



Our Second Decade - Greater Progress *with your help!*

Let's all work together to make the miracle we all crave -- ***let's cure VHL!***

I'll probably never hold a brush
That paints a masterpiece.
Probably never find a pen
That writes a symphony.
But if I love, then I will find
That I have touched another life.
And that's something
worth leaving behind. (Lee Ann Womack)

We are all working together to leave something behind. The VHL Family Alliance will celebrate its tenth anniversary in January 2003. As we look back on the growth of our organization, much progress — much positive and innovative progress — has taken place. It takes time, enthusiasm, and money to create the progress you will see in this report.

The many volunteers who bring their expertise and give of their time have brought us to where we are today. Our Board of Directors works to enhance the existing programs in place and add new and informative ones where needed.

We are an organization that is growing every year. Today we serve more than half the projected number of people with VHL in the U.S., but only 6% worldwide. In addition, the VHL Family Alliance continues to raise more funds every year for vital research as well as organize decisions about VHL. We are proud to see the VHL Family Alliance grow from a vital grass roots group to a national organization still dedicated to individuals, family and friends who are affected by VHL. When one person is sick, the entire family circle is affected.

Our newly appointed Director of Volunteer Services will encourage volunteers to offer support and services through the existing 1-800 Line, info@vhl.org, State Chapters and Contacts, and online discussion groups. We are looking to introduce some new support programs to provide more service to our Spanish speaking population and to have Regional meetings four times a year to bring VHL support closer to home.

Our new Public Relations Director brings twenty years of journalistic experience as a senior business journalist, producer and publisher. His unique media talents will be a tremendous asset in bringing awareness about VHL to the public.

Our Finance Director has spent the last twenty years working on the floor of the Chicago Mercantile Exchange. His expert abilities as a broker will assist us as an organization to move forward with our funding needs and to continue to grow in the future.

Our Treasurer is a tax attorney having served various positions with a number of nonprofit organizations. We are fortunate indeed to have such an experienced, concerned individual in the important position of Treasurer.

In addition to the Directors, there are multitudes of caring volunteers who donate much of their time to provide services to everyone in the VHL community, and many more who donate money. In this issue you will read about the exciting research ***you*** are funding, and the many services ***you*** help to sustain.

We would like our tenth anniversary year to be the best year to date. Your generous donations will help to accomplish our mission. Won't you help us through and beyond the next ten years?

Leave something behind. Be a part of helping the VHL Family Alliance grow. Help us find a cure!

Take care, stay well,

Maria Shipton

Maria Shipton, Chairman of the Board

P.S. We can't do it without you!

Let's make a miracle!

Let's cure VHL!

1.. "Something Worth Leaving Behind," by Lee Ann Womack, (MCA,2002, UPC 8817028729). Song written by:Brett Beavers & Tom Douglas, Rutledge Press.

Ohio Woman Fights VHL Disease

When Cari E. was in labor in October, 2001, her blood pressure spiked repeatedly. After giving birth to her daughter, it was discovered Cari had a large tumor on her adrenal gland.

The tumor was the result of Von Hippel-Lindau Syndrome, a genetic condition caused by a dominant gene that leads to an abnormal growth of blood vessels in some parts of the body. Most VHL tumors are benign, but some can grow to be malignant.

In addition to the adrenal tumor, Cari has also had a brain tumor removed. She knows that more tumors are possible because of the nature of VHL.

Cari, an Ohio native who works as an administrative assistant, said the disease is generally not life-threatening, but she will likely develop more tumors.

"The key to living with this is early detection," she said. "I will have to go through yearly CT scans."

Cari, 27, said she believes she inherited VHL from her mother, who died from a brain tumor in 1982, and there is a 50 percent chance her daughter, Siera, has inherited the disease.

"We're going through genetic counseling at the Cleveland Clinic to see if my daughter has this disease," she said. "It was once considered rare, but now we know it's not so rare. There are thousands of people with undiagnosed tumors."

According to the VHL Family Alliance, the disorder is more common than previously thought. More people are now diagnosed in time to help because of the use of more sophisticated imaging techniques, such as Magnetic Resonance Imaging. MRI is used to produce high quality images of the inside of the human body.

"[VHL is] one of many recently recognized and described genetic diseases that predispose people to cancer," said Dr. Steve Roshon of North Coast Cancer Center of Sandusky, Ohio. "It's fairly rare, but the scientific interest is huge, especially among those who are in genetic research."

Cari, her family and friends planned and held a series of fund-raising events to raise money for VHL research.

"Research is confident that there will one day be a pill which will suppress tumor growth," she said. "The money will go to the VHL Family Alliance."

VHL Family Alliance, Brookline, Mass., is a non-profit organization, dedicated to the diagnosis,



Cari and Siera

treatment and quality of life for people affected by VHL.

The first event was a benefit day at D.J.'s Sports Bar in Sandusky. Area bands donated their time, including TwoTheMax, Funk 'n Bluez, Dave James, Pete Bernel, Island Fever, Daisy Chain, Surrender Dorothy and Donny G. In addition, Greg Michaels of WNRR 92.1 broadcast live on the radio throughout the day. Area businesses donated door prizes, including Cleveland Indians tickets, Island Rocket tickets and 18 holes of golf for two with a cart from Sawmill Creek. The \$10 admission included entertainment, food and participation in a poker run, with a cash prize of \$150 for first place.

This was followed by a bikini car wash, which attracted a great deal of attention. And finally, Cari's dad, Dan P., held a golf scramble.

Altogether Cari, her family and friends raised \$6,117 to go toward funding research on VHL. We are all grateful to them for their efforts and join them in hope that by understanding more of what is going on in the cell we can finally get the maintenance drugs we need to keep tumors small, or keep them from ever appearing at all.

Based on an article by Trish Doller, *Sandusky Register*, June 10, 2002

*We Need Your Help Too!
Please Give Generously
Thank you!*

Research Digest

by **Myriam Gorospe, Ph.D., Director of Research and Joyce Graff**

Nine VHL research proposals were submitted to the VHLFA this year. Because of your generosity we were able to fund five of these. Nonetheless there is a great deal more work to be done. Hospitals and universities are cutting back their own spending on research, so those of us who want VHL research to move forward swiftly need to fill this gap. Even with a modest budget, however, we have made a significant contribution to the advancement of VHL research.

One of the stated goals of our research grants program is to assist young researchers in gathering sufficient data to prove the validity of their ideas so that they can qualify for other larger grants elsewhere and continue their research. In this regard, we are very happy to announce that

in 2001 Dr. Maria Czyzyk-Krzeska, whom we funded for two years (1999 – 2001), was able to obtain substantial funding from the NIH (National Institutes of Health) and the ACS (American Cancer

Society) for the continuation of her research on the **Role of VHL in Pheochromocytoma**. Similarly, Dr. Ehud Gazit at Tel-Aviv University, whom we funded last year, has won a very large grant from the Israel Cancer Research Fund, to continue his work on **'The Role of Protein Folding and Stability in the VHL Syndrome'**.

There are two aspects we are focusing on in this year's grants. First, we continue to learn more about how the VHL protein (pVHL) operates in the cell – what it regulates in normal function, and what doesn't work when pVHL is not present. Second, we are trying to move from this knowledge to real therapies. This work moves ahead more quickly when there is a "biological model", preferably one that goes through many generations in a short period of time so that genetic changes can be tracked. The mouse and even the fruit fly have a VHL gene. This shows how very essential a role the VHL gene plays in the cell.

We have renewed funding for a second year for **Dr. Robert J. Dronio** of the University of North Carolina to further his research on **E3 Ubiquitin Ligase Complexes'**. pVHL's role within the E3-ubiquitin ligase is often compared to that of a 'g Page 9arbage collector', functioning as an "off" switch by gathering up certain cellular proteins that are needed for cellular growth and proliferation. The investigators have made good progress on the goals they set out to accomplish over the past year of

funding, and are continuing and extending that work.

Dr. Georges Mer of the Mayo Clinic in Minnesota is investigating how the VHL protein binds to another key protein named HIF α . These studies increase our knowledge of how pVHL and HIF1 α interact, thus helping in search for drug molecules that can restore the normal function of pVHL.

Dr. Tien Hsu of the University of South Carolina is interested in addressing how pVHL mutations cause cancer growth and metastasis. Dr. Hsu has identified a pVHL-interacting protein named nm23 (nm: non-metastatic), which may be a good target for therapeutic intervention.

“ Thank you very much for giving me this grant. I can assure you that the funding will be put to good use. My gratitude to the VHL Family Alliance for this great opportunity.

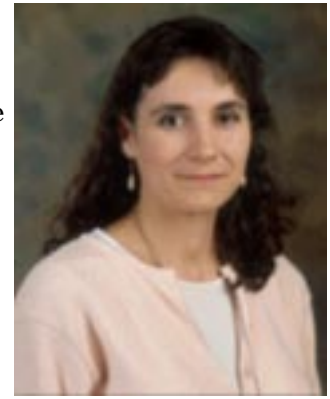
-- **Georges Mer, Mayo Clinic**

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Fortunately, nm23 belongs to a class of enzymes that have been very well studied, so drug development should be feasible.

Dr. Daniel George of the Dana Farber Cancer Research Institute in Boston proposes to use the Novartis Pharmaceuticals drug PTK/ZK to carry out a Phase II clinical trial to treat patients with VHL, especially those with advanced central nervous system disease. The VHL study is due to open to VHL patients in December 2002.

Pierre Jacomet and a team at the Catholic University Medical Center in Santiago, Chile, are studying **"Pheochromocytoma and Altered Mental Function."** The objective is to compile data on the number of people suffering from panic attacks and other personality disorders that could be traced to undetected pheochromocytomas. With the help of statistical information, he hopes to raise the visibility of this issue so that health care professionals will be more likely to suspect and diagnose a pheochromocytoma. Dr. Gorospe is Investigator Chief of the Cell Cycle Control Unit, Laboratory of Cellular and Molecular Biology, National Institute on Aging, National Institutes of Health



The VHL Family Alliance has provided enormous benefit to both clinical as well as basic investigators in the field and, most importantly, to those patients with VHL and renal cell carcinoma that we all care for. Keep up the good work, you are helping and giving hope to thousands of people. I am optimistic about the future for therapy.

-- **W. Marston Linehan, M.D., Chief of Urologic Oncology, U.S. National Cancer Institute, National Institutes of Health**

Teamwork for Health

I just came across the VHL Family Alliance Homepage. What a wonderful site! I am in awe of what an obviously dedicated organization you belong to! -- **Erica T., genetic counselor, Mass.**

It's so wonderful to know that we are not alone with VHL. There's a community of support here to help. -- **Fran M., Michigan**

Let's Cure VHL in this Decade

Improve Diagnosis: Let's find all those people with VHL who are struggling to find a diagnosis for all their mysterious symptoms.

Improve Treatment: Let's find improvements in imaging and surgical techniques that will make it easier to treat individual tumors and keep people healthy and productive.

Improve Quality of Life: By supporting one another, by keeping our spirits up, by focusing on the positive and creating real progress, we can live happier lives.

Progress!

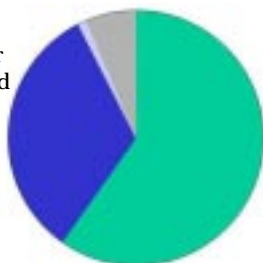
We are now reaching more than 13,000 people in 72 countries. We are in touch with more than half the projected number of people with VHL in the U.S., but only 6% worldwide. Service for English-speaking U.S. citizens has moved significantly to the internet, while service to the Spanish-speaking population in the U.S. and Latin America is beginning to build rapidly. This year we distributed 18,000 copies of the **VHL Handbook** in English, 500 copies in Spanish, and 80 in Portuguese. Operating expenses were down 7% from the prior year.

The money we raise goes directly into programming and research, with only 6% for administrative costs. We are able to do this because of the hard work of a large number of dedicated volunteers in 19 countries around the world, providing outreach in their local areas.

This year, **thanks to you**, we awarded \$131,000 in research grants, bringing the total to \$571,000 over the last six years. **Let's do it again!**

Call or write for a list of special projects that need funding. For example, we want to set up an inquiry line in Spanish language, and design better support for asymptomatic youth diagnosed through DNA testing.

Total Revenue for Fiscal 2002 (ended June 30, 2002) was \$222,152. Of this, a total of \$131,000 was allocated to research funding.



61% Research
32% Education and support
1% Fundraising
6% Administration

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 programs of education, service, and research by remembering VHLFA in your will

To make a bequest of case 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 your attorney, accountant, or tax estate planning specialist, or simply write to Director of Development, VHLFA, 171 Clinton Road, Brookline, MA 02445, info@vhl.org

Mail to: VHLFA, 171 Clinton Rd., Brookline, MA 02445

or Canadian VHLFA, 4227 Hamilton Rd., Dorchester, ON, N0L 1G3

Enclosed is my tax-deductible gift to support:

VHLFA Research only

\$ _____ \$5000 \$1000 \$500 \$100 \$50 \$ _____

(Please make checks payable to VHL Family Alliance)

Name: _____

Address: _____

City: _____ State: _____

Zip/Postcode: _____ Country: _____

Tel: _____ Fax: _____

E-mail: _____

Send quarterly newsletter Audio version needed

My employer will match my donation. I have enclosed the form.

I am a Person with VHL Family member Friend Sponsor

Health professional _____ (specialty)

Please charge my Visa Master Card Amex

Card number _____ Exp Date _____

Name as it appears on the card _____

One time payment of \$ _____

or **Monthly charges:** 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: _____
