

# Annual Report

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## We Need Your Help!

by Peggy Marshall, Chair, 800 line Committee

Living with VHL is a roller coaster existence with its ups and downs. I was diagnosed with VHL in 1962. There are nine members of my family diagnosed with VHL and the difference in each is quite unique. Everyone's case is different and we all have difficult roads to travel. We struggled for years seeking information about von Hippel-Lindau with our limited resources. For the most part, we learned about VHL the hard way -- through surgeries and experiences. We do not have to do that any longer.

Having worked closely with the VHL Family Alliance now since 1993, serving on the Board for seven years, talking with hundreds of families on the 800 line, sending information packets to all the new members, my husband Don and I are convinced that education, early diagnosis, early prevention, and appropriate treatments are the answer to living with this chronic condition.

The VHL Family Alliance provides a wealth of information about von Hippel-Lindau. Support is offered in many ways: through our website, [www.vhl.org](http://www.vhl.org), through the toll-free telephone line 1-800-767-4845, via E-mail to [info@vhl.org](mailto:info@vhl.org), through this quarterly newsletter, and through local and international meetings. We have online discussion and chat groups in four languages: English, Spanish, German, and French, all moderated by trained volunteers who have VHL themselves.

Medical information and consultation is made available to local physicians through our Clinical Care network.

These programs are supported with your membership dues and donations. Each of our programs grew more than 24% this year, while we held expenses quite steady. As you will see in this issue, research interest in VHL is increasing. Our research grants continue to be strong and hopeful with your generous support. We have more proposals each year. The number and size of the awards is dependent upon your generosity.

We need you to continue supporting our mission to improve diagnosis, treatment and quality of life for people with von Hippel-Lindau disease. Please give generously to sustain our educational programs and to make it possible for us to fund more exciting research and find a cure for VHL.

**\$100,000 for Research in 2001 -- Let's do it again!**

***What can you contribute? Every little bit helps!***

Write us in on your United Way Campaign

U.S. Federal and postal workers and military personnel can designate CFC donations for VHLFA (CFC #1098)

***Gifts of appreciated stock offer tax benefits to the donor as well as benefits to the Research Fund. Call to arrange transfer to the VHLFA account, 1-617-277-5667.***



Meet the Board: At the Board meeting in Palo Alto we honored Peggy and Don at the completion of their seven years' service on the Board, and welcomed several new members. Left to right, back row: Patricia Rasmussen, Tim Nielsen, Tom Rodenberg, Don Marshall, Matt Painter (Treasurer-elect); front row: Maria Shipton, Peggy Marshall, Sheila Tepper, Myriam Gorospe, Kathy Braden, Joyce Graff. This year's officers are: Chairman of the Board: Maria Shipton; Chairman of the Alliance: Joyce Graff; Vice-Chair, Kathy Braden. Not pictured: Treasurer Kelly Heselton and Secretary Altheada Johnson (see page 3), Jay Platt and Tom Lusk.

# Research Report

by Myriam Gorospe, Ph.D., Director of Research

Nine VHL research proposals were submitted to the VHLFA to receive funding this year. It is a remarkably high number of grants, compared with those received in the past several years: five proposals were submitted in 2000, three proposals in 1999, and two each in 1998 and 1997. Most of this year's grants were of outstanding quality, however, the VHLFA has limited funds and was only able to award four of them (up from three grants funded in 2000, three in 1999, two in 1998 and two in 1997. See Figure1)

Two of this year's awards went to investigators who were applying for a second year of grant support.

**Dr. Shahriar Koochekpour** is at the Louisiana State University, in New Orleans, Louisiana. His proposal ('*VHL-regulation of Fibronectin-integrin signaling*') addresses highly relevant questions regarding the function of the VHL protein (pVHL) in the cell. During the past year, funding by the VHLFA allowed Dr. Koochekpour to demonstrate that pVHL influences the interaction of cells with their external environment (the so-called extracellular matrix). He showed that pVHL influences the expression of *integrins*, proteins tightly linked to the communication of the cell and the extracellular environment. For an additional year of funding (2001-2002), the investigator proposes to characterize how VHL influences integrin function and integrin-associated signaling pathways, and, in turn, cell migration and invasion. He further proposes to investigate pVHL's influence on the expression of enzymes (proteases) involved in the remodeling of the extracellular matrix. Through these studies, he seeks to gain a better understanding of how pVHL affects the proliferation, differentiation, invasiveness, and metastasis of kidney cancer cells, all pivotal questions in VHL disease.

**Dr. William Rigby** is at Dartmouth College, in Lebanon, New Hampshire. His clear-cut, focused proposal is entitled '*The von Hippel-Lindau gene regulates hnRNP A2 expression: A mechanism for the post-transcriptional regulation of hypoxia-inducible genes*'. Dr. Rigby's long-term goal is to address another very important question in the fields of VHL and kidney cancer: how does pVHL influence the expression of other cellular genes? During the first year of funding, this investigator has established that a special protein named hnRNP A2 is overexpressed in pVHL-deficient cells. hnRNP A2 is, in turn, capable of influencing the expression of other important cellular proteins. These observations were written up in a manuscript that was recently



Myriam Gorospe was honored as Volunteer of the Year for her work as Research Director and as liaison with the Spanish-speaking community worldwide. A native of Spain, Myriam translated the Handbook and Family Health Tree into Spanish. Pierre Jacomet of Chile, our International Volunteer of the Year, led the project to create the first-ever book on VHL for doctors in Spanish language, produced and distributed to doctors throughout Latin America by Recalcine Pharmaceuticals.

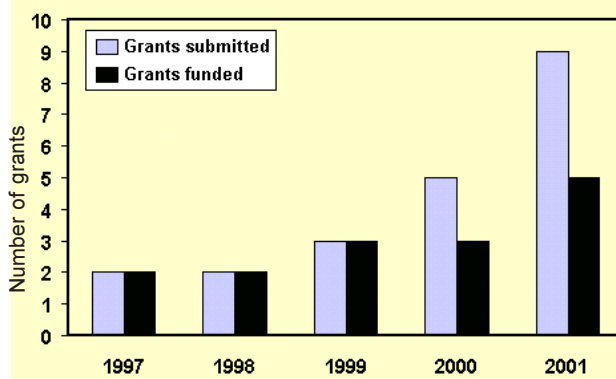


Figure 1. Comparing the number of grants funded to the number of applications received.

submitted to a prestigious biomedical journal. Over the coming year, Dr. Rigby proposes to establish whether pVHL-mediated regulation of hnRNP A2 contributes to the regulation of the expression of genes important for the growth and proliferation of kidney cancer cells. The ultimate goal of his research is to identify the protein targets of pVHL that influence tumorigenesis in order to design improved therapies to manage VHL disease.

The other two awardees will receive funding for the first time.

**Dr. Ehud Gazit**, at Tel-Aviv University (Israel), submitted his grant entitled '*The Role of Protein Folding and Stability in the VHL Syndrome*'. Dr. Gazit plans to investigate the folding, stability, and subcellular localization on wild-type pVHL, as well as those of various mutant pVHL associated with either type I VHL (characterized by the absence of pheochromocytoma) or type II VHL (where pheochromocytoma occurs). His studies are based on the hypothesis that the VHL mutations leading to type I VHL (large deletions and nonsense mutations) generally lead to alterations in protein folding and stability. By contrast, mutations leading to the type II VHL syndrome seem to affect mostly pVHL's ability to interact with other proteins. Preliminary results assessed the stability of pVHL protein in response to changes in temperature. The Principal Investigator (PI) proposes to investigate whether chemical chaperones or specific peptides can modulate the stability and folding of the mutant VHL proteins. This is a very promising direction for individuals with the VHL syndrome.

**Dr. Robert J. Duronio**'s grant is entitled '*Analysis of Drosophila Rocs, RING Finger Subunits of E3 Ubiquitin Ligase Complexes*'. This investigator, from the University of North Carolina, Chapel Hill, proposes to use a very powerful genetic system (the fruit fly) to study the function of pVHL as part of a group of proteins named 'E3-ubiquitin ligase'. pVHL's role within the E3-ubiquitin ligase is often compared to that of a 'garbage collector'. Its purpose in the cell is to eliminate certain cellular proteins that are important for cellular growth and proliferation. Overall, this outstanding proposal is likely to yield high-quality results and to increase considerably our understanding of the VHL tumor suppressor protein and the pVHL-containing E3-ubiquitin ligase complex. This grant proposal is highly relevant to the objectives of the VHL Family Alliance.

"When you think that you are the only family faced with this disease, you feel so isolated. Hearing the experiences of all the families, you realize that we are all in the same boat, and thank goodness for the VHL Family Alliance." -- Sue L., Canada



Kelly Heselton



Lois Erickson



Gerhard Alsmeier



### Jay Platt, Georgia, Director of Public Education

This year we made some inroads into the consciousness of the general public on what VHL is and how it affects those who must deal with it daily. This was done primarily through various speaking engagements throughout the country, as well as a major article written for *Coping* magazine (with an estimated 500,000 subscribers). Also, on Sunday, June 3rd, I was fortunate enough to be featured on CNN Sunday Morning Live during the National Cancer Survivors' Day Celebration to speak about my experience with VHL.



## Special Thanks . . .

. . . go to all the many volunteers who make the VHL Family Alliance work!

You have undoubtedly spoken or corresponded with one or more of the people on this page. Here are the faces that go with the names!

Peggy Marshall (center photo, left) chairs the 800 line committee, consisting of (clockwise) Barbara Redding, Eva Logan, Altheada Johnson, and Lois Erickson (left). These ladies share coverage of our primary telephone line, 1-800-767-4VHL, which can be reached free from the U.S. and Canada.

Rachael Morgenstern in Brookline logs in the receipts and sends thank-you notes.

Altheada Johnson monitors our e-mail account, [info@vhl.org](mailto:info@vhl.org), and replies to or routes messages to get timely answers. She is also a returning Board member, and we are delighted to welcome her back to the Board.

Gale Lugo and Maria Shipton moderate the English language online discussion group, [vhlfa@yahoo.com](mailto:vhlfa@yahoo.com). The German discussion is moderated by Gerhard Alsmeier of Germany; the Spanish discussion by Dr. Karina Villar of Spain; and the French discussion by Elaine Follansbee of New Hampshire.

In addition, the chapter chairs and country affiliates throughout the world form the core of our volunteer team. Their generous sharing of their time and energy make the VHL Family Alliance what it is. Your generous donations support their efforts with postage and supplies, telephone and internet charges.

Each country affiliate is a registered charity in that country. Donations go to support local programming and newsletters, and toward the research fund.

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[canada@vhl.org](mailto:canada@vhl.org), 1-800-767-4845 or +1 (519) 641-7126  
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## Challenge!

BMS Management company of Houston, Texas, which owns about 3 million square feet of office space in 30 different office buildings in the Houston area, celebrates the purchase of new properties by making donations to multiple worthy causes, one of which is the VHLFA. Their donations are in honor of Michelle, a valued employee, and her daughter Korrina. In addition to their own contributions, they challenge business associates for matching contributions. We are grateful to the good folks at BMS Management and their many partners for their generous support. Wouldn't it be great if other businesses would make contributions and challenge their associates to match them?



Rachael Morgenstern



Gale Lugo



Karina Villar



Elaine Follansbee



## Teamwork for Health

Debbie M. from Florida, found the Palo Alto meeting "wonderful and very encouraging. The conference is a must for anyone who has never had the chance to meet someone in person who is handling all the medical issues and the stress related to VHL and to see how everyone really strives to go in positive directions."

Dr. Michiel Innes, a geneticist from Alberta, Canada, "enjoyed it tremendously. As a geneticist I often find myself playing the role of case coordinator and patient advocate so hearing and learning so much from a patient perspective was very rewarding. Things have already paid off as two days after my return I saw a woman in my general genetics clinic who almost certainly has VHL and I certainly felt prepared!"

### 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!

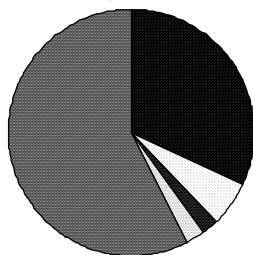
We are now reaching more than 12,000 people in 67 countries. We are in touch with nearly half the projected number of people with VHL in the U.S., but only 5% worldwide. Service for English-speaking U.S. citizens is moving significantly to the internet, while service to the Spanish-speaking population in the U.S. and Latin America is beginning to build rapidly. This year we distributed 12,000 copies of the *VHL Handbook* in English, and 900 copies in Spanish, and 7000 copies of the Spanish book for doctors. Operating expenses rose a modest 17%.

We pay no salaries, we do not rent office space. The money we raise goes directly into programming and research, with only 3% for administrative costs. We are able to do this because of the hard work of a large number of dedicated volunteers in 17 countries around the world, provide outreach in their local areas.

This year we awarded \$100,000 in research grants, bringing the total to \$440,000 over the last five years.

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 2001 (ended June 30, 2001) was \$186,636.62. Of this, a total of \$100,000 was allocated to research funding.



57% Research  
32% Education & support  
6% Public relations  
2% Fundraising  
3% Administration

## Remember VHLFA in Your Will

You can give hope to millions of people worldwide with VHL 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 cash or other property to VHLFA, your will (or supplemental codicil, if you do not wish to write a new will) should state:

"I give and bequeath to the VHL Family Alliance, Inc., a non-profit corporation, organized under the laws of the Commonwealth of Massachusetts, and having its principal office at 171 Clinton Road, Brookline, MA 02445, the sum of \$\_\_\_\_\_ or \_\_\_\_ percent of the rest, residue, and remainder of my estate to be used for general purposes of the organization."

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 more about other gift opportunities by consulting your attorney, accountant, and/or tax estate planning specialist, or simply write to VHLFA's Chairman of Development, 171 Clinton Road, Brookline, MA 02445, [info@vhl.org](mailto:info@vhl.org).

**Mail to: VHL Family Alliance, 171 Clinton Rd., Brookline, MA 02445**

or Canadian VHLFA, 905 Lawson Road, London, Ontario, N6G 4X4 Canada

Enclosed is my tax-deductible gift to support:

☐ Research ☐ Educational Programs ☐ Both Education and Research

☐ \$1000 ☐ \$500 ☐ \$100 ☐ \$50 ☐ \$25 ☐ \$\_\_\_\_\_

(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 required form.

I am a ☐ Person with VHL ☐ 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: \_\_\_\_\_

City: \_\_\_\_\_

Zip/postcode: \_\_\_\_\_ Country: \_\_\_\_\_