



Science in the Blood

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Science is in my blood. My great aunt, Ida Hyde, was a very eminent physiologist when there were almost no women scientists. My grandfather was a physician/scientist, and when I was six, he took me to his lab and showed me that science is exciting. Around the same time, I watched a movie about Daniel Boone that convinced me I wanted to be an explorer, and *Microbe Hunters*, a book about Pasteur, showed me how useful science can be.

I studied chemistry at the University of California, then got my Ph.D. under Linus Pauling at the California Institute of Technology. He was a god-like figure—so much smarter than almost anybody else.

The big question when I started my independent career in biochemistry was where do molecules come from and where do they go? One of my most exciting moments was when Edwin Umbarger and I independently discovered that a metabolic pathway shuts down if you provide its end product, so that energy isn't wasted. But nobody knew how that worked. My colleagues, especially John Gerhart, showed feedback-inhibited enzymes are built with a regulatory site, just as a furnace has a thermostat that senses too much heat and shuts it down. This was a totally new idea and was perhaps my most exciting contribution to science. I still find it thrilling.

In the 1950s, on sabbatical with Jacob François and Jacques Monod, we discovered a mechanism that determines whether a gene is expressed. Ours is considered one of the most important papers in 20th century biology, and it earned them a Nobel Prize. I learned from Jacques that you should give your novel idea a name (repression) so it sticks in people's minds. Sometimes people get credit because they give a better name to somebody else's discovery.

I've spent the last half of my life trying to make progress against cancer. My mother and my late wife, the scientist Ruth Sager, both died of cancer, and I wanted to do something about it. At the moment, things are looking pretty exciting. My lab developed a new drug, β -lapachone, which is currently in clinical trials with ArQule Inc. under the guidance of my former postdoc, Chiang Li.

Regulation of biology has been a major theme in my life. I've been interested in what regulates growth, so that cells are not made at the wrong place and the wrong time, as in cancer. Different genes are turned on and off in cancer cells compared to normal cells, and to study this, Peng Liang and I developed differential display, a new method for discovering patterns of messenger RNAs, as in cancer cells versus normal cells.

I'm a little disappointed at the way science is going now. It's not easy in the present atmosphere to be highly innovative. Today there's too much emphasis on the cautious development of established ideas, rather than innovative exploring. Much emphasis is put upon amassing huge masses of data. Most of us are brought up with the idea that you just put your nose to the grindstone to do science. In *The Art of Scientific Investigation*, W.I.B. Beveridge says that science is not just a plodding along, ant-like activity, but it involves inspiration, guess-work, intuition, and, of course, chance. I wish I had known that earlier.

If I were starting out today, I might study the brain as my wife Ann Goodman does. People are saying that this will be the century of the brain and its biology, and I might be swept away by that. But there's also an urgent need to translate basic cancer biology into something useful. We have lots of information, but we're having a hard time converting it into therapies. I'm optimistic it will happen.

—As told to Christie Aschwanden, a freelance writer based in Colorado.