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High School Teacher Helps Discover New Cancer Drug

Sixteen years ago, when Stuart Shifrin, then a chemistry teacher at John F. Kennedy High School in Silver Spring, Maryland, volunteered to be one of the first teachers in a new research internship program at the National Institutes of Health (NIH), all he expected from the experience was to see how scientific research is conducted. Instead, his summer research project has developed into a promising new chemotherapy drug.

The Student and Teacher Internship Program, sponsored by Howard Hughes Medical Institute (HHMI) and run by the Montgomery County Public Schools, places high school students and teachers in NIH labs to experience science in action. Shifrin, whose father died of colon cancer, asked to work at the National Cancer Institute (NCI). He was placed in the lab of Leonard M. Neckers, then a principal investigator in NCI's Medicine Branch. Neckers and his postdoctoral fellow, Luke Whitesell, were examining a group of drugs that appeared to turn cancerous cells into normal cells.

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— Stuart Shifrin

We asked Stuart to put some drugs called benzoquinone ansamycins on cancer cells and tell us what happened, said Neckers. The literature said these drugs worked by interfering with the cancer cells' tyrosine kinase metabolism, and we wanted to see if that was true. Tyrosine kinases are enzymes that have been implicated in cancer.

Shifrin noticed that the drugs affected some cells and not others, and Neckers and Whitesell observed that the tyrosine kinase activity in the affected cells did not appear to have changed. When they pooled their observations, Neckers' and Whitesell's interest was piqued, and they began to study the drugs in earnest.

Shifrin's original test drug was herbimycin, but Neckers and Whitesell found it to be too unstable for therapeutic use, so they focused their efforts on geldanamycin, another member of the ansamycin family. Soon they hope to add a geldanamycin derivative called 17-AAG to the cancer pharmacopoeia. The medication has already been tested successfully in human beings in five

Phase I clinical trials, which test the safety of new drugs. It is now in more than 20 Phase II trials around the country, testing its effectiveness. If the results remain promising, 17-AAG will move on to large Phase III trials, the final step before presenting a new drug to the U.S. Food and Drug Administration for approval.

Shifrin recalls his weeks in the lab with great pleasure. The best times of all were the brainstorming sessions after results came in. We would go into Len's tiny office, and that's where I saw science happen. We would debate about the data and think about the next steps. Watching them work was the most fascinating part for me, Shifrin said.

Ever since, Shifrin and Neckers have met for dinner several times a year. Each time, Shifrin said, he sits on the edge of his chair, eager to hear the next chapter in the cancer-drug story.

Now chair of the Science Department at Walt Whitman High School in Bethesda, Maryland, Shifrin said the lab experience has also transformed his teaching. Now that I know how exciting a career as a scientist can be, I really encourage students to go for it. I think it's a superstar job," he said. "I've seen how science works, and I try to pass that on to my students. I'm not just teaching facts anymore. I feel like a real advocate for science.

When the first scientific journal article on geldanamycin was published in *Cancer Research* in 1992, Shifrin was listed as second author. Neckers said he deserved it.

Stuart really helped us think along other lines and come up with other ideas to explain the initial results, Neckers explained. He was a big part of our team as we were trying to find out what was going on. Intellectually, he did a small but important piece of this work.

For the 2005-2006 school year, the HHMI Student and Teacher Internship Program placed 22 high school students and 10 teachers in NIH labs. Students worked in the labs full time during the summer and every afternoon throughout the following school year. Teachers participate only during the summer.

Sandra Shmookler, director of the program for Montgomery County Public Schools, calls the research internships at NIH a vital component of a good science education.

If we want to whet the appetite of our young people for science, the teachers have to know what's going on in science now, not when they were in school five, 10, or 20 years ago, Shmookler said. In 2006, science changes every day.

On May 18, 2006, the student participants in this year's internship program will present their research findings at a dinner symposium at HHMI headquarters in Chevy Chase, Maryland.