WHY GIVE TO VHLA?

By Jennifer Galenkamp, VHLA Board of Directors

Many of us have found the VHL Alliance at times of deep personal crisis. The information, the resources, the community are lifesavers thrown out to us, which we grip with all our might when our lives are spinning out of control.

Our family’s journey will be all too familiar to many: a sudden deterioration of vision early in the senior year of high school; a scholar-athlete aiming high, overwhelmed with college applications, SATs and exams now scheduled between appointment after medical appointment; laser, injections, surgery, headaches, adrenaline spikes and then so dizzy they can’t get out of bed; sleepless nights of pointless but relentless parental guilt, demanding of God why and praying for better, while trying desperately to keep family life as normal as possible. We made it through that first year, but shattered dreams and shattered confidence littered the foundations of our lives.

Personally, I cannot imagine how patients and their families manage without the VHL Alliance. It is the nicest club no one would ever wish to join – but I am so grateful for the calm, humanity, and knowledge of the VHLA staff, and the resources they offer. This organization is efficiently and economically run, but it does require resources – the hours and hours of time volunteered by so many members of the community, and the funds raised and donated.

Last year, approximately 2,000 different individuals gave donations of all shapes and sizes to the VHL Alliance. The funds support educational opportunities and materials, including the Annual Family Weekend and the Handbook, to maintaining the web site, MyVHL: Patient Natural History Study (have YOU participated?), numerous facilitated support group calls and the hotline.

Donations also pay for dedicated staff responding and managing the invaluable Facebook pages; work with volunteers, including Board Members, Chapter Leaders, and Clinical Care Center Liaisons, work with partner organizations; and funding research. To date, we – yes, we of the VHL community – have funded over $1.7 million in research.

Like many of you, I am reluctant to ask others to give money. But, like many of you, I am always happy to help others as I can. And I am desperate to find a cure. Desperate to find a cure not just for VHL, but through VHL, for the cancer that has afflicted so many other loved ones. Doesn't everybody want that? But, as much as I'd like to solve the problem myself, finding a Cure for Cancer through VHL is out of my reach. One thing that VHL has taught me is that to solve a problem this complex and life-changing, we need help and support from an awful lot of people, and we can't be afraid to ask for it. And, when you ask, as I

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May is VHL Awareness Month!

by Deanna W., patient

May is VHL Awareness month! Although I was diagnosed with VHL 25 years ago, I only recently became familiar with the VHL Alliance. In 2017, I became a VHLA Chapter Leader and participated in VHL Awareness month by hosting a fundraiser for the first time.

As anyone with VHL can attest, I have run into too many people who are not familiar with my disease; whether doctors, friends, coworkers, or community members.

When I decided to raise money for VHLA, I realized it was just as important to raise awareness of the disease. And while I hit my fundraising goal, the most significant experience in VHL Awareness month for me was sharing my story with others, and for the first time in my life, meeting another VHL Warrior face-to-face.

Funding for rare diseases is extremely limited. The fact that the cure for VHL is likely to lead to the cure for many other forms of cancer, makes finding a cure for VHL extremely important.

The more people who are aware of the disease, its impact, and can put a face to the disease, the more likely that people will contribute funding to find a cure.

In my opinion, there is no better time to raise awareness than during VHL Awareness Month in May. This year, do not be afraid to try your hand at fundraising and raising awareness. Start simple by telling your story to the people you encounter on a daily basis. Consider hosting a simple fundraiser such as a meal in a local restaurant. Many restaurants have programs to raise funds if someone purchases a meal and mentions an organization. It is a simple way to begin. The VHLA staff is happy to help you with any coordination, just email Heidi at heidi.leone@vhl.org.

Remember that while raising funds is important, the most important thing is to raise awareness about this disease. Every little bit helps as we strive toward Curing Cancer through VHL.

Why do we give? We give our time and money because we care, and we hope, and we fight on. Thank you for being part of this community.
by Maryetta G., patient

THEN

In 1966, I was a sixteen-year-old growing up in Baltimore, whose life centered around friends, clothes, school, and boys, when an occurrence of blurred vision took me to the Wilmer Eye Clinic at Johns Hopkins Hospital. The diagnosis was von Hippel-Lindau (VHL) and I had to withdraw from school for a year so that numerous laser surgeries, a vitrectomy surgery, and a detached retina surgery could all be done. At that time, laser treatment for VHL eye tumors was primitive at best. Anesthesia consisted of painful needles in and around the eye and post-surgery recovery involved bed-bound hospitalization for several days with sandbags on each side of the head to prevent movement. When I returned home, I was like any typical teenager, believing I was in control of my life. I moved on as if nothing more would happen to me.

Within 8 years, I was completely blind due to advanced eye tumors. I was no longer able to receive treatment because of scar tissue damage from my original surgeries. The same year that I became completely blind, I had a bilateral adrenalectomy (the removal of both adrenal glands) and added the term ‘pheochromocytoma’ to my newly growing VHL vernacular.

Dr. Zbar from the National Cancer Institute began visiting the homes of various family members to do blood work to isolate a genetic DNA marker so that a genetic blood test for VHL could be developed. Knowing about his work encouraged me to learn more about VHL, so I attended a conference where Dr. Zbar was a presenter. Being young, married, and newly blind, I was worried about the future. Would my health be stable and how would my blindness impact my independence?

Life continued and I began my family with the birth of my first child and then the adoption of my second, both girls. As a young mother, it became more apparent that awareness and education about this disease were important to me, especially since my daughter was also diagnosed with VHL. My attention was focused on learning new rehabilitation skills like walking with a cane, and embracing the daunting task of being a blind parent, such as using bells on my toddlers’ shoes.

We moved several times with my husband’s job, which gave me the opportunity to learn new environments, form new relationships, and develop new skills. I quickly learned the duality of 1: being independent (i.e. being moderator of a woman’s group and editor of a newsletter), and 2: being dependent (i.e. leaning on others to help with transportation of my children for practices and sporting events). When my daughters were approaching their teenage years, I would sometimes shop with them at the local mall. I remember on one occasion listening to them argue as to who would be walking with me, “it is not my turn, it is your turn to walk with mom, I walked with her last time”. I smiled in amusement thinking this is less about my blindness and more about being typical teenagers not wanting to be seen in public with a parent.

After being blind for 25 years, I once again was called upon to help with the care of children, this time for my two grandsons. I remember that the joy they had in showing me their ‘perfect’ artwork compensated for the fact I couldn’t see it.

NOW

At about the time my husband retired, my grandsons became teenagers and began teaching me the importance of texting and many other resources that were available to me. They were my introduction into the world of technology. I began listening to podcasts from Apple VIS for people with low and no vision, and got apps like Airs-LA (audio internet reading service), and of late, Seeing AI, which offers text reading, product identification, etc. These apps and podcasts not only kept me informed as to what is available and accessible, they are a lot of fun! I now also enjoy NFB Newsline for reading newspapers and magazines, and digital readers such as Audible and Kindle. Most recently, I joined the VHL Alliance Low/No Vision Discussion Call (vhl.org/lownovisioncall) with others that have low to no vision that allows us to connect, share, and support one another.

I have also always loved style, fashion, and interior design, and keep up-to-date on these things through apps, TV shows, magazines, and even newspapers. Friends often ask me to help them shop or choose outfits to wear and to help redecorate rooms. They especially enjoy telling their friends that they have a blind decorator or stylist, which makes me grin. (Here is a fitting place to use an ‘LOL,’ one of the first texting acronyms of many, taught to me by my grandsons.) Through

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small successes like these, and the development of a healthy self-image, I have learned that I can do much more than I thought possible. My friends continue to encourage me, my family supports me, and my faith sustains me.

Back to my more recent journey with VHL. My left eye has been removed due to a tumor whose growth could not be managed and my right will more than likely need to be removed in the future because of a growing tumor. My doctors at UVA Medical Center, a VHL Comprehensive Clinical Care Center (vhl.org/ccc) in Charlottesville, Virginia, use MRIs to monitor pancreatic cysts and numerous hemangioblastomas along all areas of the spine and in the brain. Brain surgery was needed because of a tumor and cyst, and a spinal surgery was required for a thoracic tumor. BTW (another texting shortcut taught by my grandsons), the spinal tumor turned out to be a meningioma, completely unrelated to VHL.

Lastly, my oldest daughter has undergone laser treatments on her eye tumors twice. Anesthesia consisted of drops to numb her eyes and post-surgery recovery was handled as an outpatient. I have seen 50 years of incredible progress. Wow (clearly not a texting shortcut), I am simply eager and excited about the future.

Note: For all of you reading this, I hope my story conveys that there are challenges that come with VHL, but no challenge has prevented me from living a happy and full life with VHL for over 50 years.

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**ASK THE EXPERT**

**Rules of Thumb for Pancreatic Neuroendocrine Tumors**

*by Dhaval Patel, MD, Staff Clinician, Endocrine Oncology Branch, National Institutes of Health, Center for Cancer Research, VHLA Grant Award Recipient*

Pancreatic neuroendocrine tumors (PNETs) are common in patients with VHL, and are found in about 11-20% of patients over a lifetime. Besides these tumors growing and pushing on other organs, these tumors have a risk of spreading. When should you or your physician become concerned?

Evidence from the National Institutes of Health (NIH) has shown that when the tumors are bigger than 3 centimeters (a little over an inch) in the tail of your pancreas, growing quickly (with a tumor doubling time of less than 500 days), or have spread, you should have an operation. We have also removed tumors bigger than 2 centimeters (a little over three quarters of an inch) in the head of the pancreas, because these tend to push on the bile duct, which causes problems like jaundice.

The chance of requiring an operation are low. However, imaging every year is needed to catch the tumor before it spreads. If you have a solid tumor, you should have imaging every year with either CT or MRI. If you have only cysts in your pancreas, you should have imaging every two years.

At the NIH, our new research has shown that the type of mutation can tell us if your tumor has a higher risk of spreading. We are using this new research with the generous help of the VHL Alliance to figure out what other genes are affected and why we see some patients who have tumors that spread and other patients that don't. Using tumor samples form our lab, we will test which genes are expressed at a higher level and which genes are expressed at a lower level. This might give us a clue as to why some people do better and others do worse.

In addition, we discovered that by figuring out the volume of a tumor by how much radioactive sugar (tumors like sugar) they take up, we can predict the grade of a tumor. The grade of a tumor goes from one to three. A grade 1 tumor is slow growing. A grade 3 tumor is dangerous and can spread quickly (luckily, most patients with VHL do not have a grade 3 tumor). Grade 2 is in between and sometimes acts like a grade 1 and sometimes like a grade 3. If we can figure out the grade without a biopsy or surgery, we may be able to avoid unnecessary surgery. These tumor volumes can help us figure out who needs surgery and those patients we can safely watch. These studies will hopefully help us improve our treatment of patients with VHL-associated PNETs and avoid unnecessary surgery.
The product of the VHL gene is the VHL protein (pVHL). This protein plays a central role in oxygen-sensing by targeting the protein hypoxia inducible factor alpha (HIF1α) for degradation. Under normal oxygen conditions, pVHL is equipped to recognize and clear HIF1α from the cell. Put simply, VHL halts or “applies the brakes” on undesired proliferation by removing HIF1α from the cell. In other words, loss of VHL releases the brakes leading to accumulation of HIF1α. This, in turn, induces changes to several other proteins causing a net undesired proliferation of cells. In many mutations in the VHL gene, it is not a matter of complete loss of the VHL protein. Some mutations, result in a flawed VHL protein preventing its ability to function as a tumor suppressor.

Another fundamental problem in the case of solid tumors is that the cell mass outgrows its oxygen supply and has to adapt to thriving in conditions of oxygen depletion, referred to as hypoxia. The hypoxic state makes it impossible for pVHL to clear HIF1α. Seminal studies on this phenomena has led us to believe that pVHL is inactivated by another protein in conditions of hypoxia.

Our recent discovery of a protein, Aurora Kinase A (AURKA), as a novel target of pVHL is very exciting. Our data has demonstrated that pVHL degrades and clears AURKA from the cell even in hypoxic conditions. This makes it important to understand how the VHL protein retains its ability to regulate AURKA independent of oxygen levels. Another important finding in our laboratory is that the VHL R167Q mutant retains its ability to degrade HIF1α but is ineffective at degrading AURKA. Together with the finding that a mouse model carrying the VHL R167Q mutation presents with retinal branching defects similar to those observed in patients with retinal hemangiomas suggests that VHL mutations may differ in their ability to degrade HIF1α and AURKA.

The AURKA protein is also frequently mutated and augmented in several cancers. This has led to the identification and availability of AURKA specific inhibitors. These inhibitors are commercially available and show low levels of toxicity in Phase I and II clinical trials. Given our data and with the help of a VHLA research grant, we are now poised to obtain preclinical proof of principle on the ability of the AURKA inhibitor to reverse the retinal defects in our mutant mouse model. The success of these studies would help aid the development of a potential therapy and lay the foundation for patient selection in future clinical trials.
The VHL Alliance is committed to process improvement and working with all of the hospitals and doctors in the VHL Clinical Care Center network. With the CCC Patient Liaisons leading the way, we have worked to identify key areas that require improvement and to develop and implement solutions. UVA’s CCCC is the first to run a pilot program designed to make sure that patients are aware of and receiving all of the support and resources that are available to them. We look forward to expanding it to all the Clinical Care Centers!

Overall improvement is an ongoing process that requires feedback from all of the people that utilize their services – THAT MEANS YOU! We strongly encourage everybody who receives care at a VHL Clinical Care Center to submit feedback about your experience at: vhl.org/cccfeedback. You can keep your feedback anonymous.

Please join the VHL Alliance and all of our Clinical Care Center doctors in our commitment to progress by submitting your feedback today.

Congratulations to Moffitt Cancer Center (Tampa, FL) and Memorial Sloan Kettering Cancer Center (New York, NY) on the renewal of their recognition as VHL Clinical Care Centers. Led by Dr. Philippe Spiess and Dr. Jonathan Coleman, respectively. We are excited to continue to work with them to meet the needs of VHL patients in Florida, New York, and beyond.

Clinical Trial Recruitment
Help Find a Cure!

PT2977-202: An open-label phase 2 study to evaluate PT2977 for the treatment of von Hippel-Lindau disease-associated renal cell carcinoma

Now Enrolling
The University of Texas, MD Anderson Cancer Center
Contact: Christine Robichaux, crobichaux@mdanderson.org, 713.794-4077;

Additional sites opening soon!

More information can be found at:
vhl.org/clinical-trials or clinicaltrials.gov (Study Number NCT03401788)
VHL Alliance: josh.mann@vhl.org, 617.277.5667 x4
Study sponsor: Peloton Therapeutics, Inc.
MyVHL
The VHL Patient Natural History Study

Do you want to help find a cure?

DISCOVER how your unique journey can help others

Help find a CURE for cancer through VHL

Be a part of progress in RESEARCH

PARTICIPATE NOW!!!

Register for MyVHL today at vhl.org/MyVHL! Learn more about your VHL and contribute to finding a cure. And, when you complete the surveys and upload your scans (or submit a records release form), a $50 donation will be made to VHLA.

YOUNG ADULT RETREAT

June 8-10, 2018 in Boston, MA

Looking for an opportunity to bond and connect with other young adults with VHL? Come join us for a fun and interesting weekend in beautiful Boston in June! Share your experience as a VHL patient, increase your knowledge of caring for your holistic needs, and discuss topics that are particularly relevant to young adults. The program includes a good balance of fun activities and valuable discussions, including: a private tour of Fenway Park, New England candlepin bowling, group discussions with genetic counselors and physicians and more!

Details: Open for young adults with VHL – ages 18-30. No partners or children. (Bring them to the family meeting in Denver in October!)

Cost: $75 registration fee covers lodging, meals and activities for the weekend. It does not include transportation to or from Boston.

For more details, or to register, please visit: vhl.org/yar
REGISTER NOW!

2018 VHLA ANNUAL FAMILY WEEKEND

OCTOBER 19-21, 2018 — DENVER, CO

Comedy Night Fundraiser
Annual Family Meeting
Teen Event
Young Adult Happy Hour
2018 Team VHL 5K Run/Walk

Tickets and Registration for all events
vhl.org/familyweekend