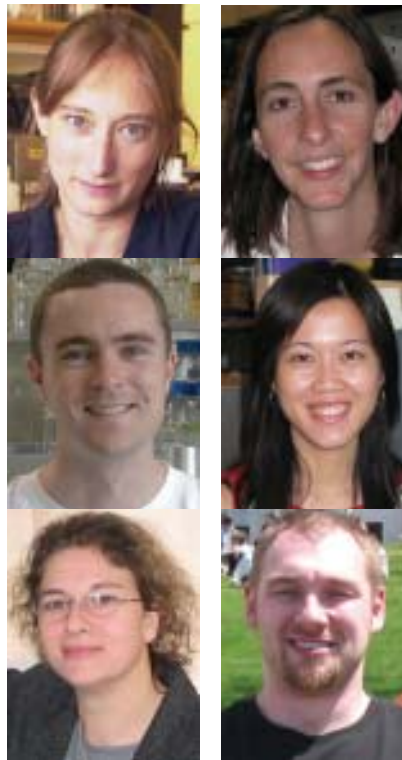
We are encouraging young researchers to study VHL, and helping them gather data so that they can solve another piece of the puzzle of VHL in particular and cancer in general. You will notice that this year much of the work focuses on kidney cancer. Drugs are somewhat easier to test in the kidney than in other organs, but the mechanism is the same and hopefully the same drugs will work throughout the body.

Dr. Judith Frydman [left top photo] of Stanford has completed her first year of the 2-year grant we awarded last year. With the support of the VHL Family Alliance she has published a paper in the prestigious journal *Cell*, which raised a great deal of interest in the scientific community and was reviewed in three other journals. Her work helps us to understand the process of "folding" which is important to the correct functioning of the VHL protein.

Teamwork for Health

Thank you for including me as a member. I will gladly spread the word to my circle of friends. I can think of nothing better than to bring more attention to VHL and the work to find a cure. -- M.A., Calif.

I was only 10 when my Dad died of VHL, so I was confused and afraid. Thank you for offering the information I was searching for. I now feel I understand what it was all about. I am overwhelmed that there is hope that a cure will be found in some years time. It will be a genetic breakthrough for all the families suffering from the effects of VHL. I admire each and everyone of you. -- N.C., England



Researchers you are supporting
2005-2006

When the protein cannot fold properly, the body invokes a kind of quality control process intended to dispose of the incorrectly folded protein, making way for correctly folded protein instead. This paper describes the different sets of "chaperone" proteins needed for correct folding, and for elimination of incorrectly folded protein.

Dr. Ian Frew [left middle], of the department of cell biology at the Swiss Federal Institute of Technology, is working toward better therapies for kidney cancer, by improving our understanding of how the VHL protein works, and specifically what other events are needed for the tumor to progress to cancer. He will study closely the interaction among the loss of VHL, a change in PTEN, and a disruption of the P13K pathway. If interactions among these are proven, this would be a very attractive target for drug development to aid in the control of kidney cancer.

Dr. Kimryn Rathmell [right top] (an oncologist) and **Dr. Shufen Chen** (a renal pathologist) at the University of North Carolina at Chapel Hill have been investigating the activities of the VHL protein which normally acts to prevent the development of kidney cancer. They are making a series of animal models (mice), each with small changes in the VHL gene, that will allow us to learn important things about the biology of VHL-induced kidney cancer, and will aid in testing proposed new therapies.

Pei-Yin Lin [right middle] is a doctoral candidate in the Graduate Group of Immunology at the University of California, Davis, working with **Dr. Robert Weiss** (nephrology). Kidney cancer does not respond well to most kinds of chemotherapy. One possible reason is that protein p21, which works against chemotherapy, is elevated in kidney cancer. Lin will be studying p21 and using a method of neutralizing some of the effects of p21, to see if the kidney will respond better to chemical treatments.

Dr. Andreea Ruxandra-Schmitzer [bottom left] is an Assistant Professor at the University of Montreal working on the chemical modification of proteins. In this project, she is working with **Dr. Shawn Collins** [bottom right] on creating "molecular clips" to stabilize and deactivate telomerase, an enzyme found in most human tumors, that has been found to be a powerful marker and therapeutic target in cancer. By doing so, they hope to prevent the progress and spread of VHL tumors.

von Hippel-Lindau Research Campaign



VHL FAMILY FORUM

Annual Report issue, 2004-2005

Family, Friends, Physicians, & Researchers dedicated to improving diagnosis, treatment, and quality of life for people affected by von Hippel-Lindau.

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November 2005

It's in the Genes ... of some Pretty Terrific People



of Miss
North Carolina ...

We need your help to find the cure. The pace of research is picking up. Every week there is something new in the news that will have implications for treatment of VHL -- just not quite yet. There is work to do in "translating" the basic research into treatments, testing those treatments for safety and effectiveness, and then getting them approved for VHL. But this year we received a number of exciting research proposals that will take us farther down this path.

Thanks to your generosity, we were able to fund four new proposals -- a total of \$120,000 or 53% of our total expenses this year.

Please join us!

We Need Your Help!

But the future is not our only concern. Meanwhile there are still people struggling to get a diagnosis, or to get optimal treatment for the tumors they are dealing with today. Our **Hotline** now serves people in three languages: English, Spanish, and French. Our **website vhl.org** serves more than 20,000 people each month, coming from 107 countries. More than 100 people attended five **regional meetings** around the United States alone. And 600 people participated in our five **online support groups** in English, Spanish, French, German, and Japanese.



of an aspiring
rap artist ...

The third edition of the **VHL Handbook** was distributed to our entire mailing list last December. The Handbook assists patients and their local doctors in monitoring VHL, finding issues early when they are more successfully treated, and choosing the best moment and method for treatment. It is important to get this information to that local doctor-patient team in order to make the biggest difference in diagnosis, treatment, and quality of life. For this reason, teams of volunteers have helped to make local language versions of the Handbook available free on the internet in Spanish, French, Chinese, Arabic, German, and Danish. Additional translations will become available this year: Croatian, Dutch, Hebrew, Italian, Japanese, Portuguese, and Ukrainian.

Funding for all our activities comes from you, our members and friends. We depend on your generosity to support our educational programs and to fund research.

You'll notice a little seal and ribbon on our report this year, an award from the Independent Charities of America (ICA), acknowledging us as one of the best charities in America. This seal is awarded to members of the ICA who have undergone rigorous independent review, and have demonstrated each year that they meet the highest standards of public accountability, program effectiveness, and cost effectiveness. Of the 1,000,000 charities operating in the United States today, it is estimated that fewer than 50,000, or 5 percent, meet or exceed these standards, and, of those, fewer than 2,000 have been awarded this Seal.

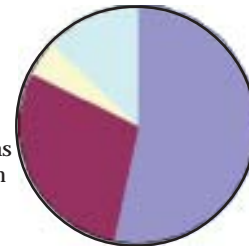
Please help us continue this important work. Thank you.



of this
young boy ...



Total Revenue for Fiscal 2005 (ended June 30, 2005) was \$217,855. Of this, \$120,000 was allocated to research funding.



Of our Expenses:
53% Research
29% Education
and support
4.6% Fundraising
13.2% Admin

*We Depend on Your
Support! Thank you!*