

## A Lifesaving Legacy

**Judah Folkman transformed our understanding of cancer. Now his groundbreaking work is leading to new strategies for fighting obesity, Alzheimer's and scores of other conditions.**

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Two years ago, a patient of mine received some terrible news. Her cancer had spread to her liver, and it had spread so extensively that she was given only a few months to live. Her doctor prescribed a new drug, Avastin. Instead of directly killing the tumor cells, this drug was designed to disrupt the tumor's blood supply, thereby causing the tumor to die while minimizing damage to the normal cells around it. It worked. She is still alive today, and there is no trace of tumor in her liver.

Although she never met him, she owes her life to Dr. Judah Folkman, as do many others. The world lost one of the great scientific minds of our time when he died two weeks ago. His life's work literally transformed our understanding of cancer and other illnesses. Folkman's ideas were truly revolutionary. Like other scientists throughout history whose ideas were ahead of their time, he endured with grace many years of deep skepticism, even ridicule, from much of the medical community until he was ultimately proved right. He inspired me by his example. Few scientists are able to witness their ideas move from the laboratory to the clinic and change the way medicine is practiced.

His remarkable breakthrough showed that tumors create a private blood supply for themselves in order to grow and spread, a process called angiogenesis. Folkman believed that disrupting this blood supply, called antiangiogenesis, could starve tumors. Undeterred by criticism, he doggedly persevered over four decades and eventually established a new field of medical research based on understanding and controlling new blood-vessel growth.

In 2003, the biotech company Genentech proved the antiangiogenesis concept with Avastin. In 2004, an [article](#) published in The New England Journal of Medicine showed that Avastin significantly prolonged the lives of patients with metastatic colon cancer. Today, 10 antiangiogenesis drugs for cancer have been approved in the United States, helping more than 1.2 million patients with cancers of colon, lung, breast, kidney, liver, pancreas, stomach and bone marrow live longer and better.

While biotech companies are beginning to rally around this idea, Mother Nature may have already given us a practical solution in certain foods. A growing body of research is showing that fruit and vegetables

contain an arsenal of naturally occurring angiogenesis inhibitors. These include substances like ellagic acid (berries), resveratrol (grapes), curcumin (turmeric), ECGC (green tea), procyanidin (cocoa) and genistein (soybeans). Increasing the intake of these substances may prove to have antiangiogenic benefits, such as cancer prevention and weight reduction. Antiangiogenesis may be yet another reason why fruits and vegetables are so beneficial. The [Angiogenesis Foundation](#), a nonprofit organization inspired by Folkman's vision, is now building a worldwide research effort to study this approach.

More than 70 diseases besides cancer are now recognized as "angiogenesis-dependent," and may yield to the same approach to therapy. These diseases include arthritis, psoriasis, endometriosis, Alzheimer's disease and even obesity. Abnormal blood-vessel growth also underlies the most common causes of blindness in Western nations, age-related macular degeneration (AMD) and diabetic retinopathy. Folkman's antiangiogenesis concept also led to the successful development of two new antiangiogenic drugs, Lucentis and Macugen, that effectively treat, and can, in some cases, even reverse vision loss. An [editorial](#) in The New England Journal of Medicine accompanying the article used the uncharacteristic word "miraculous" to describe these findings.

The importance of angiogenesis in health and disease is also leading to new insights for obesity. It turns out that fat, like tumors, also relies on a blood supply to grow. In some of his last work, Folkman and his colleagues found that antiangiogenesis drugs caused dramatic [weight loss](#) in obese mice by reducing the blood supply to fat cells. I found it especially interesting that these mice lost weight even when their food intake was unchanged, raising new possibilities in obesity research. Imagine if, one day, an antiangiogenic pill enabled you to lose weight without eating less food!

In some circumstances, angiogenesis can be healing. Therapeutic angiogenesis is a new approach in medicine whereby doctors stimulate blood vessels to promote repair and healing. For example, when arteries that feed your brain and heart get clogged with atherosclerosis, angiogenesis causes new blood vessels to grow around these blocked arteries to help prevent a heart attack or a stroke. These new blood vessels, called collaterals, are stimulated by [regular exercise](#).

In addition to exercise, scientists are now finding that they can enhance [angiogenesis](#) in the arteries that feed the heart by transplanting cells from the subcutaneous fat into the heart. Fat tissue contains angiogenic stem cells (called adipose stromal cells, or ASCs), which increase the blood supply to fat cells, promoting obesity. Cardiologists have discovered that by removing fat using liposuction, it is possible to harvest these adult stem cells and implant them into the heart, where they grow natural bypass channels, at least in mice. Should this prove effective in humans, one day we may see overweight patients with coronary disease treated by both the plastic surgeon and interventional cardiologist, then maintained on an antiangiogenic weight-control diet.

Besides residing in fat, angiogenic stem cells are stored in our bone marrow, called into action whenever they are needed for cardiovascular regeneration. Clinical trials are now underway to harvest these bone-marrow-derived angiogenic stem cells and transplant them into the heart to create a better blood supply, as an alternative to bypass surgery--a recent randomized controlled trial in humans showed some [encouraging results](#). Products are now being developed to treat coronary disease and peripheral arterial disease using genes, proteins and adult stem cells that stimulate angiogenesis in diseased tissue. Some medical researchers even believe that angiogenic stem-cell therapy may be a key to regenerating the heart, brain, liver, nerves and other vital organs.

Also, Folkman's research led to our understanding that wounds require new blood vessels to heal. In 1997, the FDA approved a topical angiogenesis-stimulating gel called Regranex that [heals](#) foot ulcers in diabetics. A 2005 [study](#) of 24,898 diabetic patients showed that patients who received this drug had a 30 percent reduced risk of having their leg amputated.

All of these remarkable advances emerged from the vision, perseverance and determination of one man, Dr. Judah Folkman, whose keen powers of observation, ability to think beyond the accepted beliefs and ability to inspire others led him to leave one of the biggest footprints in modern medicine.

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