

von Hippel-Lindau Research Campaign



VHL FAMILY FORUM

Annual Report issue, 2007-2008

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

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Exciting Progress, With Your Help . . .

In January 2009, the VHL Family Alliance turns sweet sixteen. This has been a wonderful year of celebrating what we have already achieved, and reaching out toward the future.

Over the past two years we have worked to build a Research Infrastructure that will encourage more researchers to study VHL, and facilitate their work.

Our partner and storage of tissue bank, National Disease Research Interchange (NDRI) in Philadelphia takes excellent care in transport. One tumor becomes multiple samples for research. To date 35 people have donated 412 samples. These days the researchers are often studying not just VHL, but a particular type of VHL mutation. To support this research, we began requesting a copy of the donor's VHL DNA analysis. Our members have responded wonderfully to this call; we have already accepted 20 DNA reports.



Alicia and Addison

As this resource grows, an increasing number of researchers are drawing samples from the bank.

Our Education Service activities have grown considerably this year as well. We moved the website to a more modern base, which gives us opportunities to enhance the site. You will see a continuing evolution of the site, and we hope that you will continue to provide your feedback about what you like and what needs improvement.

We continue to look for the optimal format for recorded presentations. This year we are offering a series of Webinars which people can attend live, or play the pre-recorded session. VHL 101, a session on pre-implantation genetic diagnosis, and a recap



bbb.org/charity

of the Denmark symposium are online now, with a series of excellent medical presentations slated for the next several months. Your feedback will be essential.

Take two pills a day, and you'll never get another tumor. That's the dream. How realistic is it?

This year at the Kidney Cancer Symposium in Chicago, it was almost entirely about the drugs. These drugs are based in large part on research on the VHL gene. Several of them hold promise of being able to control the development of new tumors, or to keep existing tumors small. The challenge



is to test these drugs with people with VHL, to determine whether they are effective against VHL tumors, and what their side effects look like in people with VHL. Each next-generation drug is better targeted, with fewer or less burdensome side effects. We encourage people with VHL to consider participating in a clinical trial and help us find the maintenance drug we would all love to have.

Internationally our activities have expanded this year.

Camron and Brayden

At the medical symposium in Denmark in September we had our first presentation ever from India, where a doctor in Kerala province has identified three families with VHL and has been studying them for four years. In March Altheada and Fred Johnson went with Joyce Graff to Johannesburg, South Africa, to meet with 55 patients and family members to talk about VHL, and coach them in setting up an affiliate organization there.

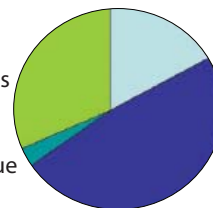
Please help us fight VHL.

Challenge grants see pg. 4

Report for Fiscal 2008 (ended June 30, 2008)

*Preliminary numbers; Audited financials will be available end of November

Total Revenue for Fiscal 2008 was \$299,278
Of this, \$75,555 was allocated to the Research program, for grants and Tissue banking.



Of our Expenses:
Research - \$75,555 (29.2%)
Education & Support - \$127,684 (49.3%)
Fundraising - \$7,688 (3.0%)
Management - \$48,039 (18.6%)

Researchers you are supporting 2007-2008

-- James T. Gnarra, Ph.D., Research Advisor

In the 15 years since finding of the VHL gene, research on the VHL gene and the protein it encodes has brought together scientists and physicians from many diverse areas. Genetic testing for VHL has become a straightforward laboratory test that not only helps diagnose VHL, but is becoming increasingly important in the clinic. Where once only a handful of laboratories were familiar with VHL, now scores of laboratories are involved in VHL research. We now know that the VHL protein is central to a number of important processes in the cell.

Among other things, the VHL protein controls the activity of hypoxia-inducible factor (HIF), a "master regulator" of cell activities, especially of angiogenesis, or the growth of new blood vessels that will feed any of a number of tumors, or form an angioma.

VHL is also important in the structural integrity of the cell, and in controlling the process. We now understand that all clear cell kidney cancer tumors in the general population have an abnormality in the VHL gene in the tumor.

Two years ago, there were no drugs to help at all with VHL, nor with kidney cancer. This year there are four approved drugs for advanced kidney cancer, but still none "for VHL." There are also many new drugs working their way toward FDA approval for one or more types of cancer. Most of these are based in whole or in part on research on the VHL gene.

The Cancer Research Fund of the VHL Family

Alliance was able to fund 3 proposals of the 13 very high quality proposals that were submitted this year. The research that will be performed by these groups will address important clinical, translational, and basic research questions that are very relevant to our understanding of VHL and how VHL patients will be treated in the future.



Thera P. Links, M.D., Ph.D., of the University of Groningen in the Netherlands, is pursuing a project of "Visualizing VEGF producing lesions in Von Hippel-Lindau."

The first thing that happens in the development of a VHL lesion is that the second copy of the VHL gene is inactivated in a cell. Without the VHL protein, there is heightened production of vascular endothelial growth factor (VEGF). The greater the production of VEGF, the higher the growth rate of the tumor.

Until recently, it was not possible to measure the VEGF levels inside the tumor without removing the tumor. Dr. Links and colleagues have developed a radioactive labeled antibody, based on bevacizumab

(Avastin) which binds to VEGF, making it possible to visualize and quantify VEGF in tumors of colorectal and melanoma patients using a PET scan.

This project will use PET scans on 30 people with VHL to detect and quantify the level of VEGF production in VHL-associated lesions. The goal is to use this information to formulate a plan of monitoring and treatment with surgery and/or drug therapy to manage the health of these patients.



Rupal Bhatt, M.D., Ph.D., of Beth Israel Deaconess Hospital and the Dana Farber/Harvard Cancer Center in Boston, will study the "Role of the Interferon Gamma Pathway in Resistance to Antiangiogenic Therapy."

People with VHL are sometimes being offered treatment with one of a class of drugs known as tyrosine kinase inhibitors (TKI's). Eventually the tumors become resistant to treatment, and begin to grow again. Even though the drug is blocking the VEGF pathway the tumor seems to find a "detour" and begin to grow again. Bhatt's team believe they have identified the "detour" being used. The project will confirm this hypothesis in mice, test it in VHL patients, and try to find a way to block this path so that these and newer TKI's can be used effectively for longer periods of time.

James Handa, M.D., of the Wilmer Eye Institute of Johns Hopkins Medical Institute in Baltimore, will study the "Use of a novel genetic animal model to study the molecular pathogenesis of retinal hemangioblastomas in VHL disease."



Retinal hemangioblastomas are the most common manifestation of VHL, occurring in the vast majority of VHL patients, often as the first sign of the disease.

It is essential to identify lesions early and control them. However, there are only limited treatment options available, which are not always successful. Better treatment options are needed.

Dr. Handa and his colleagues have recently developed an animal model that reproduces the retinal hemangioblastomas observed in patients with VHL disease. This novel genetic model represents the first animal model for VHL retinal hemangioblastomas. In this research proposal they will use this animal model to identify new methods for the early diagnosis and treatment of VHL-associated retinal hemangioblastomas.

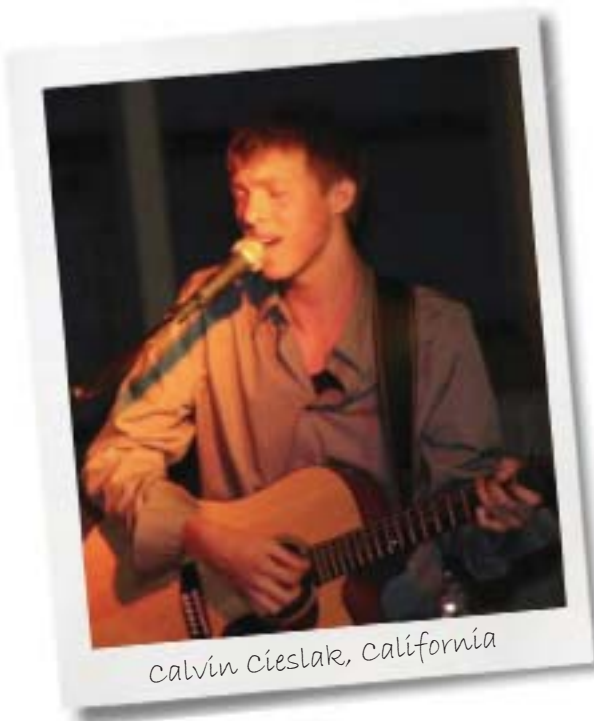
Here's How Some of You Have Helped!

At first, the plan was to have a small fundraiser/concert for friends and family – featuring me on guitar, playing some of the music I have written. Over time, however, plans for the event grew into something much larger.

Enlisting the help of my immediate family, grandparents, aunts, uncles and cousins, we invited several hundred people to join us for an evening of music, wine tasting and dessert under the stars. I called the evening VHLstock in the spirit of rock & roll. And instead of just me on guitar, we pulled together a whole band, featuring my uncle and me playing guitar, my dad on drums and my cousin playing keyboards.

Over 150 people attended and the event was a tremendous success! The event is something that has finally made me feel as though I'm doing something progressive for VHL.

Calvin and his family raised more than \$10,000 for VHL.



pete in future triathlons this summer.

Thank you to all of our friends and family for your support throughout the training process as well as all of your generous support in our fundraising efforts. We had set a goal of \$2500. So far we have raised \$4,175!! If you'd like to contribute, please see our web page,

<http://www.firstgiving.com/powowtriathlon>.

-Beth S. and her training buddies, Janet and Alicia, Massachusetts

Jenny M. and Kim H. joined 50,000 trekkers in May 2008 for the annual Bloomsday walk in Spokane, WA. Here is Jenny's description.

"We were amazed at the number of people, both participants and spectators alike, that asked us about VHL. There were 50,000 participants and many more spectators. People were cheering us on saying "Way to go VHL!" and radio stations positioned throughout the 7.46 mile course always asked what VHL stood

for and then gave us a plug over their loud speakers. It was such a great experience I encourage more people to do something similar to just get the VHL name out there -- if they see it, they will ask about it! We decided next year we will hand out cards with info to those who ask about VHL and once again we will put VHL.org on our shirts."

Jenny and Kim and friends raised over \$2000!

Jenny M. and Kim H., Washington

We did it!!!! On Saturday, July 12, 2008, we competed in the Powow Triathlon in Amesbury. We swam .5 miles in Lake Gardner, biked 12.7 miles and ran 3.2 miles. In June our training definitely been stepped up a notch. We



began swimming 4,650 yards each week, that is about 3 hours in the pool. We biked 45 miles a week in addition to running 12 miles. It was tough, but now that we are in better shape, it is much easier.

The actual event was such a blast!!! We plan to continue our training and com-



You can make a difference too!

Take The Challenge...

Thanks to the generous support of Sunny Greene and the Lusk and Horwitz families who have challenged us to make our donations go even farther! They will match all contributions of \$100 or more that we receive by December 31, 2008, up to a total of \$30,000. Please help us earn these wonderful donations!

We're offering you something you can't buy at any price -- life-saving information to help you stay healthy and give hope to millions of people worldwide with VHL, kidney cancer, and other tumors by extending your support to VHL Family Alliance.

To simply learn why your decision to contribute to VHLFA is so valuable or how the method you choose works contact: **development@vhl.org or 617-277-5667 ext. 4**

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.

**** 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
5. Music CD, "Love Being Here With You," by Cool City Band



Mail to: VHLFA, 2001 Beacon St, Ste 208, Boston, MA 02135-7787 USA
or Canadian VHLFA, 4227 Hamilton Rd., Dorchester, ON N0L 1G3

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.
 Please send me ___ VHL wristbands (minimum donation \$5 each).
 Gifts of \$100 or more will be matched by the Greene, Lusk and Horwitz families.
 With my gift of \$150 or more, please send me item # _____ above **
(Please make checks payable to VHL Family Alliance)

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 Zip/Postcode: _____ Country if not U.S.: _____
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- Send newsletter
 Audio version needed
 I would like to receive occasional alerts via e-mail from VHLFA only

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: _____

Easy Ideas to Consider

You can turn any event you can dream up into a way to support VHLFA. Create a sports event, even a birthday party or a wedding can be a simple way to encourage guests to make a donation to VHLFA.

Please call us if you are interested in helping VHLFA in this fun way. We would be happy to send you informational materials, donation forms and envelopes. Big or small, anything you can do to help people understand VHL and to fund our cause can affect everyone in a big way. Your effort is important to us, **thank you!**

People with VHL can make the most important gift of all; tissue removed during surgery is critical to finding a cure. Call or write to the VHL Tissue Bank to give permission to deposit surgically removed tissue in the Bank, write to bank@vhl.org or phone 877-221-6374 (24 hours a day) or see <http://vhl.org/bank>

We understand that choosing to make a bequest of cash or other property to VHLFA is an important decision. If you are interested in making this personal commitment to VHLFA, please don't hesitate to contact us.