PEOPLE IN OUR NEIGHBORHOOD

Dr. Maria Nedwidek: *In pursuit of the cancer pathway*

by Jenny Attiyeh

It was the culmination of many long days in the lab, days of routine, of patience, of consistently applied technique. The days had bled into the nights, adding up to the length of a Boston winter. Tail-bone ache and eye strain were the marks of the trade.

Then one morning in early March, the computer spit out a long line of letters, and Pinckney Street's Dr. Maria Nedwidek read in them a meaning. She had shown that a particular protein related to cell death had interacted with a lung cancer protein known to be involved in tumor suppression.

This interaction is as it should be in a healthy human being. But if either protein has a single point mutation, or a genetic abnormality, it could malfunction, leading to unchecked cell proliferation — and eventually, to cancer.

"The key to understanding the abnormal function is to understand the normal function," Dr. Nedwidek explained in the Signal Transduction Lab at Massachusetts General Hospital, where she is a post doctoral research fellow. "What it means is that we have a piece of the pathway that's involved in determining the fates of cells in the progression of a cancer." Nedwidek, along with 11 other researchers, works under the supervision of Dr. Joe Avruch, her advisor. Their goal is to study the biochemical mechanisms of cell proliferation and cell death.

So far, Nedwidek seems to be ahead of the game. "This interaction is concrete," she said, referring to the bonding of her two proteins. "It's new. It's now in the process of being published." Curiously, this interaction was not initially uncovered by Nedwidek, but by a member of the research team who had quit the lab. His test tube filled with mysterious cells, however, remained behind him, untouched.

This Nedwidek inherited and she subjected it to scientific rigor, exploring the significance of what he had left — that these two proteins had an affinity for each other. "I opened the box. It was there, in the freezer, and I just grabbed it and started to do stuff with it," she explained. "I took it and sequenced it, and found out what it was."

What she had glimpsed was a link in the chain reaction that can lead to cancer. Now she is in search of more of its constituent parts, more links in the chain. "What we do doesn't cure the diseases directly, but it unravels the mechanisms of the diseases so they can be tackled," she explained. "It's like fixing a car. You can't fix a car if you don't know how the parts fit together! If you don't understand it, you can't fix it."

Nedwidek, 30, moved to Beacon Hill in September of 1999 to begin a research fellowship at Harvard University, which is a partner with Mass General. She is intense, complex and precise, with a high, girlish voice that belies her forthright manner. Although she is a spiritual person, who was baptized Greek Orthodox and at times wears a Byzantine cross around her neck, she is also an ardent Darwinian. "Charles Darwin is one of my idols," she explained. "When I was about ten, my dad made me watch a PBS program about his voyage on the Beagle and I was totally mesmerized," she said. "Darwin wasn't an anti-creationist, he was trying to explain how we got here. I don't really know why it happened either."

The quest for knowledge appealed to her. Spurred on by supportive, involved parents and a first rate education at Stuyvesant High School in Manhattan, MIT and then Princeton, where she earned a Ph.D. in molecular biology, Nedwidek immersed herself in the study of the human organism.

"My parents always encouraged me to work as hard as I possibly could because, they said, it gives you power. Not that I'm power hungry," she explained, "but it gives you control. If you get an education you're open to insights that other people are not aware of."

Dr. Maria Nedwidek.

Nedwidek realizes that her work is important, but she also knows that science is a process, that there are steps to be taken one at a time. "First, verify" could be her motto. So she does her part, and she does it painstakingly. She knows this enables others to do theirs. Like the interactions of the molecules she studies, a career in science is driven in part by a chain reaction, a cascade of events each with its own chaotic possibility.

"It's kind of like opening a treasure chest, but you're blindfolded. The chest is open and you don't really know the contents, but you know there's something good inside. In general you don't really know what the outcome of the experiment is going to be before you do it," Nedwidek explained. "What usually happens is that the hypothesis is not quite right. It's usually slightly off, and in some cases it's very far off, and you have to be open to that."

Although one might speculate that the pressure in such a career is immense, Nedwidek has her life remarkably under control. For one thing, she loves her work.

For another, she makes sure to schedule time for herself to unwind. After returning from the lab, she'll cook, watch PBS, listen to music. "I listen to Bach, he's one of my favorites. I listen to Mozart when I need to think, because the patterns in that music help me think. I listen to Christmas music starting in about October," Nedwidek said, giggling. In her Beacon Hill apartment she still has a small Christmas tree by the window and is planning to wrap a cardboard cut-out of a star in gold paper to give to a friend. "My life is really good," Nedwidek said. "I do know it's a cliche, but the glass is half-full."