

**NEWSLETTER**  
*Winter 2015*

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Dear Friends,

Next August marks ten years since Paul Nabil died and we're devoting this issue of the PNB Fund Newsletter to all our donors who have made contributions to synovial sarcoma research over the past decade. Your steadfast focus and encouraging support of the scientists working in this field have resulted in important advancements in our understanding of the disease and its behavior. The publication of a number of scientific articles on synovial sarcoma, which acknowledge your support, bear this witness. Knowing the agony of having a child with this incurable cancer, we welcome the progress made towards improving treatment and finding a cure. We hoped it would take less than ten years to solve the riddle, but as we inch forward, we are deeply grateful for your enduring loyalty.

At the time of Paul Nabil's death, there were no private foundations raising money for synovial sarcoma and as we searched medical institutions throughout the country over twelve years for information and asked about basic research, we were told time and again that it was such a rare disease that little to nothing was being done. And yet, Marc Ladanyi, M.D. at Memorial Sloane Kettering Cancer Center had spent years doing research and succeeded in identifying the mutation involved in synovial sarcoma, which we only found out the year Paul Nabil died.

In response to the paucity of information on this disease, the Bustany family and close friends of Paul Nabil started The Paul Nabil Bustany Memorial Fund to raise money for basic research on synovial sarcoma. Since our inception in November 2007, we've raised close to half a million dollars and awarded annual research grants to dedicated synovial sarcoma research teams at MSKCC and the University of Utah.

As we have for the past six years, this year's grant was again awarded to Kevin B. Jones and his team at the Huntsman Cancer Institute at the University of Utah School of Medicine. You can read Dr. Jones' ten-year perspective of the evolving progress of treating patients with synovial sarcoma and an update on the research later in this issue.

Also in this issue is an interview with Dr. Marshall Rafal, who participated in our first fundraising event in Reykjavik and, along with his wife Jane, remains a close friend and supporter of the PNB Fund.

Marshall is one among many. On behalf of the Board, we appreciate all the wonderful people who have made donations to this effort. Additionally, all of our work is done by volunteers and we'd like to acknowledge the important services provided by our Board Members as well as our Research Proposal Advisor Unnur Thorgeirsson, M.D. We are indebted to these individuals without whom we would not be able to donate a substantial research grant annually.

With deepest appreciation,  
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*

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**DONOR SPOTLIGHT: DR. MARSHALL RAFAL**

*Interview by Sabrina Tom*

Marshall Rafal, CEO of OLI Systems and a father of seven, recently joined me on a trip down memory lane to talk about his legendary race walk at the Reykjavik Marathon, as well as his philanthropic interests, his son Alex, and Yankee fever.

**Tell me a little about your history with the PNB Fund.**

I met Nabil when he was three. Alex was two. So I qualify as going way back.

**You were 63-years-old when you participated in our first fundraising event in Iceland. How did you decide to walk the Reykjavik Marathon?**

Anyone who knew me from the time I was 42—I'm 72 now—knows that I was just an addicted runner. I ran too much, usually 6 days a week. And eventually, by the time of Iceland, my knees were so compromised that I could no longer run. But one of my daughters-in-law was a race walker and she got me into that.

**Do you remember your time?**

I think their rule was that they would shut down the finish line and stop giving out medals at 6 hours 30 minutes. All I know is I averaged 15 minutes a mile, so slightly under 6 hours 30 minutes.

**What was going through your mind during those twenty-six miles?**

The first part of the race, I was walking with my son, Alex. We walked together for about eight miles. And then it's much different when you're walking. You don't hit a wall. Either you enjoy the surroundings or you talk to somebody. Most of the time I found somebody who was also race walking who I could converse with. I do recall one funny moment. You know, walkers start earlier, but at some point all the runners pass you. In this case, this guy and I, we couldn't see anybody in front of us or behind us, and not any of the people who were guiding the runners, telling them which way to turn. And there were a couple of places near the end where we just had to guess which way to go and we would've missed that magic time and the medal had we not made the right choices.

**“By focusing on this one rare cancer we’re managing with a relatively small number of people to make substantive, meaningful progress.”**

**Did you talk about Nabil and why you were there?**

I'm sure I did. I took his loss very hard. He was the dearest child. He was just a sweet, sweet guy. I remember, towards the end, he got some really bad news from a doctor and it turned out that that night Alex had gotten tickets for them to see the Yankees who were playing the Red Sox in the seventh and deciding game of the 2003 Playoffs. They were both fanatic Yankees fans. This was the game in which they were losing late in the seventh inning and it looked hopeless and then they managed to score three runs against Pedro Martinez in the eighth inning to tie the game. And eventually, in the bottom of the eleventh, a guy named Aaron Boone hit a famous homerun that not only won the game, but the series, and the Yanks moved on to the World Series.

That game was such a tonic for Nabil. It's the quintessential example of how certain entertainments, like a sport, can just take us away. It's like a magic carpet from something even as profound as the bad news he received.

**About 1 to 3 individuals out of a million are diagnosed with synovial sarcoma each year. It's a rare cancer that gets very little research funding. What would you say to someone wanting to making a difference in cancer research? Why synovial sarcoma?**

The obvious reason that I'm supporting this rare cancer, which I probably would never have heard of if it wasn't because of Nabil, is Nabil and the person he was. That said, I see a bit of an analogy between our involvement with the Fund and our involvement with the San Diego Safari Park. There was a small entity in the park called the Animal Care Center. This is where they brought animals that were rejected by their mothers in the field and would have died if not for the intervention and care of the Animal Care Center. But it was kind of an orphan thing and they didn't get project funding, even though a lot of people donate to the zoo, getting millions of dollars to create a new tiger exhibit, for example. What we found was we could bite off a modest-sized project and fund it and see the results. So what I would say to someone is, yes, synovial sarcoma is a rare cancer, but by focusing on this one rare cancer we're managing with a relatively small number of people to make substantive, meaningful progress. It's different than sending your money to the Cancer Society. It's a worthy cause, but you won't see directly the result of your investment. It can be very meaningful when you're part of small group and you feel you can make a difference in the area of something as large as cancer.

*Interview has been condensed and edited.*

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**A TEN-YEAR PERSPECTIVE ON SYNOVIAL SARCOMA RESEARCH: DEVELOPING MOLECULAR TESTS, GENETIC MODELS, AND THE FIRST CLINICAL TRIAL**

*By Kevin B. Jones, M.D.*

On the tenth anniversary of Paul Nabil Bustany's death, it is fitting to take a moment to reflect where synovial sarcoma treatments were a decade ago, how they have changed, and how current research will likely change them more in the near future. Synovial sarcoma is not only unique among sarcomas for its predilection for adolescent and young adult victims, but also for its association with a very specific molecular signature.

This molecular signature, the creation of a singular, but powerful change in the cancer cells from the genetic code they otherwise share with the rest of the cells in the body, has been known about for nearly 20 years. Nonetheless, in the last ten years, it has become the standard practice throughout the community of physicians specializing in the care of sarcomas to use molecular tests to diagnose this particular cancer type. That may sound like a very technical (and perhaps not all that helpful) advance, but it is very important from the standpoint of personalized medicine. While personalized medicine is certainly a buzzword right now in the media, what it really means is that physicians must make as specific a diagnosis as possible, then let that specific diagnosis guide treatment.

The world of sarcoma-focused physicians has been slower to provide synovial-specific treatments, but the first synovial sarcoma specific clinical trial is scheduled to open soon in Canada, led by the University of British Columbia, based on research into the unique character (and vulnerabilities) of synovial sarcoma cells. The study will test the impact of a combination treatment with two drugs, quisinostat and bortezomib. Quisinostat inhibits one of the enzymes that works with the signature synovial sarcoma protein to change the expression of other genes. Quisinostat also causes the cell to degrade the synovial sarcoma protein itself. Bortezomib changes the way that proteins are processed in a cell. Both of these treatments have been tested alone and in combination in synovial sarcoma cells growing in a culture dish as well as in the mouse genetic models of synovial sarcoma that the Paul Nabil Bustany Memorial Fund has helped to develop. This trial has been a long time in coming, but it depends on the widespread ability to make the specific diagnosis, which had to be adapted by treatment centers first.

Basic research, funded by the Paul Nabil Bustany Memorial Fund, has proven that this singular genetic change in cells is not only useful for diagnosis, but also drives the entire cancer program in those cells.

Unlike almost all other cancers, synovial sarcoma cells require no other mutations or genetic changes to become a cancer. While we have not been successful in targeting that genetic change itself in our treatment strategies, our understanding of how that one change drives the cells to become a cancer is growing every year. As we identify the cellular machinery that this one change uses to effect all the other cancer programs in the cell, we will doubtless identify new, and hopefully more effective, targets for therapy. Critical to that effort has been the development of genetic models of synovial sarcoma in the mouse. These have allowed us to test not only the critical role of each type (1 and 2) of the signature synovial sarcoma protein, but also the other participants in its function, such as the enzyme that quisinostat inhibits. Current work underway will allow us to round up all the suspicious partnering proteins and even localize the protein complexes they form to their functional targets on other genes.

*Dr. Jones is an orthopedic surgeon at the University of Utah School of Medicine and a lead investigator, along with Dr. Mario R. Capecchi and Dr. Jared J. Barrott, for synovial sarcoma research.*

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### OCTOBER 2016 HOME RUN FUNDRAISER

Our Tenth Anniversary Fundraising Event will be held next October in Morristown, New Jersey. Participants are invited to join in Morristown's annual Halloween half marathon or 3-mile run around town, followed by a party for families and friends of all ages.

Many of you came with us to Iceland in 2007 to run in the Reykjavik Marathon, in Istanbul in 2010 to run across the Bosphorus, and in New York on numerous occasions to run in Central Park. We hope you will join us next October in Morristown for our "Home Run" Fundraiser.

Details will be announced later.

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### NEW PUBLICATION

Jared J. Barrott, Benjamin E. Illum, Huifeng Jin, Ju-Fen Zhu, Tim Mosbrugger, Michael J. Monument, Kyllie Smith-Fry, Matthew G. Cable, Yanliang Wang, Allie H. Grossmann, Mario R. Capecchi, Kevin B. Jones, "β-catenin stabilization enhances SS18-SSX2-driven synovial sarcomagenesis and blocks the mesenchymal to epithelial transition." *Oncotarget*, Vol. 6, No.26 (June 08, 2015).

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### 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](http://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.**