



## The Changing Face of VHL

When we first organized in 1993, before the gene was identified, it was very difficult to get a diagnosis of VHL. The clinical diagnostic criteria required that you have tumors in two different organ systems, or one tumor type plus a first-degree relative with VHL -- and the good fortune to have a doctor who thought of VHL. There was no internet, and no automated decision-support tools for doctors. In most cases, it took more than 20 years to get a diagnosis of VHL.



*Checking vision*

Today the community we serve has changed as a result of the progress we have made together. First and foremost there is DNA testing. More information about VHL is now readily accessible on the internet: on [vhl.org](http://vhl.org), in our Handbook, and in a wealth of new articles in the medical literature and in internet resources for doctors like UpToDate. While the clinical criteria have not changed, doctors who have a patient with an eye lesion or hemangioblastoma or kidney tumor at a younger age have the option now to send that person for DNA testing to determine whether this one tumor might in fact signal VHL. Families who know they are at 50% risk of passing VHL to a child have the option to test early to determine whether a child carries the VHL alteration.



[bbb.org/charity](http://bbb.org/charity)

As a result, children can be started early on the screening program outlined in the Handbook, to watch for issues and keep that child healthy. There are better treatment options today, raising the likelihood of good outcomes from procedures.

All of these improvements are

changing the face of the community we serve. When someone is diagnosed with VHL, DNA testing throughout that person's family is able to identify older relatives who do carry the mutation, but who may have been more lightly affected. Often we find that an older relative might have some kidney tumors that, if left undetected, would soon have become full-blown kidney cancer. More than one person has said to us, "my child saved my life" by making the VHL diagnosis possible before that crisis occurred.



*Checking hearing*

DNA testing has also allowed us to identify young children who carry the VHL alteration, years before any symptoms. By following the screening protocol, we are able to observe the early development of tumors as never before, and to work with prevention strategies, to soften the course of the disease. Through good nutrition, exercise and the avoidance of smoking, and through early care of the eyes, we are working to keep kids healthy with VHL.



*Having fun with friends*

This requires the participation of the child. As we have learned from other diseases, such as juvenile diabetes, children need to become managers of their own health from an early age. To help us enroll our children into that effort, we have published the *VHL Handbook: Kids' Edition*, helping children understand the key role they can play in keeping their bodies and spirits strong and healthy.

There is one other very important and growing contingent of our community -- people who are the first person in their

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family ever to have VHL. About 20% of the people we are in touch with are the first in their families ever to have VHL. Thanks to DNA testing and more easily accessible information about VHL, people are being diagnosed at younger ages with single tumors. A seven-year-old girl in California and a nine-year-old boy in Boston were first thought to have retinoblastoma, but in the course of the next two months their doctors realized that both of them had VHL, each the first person in the family to have the altered gene.

There is an important message here. VHL can

happen to anyone. Things are still happening that cause the VHL gene to change. Is it in the environment? in the water? in our food supply? Is it random chance? Whatever the cause, we need to better understand what causes genetic change, and to find a cure for VHL and for all the many cancer tumors in the general population that follow the same pattern of growth. VHL is one of the key controllers of cell division and proliferation of new blood vessels that are the hallmarks of all cancer tumors.

Please help us find a cure for VHL, and a cure for cancer.

## Clinical Care Centers - Providing Coordinated Care

We have partnered with 21 medical centers in the United States and another 11 throughout the world to form a network of Clinical Care Centers (CCC's) for VHL. Each center provides us with a single point-of-contact, so that people seeking care for VHL have a name and a telephone number to call. Each CCC has committed to work with people with VHL, to help them wend their way through the forest of medical specialists needed to manage VHL.

The complete list of centers can be found at <http://vhl.org/cc>

In this issue we meet two of the centers.

*From Maegan Roberts, MS:*

"The Mayo Clinic Florida (MCF) is excited to be recognized by the Von Hippel-Lindau Family Alliance as a VHL Clinical Care Center. MCF fills a geographic need for VHL patients being the only CCC located in Northern Florida or Georgia. The Mayo model of care aims to decrease the time and resources patients need to invest in a visit. Scheduling is efficient, with several consultations and tests grouped into the shortest time possible, usually 2 to 4 days.

"It is vital for VHL patients to be seen by medical providers who have knowledge of VHL. At MCF, our VHL patients are seen by a multi-disciplinary team. This team is directed by a Medical Geneticist, Dr. Douglas Riegert-Johnson, and a board certified

genetic counselor. There are many other physicians in a wide variety of specialties which complete the Mayo Clinic VHL CCC."

*From Gayun Chan-Smutko, M.S.:*

"The VHL CCC at the Massachusetts General Hospital (MGH) is staffed by Dr. Othon Iliopoulos, genetic counselor Gayun Chan-Smutko, and a patient coordinator. Together we provide comprehensive care and coordination of care for patients with VHL disease and other hereditary kidney cancer syndromes. In the past year, we have seen a continued growth in new referrals to the MGH CCC from the New England area. In particular, there has been an increase in referrals from internal and external providers with patients who have a single hemangioblastoma, no other symptoms or findings, and no known family history of VHL-related lesions. This has helped us continue to broaden our understanding of VHL disease from the clinical standpoint."

"Research on the VHL gene has already given us four approved drugs for kidney cancer -- it is time for us to give back to VHL patients what they have provided for the broader medical community."

-- Eric Jonasch, M.D., Genito-urinary Oncologist at University of Texas M.D. Anderson Cancer Center, Houston, Texas

## Holiday Gifts



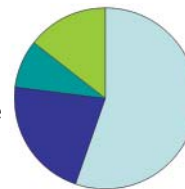
Instead of one more tie or bottle of perfume, how about a gift of research to find a cure?

We will be happy to send you blank cards to send yourself, or we can send cards to the recipients you ask us to honor. Minimum \$10 per card.

This year's card is one of the illustrations from our wonderful new *VHL Handbook Kids' Edition*.

## Report for Fiscal 2009 (ended June 30, 2009)

Total Revenue for Fiscal 2009 was \$284,613  
Of this, \$61,020 was allocated to the Research program, for grants and Tissue banking.



*Of our Expenses:*  
Research - \$61,020 (21%)  
Education & Support- \$157,705 (56%)  
Fundraising - \$25,029 (9%)  
Management - \$40,859 (14%)

## Please help us cure VHL!

## Challenge! Your Gift Goes Farther!

Four families are challenging you to make a special pledge to VHLFA this season. They will double your gift, up to a total of \$55,000! and help us raise money for research. Special thanks go to Scott & Amy Borg, Sunny Greene, Lee and Toni Horwitz, and Tom and Nancy Lusk for their generous Challenge Grants!

## Research efforts you are supporting 2008-2009



**Thera Links, M.D., Ph.D.**, of the University of Groningen in the Netherlands, has completed the preparations for the study she began for us last year. She is now ready to begin scanning patients in her project "Visualizing VEGF producing lesions in von Hippel-Lindau." When the second copy of the VHL gene is inactivated in a cell there is heightened production of the vascular endothelial growth factor (VEGF). The greater the production of VEGF, the higher the growth rate of the tumor.

Dr. Links and colleagues have developed a radioactive labeled antibody, based on bevacizumab (Avastin) which binds to VEGF, making it possible to see concentrations of VEGF on a PET scan. They will be scanning 30 people with VHL to detect and quantify the level of VEGF production in VHL-associated lesions. The goal is to use the information learned through these scans to formulate a plan for monitoring and treatment of these patients.



**Rachel Giles, M.D., Ph.D.**, of the University of Utrecht, also in the Netherlands, has developed a unique animal model for VHL, a zebrafish with no VHL gene at all. An animal model allows scientists to watch tumors develop in the body of the animal, and test the reaction of the tumor to various treatments. Small animals that go through many generations in a short period of time are preferred, allowing the researcher to see the consequences of a treatment quickly.

Zebrafish are particularly interesting because they are small and transparent. You can see right through them. With the aid of a microscope and various contrast media, you can observe changes in the blood vessels while the animal continues to live. Dr. Giles; team will be systematically testing VHL patient mutations by injecting this mutation into a zebrafish embryo and watching the development of the fish. They can inject hundreds of zebrafish embryos in a single morning and perform the phenotypic analysis within two weeks.

In the four pictures shown here, the lower two

pictures are of the eye of a fish with no VHL protein (*vhl -/-*). The top two pictures are of the eye of a fish at the same age with normal VHL protein function (*vhl +/+*). In the centers of the two left-hand pictures you can see that where the eye with normal pVHL has only three visible blood vessels, the eye with no pVHL has many blood vessels. In the two right-hand pictures, you can see those same blood vessels from the top. In full motion under the microscope, you can see the blood pulsing through these vessels, or watch cells divide. As time goes on, more blood vessels grow, forming a hemangioblastoma.

Different drugs can be tested to see if the tumor responds.

VHLFA continues to invest in building a robust **Research Infrastructure** consisting of surgically removed tissue and donations of tissues after death. These priceless biomaterials are the essential building blocks for all research. Our bank continues to grow, with 357 samples collected from 24 donors, and nearly 60 people registered with the Tissue Bank. We are working to double that number this year.

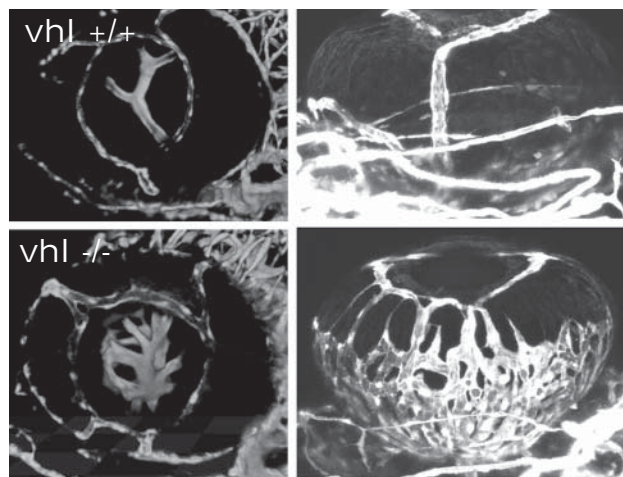


Photo taken by E. van Rooijen: Zoom-in picture of a living fish eye. The blood vessels are labeled with Enhanced Green Fluorescence Protein (GFP) as a contrast medium. Left, looking from the front; Right, as seen from above. Notice the much larger number of blood vessels seen in the eye with no VHL protein function (*vhl -/-*).

## Your Donation Goes Even Farther!

Thanks to the generous support of the Borg, Greene, Horwitz and Lusk families, *Your donation* this season will go even farther!

Sunny Greene, Scott and Amy Borg, Lee and Toni Horwitz, and Tom and Nancy Lusk have challenged us. They will match all contributions that we receive this season, up to a total of \$55,000. 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 with VHL, and targeted research projects working for a cure for VHL.

You can send holiday greetings to your friends and relations that will help match these gifts! Fill out the form below, or list addresses on other paper, to send holiday gifts *and* help us find a cure.

**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. "VHL Handbook, Kids' Edition", by Kruger et al
2. CD, Bach, "Goldberg Variations" for Piano, by Pierre Jacomet
3. CD, "Forever In His Care," by Deb Hogan
4. CD, "Wayfaring Stranger," by Clenton Winford II
5. CD, "Swing Favorites," by Shannon Forsell



## 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 educational 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  
2001 Beacon Street, Ste 208, Boston, MA 02135  
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 send e-mail to [development@vhl.org](mailto:development@vhl.org), or phone Lisa Steindel at 617-277-5667 ext. 4

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 \_\_\_ blank holiday cards (minimum donation \$10 each)  
 With my gift of \$150 or more, please send me item # \_\_\_\_\_ above \*\*  
 (Please make checks payable to VHL Family Alliance)

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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  With Holiday Greetings to...  In Honor of ...  In Memory of ... \_\_\_\_\_

Please send an acknowledgment card to ... Name: \_\_\_\_\_

Address: \_\_\_\_\_

or enter multiple holiday cards on the back of the cover letter. Card design from the VHL Handbook: Kids' Edition Page 4

