

# In Conversation:

## Clinical Fellow Jack Shern, M.D.

(Photo: B. Branson)



Jack Shern, M.D.

**CCR:** Pediatric oncology is a challenging field. How did you choose to work with kids?

**Jack:** I knew very early that I was interested in pediatrics. We have a pretty good cure rate, which means we can make a huge difference. If you save an infant, they have their whole life ahead of them. Plus, pediatrics is a fun specialty. It's amazing to see, even when they are sick, kids can keep smiling, laughing, and having fun.

**CCR:** You have a joint fellowship between NCI and Johns Hopkins. Tell us about it.

**Jack:** First, there was a very intense clinical service year of seeing patients all the time, half at Hopkins, half at NCI. For research, I knew pretty early that I wanted to be at

NCI. I met my wife when I came here as a summer research fellow, and we both knew we wanted to come back. So I started looking around the Pediatric Oncology Branch for a research opportunity. And Javed was the best salesman.

**CCR:** That's Javed Khan, Deputy Chief of our Genetics Branch and an Investigator in our Pediatric Oncology Branch. Humor aside, what interested you in his work?

**Jack:** I saw high-throughput genomics as the best way to characterize these tumors. We can survey the entire picture of what these tumors do with a couple of experiments. When I joined in 2011, his laboratory was already actively sequencing about 140 rhabdomyosarcomas and Javed suggested I lead that project. I had no experience in genomics, but it was a good place to learn. There is so much expertise in the Branch; for a novice, it is reassuring to have the world's experts mentoring you.

**CCR:** What was the biggest challenge to the project?

**Jack:** The biggest challenge was collecting enough tumors, then pooling all the data and figuring what story all this information was trying to tell us. Tumors are heterogeneous and the sequencing data can be very hard to interpret. You have to come up with statistical tools to carefully balance the false positives and negatives. It is even more challenging in a rare tumor where you have low sample numbers and recurrent mutations are infrequent.

**CCR:** What surprised you most about the results?

**Jack:** How simple, yet deadly, some of the tumors are. There was a one-year old with only two genomic alterations, one of which generated the fusion oncogene, *PAX3-FOXO1*. Of course, that change affects hundreds of genes downstream. In another big project, we are building some cell lines that can be screened by groups at the National Center for Advancing Translational Sciences (NCATS) and the RNAi core facility to help us figure out what the fusion gene is doing, who it is interacting with and ultimately, to develop novel therapies.

**CCR:** What advice would you give to your colleagues?

**Jack:** This project had so many moving parts and collaborators that it took a lot of persistence to get it to where it is today. There are lots of times in science when you get disappointed. To succeed, you need persistence.

**CCR:** Where do you see your future career?

**Jack:** I still love to see patients, but I would one day like to head my own lab. The NIH is a remarkable community where this type of "big science" can be done. It's hard not to aspire to be a principal investigator in this exhilarating environment. For me, that means I'll try to stay here and use genomics to translate our findings into new treatments for children who currently have incurable cancer.