Paul Nabil Bustany Fund
for synovial sarcoma research
www.pnbustanyfund.org

NEWSLETTER

Winter 2013

In this issue…

Giving Thanks

Dear Friends,

I'd like to give thanks to the many donors who have contributed to the Paul Nabil Bustany Fund for Synovial Sarcoma Research, both this year and during the previous six years. I am particularly grateful to you because I feel like a mother of a soldier who has lost her son in battle, except my son's battlefield was an incurable cancer. Paul Nabil fought heroically but was overcome and it is his fight that you have taken on. If our common effort and support continues, we may sooner see the day when this cancer is history, and the young people unfortunate to be struck with it, cured.

Your generosity has already translated into deeper understanding of synovial sarcoma through research carried out by teams of scientists both at Memorial Sloane Kettering and the University of Utah Medical School. In the last two years we have not been able to give grants to both teams and for this reason we asked Unnur S. Thorgeirsson, MD, who recently retired from the National Institute of Health and comes with over 30 years of experience in cancer research, to join us as an advisor and evaluate the proposals and publications of all of our prospective grantees. This year Dr. Thorgeirsson recommended the team at Huntsman Cancer Institute at The University of Utah under the leadership of Kevin B Jones, MD and Dr. Mario R. Capecchi, 2007 Nobel Laureate for Physiology and Medicine, based on their successful results gained by using the synovial sarcoma mouse model. In September 2012, The PNB Fund awarded them a grant of $50,000, and another grant of $40,000 in September 2013.

Last year, we told you that an "Achilles heel" had been found by Dr. Jones' team, where the cancer gene was vulnerable and several known drugs were potential candidates for clinical trials. As you will read in Dr. Jones' report, the scientists are now focusing on analyzing which of these drugs are most effective by testing them in human cell-lines and mice especially outfitted with synovial sarcoma. They are hopeful to start clinical trials within two years.

Also in this newsletter is an interview with Elodie Espesset. Elodie is a cancer survivor, a mother, and an active member of the Synovial Sarcoma Survivor's Network, which offers information and community to the hundreds of active members in the US and abroad.

I hope you will consider a generous donation this year to the Paul Nabil Bustany Memorial Fund for Synovial Sarcoma Research, Inc. so that we may continue to support the scientists working to find a cure.

On behalf of our Board members, I thank you.

Laufey Bustany

The Paul Nabil Bustany Fund for Synovial Sarcoma Research Board of Directors: Rami Badawy, Christine Bustany, Laufey Bustany, Samir Ted Bustany, Alex Kaplan, Asu Okyay, Alex Rafal, Anthony Rizzo, and Sabrina Tom

Research Update from Kevin B. Jones, MD, The Huntsman Cancer Institute at the University of Utah

The synovial sarcoma research team of the Huntsman Cancer Institute at the University of Utah continues to make strides toward a clearer understanding of the fundamental biology of this devastating cancer. Using our mouse model of genetically-initiated synovial sarcoma, we have identified a few molecular pathways that offer vulnerabilities we can target with available drugs. One new class of drugs blocks a cancer cell's ability to avoid apoptosis, or the program by which distressed cells destroy themselves. Another group of new drugs poisons beta-catenin, a protein critical to colon cancer and which we and others have shown is also important in synovial sarcoma. Finally, the synovial sarcoma research community is becoming increasingly convinced that this cancer is driven more by epigenetic changes than genetic changes in the cancer cells.

Many cancers develop by the accumulation of multiple genetic errors and mutations. Eventually, they progress by the loss of genetic stability, meaning they start to accumulate errors faster and faster. Synovial sarcoma is quite different, maintaining a very stable complement of genes in each cell with few errors. In many synovial sarcomas, we cannot find gene errors beyond that which produces the single driving fusion gene SS18-SSX. Instead of depending on the accumulation of many other gene mutations, synovial sarcoma reprograms the packaging and utilization of the normal genes. These broad changes in gene packaging and utilization are controlled by what we call epigenetics. We are beginning to test a variety of drugs that alter the epigenetic forces at play in synovial sarcoma. Currently trying to hone in on the best available combination of drugs in cell culture and in the mice, we hope to identify this regimen and move toward clinical trials in patients over the next 2 years. We have articles forthcoming regarding the mechanism of a new epigenetic drug class called histone deacetylase inhibitors, the impact of beta-catenin signaling in synovial sarcoma, and the importance of which SS18-SSX gene a specific synovial sarcoma expresses.

Our ongoing work this year supported by the Paul Nabil Bustany Fund for Synovial Sarcoma research focuses on a specific question: how valid are our cell-based synovial sarcoma models? Combination drug screens are generally done on cells in a culture dish due to the high-throughput efficiency of cell-based screens. However, we do not yet know how cells in a dish differ from cells in a tumor in a patient. Using a variety of new sequencing technologies, we are working to decipher the predictable discrepancies between cells in their native tumor environment and cells in a culture dish, whether mouse or human.

Elodie Espesset on Synovial Sarcoma and the Survivor's Life

Interview by Sabrina Tom

Originally from Toulouse, Elodie Espesset moved to America in 1998 to work in optoelectronics engineering. She was diagnosed with synovial sarcoma in 2003. The tumor was located behind her knee joint and her initial treatment included six rounds of chemotherapy and amputation above the knee. She was 31 years old and had just given birth to her son. Ten years on, Elodie continues to fight the disease while offering support for others in the online community Synovial Sarcoma Survivors' Network. I had a chance to speak with her the day after Thanksgiving about family, life, and her thoughts on being a synovial sarcoma survivor.

How was your Thanksgiving?
We were invited to a small party with friends.

Do you have a lot of family here?
Just my husband and my son.

What's your son's name?
Alandis.

That's not a French name.
No, it's not. My husband is Russian and he liked some Russian names, but I didn't like them, and he didn't like the French names I liked. We decided to go to neutral territory so we looked at American names. My husband is a database programmer so he had access to a database of names. He printed all the first names and we went through them. We stopped at the first name we agreed on. And obviously Alandis starts with an A so it was a relief.

Do you want more children?
Maybe I had a window of opportunity between my amputation and when my disease came back, and I tried at that time, but it didn't work. And now it's too late, I think.

How many treatments have you had?
Many. When I was diagnosed I had six cycles of chemotherapy and they did an amputation of my leg above my knee. They told me that the tumor was too close to the artery and the main nerve so that's why they thought it was better to amputate. Well the disease came back three and a half years later in my lungs. It was probably already there when they amputated only I didn't know. When it came back I did more chemo, I did more radiation. I had lung surgery. That was in 2008. Since then I've had a total of six lung surgeries. It's becoming a chronic disease.

When was your last surgery?
Last summer.

How are you feeling now?
Now I feel good. It's good to be in remission every time. Even if you have all these treatments, if you have some months when you don't have treatments it's nice.

Tell me about the Synovial Sarcoma Survivors' Network.
It's a community. It's a place where you can meet other people with the same disease. You can start discussions. You can blog. You can share information about yourself. It's empowering.

You're very active on the site. You're always wishing people happy birthday and asking about their families.
Well I'm trying to find out what's going on with them. I think it's very useful to know what happens to other people. I cannot foresee my future. At one point I may have to make some decisions about my health and to know what's happened to other people can help me make those decisions.

You're also an advocate for seeing a synovial sarcoma specialist.
I think it's important. It's a rare disease and if you don't take care of it right away the right way, that can make a big difference.

Is this coming from personal experience?
Yes, and from stories I've heard from other people. Some people regret not having been more aggressive with the disease at the beginning stage and then the disease comes back and they feel they didn't do everything right. I don't want people to regret anything. I think they should see someone who is familiar with the disease, not someone who's only seen one case.

What's your relationship to this online community?
I feel a lot of empathy for people because I'm going through the same thing so I feel close in that way.

That says a lot about your spirit.
I don't know how to express it. When I talk about my disease to my friends—my real friends that I see everyday—I don't feel comfortable. I feel they feel sorry for me. But for these people who have this same disease I feel more free to talk about it.

You have a common language.
Yes, exactly.

What's been your experience with the healthcare system?
Pretty awful. In France it's government-run health care. Everything is virtually free. You never have to worry about it. When I was diagnosed here I had to worry about it. For example, where they sent me first for my biopsy, the hospital was not covered by my insurance. So I tried to find a different surgeon who would be covered by my insurance and I wasn't able to do so. My insurance wasn't

covering any sarcoma surgeons that I could find on the internet. I asked my doctor to refer me to a sarcoma surgeon and the only one he knew was at the Newark hospital and that hospital wasn't covered by my insurance. So I asked more surgeons, "Do you know any other guys?," and they didn't want to tell me any other names.

So what did you do?
I did the biopsy with the surgeon and then once I got the diagnosis I decided to get a different opinion from an oncologist who was not in my insurance, either. But I was very impressed with him and his hospital was covered so I decided to go with him. I did have to pay out of my pocket his fees. I was lucky in the sense that my work had short-term insurance so even though I wasn't working during the treatments I was receiving 60% of my salary. So that helped me pay for it. Without that it would've been difficult because my husband and I had just bought a house, just had a baby, so maybe it was the worse time really.

You must have compared notes about your experience with members living abroad.
I met a patient who had synovial sarcoma in France and he had a little bit different treatment than I did. But I know it was kind of great for him. For example he could go to the hospital in a taxi and the government pays for it. He lived in the countryside and they were taking him to Paris. So that was pretty nice.

Have you been satisfied with the care you've been given?
I'm still alive so I cannot complain. I mean, my friend in France, he passed away. But if he had been here, would he be alive? Probably not. A lot of people die here, too.

What would you say to our community about living with this disease?
I do hope they find a cure quickly. We really need some new treatment. It can get depressing when I look at all the people I've met that have passed away. And people are young. Sometimes they have young kids. It's really sad.

There are so many cancers and this doesn't seem to be one that gets attention.
When something is rare, it's not interesting for the big pharmaceuticals. How do you get the funding to go forward with the research, all the clinical trials and everything?

It's important to keep being an advocate and show that there are a lot of people fighting this disease. Real people.
There it is.

Visit the Synovial Sarcoma Survivors' Network at www.synovialsarcomasurvivorsnetwork.com.

Upcoming Events

We are currently planning a benefit event for early 2014. Stay tuned for more details.

How to Donate

Option 1: Write a check to *The Paul Nabil Bustany Fund for Synovial Sarcoma Research*. Send your check to: 15 Footes Lane, Morristown, NJ, 07960.

Option 2: Donate online at **www.pnbustanyfund.org**.

The PNB Fund is a 501(c)(3) nonprofit organization. All donations are tax deductible.

The purpose of the Paul Nabil Bustany Fund for Synovial Sarcoma Research is to raise money for basic scientific research on synovial sarcoma. The PNB Fund is entirely run by volunteers and all donations go directly to synovial sarcoma research. Thank you for your support.