



Dedicated to the memory of John Petito, Founder and Editor-in-Chief, NF2 Review

THE



REVIEW

WINTER 2004 VOL. 11 ISSUE 2

A REVIEW OF RESOURCES FOR LIVING WITH NEUROFIBROMATOSIS TYPE 2 (NF2)

Welcome to the Winter issue of the NF2 Review.



Back in September, when the floodwaters of Hurricane Ivan nearly swept away the state of Pennsylvania, they almost took **Marie Drew**, NF2 Chapter Representative for NF, Inc., out with it. The story of her harrowing rescue is our **cover feature**.

Living with a diagnosis of NF2 as a young adult can produce a whole other kind of flooding ... of emotions. **Katie Anderson**, PABI #1, found that putting pen to paper can help to sort through them. She shares with us a page out of her diary on page 2.

Identifying and developing promising new drug therapies for the treatment or management of NF is an ongoing process. On page 3, **Dr. Hiroshi Maruta** from Melbourne, Australia, brings us up-to-date on some of those research efforts.

As we celebrate and honor our memories of **Jayne Johnston** (page 8) and **Kathie Hering** (page 9) we recognize the significance of their legacies, which will impact the NF2 community for a long time to come.

But one doesn't need to be politically active, or organize a support group in order to leave a mark in the world. **Lynn Bluett-Knox**, who passed away on December 2, left her "mark", too ... on the hearts of all who came in contact with her. Her resplendent smile, words of wisdom and warm hugs will be sorely missed.

This issue of the newsletter is dedicated to all of these remarkable women who, through their compassion, dedication and humor, made a world of difference in our lives.

All too Real TV



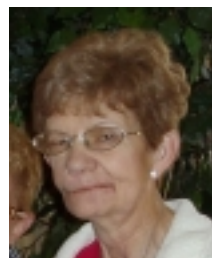
Rescuers in Cecil 'paid it forward'

By **Byron Smialek**  
for *The Observer-Reporter*  
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SEPTEMBER 21, 2004 – Look under “H” in your dictionary for hero and you’re liable to find the picture of **Sgt. Tom Weaver**. He’s the Cecil Township policeman who saved a woman from what would have been certain death in the floodwaters of Millers Run Creek.

What Weaver did Friday afternoon at the height of the rainstorm that was left over from Hurricane Ivan perfectly fits the definition of a real-life hero. A news cameraman from Channel 11 captured the rescue as it happened.

Weaver went forward when others, perhaps, would have gone the other way.  
*Please see **Rescue** on page 7*



**Marie Drew** ... rescued from the flood

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*A Page from the Heart ...*

# Dear Diary...

*Story and photo courtesy of House Ear Institute*

I was diagnosed with Neurofibromatosis Type 2 (NF2) at age 14, when I was an eighth grader in junior high. The school district audiologist discovered my hearing loss and suspected the cause, so I went for an MRI. I'd realized before my diagnosis that I was experiencing some hearing loss, but I had no idea the cause was so serious. I was pretty down and sad about it when I found out.

Before I lost my hearing I played the flute. Over time, it got harder for me to hear well enough to play, so I stopped playing in my sophomore year in high school. Once my hearing loss was diagnosed and I received a hearing aid, I was very self-conscious about it. I used to wear my hair over my ears so others couldn't see my hearing aid. Now I've gotten used to coping with hearing loss, and I don't care what people think or say about me. I wear my hair however I want, and the external components for my PABI are in plain view most of the time.

In the beginning, my hearing loss really affected my social life. Obviously, I stopped racing to answer the phone. I was so frustrated that I couldn't hear the phone ring or the doorbell. I'm a very shy person anyway, and it's hard for me to go out and make new friends. With the loss of hearing, I withdrew even more. Not many of my peers spoke to me at school, and I felt like a ghost most of the time because I'd sit in the lunchroom and no one would notice I was there. I found it too difficult to reach out and initiate a conversation.

I wish I could say I developed lots of new coping skills to compensate for my hearing loss, but I really just shut people out. I would go to my parents if I had a problem, but otherwise I was happy to turn off my hearing aid and go up to my room and read for hours on end. Like many teenage girls, I loved to read romance novels, and that was my escape.

I think having to cope with NF2, this rare and difficult disease, is a lot for a teenager to handle. My family has supported me a lot through this and so has my church. I received a priesthood blessing before I had my tumor removal surgeries, and that helped a lot.



When I heard that I might be a candidate for the clinical trial of the penetrating electrode auditory brainstem implant (PABI) in late 2003, I was excited by the possibility that I might hear some sound again, even if it wasn't the same as before. And of course, I was afraid it wouldn't work for me, and I'd be stuck with no hearing at all. Overall, I had a very positive attitude about being the first person to receive the PABI because it offered hope and bring me out of my isolation.

Since receiving the PABI at the House Clinic and House Ear Institute, things have definitely improved. Even though I don't receive the maximum benefit we'd all hoped from the new microelectrode feature of the PABI, I hear enough with the surface electrodes to communicate pretty well. I can even hear certain voices on the phone. I've become a bit more social and am looking for a new job.

I was excited to be interviewed for an article in the Los Angeles Times Magazine, which emphasized how important my participation in this early trial is for the development of the technology, which made me feel good. I hope that other people with NF2 will take advantage of this wonderful new technology that was invented for people like me. They should keep in mind that they are not alone, and should reach out when the going gets tough in the hearing world.

I turned 20 last Tuesday, and I'm looking forward to the future with a lot of hope.

**Katie Anderson ... first recipient of the PABI (Penetrating Auditory Brainstem Implant)**





Each year the Association of Late-Deafened Adults (ALDA) holds an annual convention – ALDAcon – for people of all ages who may be late-deafened, hard of hearing, newly experiencing any degree of hearing loss, or have family or friends who are coping with such a loss. Along with various social events, ALDAcon also features speakers and/or workshops that offer a wide range of topics that relate to hearing loss.

Among the NF2-related workshops offered at this year's ALDAcon, was a presentation by **Hiroshi Maruta, Ph.D.**, head of the Tumor Suppressor Laboratory at the Ludwig Institute for Cancer Research in Melbourne, Australia. Dr. Maruta described the cell signaling of NF tumors, and talked about recent critical breakthroughs that are providing vital clues in identifying and developing drugs that may chemically replace the tumor-suppressing function of the NF2 gene.

Although the following contains edited portions of Dr. Maruta's presentation, the transcript in its entirety can be found on the NF, Inc. Website at: <http://www.nfinc.org/nf2news.shtml>, and is reprinted here with permission.

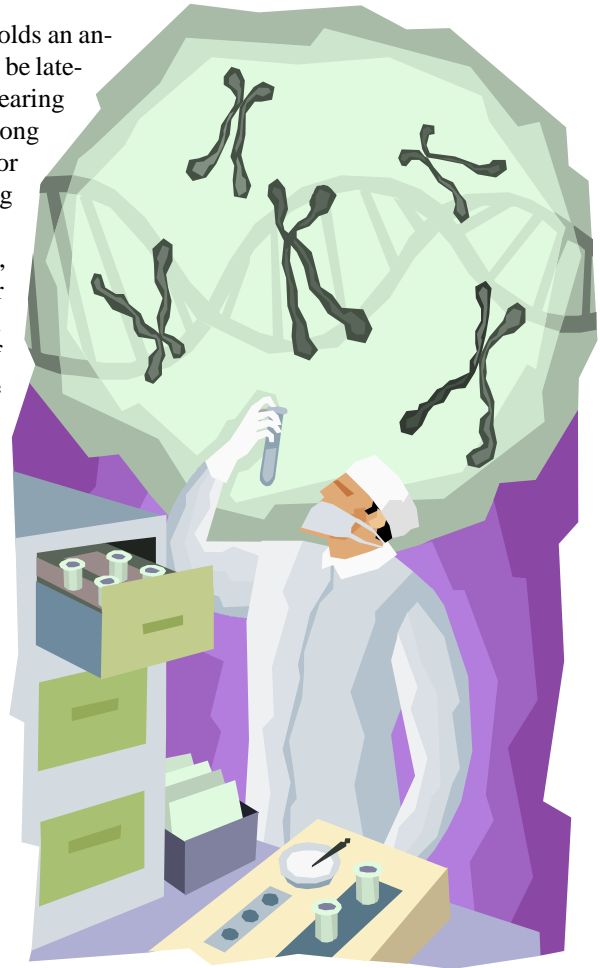
#### The Merlin-Pak Connection Revealed:

## The Turning Point in the Development of Therapeutics for NF?

By **Hiroshi Maruta, Ph.D.**

My original research had been focused on certain cancers that are caused by a particular gene called **RAS** (Renin-Angiotensin System). This causes more than 90% of pancreatic and more than 50% of colon cancers. But during our research we noticed that there is a very close relationship between neurofibromatosis type 1 and type 2 (NF1 and NF2) and RAS cancers.

About a decade ago, as soon as the genes for both NF1 and NF2 were cloned or discovered, we started working on NF. By the end of this talk you'll see that NF1 and NF2 are not isolated from other cancers, but share many common things. In fact, at the molecular level, more than 50% of all cancers are closely related to NF types 1 and 2. That's the reason why we think the drugs that block a particular enzyme called **PAK** could potentially be the first cure for NF, as well as many cancers. My talk today will focus on the relationship between RAS cancers and neurofibromatosis, with my focus on the enzyme called PAK.



I think you are more familiar than myself about what NF2 is. Before I discuss in detail how RAS cancers and NF are related, I'd like to give you a very short introduction – in particular, the current situation of NF2 treatment.

As you know, more than one and a half million people on this planet are suffering from neurofibromatosis type 1 or type 2. However, the status of NF treatment is very far from satisfactory. One of the reasons is that treatment is limited to only surgery and radiotherapy. However, these two types of treatment are not complete.

There are two reasons. One is that neurofibromatosis is highly metastatic so that, although the original tumor is developed in the brain or along the spinal cord, eventually the tumor spreads over the whole body so that the local treatment by surgery or radiotherapy wouldn't be sufficient for a complete cure. The second reason is that the sites where the tumors grow are in the brain and on the spinal cord so that it would be very difficult to remove or destroy the tumors without affecting the surrounding healthy nerve. As yet, no

*Please see **Turning Point** on page 4*



### *Turning Point ... from page 3*

therapeutics have been developed for the complete cure for neurofibromatosis.

One question you might ask is why conventional anti-cancer drugs are not used for the treatment of NF1 or NF2. Well, there is a reason. Conventional therapeutics are not effective simply because they were developed to target fast-growing malignant tumors. As you know, the majority of NF tumors are not malignant (only 10% or less are so-called cancerous). Also, the growth rate of these tumors is very slow. Conventional drugs targeting fast-growing tumors, like leukemia, never work on slow-growing tumors.

These chemotherapeutics also have severe side effects on some normal cells, such as hair and bone marrow cells, which also grow fast. That's why we – not only my own group, but also many other cancer research groups – decided to develop new types of chemical compounds which block the specific signaling pathways essential for tumor growth. That's one of the reasons why we started with RAS. RAS is probably the best-known oncogenic or cancerous gene product, and the biochemistry of signaling pathways downstream of RAS has been the most comprehensively studied during the last two decades. In the end we found that both NF1 and NF2 share a common signal with RAS and many other major cancers. So, first, let me try to tell you how RAS works.

RAS is a signal-transducing protein, and there are two stages, or forms. One is the active form, which binds a certain nucleotide called GTP. In normal cells, RAS cycles between inactive form and active form. Through two other proteins, "A" converting RAS from the active form to inactive form (GDP-bound form), or "B" only upon the stimulation of cells by growth factors, reactivating the RAS. Normal RAS stays only transiently in the active form. That's why normal cells will never become malignant. However, when the RAS gene is mutated permanently, it is kept frozen in this active form, continuously sending a signal to its downstream effectors. Then it causes tumors.

I'd like to explain how RAS activates other proteins simply called "A", "B" and "C". "A" activates "B", and "B" in turn activates "C" through this signal cascade. In the end, the key enzyme we're working on (PAK) is activated. So, RAS activates PAK through



these signal transducers ("A", "B" and "C"). We know that RAS requires this enzyme PAK to induce tumors. We've been working on PAK for almost 30 years, so we know every property of this enzyme and are in the best position to develop its inhibitors.

Neurofibromatosis type 1 (NF1) is caused by the dysfunction or loss of a gene. The gene product for NF1 happens to be an attenuator of normal RAS. So when the NF1 gene is missing, the normal RAS becomes abnormally activated. Then eventually, through this "A", "B" and "C" pathway, PAK is activated. So, in terms of the signal, the NF1 behaves in the same way as RAS cancers, such as pancreatic and colon cancer.

Several years ago, Jeff Field's group at University of Pennsylvania showed that this enzyme is essential for NF1. It means that if we had had a specific inhibitor for PAK, we could have at least been treating type 1 neurofibromatosis. But until very recently nobody has developed any anti-PAK chemical compound. That is why there is, so far, no treatment or chemotherapeutics to treat NF1.

Neurofibromatosis type 2 (NF2) is caused by the mutation of a gene, resulting in a loss of its tumor suppressor function. But NF1 and NF2 gene products are structurally so different, it was very difficult for us to find the exact function of the NF2 gene product that we call **Merlin** (named after a magician in the legend of King Arthur). As soon as Jim Gusella's group at Massachusetts General Hospital (MGH) and a French group in Paris discovered the NF2 gene, we decided to test whether NF2/Merlin is a tumor suppressor. So putting this gene in a RAS cancer, we watched what would happen.

As expected, the malignant transformation was reversed. So we know that both NF1 and NF2 genes create a block somewhere in this oncogenic RAS pathway. However, it has been difficult to sort out what the primary target of this Merlin is (it turns out to bind *several* proteins). Two years ago we found that the Merlin acts as an inhibitor in PAK. In other words, when this NF2 gene is missing, or mutated, PAK is abnormally activated, just like the loss of NF1 or the mutation of RAS. So actually, the type 1 and type 2 of neurofibromatosis are in the same family as the RAS cancers.

*Please see **Turning Point** on page 5*



### Turning Point ... from page 4

We have [looked at] two types of mesothelioma cancer cells, which are derived from lung cancers caused by asbestos. But one normally expresses the NF2 gene, while the other is NF2-deficient. We then compared the PAK activity between these two cell lines, using a RAS cancer as a positive control, which has a very high PAK activity compared with normal cells.

The PAK activity in normal cells is only one-tenth of that in RAS cancer. When Merlin is missing in cells, PAK activity becomes very high – quite similar to RAS cancer. But in the cells normally expressing the NF2 gene, the PAK activity remains very low (like normal cells).

The next question is whether this PAK is actually essential for the growth of NF2 tumors. We have two inhibitors for PAK. One is a **peptide\***, which blocks the interaction between two proteins, PAK and **PIX**. I will not go into details, but the part of PAK has some 18 amino acids stretch. This is required for its interaction with the PIX that activates PAK. So if we use this peptide/stretch, we have to make it cell-permeable before putting in a medium. Then it blocks this interaction (within cells).

We also used another inhibitor, a chemical compound called **CEP-1347**. This is also a specific inhibitor for PAK. Using these inhibitors, we tested how the growth of NF2-deficient and NF2-positive cancer cells is affected. Both the chemical compound and peptide inhibited the growth of only NF2-deficient cancer cells, having no effect on NF2-positive cells. This clearly shows that the NF2-deficient cancer cells require PAK for their growth. However, these inhibitors have relatively high **IC50** (they are not so potent). IC50 is the concentration of a chemical compound that shows 50% inhibition of the growth. The lower the IC50 is, the more potent it is. So we are looking for something whose IC50 is very low.

So, we tried to find a more potent PAK inhibitor that could be useful for a clinical trial. In the end we found another chemical compound called **FK228**. Even at 0.1 nM, ten thousand times lower than the IC50 of CEP-

1347, FK228 can completely block the growth of NF2-deficient cells. Its chemical structure shows it is a ring peptide. The compound FK228 works by blocking the PAK pathway. This chemical compound does not directly bind PAK, but blocks both the upstream and downstream of PAK. This chemical compound has been clinical trials for a variety of tumors or cancers, but not yet for NF tumors. FK228 was originally developed as an anti-RAS cancer drug by a Japanese pharmaceutical company called “Fujisawa”. But, until recently, nobody knew how it blocked the growth of RAS cancers.

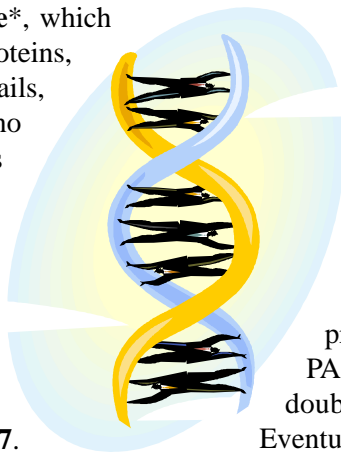
A few years ago they found that this chemical compound changed the structure of chromatin, a complex of genes, and a subset of genes are activated by this chemical compound. Two of them happen to be the tumor suppressors **Gelsolin** and **P21**. This scheme shows how RAS activates the cell division through PAK. The Gelsolin blocks the enzyme “A” right after RAS. So, in the presence of this chemical compound, PAK is no longer activated. That’s why this compound blocks the growth of RAS cancers.

This chemical compound, through another protein called P21, blocks the downstream of PAK. So, this single chemical compound gives a double-punch to this oncogenic RAS pathway.

Eventually we actually showed that this chemical compound reduces the PAK activity in RAS transformed cells. The control cells show a very high PAK kinase activity, but when you treated cells with this drug at this concentration, the PAK activity is significantly reduced. So, it’s now clear that this compound blocks the PAK activation. To see if both NF1 and NF2 deficient tumors require PAK for their growth, we tested whether this compound has any affect on their growth. As we see (in these slides), when you treat these two cell lines with this drug, none of them grows.

At this concentration (0.1 nM), the inhibition is 100 percent. Then we determined the IC50 – the concentration of chemical compounds that inhibits the growth by 50%. It turned out to be around 5 pM. Very, very low concentration. We used the cell line H-MESO, derived from a lung cancer (mesothelioma) caused by asbestos, as this is the fastest growing among NF2-deficient cell lines. Most NF tumors grow very slowly. So it is hard to do any animal experiments with NF

Please see **Turning Point** on page 6



\***peptide** – Any of various amides that are derived from two or more amino acids by combination of the amino group of one acid with the carboxyl group of another and are usually obtained by partial hydrolysis of proteins.



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tumors.

Using this cell line, we can have two types of xenograft by transplanting this human cell line into immuno-deficient mice (called “nude” mice). One is a solid tumor, which grows very slowly. The other one is **ascites\***, which is supposed to grow much faster. To see whether this chemical compound suppresses the growth of NF2-deficient cells will probably take a few more months, even using this ascites tumor. The prime reason is that growth of these cell lines is much slower than the major cancers, such as pancreatic and breast cancers.

So, meanwhile, we chose a much faster growing human cancer to find out the best condition, or so-called minimum effective dose, of FK228. Once we know the minimum dose we can start a clinical trial for NF1 and NF2.

There are two reasons why we chose breast cancers. Firstly, about three-quarters of breast cancers are estrogen-dependent, and the estrogen receptor and the key enzyme PAK form a vicious cycle. The receptor activates PAK, which in turn activates the receptor. So, we thought if you block the PAK, then the estrogen-dependent growth of these breast cancers could be inhibited.

Also, about 30% of breast cancers are developed by mutation of other receptors called **ERBB1** and **ERBB2**. Peptide hormones activate these receptors, and the receptors eventually activate PAK through the RAS pathway that I have explained to you. These breast cancers are also probably sensitive to FK228. So, we recently started to determine the concentration that FK228 needs to block the growth of the breast cancer. We learned that it is around 5 – 10  $\mu\text{M}$ , very similar concentration at which the growth of NF1 and NF2 cells is inhibited. In terms of sensitivity, this breast cancer is very similar to NF1 or NF2 tumor cells. Since this breast cancer develops a tumor very fast in nude mice, we thought this would be a good model for determining the minimum effective dose of this chemical compound in vivo.

Right now we have a xenograft of this human breast cancer in mice. Since the pharmaceutical company

provided us with FK228, we cannot release the detailed data right now without their permission. But I will tell you that the growth of this breast cancer is almost completely blocked by this drug with a certain dose. In our remaining time, I'll show you a few other anti-PAK drugs, which block either the upstream or downstream of PAK.

You have seen that FK228 suppresses not only NF1 and NF2, but also breast cancer and RAS cancer. It was published last year that the same compound also blocks the growth of prostate cancer, indicating that anti-PAK inhibitors such as FK228 can treat more than 70% of all human cancers/tumors. But even miracle drugs would not lead to a complete cure, simply because some mutated tumors then begin to show resistance to this drug. So we like to have multiple drugs (more than one) which block different target enzymes, but in the same pathway.



That is one of the reasons we developed another inhibitor called **AG 879**, which blocks the interaction between PAK and **ETK**. The ETK is another enzyme required for the activation of PAK. The PAK requires so many proteins for the activation in cells. So if you block this ETK, you can block the RAS pathway, and therefore AG 879 could also be useful for the treatment of NF.

Besides, we are trying to develop a direct PAK-specific inhibitor called **ST-2004** by a specific chemical modification of a non-specific inhibitor called **ST-2001**. The original compound, found in a marine sponge on Guam Island, is a very potent inhibitor for PAK, but it inhibits so many other enzymes as well. It causes even the death of normal cells. So, you can't use it as a drug. However, we know how to modify it chemically to reduce these side effects selectively, so that its derivative ST-2004 blocks out only PAK in the end. We are making this “magic bullet”.

Also, a drug company called Bayer and a biotechnology company called Onyx, together developed another inhibitor called **BAY 43-9006**. This is specific for another enzyme called RAF, just downstream of PAK. This is now in clinical trials for RAS and many other cancers. This is also potentially useful for the treatment of NF1 and NF2, because it blocks right downstream of PAK, and this pathway is actually required for the growth of NF2 tumors.

Using just the last few minutes, I will explain how to

\***ascites** – is the accumulation of serous fluid in the spaces between tissues and organs in the cavity of the abdomen.

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### *Turning Point ... from page 6*

modify and convert the non-specific PAK inhibitor to a potent PAK-specific inhibitor. Actually, I have mentioned to you that the CEP-1347 is a specific inhibitor, but the IC50 is very high, around 1 micro M, and in our common sense we can't use it for a so-called in vivo (animal or clinical) experiment, because we have to use a very high dose to see the effect.

So we began to focus on the compound ST-2001, the marine sponge product. This is a thousand times more potent than CEP-1347. The PAK-specificity of CEP-1347 is based on the unique property of PAK that distinguishes itself from other enzymes. The drug-binding domain of the enzyme PAK is bigger than any of the other enzymes in the kinase family. If you take these bulky side chains to CEP-1347, only PAK can accept this compound. Although ST-2001 itself binds any other enzymes non-specifically, if you put this bulky side chain to this compound, converting this one to ST-2004, it is then expected to inhibit only PAK, no other enzymes, and is very potent. That is what we are making in collaboration with people in Guam Island and organic chemists at Yale. Because we need a large quantity of ST-2001, it takes some time. But hopefully, by the end of the year, we will get this starting compound in a large scale, and then convert it to this PAK-specific potent inhibitor.

One of the chemical compounds that work, at least in RAS cancer in mice, is **AG 879**. It blocks interaction between PAK and ETK, but inhibits the growth of RAS cancer by only 50%. There is another chemical compound called **PP1**, which was originally developed by Pfizer, the pharmaceutical company, several years ago. This inhibits another enzyme in the sarc family. Again, it alone inhibits the cancer growth by only 50%.

If you combine these two compounds, the growth of RAS cancer is almost completely blocked. We are going to do the same experiments with human NF1 and NF2 tumors. If, like RAS cancers, it is proven to work with NF tumors, we can shift to clinical trials. I have talked about a few chemical compounds that block upstream or downstream of PAK, but just before closing my talk, I will show you another way to treat NF, both types 1 and 2. This is a little complicated. I'll just try to make it simpler. This approach is somehow opposite to the chemical approach.

There is a unique virus called REOVIRUS. This is a deadly virus for mice, but harmless for humans. Most people have probably never heard about it. It became known several years ago that REOVIRUS could de-

stroy only cancer cells in which RAS is activated. Thus, RAS cancers are the major targets of this virus. This REOVIRUS does not cause harm to normal cells. So it's now in clinical trials (I think phase 1 or 2), and it shows some promising results.

Recently we found how RAS allows this virus to infect cells. The responsible enzyme that allows the REOVIRUS to infect cancer cells is actually PAK, because PAK interacts with this and other proteins anyhow. In principal, all the cancers in which PAK is activated, like RAS cancers and NF tumors, are sensitive to this REOVIRUS. So after the treatment with so-called PAK inhibitors of NF1 and NF2 tumors, and if we find that some of the tumors become resistant to the anti-PAK drugs, we know that PAK is fully activated in those cancers, and therefore the tumor is sensitive to this REOVIRUS. Instead of blocking the PAK pathway, we can actually treat neurofibromatosis by using the PAK pathway.

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**T**hese are our hope ... and some of the viruses or chemical compounds are *now* in clinical trials. The only thing that we have to show (prior to NF clinical trials) is that these viruses or chemical compounds work at least in mouse NF models. Then we are allowed to shift to the clinical trials.

That is our current situation. There is a hope for NF1 and NF2 peoples.

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### *Rescue ... from the Cover*

That's what a hero does. Joe Marm, the Washington man who earned a Medal of Honor in Vietnam, said that's what makes a hero. That's what he told me he did to earn his medal almost 40 years ago. He went forward.

That's exactly what Weaver, a 20-year veteran police officer, did when he got 63-year-old **Marie Drew** out of her car and carried her through the raging water to safety. He's her hero, for sure. Ours, too, because he went the other way – forward – without hesitation, without concern for his own safety, without a life jacket or a rope around his waist, and without possessing the ability to swim.

"I'm not a swimmer; I can dog paddle a little," Weaver, 56, told Observer-Reporter staff writer Barbara S. Miller late Saturday after having worked a double shift Friday afternoon and evening and into Saturday morning.

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### Rescue ... from page 7

"You don't think about something like that," he said. "I have a 6-year-old granddaughter who can out swim me."

Drew, former volunteer coordinator at Western Center until it closed in 1999, became trapped in her small sedan when she tried to drive through the Montour Railroad tunnel at the intersection of Routes 50 and 980 in Venice. She was coming from her mother's home in the Gladden Heights section of the township outside McDonald and was on her way to her own home in Canonsburg when her car floated through the tunnel to become wedged by water pressure against the bridge railing.

"In my deafness, I misunderstood what I was told. I thought the water had been pumped out of the underpass and the road had reopened," Drew said Monday morning. "As soon as I started into the tunnel, I knew I'd made a mistake. Before I could put the car into reverse, it started floating through the tunnel. Thank God that it did. That's how I was found."

A Channel 11 cameraman noticed her in the car, waving from the driver's window. News people in the Pittsburgh studio called Washington County 911 dispatchers to apprise them of the situation and the location. Weaver and Cecil No. 3 volunteer firemen rushed to the scene.

"Sgt. Weaver came walking through the water to me," said Drew, who lost her hearing four years ago, the result of an operation, her seventh, to remove a

brain tumor. "For him, it looked like it was a Sunday walk in the park.

"I wasn't scared; at least I hadn't gotten to the point of praying for my life," she said. "He conveyed complete confidence with every step he took. He made me calm just by his body language. I had the feeling that he was in total control."

Weaver got her to let go of the steering wheel and to take her foot off the brake pedal. Then he grabbed her up and started walking back through the water to the waiting firemen and the safety lines that they had strung across the flooded road.

"I didn't know she was deaf until afterward," Weaver told Miller, "I just thought she couldn't understand me because of all the noise from the rushing water. She's a pretty good lip-reader."

Weaver, who was flown Monday evening to New York City for a taping session for the Jane Pauley Show, was not the only Cecil Township officer to pull people from cars stalled in the floodwaters.

Two miles down Route 50, near Bunny's Tavern at the intersection of Muse-Bishop Road and Wilson Avenue, Patrolman Keith Strain helped rescue two people from their stalled cars.

There was no TV cameraman to catch that rescue action on videotape, however. Strain also went forward. He, too, is a hero. Look it up.

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Byron Smialek is columnist and senior writer for The Observer-Reporter. Reprinted with permission.



## Not Forgotten

**J**ayne Audrey Johnston passed away at home surrounded by her loving family on September 24, 2004 from complications of Neurofibromatosis type 2. She was 34 years old.

After graduating from Winthrop High School Class in 1988, Jayne entered Northeastern University where she received the Northeastern University Distinguished Leader Award in 1995 and was a member of the National Honor Society and an officer and member of the N.U. Deaf Club.

She was active in the Boston Deaf Community and



the Massachusetts Association for the Deaf, and was an esteemed member of ALDA (Association of Late Deafened Adults) and the NF Crew online support group.

"Support" seemed to be Jayne's *other* middle name. She was a passionate across-the-board advocate for women's issues and the disabled. As a member of NF, Inc. New England, Jayne helped in lobby efforts for the federal funding of NF research by writing letters to Congress. She also embraced the role of advisor during the development of their web site.

In all of these endeavors she tirelessly served the NF2 community, but they were nothing less than labors of love from someone who truly celebrated life every day.



### Editor's Note:

When **Kathie Hering** passed away on October 22, a loving tribute to her remarkable life made by family members, friends and associates was published in the November-December issue of "ALDA Chicago Style", newsletter for the Chicago Chapter of ALDA (Association of Late Deafened Adults). Kathie, together with **Bill Graham**, had co-founded ALDA in 1987. Tributes written for that special issue by Bill Graham and Kathie's brother, **Rick Skyer**, are reprinted here with permission.

# The Gift of Kathie Hering

By **Bill Graham**

I heard the name Kathie Hering for the first time in late 1986. She had organized a self-help group at Ravenswood Hospital for people who lose their hearing as adults. I thought this was an interesting idea. After becoming deaf about ten years before, I began moving tentatively in deaf and hard-of-hearing circles. I had learned a sputtering form of sign language, joined an interpreted theater organization, attended a SHHH meeting or two, went to big "D" Deaf clubs a few times, and owned a TTY. A big change in life, for sure, achieved only through the encouragement of people who could see that I was, in fact, lost.

I attended Kathie's self-help group for the first time a few months later. I walked back and forth past the room a number of times before summoning up the courage to walk in. There were only two people in the room, two women sitting face-to-face in folding chairs at close range, working hard to communicate. They didn't see me standing at the door for what seemed like several minutes. I had time to get out of there unnoticed, maybe

go home and take my dog for a walk instead. But in I went.

Kathie greeted me. I had never met a person with NF2 before. At the time, I didn't know what NF was. I was startled by the facial paralysis. I need to read lips to understand what people say – even when they sign – and Kathie's lips didn't move much.

This did not look like a place I wanted to be. But Kathie motioned me to a chair next to the other woman, Paulette Pounds, and I sat down.

I remember absolutely nothing about our conversation that night. We were in that room together for over an hour and it was a struggle to understand anything at all. I had trouble with Kathie's signing and I couldn't read her lips. Paulette couldn't understand either one of us. Kathie repeated whatever she said over and over; she seemed patient and composed although it was hard to tell really because NF had robbed so much expression from her face. I left the meeting un-nerved.

It was only after a few days that I started to sense anything positive in what I had experienced. Kathie had kept us "on point", which is another way of saying that she wouldn't let us bluff and move a nonexistent conversation along. We may not have covered much ground, but we did cover that ground. This was not my usual experience with communication. There was an odd attraction about it that I couldn't articulate at the time. So I went back. And it changed my life completely.

I gradually realized that the self-help group was an honest place. One of the hardest things for people who lose their hearing is honesty, with themselves and with others. Kathie kept us honest about our deafness. This wasn't particularly fun, but not everything of value has a laugh track.

We met three or four more times before Kathie couldn't come anymore. She lived in the far south suburbs and Ravenswood was on the north side of the city. That's a long way to drive, especially at night. But, if I remember correctly, she stopped coming because she wasn't well. Although she didn't advertise such things, I assume this was one of her many sur-

*Please see Gift on page 10*





*Gift ... from page 9*

geries to chase down NF's unrelenting tumors.

By then, I had begun looking forward to Kathie's self-help group. I wasn't ready for it to end. Kathie worked as a rehabilitation counselor for the deaf and had compiled a list of late-deafened clients. I asked her for the list so I could contact these people. After a few social get-togethers, we had forged an increasingly strong support network that evolved into the Association of Late-Deafened Adults.

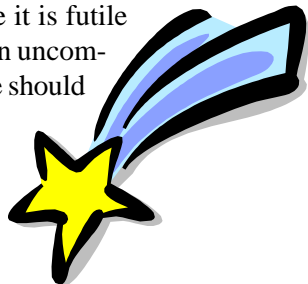
As ALDA grew, so did the number of NF2 people in the organization. They formed 5 to 10 percent of the membership during ALDA's early years. They were conspicuous at ALDA conventions, with the telltale facial paralysis, their often-uncertain gait, and the special challenge they presented in deciphering their speech and signs.

Kathie, her sister Mary, brother Rick and Helen Mendelsohn were the chief NF2 recruitment officers in ALDA. But Kathie was clearly the center, the person who reached out to NF2 people the most visibly and effectively; the one who steered them into ALDA's mainstream and made it all work.

It's not a stretch to say that Kathie and the NF2 subgroup embody the soul of ALDA. Deafness is often called an invisible disability; you can't see hearing loss and most deaf people can blend in with the hearing population undiscovered if they want to play their cards that way. People with NF2, on the other hand, cannot hide their disability – it's immediately apparent and consequently, there is no choice but to deal with it head-on. That must be extremely hard. But it's also honest. And it is a beautiful thing.

It's always easy to get caught up in the fun of ALDA – the hugs, the laughter, the karaoke parties, the old friendships renewed. But the heart of ALDA is the honesty of people being totally themselves, deaf warts and all. Without this simple yet elusive virtue, ALDA's unmistakable beauty starts to fade.

Kathie knew this. Her integrity was unassailable as was her extraordinary courage. With honesty and quiet grace, Kathie gave solace, support, hope and finally strength to so many people it is futile to begin a count. She was an uncommonly beautiful person. We should keep her in our hearts.



By **Rick Skyer**

**K**athie was like most of us in many ways, but very different in others. When she saw a real need, she set out for the "cause" as was her word.

She saw the deafened and realized there was nothing available to help us. No support network to talk to about becoming deaf, being late deafened or general "talk" since isolation was a very real monster.

ALDA solved this. It was and is amazing. It is now a worldwide network! That, in itself, is something few of us ever do – affecting the lives of others in a positive way. What's even more humbling is that she didn't gloat over her huge achievements and yes, the immortality that she obtained.

You talk about animals and her fondness. Even before she was deafened they were a big part of her. After, they remained so as they were uncommitted and totally impartial to the physical changes she endured. She loved them and they loved her; it's that simple.

Another talent was that she would only see "good" in people. We all know there is a lot of "bad" in people, too, but she never dwelled on the negative and only supported the positive.

Some of the biggest memories she provided were her "magical smile" when she was dancing. She was absolutely fabulous when she used to dance. It's funny now, but every time I watch the TV show "American Dreams", or see Meg dancing and hopping around in the previews, I think of Kathie and no one else.

When she smiled and danced, the only other comparable moment of blissfulness is how proud of herself she was when she would water ski – starting on two skis' and dropping one.

Lots of small, cherished things come to mind. I just hope we can see them through our tears.

**NF, INC. NEWS****NF, Inc.**

9320 Annapolis Road #300  
Lanham, MD 20706-3123  
E-mail: [info@nfinc.org](mailto:info@nfinc.org)

**Upcoming Events**

The next **Camp New Friends** is scheduled for **July 23 – July 29, 2005**. Camp fee is \$600 per camper; camperships are available. Prospective Campers, Counselors, and Counselors-In-Training can obtain more information about the camp by e-mailing [NFMidAtlantic@aol.com](mailto:NFMidAtlantic@aol.com). You may also contact **Sandy Cushner-Weinstein, MSW**, at Children's National Medical Center, by phone at 202-884-5142, or via e-mail at: [scushwei@cnmc.org](mailto:scushwei@cnmc.org) (please use "NF Camp" in the subject line).

**NF, Inc. Chapters**

**NEUROFIBROMATOSIS, INC.** is comprised of seven independent, state and regional Chapters. It is through the efforts of these chapters that NF, Inc. is able to provide information, make referrals, assist with community support services, provide research funding, and educate federal, state and local governments of the needs of NF families.

Please feel free to contact the local chapter in your area (below), or us at NF, Inc., for assistance in finding out how you might be able to make a difference.

**◆Neurofibromatosis, Inc. – NF2**

Due to the statistical rarity of NF-2 and the special needs of the NF-2 population, NF, Inc. has given the NF-2 representative Chapter status. Those with NF-2 throughout the country are encouraged to communicate with NF, Inc. through Marie Drew, the NF-2 Chapter Representative.  
E-Mail: [Marie.Drew@comcast.net](mailto:Marie.Drew@comcast.net)

**◆Neurofibromatosis Association of Arizona**

PO Box 2718, Chandler, AZ 85244  
Phone: (480) 945-9650  
E-Mail: [nfaz1@cox.net](mailto:nfaz1@cox.net)

For current news and events related to the Arizona chapter, please visit their new website at [www.nfaz.org](http://www.nfaz.org)

**◆Illinois NF, Inc.**

PO Box 1923, Lombard, IL 60148  
Phone: (630) 932-8111 or 800-322-NFNF (Illinois only)  
E-mail: [ilnfinc@sbcglobal.net](mailto:ilnfinc@sbcglobal.net)

**◆NF, Inc. – Indiana**

1173 Hague Court, Franklin, IN 46131  
Phone: (317) 736-7577 or (765) 339-7206  
E-mail: [pdavis@athensmed.org](mailto:pdavis@athensmed.org)

**◆Neurofibromatosis Kansas & Central Plains**

P.O. Box 1792, Hutchinson, KS 67504-1792  
Phone: 1-800-942-6825  
E-Mail: [gfprieb@kcisp.net](mailto:gfprieb@kcisp.net) or [nprieb@southwind.net](mailto:nprieb@southwind.net)

**◆Neurofibromatosis, Inc. – Mid-Atlantic**

8855 Annapolis Road, Suite 110, Lanham, MD 20706-2924  
Phone: (301) 577-8984 / (Toll Free) 1-866-261-1271  
E-mail: [NFMidAtlantic@aol.com](mailto:NFMidAtlantic@aol.com)

The Mid-Atlantic Chapter services Maryland, Virginia, the District of Columbia, Delaware, Pennsylvania, New Jersey, West Virginia, and North Carolina. The Chapter is dedicated to individuals affected by NF, their families, and the professionals who provide services to them. We are here to help in any way that we can.

**Mid-Atlantic News / Events**

*Presented by*

**The Johns Hopkins Hospital  
Comprehensive Neurofibromatosis Center**  
Co-chairs, **Dr. Allan Belzberg**, Neurosurgery  
and **Dr. Kaleb Yohay**, Neurology

On November 6, the Johns Hopkins Hospital Comprehensive Neurofibromatosis Center held its first **Informational Meeting for Individuals with NF**, their families and friends. People impacted by NF1 and NF2 came from all over the country – as close as D.C., Pennsylvania, New Jersey and Virginia and as far as Arkansas, Florida, Michigan and Wisconsin. For questions or more information please call Dr. Belzberg at 410-955-5810 or Dr. Yohay at 410-955-3806.

**◆NF, Inc. – Minnesota**

PO Box 18246, Minneapolis, MN 55418  
Phone: 612-362-4413 (work)  
E-mail: [JohnE@cipmn.org](mailto:JohnE@cipmn.org)

**◆Neurofibromatosis, Inc. – New England**

9 Bedford Street, Burlington, MA 01803  
Phone: (781) 272-9936  
E-Mail: [info@nfincne.org](mailto:info@nfincne.org)  
Please visit our beautiful new website at [www.nfincne.org](http://www.nfincne.org) for chapter information and events.

**◆NF, Inc. – Northern California**

P.O. Box 1234  
Vacaville, CA 95696  
Phone: (707) 469-0467  
E-mail: [dbell@nfnocal.org](mailto:dbell@nfnocal.org)






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**NNFF NEWS**


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**The NF Marathon Team hits the streets of New York ...**

The NF Marathon Team has run from Anchorage Alaska to Dublin Ireland, but for the first time had a team running in the New York City Marathon. "Jessica's Team" was named for Dan and Robin Altman's two-year-old daughter Jessica, who was diagnosed with NF earlier this year. Joining Dan was Ron Bowman, who ran for his close friends John & Florence McCarthy, whose 4-year-old daughter Aidan also has NF. Dan and the McCarthys recruited an exceptional group of friends to join the team and made our first entry in the New York Marathon a success both in raising funds for NF Research and for increasing public awareness of NF.

For more information on this and other upcoming NF Team Marathon events, please contact:

**The NNFF Marathon Team Program**

Phone: (212) 344-6633 ext. 251

or (800) 323-7938 ext. 25

Fax: (212) 747-0004

Email: [nfmarathon@nf.org](mailto:nfmarathon@nf.org)


**NF Gala ...**

Over 280 Guests celebrated the 25th Anniversary of the Foundation at the New York Mandarin Hotel on Tuesday night November 9th. Jane Hanson, NBC News Anchor, hosted the event. The program included a short film on our 25th Anniversary Ambassadors, Bara Colodne & Adam Goodkind, the unveiling of our new name, logo and television public service announcement by Board member Al Kahn, and a memorable musical performance by The Manhattan Rhythm Kings. The event raised over \$250,000 for NF research and public awareness.





## NF2 Resources

# OnLine...

# ... and OffLine

### NF2 Crew

The NF2 Crew is an online information, support and sharing group for persons with NF2 and their family members and friends. Members discuss treatment options, share experiences and coping skills, jokes and friendships. To join the NF2 Crew, the address is:

**NF2\_Crew-subscribe@yahoo.com**

or contact **Jennette Braaten** at:

**(new!) jennette2@charter.net (new!)**



## WebSightings

The Internet is a storehouse of information for researchers, doctors and other health care professionals, as well as a resource of personal support for NF2ers, their families and friends. The aim of *WebSightings* is to offer readers a sample selection of NF2-related websites that offer just such support and information. If you have a website that you would like to see mentioned here, please submit them ...

### NF2 Crew Website [www.nf2crew.org](http://www.nf2crew.org)

The NF2 Crew Website continues to be one of the leading NF2 support sites online ... "the only place on the World Wide Web for people with NF2 (and their families) to come together, face our challenges, and learn through sharing."

The home page offers a wide range of **Links** to explore, including information about NF2, an **NF2 Doctors** list with patient-recommended physicians from all over the country, and an ever-expanding **Photo Gallery**. There is also a *new* section for members-only, an **Events** section that lists and describes upcoming NF2-related events, and an **NF2 Glossary** with explanations of lots of NF2 terms.

Information on how to join various NF2 Crew **E-Mail Lists** is available, and for those wanting to talk in "real time" with other Crew members, we also pro-

*Please see WebSightings on page 14*

The following listings contain the mailing addresses and/or phone numbers (both VOICE and TTY, when available) for some of the organizations and support groups found under **NF2 Resources Online**. After all, not *everyone* has access to a computer (smile).

If there is an organization or a support source that you would like to see listed here, please submit them.

#### Neurofibromatosis, Inc.

9320 Annapolis Road, Suite 300

Lanham, MD 20706-3123

Telephone: **1-800-942-6825** (Toll Free)

or **301-918-4600** / Fax: **301-918-0004**

#### The National Neurofibromatosis Foundation, Inc.

95 Pine Street, 16<sup>th</sup> Floor, New York, New York 10005

Telephone: **1-800-323-7938** (Toll Free)

or **212-344-6633** / Fax: **212-747-0004**

#### ALDA Inc.

1131 Lake St., # 204, Oak Park, Illinois 60301

Telephone: (Voice/Fax) **877-907-1738** (US only)

or (TTY) **708-358-0135**

#### The Neurofibromatosis Association – U.K.

82 London Road, Kingston on Thames,

Surrey, KT2 6PX / Telephone: **0208 547 1636**

Fax: **0208 974 5601** or Minicom: **0208 392 0184**

~ ALSO ~

#### ♦ Neurofibromatosis Clinics Association Inc.

PO Box 14185, Pittsburgh, PA 15239

Telephone: **412-795-3029** / Fax: **412-795-3098**

Online: <http://trfn.clpgh.org/nfca>

#### ♦ British Columbia

#### Neurofibromatosis Foundation (BCNF)

203-1001 Cloverdale Ave., Victoria, B.C. V8X 4C9

Telephone: **250-370-7597** / **1-800-385-BCNF** (2263)

Online: [www.bcnf.bc.ca](http://www.bcnf.bc.ca)

#### ♦ Angel Flight, Tulsa, OK (918) 749-8992

#### ♦ Mercy Medical Airlift, Chesapeake, VA

**1-800-296-1217**

#### ♦ National Association of Hospital Hospitality Houses, Inc., Hospitality Hotline **1-800-542-9730**

(daily 9 a.m. to 5 p.m. EST)



### *WebSightings ... from page 13*

vide you with details about the Crew AIM chats.

Because there is so much information on different approaches to treating and living with NF2, we will do our best to list what's available on the web on our site.

### **NF, Inc.**

*“Serving NF Families Since 1988”*

**www.nfinc.org**

**N**F, Inc. is an organization made up of independent state and regional chapters, providing support and services to NF families. We are a non-profit organization dedicated to individuals and families affected by neurofibromatosis and related disorders.

We serve these needs through coordinated educational and personal support, as well as clinical and research programs. NF, Inc. also promotes national, state and local community involvement. We have a packet of NF2 materials that we can distribute upon request, a physician's referral listing, a video that is open-captioned and conduct meetings with the aid of “Real Time Captioning.” Some of the meeting presentations are also posted on the NF, Inc. website.

In addition to assisting individuals and families, NF, Inc. works closely with clinical and research professionals who specialize in the treatment of NF.

### **National Neurofibromatosis Foundation (NNFF)**

**www.nf.org**

**T**he NF Website – a leading resource for information and support for the NF community – now incorporates more information than before, to better serve patients, families, medical professionals, scientists and the public.

By logging on to The NF Website, visitors can instantly obtain information on the latest news in research, NNFF programs, or how to become a member. The interactive Bulletin Board, containing more than 25,000 messages, and chat rooms help to keep people connected and provide support and encouragement for those living with the NF.

The NF Website is interactive and has 18 foreign language pages. Medical professionals and the general public can use the website to learn, share information and provide support from anywhere in the world.

### **Association of Late-Deafened Adults (ALDA)** **www.alda.org**

**A**LDA was formed in Chicago, Illinois in 1987. Most of those that gathered there were total strangers who had never met or talked to another deafened person, yet they found themselves wonderfully comfortable with one another. The marvelous sense of fellowship lasted and led to more social gatherings and self-help support groups, which swiftly evolved into the Association of Late-Deafened Adults (ALDA).

Today, ALDA's membership is international in scope. ALDA works collaboratively with other organizations around the world serving the needs of late-deafened people and extends a welcome to everyone, late-deafened or not, who supports our goals.

### **American Sign Language**

- ◆ [www.lifeprint.com/index.htm](http://www.lifeprint.com/index.htm)
- ◆ [www.disabilityresources.org/SIGN.html](http://www.disabilityresources.org/SIGN.html)
- ◆ [www.handspeak.com](http://www.handspeak.com)  
(subscription-based)
- ◆ <http://commtechlab.msu.edu/sites/aslweb/browser.htm>
- ◆ [www.coloroflanguage.com](http://www.coloroflanguage.com)

### **Open Caption Programs & Opportunities**

#### **InSight Cinema**

*The Audience is Reading*

**www.insightcinema.org**

**I**nSight Cinema is a non-profit organization dedicated to bringing the Big Screen Movie-Going Experience to Deaf and Hard of Hearing Audiences across the U.S.

Open captioned films make major motion pictures – top box office hits like “BRIDGETTE JONES: THE EDGE OF REASON”, “THE INCREDIBLES” and “RAY” – available quickly (usually within 4 weeks of national release) and on a wide scale. Captioning technology has made viewing open captioned films more

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### *WebSightings ... from page 14*

pleasurable not only for deaf and hard of hearing audiences, but also an experience to be shared with their hearing friends and family as well.

Be sure to check the website for updates and current confirmations. You can also write to us at:

**InSight Cinema**, 6080 Center Drive,  
Suite 600, Los Angeles, CA 90045.

## **Captioned Media Program (CMP)**

[www.cfv.org](http://www.cfv.org)

The mission of the Captioned Media Program (CMP) is to provide all persons who are deaf or hard of hearing awareness of and equal access to communication and learning through the use of captioned educational media and supportive collateral materials. The CMP also acts as a captioning information and training center. The ultimate goal of the CMP is to permit media to be an integral part in the lifelong learning process for all stakeholders in the deaf and hard of hearing community: adults, students, parents, and educators.

The CMP supports the U.S. Department of Education Strategic Plan for 2002-2007 and will focus on:

- ♦ Ensuring that all deaf and hard of hearing students have the opportunity to achieve the standards of academic excellence.
- ♦ Advocating for accessible media, as well as the establishment and maintenance of quality for CMP captioning.
- ♦ Involving its constituents in the selection, evaluation, production, and distribution of its products.
- ♦ Exploring and adapting new media and technologies, which assist people who are deaf and hard of hearing in obtaining and using available information.

## **Vocation/Education Services**

### **The Sierra Group**

[www.thesierragroup.com](http://www.thesierragroup.com)

*Enhancing Human Potential  
Through Technology and Strategies*

### **Changing America's Workplace**

The Sierra Group works in the area of disability and employment. The nexus of expertise that brought the organization to the forefront of the industry is our ability to use technology and assistive tech-

nology to drive employment opportunities for individuals with disabilities – even severe disabilities.

By thinking “integrated performance” we reduce discomfort, improve accessibility and help to create systems for optimal employee interactions. Our team of qualified engineers, trainers, rehabilitation counselors, ergonomists, and case managers, direct vocational rehabilitation services for our customers and clients.

The Sierra Group, an award winning, certified women’s business enterprise has been serving individuals, governmental organizations, agencies and corporations since 1991. Our diverse team has expertise in the following areas:

♦ **Rehabilitation Engineering** ♦ **Assistive Technology and Section 508 Compliance** ♦ **Vocational Rehabilitation** ♦ **Ergonomics** ♦ **Independent Living** ♦ **IT and Website Accessibility** ♦ **Consulting, Training, Planning and Outsourcing** ♦ **Disability Management**

The Sierra Group stands for reversing the rate of unemployment for individuals with disabling conditions in America.

Interested? Please contact The Sierra Group via e-mail at: [info@thesierragroup.com](mailto:info@thesierragroup.com), or by phone at **1-800-973-7687**.

## **Medical-related Travel and Lodging Services**

### **The National Association of Hospital Hospitality Houses, Inc.**

[www.nahhh.org](http://www.nahhh.org)

Established in 1986, the National Association of Hospital Hospitality Houses, Inc. is a caring association of more than 150 nonprofit organizations located throughout the U.S. that provide family-centered lodging and support services to families and their loved ones who are receiving medical treatment far from their home communities.

### **Healthcare Costs Reduced**

The need for family-centered lodging during long-term illnesses has become an increasing concern with the medical community. As hospitals address the matter of cost containment, more and more procedures are performed today on an out-patient basis, often including same-day surgical care. On-going treatments, like radiation or chemotherapy, may not require overnight hospitalization, but usually involve a series of ex-

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### WebSightings ... from page 15

hausting treatments for patients, especially if daily-round trips to the hospital are required. Even when medical treatment is covered by insurance, living expenses are not. Families cannot afford expensive hotels or motels.

To reduce healthcare costs, NAHHH member/houses offer inexpensive accommodations (usually \$5 to \$15, sometimes free) during hospitalizations, before and after surgery, and during repeated visits. A hospitality house truly becomes a family's "home away from home."

The NAHHH maintains information on all known facilities offering accommodations to people during medical treatment away from home. A directory of NAHHH member/houses is updated regularly and published annually. Free copies are available to all members. Our "Hospitality Hotline" (800-542-9730 daily 9 a.m. to 5 p.m. EST) and this World Wide Web site makes information on all hospitality houses available to anyone at no charge.

### Angel Flight, Inc.

[www.angelflight.com](http://www.angelflight.com)

Angel Flight is a non-profit organization of pilots and other volunteers dedicated to serving the community by arranging free private air transportation for

medical patients who cannot afford to utilize normal, commercial transportation. Angel Flight also provides services to blood, organ and tissue banks.

Angel Flight is a member of Air Care Alliance, a group of 37 organizations providing similar services throughout the United States.

### Mercy Medical Airlift (MMA)

[www.PatientTravel.org](http://www.PatientTravel.org)

**PatientTravel.org** is a service of the **National Patient Travel Center** – the facility housing all the programs of **Mercy Medical Airlift (MMA)**, a national charity. The Center is in Virginia Beach, Virginia, and provides a variety of services to those seeking a way to travel long-distances for specialized medical evaluation, diagnosis and treatment.

The **National Patient Travel Helpline, 1-800-296-1217**, provides information about all forms of charitable, long-distance medical air transportation and provides referrals to all appropriate sources of help available in the national charitable medical air transportation network.

## Disability-Related Information & Resources

### DisabilityInfo.Gov

[www.disabilityinfo.gov](http://www.disabilityinfo.gov)

**D**isabilityInfo.gov is designed to be a single point of entry to access government services and information relevant to people with disabilities. The site contains information on civil rights, education, employment, job accommodations, housing, technology, Medicaid and Medicare and emergency preparedness. The Office of Disability Employment Policy in the Labor department established and manages the site with ongoing content development shared by multiple agencies.

## Health Management Info

### Mayo Clinic Health Information

[www.MayoClinic.com](http://www.MayoClinic.com)

**M**ayo Clinic Health Information's award-winning consumer Web site offers health information, and self-improvement and disease management tools. MayoClinic.com's medical experts and editorial pro-



Reprinted from The Funny Times, 2002

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professionals bring you access to the knowledge and experience of Mayo Clinic for all of your consumer health information needs, from cancer, diabetes and heart disease to nutrition, exercise and pregnancy.

**www.MayoClinic.com** articles are continuously reviewed and updated with significant changes or advances, with scheduled updates occurring at least every two years. Please check the site regularly to ensure you are reviewing the latest health information.

## Patient Services

### Patient Updates

**www.patientupdates.org**

When a loved one is hospitalized, it is sometimes difficult to get updates about their prognosis and progress. Concerned friends and family may be reluctant to call for fear of disturbing someone at a difficult time. Likewise, those who are charged with keeping everyone informed may find it fatiguing to repeat the same information again and again.

That's where PatientUpdates.org comes in.

PatientUpdates.org is both a website and a nonprofit organization that was created to provide a convenient and reliable way to keep friends and family updated on the condition of a hospitalized loved one **free of charge**. This website is provided as a public service – there is **no fee** to use this site. Simply enter the name of your loved one to view the latest update on their condition, or you can create a new patient account to keep others informed.

## International Sightings



**The Neurofibromatosis Association – U.K.**  
**www.nfauk.org**

The Neurofibromatosis Association, originally founded in 1981, today has four main aims:

- ♦ To provide information on NF to patients, medical practitioners and others, and to provide support to those affected by NF, and their families, which also includes helping to link them with the medical profession to their mutual benefit. In doing so, we are able to promote

awareness and understanding of the problems encountered with the disorder.

- ♦ Raising funds to support research into NF.
- ♦ Organizing seminars or symposia to study, discuss and disseminate information and research findings.
- ♦ Maintaining liaison with like-minded organizations and medical professionals both nationally and internationally.

The Neurofibromatosis Association also provides support for children, teenagers and young adults by holding special camps for them.

### The Acoustic Neuroma Association of Canada (ANAC)

**www.anac.ca**

The purpose of this website is to increase and expand the accessibility of current and relevant information about acoustic neuroma for patients and their families and for health professionals.

You may also contact them by E-mail at:

**anac@compusmart.ab.ca**

### Neurofibromatosis

**Association of Australia Inc.**

**www.nfaa.org.au**

The Neurofibromatosis Association of Australia (NFAA) Inc. was founded in 1985 with the aim of bringing together individuals and families with Neurofibromatosis (NF) for mutual support. The NFAA has a medical and scientific advisory board and close affiliation with similar NF groups overseas.

The aims of the Association are to:

- ♦ Support members
- ♦ Increase public awareness
- ♦ Increase awareness amongst medical and health care professionals
- ♦ Alert educational authorities to learning problems
- ♦ Promote research

**Neurofibromatosis Association of Australia Inc.**

PO Box 84 West Ryde, NSW 1685, Australia  
Telephone: +61 2 98740844 / Fax: +61 2 98740144

~ ALSO ~

**Brazil ~ Associação de Neurofibromatose**

**www.nf.org.br**



## NF2 EVENTS

11th Annual

# Las Vegas NF2con

Warm up the old 'slot machine' arm and save those nickels, because plans are once again in the works for the gathering of the faithful in Las Vegas.



Unfortunately, as of this printing, important little details such as *where* and *when* were still a bit sketchy. So, for those interested in attending and would like more information, please write to NF2con Host, **Pat Dillon**, 401 Agate Drive, Carson City, Nevada, 89706.

You can also e-mail Pat at: [pdillon438@aol.com](mailto:pdillon438@aol.com).

## Laughter ... good for what ails you



At great expense, people join health clubs for cardiovascular exercise. Laughter can produce similar results at far less cost. It stirs up the blood, expands the chest, electrifies the nerves, and clears the brain.

Laughter provides refreshment to the entire body. It can lower blood pressure, increase muscle flexion, and trigger a flood of endorphins – the brain chemicals that can bring on euphoria.

But laughter most profoundly affects our immune system. Gamma-interferon, a disease-fighting protein, rises with laughter. So do B-cells, which produce disease-destroying antibodies, and T-cells, which orchestrate our body's immune response.\*

With all that in mind, it is hoped that you will get a medicinal giggle or two from the contributions here. If you have something you'd like to contribute – an amusing joke, poem, story or cartoon, please write to us with your funnies.

\* Sources: American Association for Therapeutic Humor; Lee Berk, M.D. and Stanley Tan, M.D., Loma Linda University

## From the E-Mail Bag

More of ...

### Modern Medical Terminology:

**FIBULA:** A small lie.

**ENEMA:** Not a friend.

**SEIZURE:** Roman emperor.



**RECOVERY ROOM:** Place to do upholstery.

**CAUTERIZE:** Made eye contact with her.

**LABOR PAIN:** Getting hurt at work.

**BACTERIA:** Back door to the cafeteria.

**PAP SMEAR:** A fatherhood test.

## The History of Medicine

**2000 B.C.** – Here, eat this root

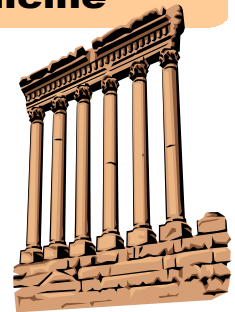
**1000 A.D.** – That root is heathen. Here, say this prayer.

**1850 A.D.** – That prayer is superstition. Here, drink this potion.

**1940 A.D.** – That potion is snake oil. Here, swallow this pill.

**1985 A.D.** – No, that pill is ineffective. Here, take this antibiotic.

**2000 A.D.** – Oh, no ... that antibiotic doesn't work anymore. Here, eat this root.



"Howard, I think the dog wants to go out."

Reprinted from The New Yorker magazine



# CONNEXIONS



*This column is dedicated, with love, to Caren Miller.*



I was the model for this snow woman. Hey, even editors have "bad hair" days.

Hi ... and welcome to Connexions, a pen pal column for those who would like to meet and connect with life long friends the "old-fashioned" way – via the post office.

If you would like to join Connexions, or have any questions, ideas or suggestions for the column, please write to: **Gail Petito, The NF2 Review, c/o The House Ear Institute, 2100 West Third Street, Second Floor, Los Angeles, CA, 90057.** You can also e-mail me at: **johnpetito@prodigy.net.**

If you'd like to be a pen pal, don't forget to include a little description of yourself along with your postal mailing address.

*We hope to hear from you soon!*

## Pen Pals

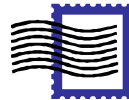


Hi! My name is Karina. I'm 30-something and I live in Colorado with my parents. I'm a little shy, but I enjoy going out, doing lots of things and just having fun. I love pets, traveling, and attending Gem Shows with my parents. I enjoy making new friends and would love to correspond with you!

You can also e-mail me at: **karinalee73@earthlink.net.**



**Karina L. Davis**  
2444 S. Laredo St.  
Aurora, CO 80013



**Felicity Lingo**  
68 Cottage Street  
Easthampton, MA 01027

Brian Johnson is divorced with two grown kids and "4 precious grandkids." If you would like to have a new friend in Brian, you may write him at:



**Brian Johnson**  
1010 S. Starr Avenue  
New Richmond, WI 84017-2341

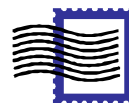
I am into computer programming, Jay Leno's head lines and general silliness. I love getting postcards from faraway places, and scanning them with my flatbed scanner. Need a laugh? I have several joke databases to draw from. They brighten your day, if nothing else. Have been pen paling forever.



**Keith Keller**  
304 4th Ave. W Apt. 2  
Grinnell, IA 50112



Marcus McCallum enjoys e-mailing his friends on the NF2 Crew, but he also appreciates the fine art of letter writing. Marcus lives in Runaway Bay, Australia, which is in the city of Gold Coast, in Queensland state. All of this is located on the east coast of OZ (nickname for Australia). If you'd like to drop Marcus a line and say 'G'Day', please write to:



**Marcus McCallum**  
56 Anchorage Way  
Runaway Bay 4216  
Gold Coast  
Queensland, Australia





## JOURNAL ARTICLES ABOUT NEUROFIBROMATOSIS TYPE 2

The following scientific articles on NF2 have been published since the last issue of the NF2 Review. The summaries and abstracts of most of these and other articles can be accessed through the web on PubMed at: <http://www.ncbi.nlm.nih.gov/PubMed>.

Source: *Oncogene*. 2004 Dec 06;  
[Epub ahead of print]

### Cell cycle-dependent nucleocytoplasmic shuttling of the neurofibromatosis 2 tumour suppressor merlin.

Authors: *Muranen T, Gronholm M, Renkema GH, Carpen O*

The neurofibromatosis 2 tumour suppressor merlin/schwannomin is structurally related to the ezrin-radixin-moesin family of proteins, which anchor actin cytoskeleton to specific membrane proteins and participate in cell signaling. Merlin inhibits cell growth with a yet unknown mechanism. As most tumour suppressors are linked to cell cycle control, we investigated merlin's behaviour during cell cycle. In glioma and osteosarcoma cells, endogenous merlin was targeted to the nucleus in a cell cycle-specific manner. Merlin accumulated perinuclearly at the G2/M phase, and shifted to the nucleus at early G1. During mitosis, merlin localized to mitotic spindles and at the contractile ring. Nuclear merlin was strongly reduced in confluent cells. Blocking of the CRM1/exportin nuclear export pathway led to accumulation of merlin in the nucleus. Activation of the p21-activated kinase or protein kinase A, which result in phosphorylation of merlin, did not affect its nuclear localization. Merlin regulates the activity of extracellular signal-regulated kinase 2 (ERK2) and nuclear localization of both proteins was induced by cell adhesion. Unlike ERK2, nuclear localization of merlin was not, however, dependent on intact actin cytoskeleton. These results link merlin to events related to cell cycle control and may help to resolve its tumour suppressor function. *Oncogene* advance online publication, 6 December 2004; doi:10.1038/sj.onc.1208283.

Source: *Am J Hum Genet*. 2004 Aug;75(2):231-9.  
Epub 2004 Jun 09.

### Genotype-phenotype correlations for nervous system tumors in neurofibromatosis 2: a population-based study.

Authors: *Baser ME, Kuramoto L, Joe H, Friedman JM, Wallace AJ, Gillespie JE, Ramsden RT, Evans DG*

Neurofibromatosis 2 (NF2) is an autosomal dominant disease that is characterized by tumors on the vestibular branch of the VIII cranial nerve, but other types of nervous system tumors usually occur as well. Genotype-phenotype

correlations are well documented for overall NF2 disease severity but have not been definitively evaluated for specific types of non-VIII nerve tumors. We evaluated genotype-phenotype correlations for various types of non-VIII nerve tumors in 406 patients from the population-based United Kingdom NF2 registry, using regression models with the additional covariates of current age and type of treatment center (specialty or nonspecialty). The models also permitted consideration of intrafamilial correlation. We found statistically significant genotype-phenotype correlations for intracranial meningiomas, spinal tumors, and peripheral nerve tumors. People with constitutional NF2 missense mutations, splice-site mutations, large deletions, or somatic mosaicism had significantly fewer tumors than did people with constitutional nonsense or frameshift NF2 mutations. In addition, there were significant intrafamilial correlations for intracranial meningiomas and spinal tumors, after adjustment for the type of constitutional NF2 mutation. The type of constitutional NF2 mutation is an important determinant of the number of NF2-associated intracranial meningiomas, spinal tumors, and peripheral nerve tumors.

Source: *Otol Neurotol*. 2004 Sep;25(5):811-7.

### Vestibular schwannoma growth rates in neurofibromatosis type 2 natural history consortium subjects.

Authors: *Slattery WH 3rd, Fisher LM, Iqbal Z, Oppenheimer M*

**OBJECTIVE:** To determine the amount of growth in vestibular schwannomas in Neurofibromatosis type 2 (NF2) patients from diagnosis through short-term (up to 2 yr) and long-term (up to 4 yr) follow-up.

**STUDY DESIGN:** Retrospective magnetic resonance imaging (MRI) films were obtained on subjects enrolled in the NF2 Natural History study and examined for changes in vestibular schwannoma size over time.

**SETTING:** Data were collected from nine foreign and domestic NF2 centers, including hospital-based, academic, and tertiary care centers.

**SUBJECTS:** NF2 patients with MRI data and at least one follow-up examination within 9 months to 2 years of diagnosis were included; n=56 patients with 84 lesions for evaluation of growth.

**INTERVENTION:** Routine, clinically obtained, magnetic resonance images were digitized and measured using image management software. Short-term follow-up was defined as up to 2 years (n=84 lesions), and long-term follow-up was defined as 3 to 4 years (n=29 lesions).

**OUTCOME MEASURES:** Vestibular schwannoma size was assessed using anterior-posterior, medial-lateral, and greatest diameter linear measurements.

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**RESULTS:** Vestibular schwannomas increased in size (at least 5 mm) in 8% of the vestibular schwannomas across short-term follow-up. At long-term follow-up, 13% of the tumors had increased in size. On average, schwannomas increased in greatest diameter 1.3 mm per year across short-term follow-up.

**CONCLUSION:** Slightly greater than 1 in 10 diagnosed NF2-related vestibular schwannomas increased in size by at least 5 mm by 4 years of follow-up, if still untreated at that time.

Source: *Cancer Res.* 2004 May 15;64(10):3718-24.

#### **Comparative pathology of nerve sheath tumors in mouse models and humans.**

Authors: *Stemmer-Rachamimov AO, Louis DN, Nielsen GP, Antonescu CR, Borowsky AD, Bronson RT, Burns DK, Cervera P, McLaughlin ME, Reifenberger G, Schmale MC, MacCollin M, Chao RC, Cichowski K, Kalamarides M, Messerli SM, McClatchey AI, Niwa-Kawakita M, Ratner N, Reilly KM, Zhu Y, Giovannini M*

Despite the progress made in our understanding of the biology of neurofibromatosis (NF), the long-term clinical outcome for affected patients has not changed significantly in the past decades, and both NF1 and NF2 are still associated with a significant morbidity and a decreased life span. A number of NF1 and NF2 murine models have been generated to aid in the study of NF tumor biology and in the development of targeted therapies for NF patients. A single, universal pathological classification of the lesions generated in these murine models is essential for the validation of the models, for their analysis and comparison with other models, and for their future effective use in preclinical treatment trials. For the formulation of a pathological classification of these lesions, the WHO classification of human tumors was used as a reference. However, it was not adopted for the classification of the GEM lesions because of some important differences between the human and murine lesions. A novel classification scheme for peripheral nerve sheath tumors in murine models was therefore devised.

Source: *Oncogene.* 2004 Nov 18;23(54):8815-25.

#### **Magicin, a novel cytoskeletal protein associates with the NF2 tumor suppressor merlin and Grb2.**

Authors: *Wiederhold T, Lee MF, James M, Neujahr R, Smith N, Murthy A, Hartwig J, Gusella JF, Ramesh V*

Neurofibromatosis 2 (NF2) is a dominantly inherited disorder characterized by bilateral vestibular schwannomas and meningiomas. Merlin, the neurofibroma-

tosis 2 tumor suppressor protein, is related to the ERM (ezrin, radixin, moesin) proteins and, like its family members, is thought to play a role in plasma membrane-cytoskeletal interactions. We report a novel protein as a merlin-specific binding partner that we have named magicin (merlin and Grb2 interacting cytoskeletal protein) and show that the two proteins interact in vitro and in vivo as well as colocalize beneath the plasma membrane. Magicin is a 24 kDa protein that is expressed in many cell lines and tissues. Magicin, similar to merlin, associates with the actin cytoskeleton as determined by cofractionation, immunofluorescence and electron microscopy. Analysis of the magicin sequence reveals binding motifs for the adaptor protein Grb2. Employing affinity binding, blot overlay and co-immunoprecipitation assays, we demonstrate an interaction between Grb2 and magicin. In addition, merlin is capable of forming a ternary complex with magicin and Grb2. These results support a role for merlin in receptor-mediated signaling at the cell surface, and may have implications in the regulation of cytoskeletal reorganization.

Source: *Oncogene.* 2004 Nov 4;23(52):8447-54.

#### **Serine 518 phosphorylation modulates merlin intramolecular association and binding to critical effectors important for NF2 growth suppression.**

Authors: *Rong R, Surace EI, Haipek CA, Gutmann DH, Ye K*

The neurofibromatosis 2 (NF2) tumor suppressor protein, merlin, functions as a negative growth regulator; however, the molecular mechanisms that underlie merlin regulation remain elusive. Recent studies have implicated merlin phosphorylation in regulating merlin subcellular localization and growth suppression. P21-activated kinase (PAK), a downstream target of Rac1/Cdc42, directly phosphorylates merlin at Serine 518. In this report, we show that PAK2 directly phosphorylates wild-type merlin, whereas merlin truncation mutants with impaired GST-amino-terminal domain (N-term or NTD)/GST-carboxy-terminal domain (C-term or CTD) intramolecular association exhibit impaired S518 phosphorylation. We directly demonstrate that PAK2 phosphorylation impairs merlin N-term/C-term binding in vitro and in vivo. Lastly, we show that PAK2 phosphorylation impairs the ability of merlin to bind to two interacting proteins, CD44 and hepatocyte growth factor-regulated tyrosine kinase substrate (HRS), both critical for merlin growth suppression. These observations suggest that merlin S518 phosphorylation directly modulates merlin intramolecular and intermolecular associations important for the ability of merlin to function as a tumor suppressor.

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*Journal articles ... from page 21*

Source: Otol Neurotol. 2004 Jul;25(4):587-93.

**Serial analysis of gene expression in neurofibromatosis type 2-associated vestibular schwannoma.**

**Authors:** Halum SL, Popper P, Cioffi JA, Wackym PA

**HYPOTHESIS:** The genesis, morphology, and growth characteristics of vestibular schwannomas are determined by genetic alterations which vary gene transcript expression and this transcript expression can be qualitatively and quantitatively evaluated using the SAGE technique. By use of such technique, gene products with tumorigenic potential may be identified, providing insight and targets for future study.

**BACKGROUND:** Serial analysis of gene expression (SAGE) is a powerful new technique that allows detailed qualitative and quantitative evaluation of cellular gene transcript expression. Tissue in limited quantity (5 x 10 to 2 x 10 cells) may be analyzed by a modified version of SAGE called microSAGE. Application of SAGE or microSAGE to study vestibular schwannoma gene expression has not been previously reported.

**METHODS:** Fresh, vestibular schwannoma specimen from an individual with the diagnosis of neurofibromatosis type 2 was attained intraoperatively and maintained in a sealed container at -80degreesC until the time of analysis. The tissue was processed according to the microSAGE protocol, using 180 mg of vestibular schwannoma as starting material.

**RESULTS:** The protocol resulted in the generation and sequencing of a tag library involving 458 tags representing 277 different gene products, including many transcripts known to be expressed in vestibular schwannomas. Several gene products with tumorigenic potential were identified.

**CONCLUSIONS:** These data demonstrate that microSAGE is a useful technique to study vestibular schwannoma gene expression. Future studies will include building more comprehensive libraries and comparing libraries from various vestibular schwannoma phenotypes to identify useful diagnostic or prognostic markers, and targets for therapeutic intervention.

Source: AJNR Am J Neuroradiol. 2004 Sep;25(8):1414-6.

**N-butylcyanoacrylate embolization of a middle meningeal artery aneurysm in a patient with neurofibromatosis type 2.**

**Authors:** Lesley WS, Thomas MR, Abdulrauf SI

**A**neurysms of the middle meningeal artery are rare, with no documented association with neurofibromatosis type 2 (NF2). Middle meningeal artery aneurysm embolization with N-butylcyanoacrylate has not been described, and altogether, few accounts exist regarding the endovascular management

of these unusual aneurysms. In this case report of a patient with NF2, an unruptured middle meningeal artery aneurysm was prophylactically embolized in a previously unreported fashion by using N-butylcyanoacrylate acrylic glue.

Source: Curr Opin Neurol. 2004 Dec;17(6):687-92.

**Meningioma: an update.**

**Authors:** Lusic E, Gutmann DH

**PURPOSE OF REVIEW:** Recent clinical and molecular research has shed new light on the biology of meningiomas - a common but understudied CNS neoplasm. This review will focus on recent advances and their significance for future research and treatment.

**RECENT FINDINGS:** Meningiomas represent the second most common brain tumor in adults, and while improved diagnostic modalities are available, these tumors remain underreported. Radiosurgery is an effective adjuvant therapy against meningioma; however, no effective chemotherapy exists. In addition to histologic grading and estimates of the extent of resection, biomarkers, such as progesterone receptor, cyclooxygenase 2, S100A5 and ornithine decarboxylase may be useful in predicting tumor recurrence and/or progression potential in patients with meningioma. On the genetic level, cytogenetic losses on chromosomes 1, 7, 10 and 14 and telomerase activation are observed in clinically aggressive meningioma, whereas monosomy 22 is a common early molecular event in tumor formation. Several candidate growth regulatory genes have been identified, including the Neurofibromatosis 2 (NF2), Tumor Suppressor in Lung Cancer-1 (TSLC1), Protein 4.1B, p53/MDM2 and S6-Kinase genes. The roles of these genes in meningioma formation and progression, as well as the clinical implications of these genetic changes, are discussed.

**SUMMARY:** The recent insights into the molecular biology and genetics of meningioma provide new avenues for basic science research aimed at understanding the mechanisms underlying meningioma formation and malignant progression. These advances may be useful in improving our ability to predict clinical outcome and developing targeted therapies to improve outcomes in patients with clinically aggressive meningiomas.

Source: Proc Natl Acad Sci U S A. 2004 Dec 14; [Epub ahead of print]

**Neurofibromatosis 2 (NF2) tumor suppressor merlin inhibits phosphatidylinositol 3-kinase through binding to PIKE-L.**

**Authors:** Rong R, Tang X, Gutmann DH, Ye K

**N**eurofibromatosis 2 (NF2) is a tumor suppressor, although the molecular mechanism accounting for this effect remains unknown. Here, we show that merlin exerts its activity by inhibiting phosphatidylinositol 3-kinase (PI3-kinase), through binding to PIKE-L. Wild-type merlin, but not

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patient-derived mutant (L64P), binds PIKE-L and inhibits PI3-kinase activity. This suppression of PI3-kinase activity results from merlin disrupting the binding of PIKE-L to PI3-kinase. In addition, merlin suppression of PI3-kinase activity as well as schwannoma cell growth is abrogated by a single PIKE-L point mutation (P187L) that cannot bind merlin but can still activate PI3-kinase. Knocking down PIKE-L with RNA interference abolishes merlin's tumor-suppressive activity. Our data support the hypothesis that PIKE-L is an important mediator of merlin growth suppression.

Source: *Laryngoscope*. 2004 Dec;114(12):2135-46.

**Auditory brainstem implantation in patients with neurofibromatosis type 2.**

Authors: *Kanowitz SJ, Shapiro WH, Golfinos JG, Cohen NL, Roland JT Jr.*

**OBJECTIVES:** Multichannel auditory brainstem implants (ABI) are currently indicated for patients with neurofibromatosis type II (NF2) and schwannomas involving the internal auditory canal (IAC) or cerebellopontine angle (CPA), regardless of hearing loss (HL). The implant is usually placed in the lateral recess of the fourth ventricle at the time of tumor resection to stimulate the cochlear nucleus. This study aims to review the surgical and audiologic outcomes in 18 patients implanted by our Skull Base Surgery Team from 1994 through 2003.

**STUDY DESIGN:** A retrospective chart review of 18 patients with ABIs.

**METHODS:** We evaluated demographic data including age at implantation, number of tumor resections before implantation, tumor size, surgical approach, and postoperative surgical complications. The ABI auditory results at 1 year were then evaluated for number of functioning electrodes and channels, hours per day of use, nonauditory side effect profile and hearing results. Audiologic data including Monosyllable, Spondee, Trochee test (MTS) Word and Stress scores, Northwestern University Children's Perception of Speech (NU-CHIPS), and auditory sensitivity are reported.

**RESULTS:** No surgical complications caused by ABI implantation were revealed. A probe for lateral recess and cochlear nucleus localization was helpful in several patients. A range of auditory performance is reported, and two patients had no auditory perceptions. Electrode paddle migration occurred in two patients. Patient education and encouragement is very important to obtain maximum benefit.

**CONCLUSIONS:** ABIs are safe, do not increase surgical morbidity, and allow most patients to experience improved communication as well as access to environmental sounds. Selecting proper stimulation patterns can minimize non-auditory side effects. The ABI continues to be an emerging field for hearing rehabilitation in patients who are deafened by NF2.

Source: *Cancer Res*. 2004 Apr 15;64(8):2717-24.

**Activation of the tumor suppressor merlin modulates its interaction with lipid rafts.**

Authors: *Stickney JT, Bacon WC, Rojas M, Ratner N, Ip W*

**N**eurofibromatosis type 2 (NF2) is a genetic disorder characterized by bilateral schwannomas of the eighth cranial nerve. The NF2 tumor suppressor protein, merlin, is related to the ERM (ezrin, radixin, and moesin) family of membrane/F-actin linkers. Merlin resists solubilization by the detergent Triton X-100 (TX-100), a property commonly attributed to association with the cytoskeleton. Accordingly, NF2 patient mutations that encode merlins with enhanced TX-100 solubility have been explained previously in terms of loss of cytoskeletal attachment. However, here we present data to suggest that the detergent resistance of merlin is a result of its constitutive residence in lipid rafts. Furthermore, when cells are grown to high density, merlin shifts to a more buoyant lipid raft fraction in a density gradient. This shift is mimicked in subconfluent cells treated with cytochalasin D, suggesting that the shift results from merlin dissociation from the actin cytoskeleton, but not from lipid rafts. Intramolecular NH(2)- and COOH-terminal binding, which occurs when merlin transitions to the growth-suppressive form, also brings about a similar change in buoyant density. Our results suggest that constitutive residence of merlin in lipid rafts is crucial for its function and that as merlin becomes growth suppressive *in vivo*, one significant molecular event may be the loss of interaction with the actin cytoskeleton. To our knowledge, merlin is the first tumor suppressor known to reside within lipid rafts, and the significance of this finding is underscored by known loss-of-function NF2 patient mutations that encode merlins with enhanced TX-100 solubility.

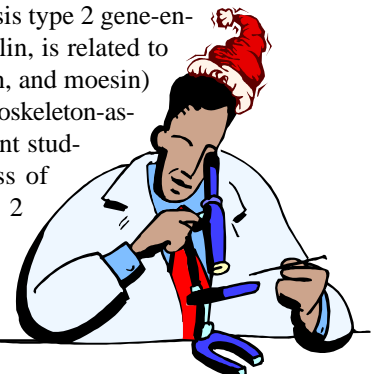
Source: *J Biol Chem*. 2004 Jul 16;279(29):30265-73.  
Epub 2004 Apr 27.

**Merlin, a tumor suppressor, interacts with transactivation-responsive RNA-binding protein and inhibits its oncogenic activity.**

Authors: *Lee JY, Kim H, Ryu CH, Kim JY, Choi BH, Lim Y, Huh PW, Kim YH, Lee KH, Jun TY, Rha HK, Kang JK, Choi CR*

**T**he neurofibromatosis type 2 gene-encoded protein, merlin, is related to the ERM (ezrin, radixin, and moesin) family of membrane-cytoskeleton-associated proteins. Recent studies suggest that the loss of neurofibromatosis type 2

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function contributes to tumor development and metastasis. Although the cellular functions of merlin as a tumor suppressor are relatively well characterized, the cellular mechanism whereby merlin controls cell proliferation from membrane locations is still poorly understood. During our efforts to find potential merlin modulators through protein-protein interactions, we identified transactivation-responsive RNA-binding protein (TRBP) as a merlin-binding protein in a yeast two-hybrid screen. The interaction between TRBP and merlin was confirmed by glutathione S-transferase pull-down assays, co-immunoprecipitation, and co-localization experiments. The carboxyl-terminal regions of each protein were responsible for their interaction. Cells overexpressing TRBP showed enhanced cell growth in cell proliferation assays and also exhibited transformed phenotypes, such as anchorage-independent cell growth and tumor development in mouse xenografts. Merlin efficiently inhibited these oncogenic activities of TRBP in our experiments. These results provide the first clue to the functional interaction between TRBP and merlin and suggest a novel mechanism for the tumor suppressor function of merlin both in vitro and in vivo.

*Some journal articles may be available to readers upon request. Please mail or FAX all requests to:*

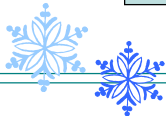
#### The NF2 Review

c/o The House Ear Institute  
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upon request.

### The NF2 Review OnLine!

**T**he NF2 community can now access the NF2 Review newsletter online courtesy of the **National Neurofibromatosis Foundation** Website at: [www.nf.org](http://www.nf.org), the **NF, Inc.** Website at: [www.nfinc.org](http://www.nfinc.org), and the **House Ear Institute** Website at: [www.hei.org/news/publications/publish.html](http://www.hei.org/news/publications/publish.html).



**F**or those who wish to, donations in memory of NF2 Review Founder John Petito may be made to the following memorial funds:


The **John Petito Memorial Fund** at the **House Ear Institute**, which supports the ongoing publication of The NF2 Review. Contributions may be sent to:

#### The John Petito Memorial Fund

c/o House Ear Institute  
2100 West Third Street  
Los Angeles, California 90057

Donations can also be made to the **John Petito Memorial Travel Fund** at **NF, Inc.**, where funds will allow people with NF2 to attend NF2 gatherings. Contributions may be sent to:

#### John Petito Memorial Travel Fund

c/o Neurofibromatosis, Inc.  
 9320 Annapolis Road, Suite 300  
Lanham, MD 20706-3123

Write To!Us!



**W**e'd like to know what you think. Let us know what topics you'd like to see discussed or tell us what you think of something that has appeared.

The NF2 Review is printed three times a year... well, we try to anyway (smile). If you would like to contribute ideas, items or a letter, here's how to contact us:

Gail Petito, Editor

E-mail: [johnpetito@prodigy.net](mailto:johnpetito@prodigy.net)

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*We welcome all opinions, suggestions and comments. If you write to The NF2 Review, please indicate if you do **not** want your letter published. The opinions expressed in The NF2 Review do not necessarily reflect the opinions of the Editor, or the House Ear Institute, and belong entirely to the individual(s) credited.*

Disclaimer:

The NF2 Review is a review of resources for living with Neurofibromatosis Type 2 (NF2), and does not constitute medical advice. Informed doctors must be consulted for the diagnosis, management and treatment of Neurofibromatosis Type 2.