

**BIOMEDICAL RESEARCH AND MY LIFE**

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Two months ago, my friend Karen received some very bad news: her colon cancer had returned and her doctor believed that it was in stage 3. Normally Karen is a very buoyant person, but the thought of facing more surgery, chemotherapy, and radiation with a poor prognosis, dampened even her bright spirits. I started reading about new cancer treatments that might be helpful and found a novel approach to cancer treatment – antiangiogenesis.

In the 1970s, Harvard researcher Judah Folkman observed that tumor growth was dependent upon angiogenesis – growing new blood vessels to support the tumor’s growth. Folkman thought that a better approach to treating cancer, one that might be less toxic than massive doses of chemotherapy and radiation, would be to find ways to *inhibit* the growth of these vessels - thereby cutting off the blood supply and “starving” the tumor.

He and his colleagues searched the literature for antiangiogenic drugs to test this theory. They found a likely candidate in thalidomide, a drug marketed to pregnant women for morning sickness in the 1950s. Because early fetal development, like cancer cells, depends on rapid vascularization, if you reduce vascularization at critical times, the fetus’ limb development will be cut short. After thousands of babies were born with missing limbs, thalidomide’s terrible side effects were realized. Thalidomide was removed from the market and a new law requiring that drugs must undergo a safety-during-pregnancy test was enacted.

Folkman’s lab got permission to work with the banned drug. Their experiments proved that thalidomide could shrink malignant tumors 80 percent of the time in mice. They hoped that this effect would also be true in humans and that by fine-tuning the antiangiogenic drugs; at least some cancers might be cured. Early results were promising but after some months, the tumors usually returned. Surprisingly, some antiangiogenic drugs like Avastin did not prolong human life on their own, but they did increase survival rate when added to chemotherapy. This

presented a paradox: If antiangiogenic drugs like Avastin or thalidomide “cut off” the tumor’s blood supply, then the poison (chemotherapy) would have no way to get inside the tumor.

Something more must be going on.

Another Harvard researcher, Rakesh K. Jain, and his colleagues had done a vast amount of research on tumor vessels. They discovered that malignant tumors are abnormal in several respects: they are permeable or leaky, allowing cancer cells to escape and travel to new sites (metastasize), they create unhealthy interstitial pressure which can cause dangerous swelling in the brain and body cavities, and they are twisted and uneven, with some parts of the tumor oversupplied with vessels, and some parts having no blood supply at all. Because of these many abnormalities, cancer medicines can’t reach and destroy all parts of the tumor.

By administering antiangiogenic drugs and carefully observing the changes in tumor vasculature, Jain discovered that antiangiogenic drugs don’t simply destroy the blood vessels leading to malignant tumors, they *prune* and *normalize* them. Some malformed or immature vessels die off, leaving the remaining vessels healthier and better functioning. In some cases, this leads to a proliferation of cancer cells, which would be very bad news except that rapidly dividing cells are also highly sensitive to chemotherapy drugs, which are designed to target them. Thus, a window of opportunity exists, following the pruning, for more effective anti-cancer treatment. Timing, says Jain, is critical. His lab is also searching for non-invasive biomarkers like a simple urine or blood test that could determine the presence of early cancers. If antiangiogenic and other drugs were give *before* new tumors could implant and grow, the many cancers that are in situ (small non-invasive tumors that are believed to be harbored by up to 30 percent of the population) might be prevented from turning into active disease!

## **Reflections:**

Animal research is very important when it comes to researching new cancer drugs. If we couldn't test on animals, it would be very hard to get new drugs approved because with every test we would endanger human lives. Some people say that animal testing is cruel, but when a positive breakthrough is made, it can benefit animals as well as humans. And despite what some animal rights activists claim, a child is not a rat or an ant! Tragedies like the thalidomide babies could have been prevented by more and better animal research.

I'm glad I was able to learn more about cancer and cancer treatments while researching this essay, and gladder still that Karen's latest tumor turned out to be benign. She will still need treatment, but her cancer is not as advanced as her doctor thought. I am looking forward to the day when cancer is a treatable condition and I am hopeful that Karen's life and many others will be saved by the advances in medicine made possible by animal and human research.

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Period 3

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