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

NEWSLETTER
Winter 2014

In this issue…

Dear Friends,

Seven years ago, when the Paul Nabil Bustany Memorial Fund for Synovial Sarcoma Research was started, there were, as far as we knew, only two US institutions focusing specifically on synovial sarcoma. This year, basic research is going on in at least six US institutions: Dana Farber Institute, Harvard University; Huntsman Cancer Institute, University of Utah; Memorial Sloan Kettering Cancer Center, which is now working in collaboration with synovial sarcoma specialists in Canada and Holland; National Cancer Institute, Bethesda, MD; Vanderbilt University; and Washington University in St. Louis. This is fantastic news. Recent publications indicate several new possible routes toward drug targets, which will now be tested by teams of scientists around the country and elsewhere. Although this development is encouraging, we still have to be patient until a cure is found and continue our support of this vital research. This is particularly important for the many young survivors of this disease like our Peruvian friend, Alejandra Camacho, whom we interviewed for this issue and is among the thousands of young people waiting for a cure.

In 2014 the PNB Fund awarded a grant of $40,000 to Kevin B. Jones M.D., and his team at the Huntsman Cancer Institute, University of Utah. Joining Dr. Jones as co-investigators are Dr. Mario R. Cappecchi, 2007 Nobel Laureate for Medicine and Biology, Howard Hughes Medical Institute, University of Utah School of Medicine, and Dr. Jared J. Barrott, who rejoined the team this summer after receiving his Doctorate in Pharmacology and Cancer Biology from Duke University, researching cancer drug targets. The focus of their research this year is on understanding the epigenetic regulation of SS-18-SSX in synovial sarcomagenesis.

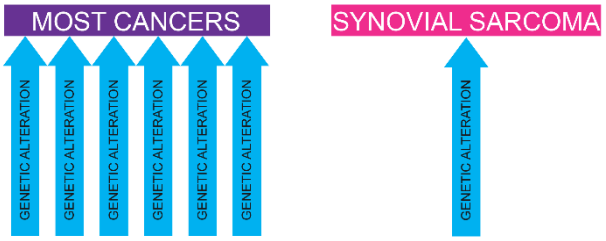
On behalf of the Board of Directors, I appreciate all the wonderful people who have made donations to this effort, in some cases, over many years. All of our work is done by volunteers and I want to acknowledge the important services provided by our Board Members as well as our Research Proposal Advisor Unnur Stefansdottir, M.D. We are indebted to these individuals, without whom, we would not be able to donate a substantial Research Grant annually.

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

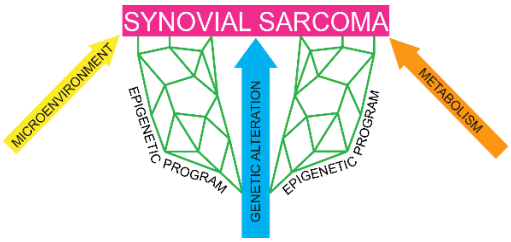
RESEARCH UPDATE FROM KEVIN B. JONES, M.D.
THE HUNTSMAN CANCER INSTITUTE, UNIVERSITY OF UTAH

Synovial sarcoma remains a devastating cancer. Although somewhat rare in the population, it too often strikes young people in the prime of life. What is perhaps most troubling about synovial sarcoma to those of us who study the biology of cancer is that synovial sarcoma *ought* to be more treatable. Synovial sarcoma tends to lack many of the genetic complexities that make other cancers so difficult to treat. Somehow, synovial sarcoma manages to program all of the complexities of cancer biology from a single genetic alteration in the cancer cell, a translocation.



The difficulty with most cancers is easy to appreciate. One cannot easily topple a structure by only attacking any one of many supporting pillars. From the sequencing work we have done, we know that synovial sarcomas do not have these redundant, supportive pillars of many genetic alterations. The tumor's unique dependence on a single pillar should render it easier to unbalance and destroy. Nonetheless, we remain entirely bereft of any ultimately effective treatments, other than surgery for early stage cases.

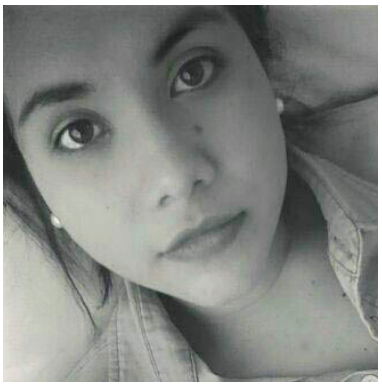
The Paul Nabil Bustany Memorial Fund for Synovial Sarcoma Research has supported our laboratory's efforts to understand better than we did before how synovial sarcoma maintains what should be a precarious balance. The cancer depends heavily on its environment, on altered metabolism, and on a complex network of what we call epigenetic factors. We are just beginning to understand how the cancer cell's environment impacts its characteristics. That environment is comprised of other nearby cells, the characteristics of the matrix, or proteins in which cells are embedded, and the availability of nutrients and oxygen. Alterations in cell metabolism, from the way that cancer cells break down sugars for energy to the way that they generate the building blocks they use for growth, are other powerful struts that prop-up the cancer. All these environmental and metabolic factors both impact and are heavily impacted by the epigenetic state of the synovial sarcoma cell. The epigenetic state is primarily defined in any cell by the way its DNA genetic code is packaged. Alterations in the packaging of individual genes make those genes either more or less available to be turned on.



The machinery that maintains this state is highly complex. The single genetic alteration of the synovial sarcoma translocation orchestrates the repurposing of normal epigenetic machinery to reprogram the cell into a cancer. Our current efforts focus on characterizing and targeting these epigenetic support struts. Such approaches have offered very favorable results for some other cancers. We anticipate that synovial sarcoma, which is almost entirely driven by these epigenetic mechanisms, may be the perfect match to this kind of approach.

"THERE'S NO CULTURE OF AWARENESS"

Interview by Sabrina Tom



Maria Alejandra Camacho, a college student at the Universidad de Lima in Peru, is a busy young woman. For four years, she saw one doctor after another to find out what was causing the pain and lump in her back. Finally, at the age of nineteen, she was diagnosed with synovial sarcoma. We recently spoke about the time she spends at the Instituto Nacional de Enfermedades Neoplásicas, where she is currently one of two synovial sarcoma patients, her future, and her thoughts on *The Fault in Our Stars*, the popular book and movie about teenagers living with cancer.

You were misdiagnosed for four years.

I had horrible pain in my back and whenever I moved my right arm. I went to several doctors about my pain but they told me it was scoliosis or things like that. There was also this huge lump on my back, but when I asked them about it, they always said, "Don't worry," "You can go swimming," "It's nothing bad." My parents didn't believe me, either. They thought I was making it up to not go to school. So I insisted. I told them I'm going to pay for all the exams they want to do to me, just please let me go to another

doctor. I finally got a scan and the doctor told me it was a malignant tumor. Of course my parents were really worried and, knowing my dad's family history, they took me to a cancer hospital. When I told the doctor there that I had this huge lump for about four years, he looked at me like I was in pretty bad condition and asked me to have a biopsy done that same day. Two weeks later I was diagnosed with synovial sarcoma. I didn't take it badly. I was relieved I at least knew what it was and was going to get treatment for it.

What was your treatment?

The initial plan was six rounds of chemo—Dexorrubicina and Ifosfamide—but two rounds in they noticed it wasn't working so they changed my treatment to five rounds of Docetaxel and Gemzar and added 33 sessions of radiation. That didn't work either. They sent me to surgery and removed two-thirds of my right scapula as well as a nerve and a muscle that had been compromised by the tumor. After four rounds of surgery I came out clean and then I finished four rounds of chemo.

Are you on any treatment now?

Radiation left me with pulmonary fibrosis. I take pills for my respiratory issues. I'm on pain meds for my back pain. I also have seromas—six in the past year.

How has all this affected your life?

I had such a hard time going back to school. I felt weak. I felt my friends and teachers treated me differently. As far as my family, they can support me, which is probably not a bad thing, but they're very protective of me now. They're scared every time I get a cold.

You've also sought psychological help.

I still see my shrink. I started in July 2013 because I had a breakdown. When I was in treatment, I felt like I had to be strong for my family and friends. I kept this image of "good Alejandra." One day I went to see my doctor, but he wasn't there, so I saw another doctor who told me that I was okay. You can come back in six months, he said. Everything's fine. No scans. Nothing. And I was like, what? What about the pain in my back? Tell me *something*. So I went home and started crying my eyes out. My mom said, you have to get psychological help. At first I didn't want to go. Then I knew it would help me. Cancer is traumatic. You go through so many things that you have to let them out somehow.

You mentioned your father's family has a history of cancer.

Almost everyone, but no synovial sarcomas. I'm the first.

How many cases of synovial sarcoma have been diagnosed in Peru?

I don't know. It's pretty rare here. As of now there's two of us [at the hospital]. He's a year older than me. We stick together. I knew a girl who had synovial sarcoma, but she passed away. I had never heard of synovial sarcoma prior to my diagnosis.

What are your future plans?

One of my fears with chemo was that I wouldn't be able to have kids. That was one of the first things I asked my doctor, but he told me not to worry about it, that I'm going to lead a perfectly normal life after treatment. I also see myself working at hospitals and helping others.

Have you seen *The Fault in Our Stars*?

I want to see it! I have the book, too. I think it portrays real teenagers battling cancer. It's not always tears and pain. We laugh, too. Then again, besides showing the happy and funny sides, it also shows the bad side, you know? [When you're in treatment] they tell you things like, you're brave, this is something heroic, etc., but what's heroic about cancer? Sometimes, you don't need people telling you

you're going to be okay. Sometimes, all you need is someone to understand the difficulty of battling this disease and your bad days.

Another connection I feel is with Hazel. She has sarcoma, too, and we had the same way of dealing with our cancer. We both worried about what would happen to our loved ones if we died, so we closed off our feelings. I also see my doctor as my Augustus, not in a romantic way, of course, but he was the one who gave me hope. When they told me that my treatment wasn't working, I really thought I was going to die. It was a really dark time for me. My doctor was the one who was there when I needed reassurance that I was going to make it. I just feel so lucky to have formed such a special relationship with him. I see him as my friend and wish every patient could experience that.

What more do you want to say about what you've gone through and what you hope will happen in the future?

To my fellow cancer patients, I'd say you have to learn to live with the possibility of cancer coming back. The fear is always going to be there, but you have to enjoy your life. Don't let it ever stop you. Also, even though most people battling cancer are sick of hearing this, it does get better so, please, don't give up.

And to whoever is reading this, please donate so it can get better for us faster. I think the rare diseases like sarcoma deserve attention, too, if not more so than common diseases because there's no culture of awareness. What if I hadn't been constant about going to the doctor those four years when I was misdiagnosed? I probably wouldn't be here right now. My mom thinks I'm obsessed with going to the doctor, but it's not like that. It's my constant fear of being misdiagnosed again. I'm still learning to deal with it. It's not an easy thing to do. It takes time, but I'm getting there.

INTERVIEW HAS BEEN CONDENSED AND EDITED.

UPCOMING EVENTS

We welcome your suggestions and assistance for our next event. Contact us at: pnbfund@gmail.com

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.