

Dealing with Inconclusive DNA Testing

Reporting a podcast discussion on the Powerful Patient

In making a diagnosis, DNA diagnostics are often considered the final arbiter of whether or not you have certain conditions. But what if the DNA testing is inconclusive? Three guests joined Joyce for a discussion of the practical and emotional turmoil this can create: Catherine Stolle, Ph.D., head of one of the top DNA testing units in the U.S.; Gayun Chan-Smutko, MSGC, of Massachusetts General Hospital; and Gary L. Wood, Psy.D., a clinical psychologist who understands first-hand the anxieties of having a genetic condition in the family.

What happens when your DNA test comes back with a fuzzy answer? Where do we go from here?

VHL was described over 100 years ago. For 90 years the only way to diagnose VHL was through clinical criteria: if you have two or more different kinds of VHL-related tumors, or one kind of tumors and a first-degree relative with a diagnosis of VHL, then you have a clinical diagnosis of VHL.

Today there is a DNA test for VHL. The DNA test is now considered to be the conclusive way of determining whether someone has VHL. But there are a number of reasons why that test might in fact not be conclusive.

We talked about a fictional person with VHL, "Sam," who has a hemangioblastoma and is talking with his neurosurgeon about whether or not it might be VHL. One option is for the neurosurgeon to order the test himself. The problem with that is that the test results, which are somewhat cryptic, come back to the ordering physician, and someone has to communicate them to the patient. The neurosurgeon is unlikely to be prepared to spend the time with the patient that it usually takes for the patient to understand and absorb the results. This is not just a blood test like a cholesterol test with a relatively simple message for what you should do to treat it. It has far-reaching implications, not just for the current treatment, but also for lifelong management for Sam, as well as potential implications for others in his family.

For these reasons it is strongly recommended

that the patient be referred to a genetics professional who can discuss with the patient the family history and potential implications for the family. Dr. Wood suggested that Sam visit a geneticist or genetic counselor and create a relationship with that professional so that even before the test there is a comfort level with the genetics professional that will help him hear and understand the results.

Genetics professionals are trained in the ethics of having those discussions – training that other physicians may or may not have had. They also understand that this information does not always "take" the first time you hear it. As Ms. Chan said, it's a bit like taking a drink from a fire hose. The patient should feel empowered to call again and ask again until they understand what it means to them. Dr. Wood added that just knowing that it is okay to call again, gives the patient some feeling of control. It is much easier to understand difficult information when you are relaxed and not tense.

OK, so let's say that "Sam" has multiple kinds of VHL tumors so we are pretty confident going into the DNA testing that he has a clinical diagnosis of VHL. But when the DNA test comes back, the results are inconclusive. What happens next?

Dr. Stolle said that she would review the case with the physician to make sure that the clinical findings are in fact consistent with VHL, and she

Inside this issue!

Stormtroopers Unite	Birthday Wishes to You!
Report from Anaheim	Steven's Journey
Three new Clinical Care Centers	Honoring Gale Lugo
Crab Fest in Maryland	New Affiliate: Argentina
City Wide Fundraiser	Pierre Jacomet
Beth Smith and Friends	Finding Support
Fixing VHL	Vote for VHLFA!
	Meetings Coming Up

would even do the test again to make sure that the lab did not make a mistake. It is also important to remember that not every DNA testing lab has a high "hit rate" – if, for example, their results are accurate 85% of the time, that means they are not accurate 15% of the time. So it would be important to look at the quality of the testing lab and their relationship with a research team. Dr. Stolle's lab has the highest "hit rate" for VHL, higher than 99%, and she works closely with the largest U.S. VHL research team.

For that reason, the VHL Family Alliance recommends that anyone who is the first person tested in their family should only go to a very high quality testing lab like Dr. Stolle's lab. A "yes" answer from nearly any lab is likely a "yes," but a "no" answer from a testing lab that has an 85% hit rate is really a "maybe" – there's a 15% chance that it might in fact be a "yes." In that case, it would be good to re-test at a more thorough lab.

Another possibility is mosaicism, which only occurs in the first person in a family to have VHL.

Jennifer called in to say that her family has clear clinical diagnoses of VHL for three generations, but very good labs have not been able to find the mutation. The testing was done in 2007. If the testing had been done before 2002, it would be worthwhile to try testing again. But a test done by a good lab in 2007 should be as accurate as it can be.

In Jennifer's family they have been able to identify through linkage analysis that there is a common pattern in the gene that seems to be passed from one affected person to another, even though they can't see the mutation. Dr. Wood asked Jennifer how her family copes with this uncertainty. Her parents feel that people have children who pass away every day from horrible things you can't predict. "We can't live our lives in fear. Knowledge has helped us. My parents were adamant that my brother and I go to college and be able to provide a good living and insurance for our families just in case of health problems. And at least we know what to look out for to protect ourselves."

Dr. Wood said that for himself, "I cope with living while VHL is happening. Life has uncertainties of its own, no matter what your genetic condition."

At a certain point we have to admit that we still don't understand everything there is to know about genetics. There are other ways that genes can be turned off. There might also be a change in a closely related gene that causes much the same thing. It may be perfectly spelled and still not be working correctly for some as yet unknown reason.

Ms. Chan said that we should view genetic testing as a tool which can be used to confirm a clinical suspicion. A negative or inconclusive test

cannot rule out a diagnosis of VHL. It is important for the healthcare provider to explain to patients beforehand that genetic testing is not a perfect science. It is helpful to confirm a diagnosis, but when it's unclear the best we can do is to screen the children to make sure that if they have VHL we will find any issues early and deal with them appropriately.

Dr. Wood said that he feels we should be looking for clarification, not certainty. We can often gain enough information to make reasonable estimations and offer advice, without achieving certainty. Almost no lab test is 100% certain. We get guidance, not certainty. Joyce said that people will sometimes call and say, "They tell me this test is 99% accurate. How do I close that gap?" Joyce responds, "99% is about as good as it gets in Nature. 85% I would worry about, but 99% I would not worry about."

Two other patients with clinical diagnoses of VHL have reported having a change in a place in the gene between the exons, in the area that used to be called "junk DNA", that has not been reported to be "causative of VHL". Ms. Chan spoke about the investigations she would do with such a patient to double-check the pathology, the clinical testing, and the family history, to make sure that it's VHL and not some very similar condition. But at some point we have to simply say that the DNA testing is not going to bring us the clarity we had hoped for. Many people had children before there was DNA testing. All we knew was that each child was "at risk" for having VHL. With medical surveillance and watchfulness, we can still have some control in the situation. We can simply manage based on the clinical diagnosis of VHL.

Joyce manages uncertainty by making a list and making a plan. Dr. Wood added that not everyone can do that alone. They may be overwhelmed – the "victim" hijacks the thinking part of the brain. That's where a genetic counselor comes into play to help the person clarify their thinking. When we can't blame it on anything else, we often blame ourselves. He works with people to perform "blame-ectomies".

When we go for DNA diagnosis we are usually looking for guidance on three planes: current treatment, surveillance and management for the rest of this person's life, and the implications for the family. Dr. Wood encourages families to talk with each other, and go toward each other. Having a disease like VHL can be very isolating, and the support of family and friends is extremely important.

Listen to the full show at your convenience, or subscribe to the podcast at <http://powerfulpatient.org>. Shows are recorded live at <http://www.blogtalkradio.com/powerful-patient>, usually Thursdays at 3 pm Eastern U.S. time, which is 9 pm in Europe and 5 am Friday in Sydney.

Stormtroopers Unite

Jeff Romanoff of Pennsylvania is the recipient of a new kidney, through the help of the 501st Legion of Star Wars Stormtroopers..

Following multiple kidney surgeries for von Hippel-Lindau, Jeff's right kidney was gone, and his left kidney was failing. He needed a kidney transplant to save his life.

Jeff and his brother attended a Storm Troopers event in Philadelphia, gathering fans and costumers from all over the region. The 501st Legion is one of the many fan groups that wear authentic-looking costumes from the Star Wars movies and appear at charity events. His brother got the word out among club members that Jeff needed a kidney. Members immediately began signing up to be tested.

They met Eric Seemann there from Long Island. "He found out about my situation," Jeff says, "and he said he wanted to be tested. And miraculously ... he was a match!"

Asked why he would give up his kidney to a guy he had just met through a Star Wars club, Eric replied, "You never knew when your time is going to stop in this world. Sometimes you just have to step up. You don't just walk past someone who is in pain, you have to stop and help them. And that's what I decided to do."

It's not unusual to hear of someone giving a kidney to a family member, but Eric really didn't know him that well. Why did he do it?

"I'm not the first person in my family to donate a kidney. My elder brother donated a kidney to my sister-in-law's cousin about ten years ago. I've also had the opportunity to see things from both sides of the fence. About two years ago my mother was in a car accident and was diagnosed with leukemia and needed a bone marrow transplant. So I've watched someone lie there and hope that someone will step up and make a match, and to see what it's like to be a donor. But I've always been registered as an organ donor."

After weeks of testing and confirmation that Eric was a good match, both men traveled to the Cleveland Clinic where the transplant was performed by a team headed by Dr. David Goldfarb. During their recovery, members of the 501st Legion visited them in the hospital, and they spoke at an event promoting transplantation.

"Words can never express my gratitude. Although it seems trite, Eric saved my life. He's my hero. It's my job now to be worthy of his sacrifice and his gift to me. My family, my wife Jane and son Nicholas have been wonderfully supportive, and also the Police Department I work with, but Eric is



The picture above is Romanoff giving Darth Vader (played by Mark Gau) a big hug. Photo: Cleveland Clinic.

my hero."

The 501st Legion promotes the Star Wars movie and gives back to the community. Romanoff himself joined in 1999 when he first put on a Stormtrooper costume. Seeman joined in 2007 when Romanoff's garrison was in New York City raising money for Albin Johnson, the daughter of the 501st Legion's founder.

"He saved my life," stated Romanoff in regards to Seemann. "I'm completely cancer-free and I have a brand new kidney. There aren't many words that can describe what he's done for me."

Editor's Note: As long as the size of the largest tumor removed from the kidney was sufficiently small (under 3 cm), the risk of metastatic disease may be considered small enough that a kidney transplant might be performed at the same time as the removal of the last bit of remaining kidney. This is a decision that can only be made by the urologist at the time. If there is any danger that cancer cells might have escaped, there may still be a recommendation to wait two years after removal of the last bit of kidney.

Please Join Us!

**Local meetings are being planned in
Massachusetts and New Hampshire.**

Please watch vhl.org/meetings for details

Report from the Anaheim Meeting

Members from around the country gathered in Anaheim, California, to be together and learn more about VHL. Our focus for this meeting was on what we can do to manage our health, including two important presentations on nutrition, one at the beginning and one at the end of the day. Videos and handouts from all presentations may be found at http://vhl.org/videos/2009_anaheim. There is also an audio report of this conference on the Powerful Patient. [See References at the end of this article.]

Nutrition

Haylie Pomroy, a wellness consultant and nutritional counselor, explained key nutrition concepts to enhance your body's own powers of self-repair. A healthy immune system is a key ingredient in minimizing tumor growth. What we eat directly affects the strength and efficiency of our immune system.

Haylie suggests that we not just look at food as a way to appease hunger, but that healthy food is the most important medicine that we need to manage our health. It is estimated that one-third of the cancer in the United States is due to lack of key nutrients and exercise.

As one example, our bodies have T-cells whose job is essentially to function as a spell-checker, to make sure that genes are copied correctly. If they find a cell that is not in good order, they can instruct that cell to self-destruct and make another healthy cell. One teaspoon of refined sugar will cut T-cell production in half for a 3-hour period. One soda has 7-14 teaspoons of sugar. The average American eats 2-3 pounds of sugar each week. Much of this is ingested from soft drinks and prepared foods.

"If you ever plan on eating, drinking, breathing or sleeping, you will be subjected to various kind of stress," Haylie said. "We don't want to walk in fear of what can happen, but walk in strength to keep your body strong and ready for action. We need to learn to manage stress – beginning with healthy foods and exercise."

She told us that she found VHLFA very inspirational, and applauds us for taking a preventive perspective on the condition. She has a number of good recipes and food advice on her website at www.hayliepomroy.com, and she offers VHLFA members a 30-minute consultation for free.

Eye Tumors

Dr. Michael Gorin of UCLA spoke with us about managing eye lesions. He recommends treating all lesions, even very small ones, with laser in order to keep them small. Once they grow to a larger size,

the risk is greater that the treatment will affect the vision, or that the tumor may have accumulated enough fluid behind the retina to cause some detachment of the retina. A little prevention at early stages can prevent much more involved procedures later.



Haylie Pomroy

The exception is the peripapillary tumors near the optic disc or adjacent to the optic nerve. These are best left alone unless they are growing, as they are nearly impossible to treat without causing harm to the vision. Some retinal specialists have had some success with photodynamic therapy (PDT) used in very small doses, repeated as necessary, but this is still considered experimental.

Research

Dr. James Gnarra of the University of Pittsburgh, Director of Research for the VHL Family Alliance, summarized for us the current state of VHL research. He presented a series of cartoons that showed the interaction of three key proteins in the cell: VHL, HIF, and VEGF. When a tumor is beginning to grow, these proteins collaborate to create new blood vessels, a process called angiogenesis, in order to bring oxygen to the growing tumor, to nourish it. A group of new drugs called "angiogenesis inhibitors" attempt to foil this process and keep the new blood vessels from growing. Without a sufficient supply of blood and oxygen, the tumor will die. This process is important not only for VHL, but in nearly all solid cancer tumors.

A complete strategy for combatting VHL will include early detection, better treatment, and also a focus on prevention. Prevention includes things like quitting smoking, protecting yourself from harmful rays of the sun, clean water, chemoprevention, anti-cancer vaccines, healthy diet, and exercise. Chemoprevention includes the nutritional advice we have been hearing at this meeting, like eating cruciferous vegetables (broccoli and such), but no one thing is the whole story. This is a complex problem and will have a complex, multi-pronged solution.

Kids' Handbook

Melissa Kruger, the lead author of the Kids' Handbook, introduced the four authors of the

book, discussed their strategy, and presented a number of the wonderful illustrations. Produced by a committee of parents and professionals, the book was illustrated by kids with VHL and their friends. It is designed for children of all ages and their parents, to help them have a constructive conversation about VHL, and learn to take responsibility for managing their own health.

The book includes a Foreword by Dr. Anna Muriel, a child psychologist, to suggest some ways that parents might use the book. The book is in a question-answer format, posing commonly asked questions and presenting simple answers that children can understand. It works to empower the child with things we can do to stay healthy, both physically and mentally.

Pheochromocytoma

We then viewed an episode of the Mystery Diagnosis television show, in which Malinda S. from Pennsylvania tells her story of sixteen years of symptoms with no diagnosis. Multiple times she went to the doctor and was sent home with antidepressants or advice to relax, but no careful analysis of her symptoms and no effective advice. For the first eight years she suffered intense headaches, heavy sweating, terrible anxiety attacks, and increasing desperation that the medical world had no answers for her.



*James Gnarra, Ph.D.
Director of Research*

After the first eight years, another symptom began to occur: reactions of intense anger to the tiniest upset. At this point what had begun as a medical condition was becoming a serious problem in her marriage, and interfering with her ability to take care of herself or her children.

On one occasion, she went to see a new doctor and was sternly told that there was nothing wrong with her. On the way out, she passed out on the floor of the waiting room. For “nothing wrong” her symptoms were now intense. She was down to 85 pounds, all skin and bones. One day she felt a large lump under her ribcage. This time the doctor was concerned, and did an MRI, which revealed a mass the size of a grapefruit on her adrenal gland.

Fortunately she found a surgeon who had worked with pheochromocytoma before and knew the importance of “blocking” or medicating her before surgery to neutralize the effects of the pheo so that her blood pressure would remain steady during the

surgery. Similarly, he knew that once he removed the pheo and the hormones it was pumping into her system, her body would need time to “withdraw” from the effects of these hormones and stabilize at its new chemical levels. He kept her heavily sedated for nearly a week following the surgery as a safety precaution, monitoring her vital signs closely.

Now she is doing very well, is back to work, and her relationships with husband and children are back on an even keel. All the panic and rage is gone as well as the physical symptoms. As she says “It is good to be *me* again.” Nonetheless, those years of undiagnosed pheo did damage to her heart, which she is still living with.

Her story gave us a good chance to talk about the importance of persisting, even when the doctors discount your symptoms. If the doctor doesn’t listen, perhaps you need a new doctor. Perhaps you need to keep a log of your symptoms so that you have a more complete story to present to the doctor, with more information to show whatever pattern there might be to the symptoms. And if you know you have VHL, remind the doctor to please test for a pheo. If Malinda’s pheo had been identified and treated any time within the first eight years of symptoms, she would never have gotten to the point of rage, and never have incurred the significant heart damage she is dealing with.

Treating Pheochromocytoma

Dr. Michael Yeh of the Department of Endocrinology at UCLA introduced us to his department, and to the new VHL Clinical Care Center he is heading at UCLA. While there are a number of physicians at UCLA who have worked with people with VHL, they have always done so one specialty at a time. Now they are embarking on a team approach, as part of the VHL Clinical Care Centers program.

Dr. Yeh explained the different kinds of tests for pheo, and how they are interpreted to determine whether a pheo is present. Once we know chemically that a pheo is present, the next challenge is to “localize” or locate the tumor. In VHL, 80% of pheos will be on or near the adrenal gland. Twenty percent, however, will be somewhere else in the body. Imaging tests that can help to find the tumor include: CT, MRI, MIBG, or F-DOPA PET.

CT, MRI, and MIBG are all explained in the VHL Handbook. F-DOPA PET is new. MIBG and PET scanning (positron emission tomography) do “functional imaging.” While CT and MRI give you a map showing where a mass is, functional imaging gives you some information about the cell type. You are injected with a radioactive tracer that seeks out cells that make adrenaline. The scan then shows the specific areas where the tracer has concentrated.

MIBG finds about 85% of the pheos present, while F-DOPA PET finds nearly 100%.

F-DOPA PET is not yet widely available in the United States, though it is fairly readily available in Europe. NIH and UCLA have research programs using F-DOPA PET.

Pomegranate Juice

Dr. Allen Pantuck, also of UCLA, has been studying the effects of the polyphenols in pomegranate juice on cancer tumors. In one study, men with early stage prostate cancer and rising PSA levels drank 8 ounces of pomegranate juice each day. In two years, the time needed to double their PSA levels slowed from 15 months to 60 months.

Dr. Pantuck's team is studying the pathway, the sequence of events that occur as cancer progresses, trying to learn how to slow this process. They have learned in the lab that the polyphenols in pomegranate juice slow the action of NF κ B (NF-kappa-beta) in cancer cells.

Similarly, in clear cell renal cell carcinoma, the VHL gene is damaged in most kidney cancer tumors. When the VHL protein is lost, HIF becomes overabundant and turns on NF κ B (NF-kappa-beta), which has been associated with proliferation of cancer cells. Pantuck and associates are studying the effects of the polyphenols in pomegranate juice in inhibiting NF κ B and slowing the growth of many kinds of tumors including prostate, kidney, breast, and colon.

Being Together

When we first met in Kansas City in 1994, we had people in the room who had been diagnosed usually somewhere in their teenage years, through age 50, but always because of some tumor that made itself known and needed immediate attention. Today we have an increasing number of children diagnosed before or shortly after birth, long before any tumor activity has begun. Early diagnosis gives us the opportunity to do more with prevention than ever before. We look forward to learning together how to prevent tumors, or slow down tumor growth.

As always, in addition to all our wonderful speakers, the biggest benefit was simply being together, sharing stories and hugs, and knowing we are not alone. Brian N. participated with Joyce in a Powerful Patient radio show about the experience of attending the conference. We hope that you will join us June 19, 2010, in St. Louis, Missouri, for the the 17th Annual VHL Family Alliance Conference.

Report from the conference (audio):

http://powerfulpatient.org/archive/2009_anaheim

Recordings of all talks and copies of the handout sets:

http://vhl.org/videos/2009_anaheim



Camron King, Calvin Cieslak, Michael Yeh MD, Allan Pantuck MD, Michelle Cieslak, Joyce Graff, announcing the UCLA Clinical Care Center for VHL

Three New Clinical Care Centers

Three additional medical centers have joined the VHL Clinical Care Centers Program:

California:

University of California Los Angeles (UCLA),

Los Angeles, CA. Michelle Fox, genetic counselor.

Tel: +1 (310) 206-6581; Fax: +1 (310) 206-8616.

E-mail: mfox@mednet.ucla.edu

Florida:

Mayo Clinic Jacksonville, Dr. Douglas Riegert-

Johnson, gastroenterology, Tel: (904) 953-2221.

University of Miami, Mustafa Tekin, M.D., geneticist,

Tel: +1 (305) 243-2381; Fax: +1 (305) 243-2396;

E-mail: mtekin@med.miami.edu

For the complete list of registered centers, please see <http://vhl.org/cc>

Remembering Rob Schoenhals

The Anaheim meeting was dedicated to the memory of Robert E. Schoenhals Jr., 50, of Michigan, Treasurer of the VHL Family Alliance 2004-08, who passed away at his home in May 2009 from complications of von Hippel-Lindau Syndrome (VHL). We extend our love and condolences to his wife Anita and their five children, and to Rob's two sisters, Susan Sorenson and Mary Lynn Pearson, co-chairs of our Utah chapter. Rob was a graduate of the University of Utah. He received his MBA from BYU's Marriott School of Management. He worked the last 22 years for Chrysler Corporation. Rob was compassionate, cheerful, grateful, and an inspiration to all. His keen mind and kind nature will be greatly missed. Rob's favorite memories included watching his children play and compete in tennis.





Crab Fest in Maryland

Kelley M., Maryland

With wonderful help from family and friends, the VHL Crab Fest was held in June. It was way more than a fundraiser -- it was a reminder to all of us involved in the ultimate importance of friendships from friends and family, the reminder that when the chips are down in life's trials we are not alone.

If we all made a donation to this cause without the blood, sweat and tears the profit column may be greater. However, the time spent together for a common goal is truly a greater contribution to the cause as in shared feelings, understanding and awareness. We were able to raise \$4000! Not bad for our first ever event.

Needless to say, this could not have been done without our wonderful volunteers. With these things said from the bottom of our hearts we thank all our supporters for caring enough to have shared our vision and believed in our cause.



In the tent at the Maryland Crab Fest.



Amy A. (left), Grandma Judy F., and two friends from Eugene Tighe School, selling T-shirts at their VHL booth.

City Wide Fundraiser

Alex Anderson and his family and friends sponsored a City Wide Fundraiser for Alex Jay VHL Day in the seaside resort town of Margate, New Jersey. Booths staffed by teenage volunteers were strategically placed around the city to attract and capture the attention of as many passers-by as we could. The weather was beautiful and our volunteers worked with the donors explaining about VHL and that we were raising funds to help their classmate, Alex.



Alicia, Beth, and Janet

Beth Smith and friends.

We did it again!!! Janet, Alicia and I completed the Powow Triathlon in Amesbury on July 11th. We met at Lake Gardner 4 times a week for training to run, bike and swim. The bike course was a little different this year and thankfully a little easier without a steep hill in the beginning. We swam in the lake a bunch of times too, thanks to some borrowed wetsuits. We really trained hard this year so we could achieve some improved times.

Thanks to all of your generous support, we raised over \$4,000 again this year for a great cause. In these difficult times, non-profit organizations need our help more than ever. We understand that times are tough for everyone, so we appreciate anything that you can give. Every penny counts! Your donations help provide information to families and physicians about this disorder, as well as local self-help support groups for families affected with VHL. To find out more about VHL and the VHL Family Alliance, please visit www.vhl.org.

Fixing VHL

Question:

In Ariel's Story in the May 2009 issue of VHLFF, she says: "A person with VHL is lacking the von Hippel-Lindau tumor suppressor gene; this gene produces a protein that helps to control cellular growth. Without this gene, and hence, without the protein, tumors are predisposed to grow in places rich with blood vessels, like the brain, eyes, spine, pancreas, adrenal gland, and kidneys."

If the problem is the lack of the VHL protein, couldn't we simply make VHL protein and inject it into the tumor? or take it as a supplement?

-- *Curious in Michigan*

Response:

People with VHL actually have quite a bit of VHL protein in most cells of the body. Everyone has two copies of the VHL gene. In a person with VHL, there is one tiny misspelling in one copy of the gene, but the second copy is correct and makes good VHL protein (abbreviated pVHL). If that second copy becomes disabled for some reason, a tumor may begin to form. It may take years for the tumor to get to a size where we can even see it on the best scan.

The pVHL is present in most cells, but missing from these tumor cells. So in theory if we could add some pVHL back into the cells of the tumor, we should be able to reverse tumor growth. However, this is not possible with today's technology. The protein is very unstable outside the cell, so even preparing it to inject would be very difficult. And we do not have the technology today to deliver it inside the cell, where it would need to be. Furthermore, the protein turns over every 1-2 days: normally you make more inside the cell. But as a therapy, we would need to deliver new pVHL inside the cell every 1-2 days. If we had the technology to do this, we could solve lots of medical problems, not just VHL.

Dr. William G. Kaelin of the Dana-Farber Cancer Research Institute in Boston refers to this as the "holy grail" of medicine. There is a great deal of experimentation going on to find a delivery mechanism to accomplish this. Perhaps one day through nanotechnology or some such thing we will have the capability to do it. But today, we simply don't have the technology needed to do it.

What is more feasible with today's technology is controlling some of the "downstream" proteins. When there is too little pVHL, there is too much HIF, which makes too much vascular endothelial growth factor (VEGF), which in turn stimulates the growth of new blood vessels. There are known ways to

control HIF and VEGF, a category of drugs known as angiogenesis inhibitors (drugs that inhibit the creation of new blood vessels). This is the primary mechanism of drugs such as Bevacizumab (Avastin), Sunitinib (Sutent), Ranibizumab (Lucentis), and others being tried in clinical trials with VHL. There are another twenty or more such drugs "in the pipeline," somewhere in the development process. As we move forward, they are getting more "specific" and with fewer side effects. As Dr. Kaelin once described it to me, classic chemotherapy is rather like using a sledge hammer. What we really want is a tweezers to get right to the very spot and do the job carefully, with least damage to surrounding tissues, and with fewest side effects.

The research continues!

Birthday Wishes to YOU!

Cheryl & Peter G., New Jersey

After reading about fundraising birthdays in a kid's magazine, my daughter Blythe decided to have a fundraising birthday party.

So, on Friday, April 24, 2009, she had her 8th birthday party.

Instead of gifts, she asked her guests to consider a voluntary donation to the VHL Family Alliance as her father, sisters and many of her family members either have the genetic defect or are actually affected by Von Hippel-Lindau disease. Blythe's guests donated a total of \$180!

So, the Graziano family matched the donations with another \$180 for a total gift of \$360! We would like to acknowledge everyone's generosity!

Thank you for all you do for VHL!



Blythe and her family working for a cure!

Steven's Journey

Beverly Angotti, chairman, Florida

Steven began complaining of dizziness in December, 2004. He seemed healthy, but the headaches became more constant. In January we took him to the pediatrician who referred us to a series of specialists.

Our first trip to the neurosurgeon's office prompted more questions than answers. The only firm answers were that Steven was neither to play soccer nor drive until further notice. Steven had a brain tumor. The radiologist suggested that this tumor might be part of a syndrome called von Hippel-Lindau (VHL), but not all the classic symptoms were present.

The surgery proceeded without complications, but the results were surprising. Instead of a typical hard tumor, the lesions were made up of blood vessels – structures called hemangioblastomas. That evening I began researching and learned that this was indicative of VHL. I found the VHL Family Alliance website and began to read.

Eventually we went to see a geneticist. The genetic counselor and the geneticist reiterated that it sounded like VHL. DNA testing confirmed it: a tiny change in one gene that would put him at increased risk for tumors. My brave and beautiful son has VHL.

Steven is the first and only person in his family ever to have VHL. Neither his parents, nor his brother and sister, have the alteration. Steven is one of the many people diagnosed each year with a *de novo* (new) mutation in the VHL gene. Why? We don't know. But at least 20% of people with VHL are the first in their families to be affected. Something is causing new mutations in the VHL gene. Once this change is in the genes, it is heritable -- there is a 50% chance of passing it to a child.

VHL will be a lifelong challenge. I do not want Steven to live an uncertain life with an incurable disease. I want Steven to live a brave and beautiful life in spite of this disease. With the help of the VHL Family Alliance we are learning all we can – and we need your help too. Please give to the Cancer Research Fund of the VHL Family Alliance. Help us cure Steven and all people with VHL and related tumors. Help us learn what makes genes change so we can prevent cancer.

Steven created a video about his life with VHL. His message conveys the strength and determination he and his family have brought to bear in dealing with VHL.

Beverly writes a blog about her own and Steven's experiences. You can write to her at us-fl@vhl.org
See Steven's video at <http://www.youtube.com/vhlfa>

Hi, My name is Steven.
I am twenty years old.
Four years ago I was told
I would never play soccer again ... but I'm back!
I had brain tumors
Caused by von Hippel-Lindau
VHL is a rare disease
My doctors knew very little about it
I was literally thrown into a world of unknowns.
I'm glad the VHL Family Alliance was there
To help me and my doctors find the best information
On how to fix my tumors
And manage my health.
VHLFA helped my family
See that there is hope
There is a way to live with VHL.
Someday
I hope
There will be a cure.
Until then,
I live by possibility.
Please give to the Cancer
Research Fund of the
VHL Family Alliance.



Honoring Gale Lugo

Gale Lugo retired this year after sixteen years as the State Chair for Florida and Regional Chair for the Southeast Region. She has been a wonderful resource to all of us, and a great coach to other chapter leaders in the southeast.

She is enjoying being at home with her husband Cesar and their two dogs, with fresh grapefruit and lemons in the back yard. Thank you, Gale, for your outstanding service. We wish you well.

Gale was recognized as Chapter Chair of the Year 2004 and Volunteer of the Year 2005. In addition to state chairmanship she was an active moderator of the online list at Yahoo, and was a key resource in the migration to Inspire. She is one of our primary resources for the use of nutrition and herbs in moderating the course of VHL.

With Gale's good assistance, her state-level responsibilities have moved to Beverly Angotti. Her regional activities will be handled by Mary Lou Linn in the VHLFA office.

You can contact the Florida chapter at us-fl@vhl.org



New Affiliate in Argentina

Translated by Myriam Gorospe, Ph.D.

Greetings to all VHL families. My name is Carlos Alberto Fredes. I am 45 years old, married and with 3 daughters, and I have VHL. I am President of the Association of von Hippel-Lindau families in Argentina (AAF-VHL). Our Association was created by a group of friends and families, all of whom did not hesitate to join forces to work for VHL families. The Association base office is located in the city of Necochea, about 650 Km (about 400 miles) southeast of the city of Buenos Aires, on the Atlantic Ocean coast.

In our country, those affected with VHL have the same problems as those with VHL in other countries: poor information and lack of knowledge on the part of the medical and scientific communities about VHL. Added to this, we have major legal hurdles; for this reason, since its formation, the Association has been fortunate to have Dr. Daniela Cangiano, a specialist in Civil Law, as its vice president. She fulfills the duty of working for the rights of those affected with VHL and their families, from medical care to employment issues. We are also privileged to have Dr. Jorge Omar Villalba, a physician and political advisor.

At present, we are working with national and provincial government representatives in the arduous task of disseminating information about VHL. First, we requested that they print the VHL Manual, brochures, and check-up schedules. Deputy Horacio Piemonte presented these requests to the Chamber of Deputies of the province of Buenos Aires. In addition, we asked that the Executive branch, implement a wide information campaign to spread knowledge about VHL.

This information campaign will include the first conference devoted to disseminating information on VHL in Argentina. The dates have not been confirmed, but we anticipate holding them in March or April 2010. They will be directed to physicians, nurses, special education teachers, affected persons, and the general public. They are supported by Necochea city government, sponsored by Dr. Jorge Omar Villalba, Pediatrician and legal counselor to Deputy Horacio Piemonte, who after learning of our situation, offered us all of his skills and expertise, and has been working diligently with us since. It is important to note that Dr. Jorge Omar Villalba has previous experience working with other Associations and has previously collaborated in disseminating information of other rare diseases, underscoring not only his caring personality, but also his solidarity with and commitment to our Association.



*Carlos Fredes,
Argentina*

We have also requested from the Chamber of Deputies, both national and from the Buenos Aires province, the designation of one public hospital of reference, with a multidisciplinary team to manage in an integrated manner the health care of persons affected with VHL and their families, including those who have social coverage as well as those who do not. This public hospital of reference will cover the costs of tests and medical treatment, so that everyone with VHL may have the best possible medical care.

We have requested from our Congress the creation of a VHL Tissue and Tumor Bank, to which all persons with VHL can contribute and thereby advance VHL Cancer Research. We have also requested the creation of a fund for the study of DNA for those with VHL and their families.

We plan to sign agreements with hotels, so that when a public hospital of reference is designated, the persons affected will be able to receive low-cost room and board. Using a similar principle, we want to make available our region and its hotels to VHL families, so that they can enjoy our touristic cities and coasts, while resting and relaxing.

We also plan to secure funds for our physicians and scientists to attend international symposia. We also hope to create, in the near future, a regional structure, given the size of our country.

As an individual with VHL and as President of the AAF-VHL, I extend my appreciation to several people who have been extremely supportive of me since my diagnosis one year ago: to Mrs. Joyce W. Graff, VHL Family Alliance Director, to Dr. Myriam Gorospe, to Ms. Jesusa Martínez Gómez, President of the Spanish VHL Family Alliance, and to Dr. Karina Villar Gómez de las Heras, Vice president of the Spanish VHL Family Alliance. I also thank Dr. Jorge Omar Villalba for all of his help and efforts as we work to disseminate information about the VHL Syndrome. My thanks also to my family, my friends, and all of those people who help and support us in one way or another, every single day.

We know that the work ahead will be hard and we will encounter hurdles along the way. We may

be slowed down, but we will not give up, since we have a mission to fulfill: to work on behalf of all of those affected by VHL and of their families, so that we will improve the quality of life and dignity of those living with VHL, and so that we leave a mark not because of what we did, but because of what we were.

Many thanks to all.

Carlos Alberto Fredes, President (AAF-VHL)
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argentina@vhl.org

Pierre Jacomet

Philosopher, Musician, and Advocate

by Gloria Valdés, MD, Santiago, Chile

It is with sadness that I communicate the death of Pierre Jacomet on the 28 of August, of a cause unrelated to VHL. He was 76 years old. As you well know he was instrumental in creating awareness of VHL and pheochromocytomas in Chile. As a consequence of his efforts we associated with him as a referral center for VHL patients, and through many years we received patients and families referred by him. During this time we came to appreciate his personal interest in the course of each patient, and the compassionate support he gave them. His life is an example of dedication to a cause that he understood from within.

It is interesting to note that in Chile he is very much appreciated as television personality, an expert in literature, and that his book "Travels through my library" has enticed many people to read his preferred authors. His knowledge of literature and languages was so extensive in part as a consequence of the hyperactivity caused by the tumoral production of catecholamines; thus he was able to turn his disease into a "blessing in disguise".

Wishing that the contact between the VHL Alliance and the Catholic University created by him will continue, I remain sincerely yours,

*Dr. Gloria Valdés, Professor, Escuela de Medicina
Pontificia Universidad Católica, Santiago, Chile*

Pierre created the first book about VHL in Spanish for doctors, and translated the VHL Handbook into Latin American Spanish for patients. He was tireless in working with families in Chile, and provided assistance to others throughout Latin America. He was an active moderator of the VHLFA online support group in Spanish.

See his story at <http://www.vhl.org/newsletter/vhl1998/98blpier.php>

Green Membership!

VHLFA introduces the Green Membership, a new way for you to make a long-term impact on VHL and the environment. Green members receive benefits and communications electronically, which helps shrink your carbon footprint, plus an automatic annual renewal feature means less paper in your mailbox.

Green Memberships start at just \$25 annually and your automatically renewed contribution will help sustain the programs of the VHL Family Alliance. Sign up on page 15.

Thank you for supporting VHLFA while doing your part for the earth!

Hold the Date!

**Annual Meeting, June 19, 2010
St. Louis, Missouri**



Pierre Jacomet, 1933-2009

Finding Support

Don't forget

that no matter where you are, people with VHL are there to support you!

- On the internet, at vhl.inspire.com, 24 hours a day
- On the telephone at 800-767-4VHL (that's -4845) toll-free from the U.S. and Canada
- In person at various state and regional meetings throughout the year. In the next few months, there will be meetings in Texas, Massachusetts, New Hampshire and others
- and at annual conferences in the U.S., Germany, Netherlands, and many other countries.

See the listing of forthcoming meetings on page 16 of this issue and online at vhl.org/meetings

See you soon? ... Be there!

Nothing near you? Help to create it!

call MaryLou Linn at 800-767-4845, ext 4.

Vote for VHLFA!

GreatNonprofits is asking you to rate your favorite cancer-fighting nonprofits. The 2010 awards will be announced in August 2010. You can vote any time during the year.

We would very much appreciate your going there and letting them know what VHLFA means to you, and how we are working to fight cancer – not only through research, but in finding help today, and in managing life with VHL.

With your help, we are hoping that next year the VHL Family Alliance will be included in the top cancer fighting charities!

The contest is sponsored by GreatNonprofits, GuideStar, and Planet Cancer.

First Descents was this year's winner in the category that VHLFA would be competing in:

<http://greatnonprofits.org/reviews/first-descents>

First Descents works to cure young adult cancer patients of the emotional effects of cancer. Through whitewater kayaking and other adventure sports, it challenges and empowers people to regain control of their lives in a safe, fun, and supportive environment. This year they will conduct nine week-long programs in six different states.

"First Descents provided me with an incredible experience that allowed me to truly "live my life to the fullest," a feat I had never actually tried to achieve before. I was able to share a week of adventure, relaxation, and fun with a terrific group of volunteers and other young adult cancer survivors who allowed me to feel as if I could completely be myself. It was the first time in 3 years, since my cancer diagnosis, that I truly felt comfortable."

The thank-you list appears only in the print edition. The thank-you list appears only in the print edition.

cont'd

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☐ I would like to receive occasional alerts via e-mail ☐ I want to Go Green!

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☐ *Go Green!* Please send all materials by e-mail to reduce costs and save the earth too!

Send me some great stuff!

☐ VHL T-Shirt, sizes S, M, L, XL, Members, \$15 ea, Non-Members \$20 each \$ _____

☐ VHL T-Shirt, sizes XXL, XXXL Members, \$18 ea, Non-Members \$25 each \$ _____

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Canadians, please send checks to:

Canadian VHL Family Alliance, c/o Jill Shields, 4227 Hamilton Road, Dorchester, Ontario, N0L 1G0 Canada



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Houston Meeting

November 7, 2009

for details see vhl.org/meetings

9:00 Introduction - Eric Jonasch
9:15 Radiotherapy and VHL - Anita Mahajan
9:45 Endolymphatic Sac Tumors - Ian McCutcheon
10:15 Break
10:30 Pheochromocytoma - Camilo Jimenez
11:00 Epididymal Cysts - Surena Matin
11:30 Targeted Agents and VHL - Eric Jonasch
12:00 Lunch
12:45 Prenatal Diagnosis and PGD - Molly Daniels
and Thereasa Rich
13:15 Family Forum - Joyce Graff

St. Louis, 2010

VHLFA Annual Meeting
St. Louis, Missouri
Saturday, June 19, 2010

Hold the date!

Please plan to join us!

Additional meetings are expected in
Massachusetts and New Hampshire
and possibly other states
Please see vhl.org/meetings for the latest
information.

Page 16

Berlin

German National VHL Meeting
in German language
10th Birthday Celebration!
16-18 October, 2009, Berlin, Germany

St. Petersburg

Kidney Cancer Conference
in Russian language
St. Petersburg, Russia, October 2009
Dr. Gennady Bratslavsky of the US National
Cancer Institute is representing VHL!

Argentina

March/ April 2010 in Buenos Aires
in Spanish language
details will be posted at vhl.org/meetings

International Medical Symposium on VHL

Rio de Janeiro, Brazil
October 23-24, 2010
(dates may not yet be final)
details will be posted at vhl.org/conf2010