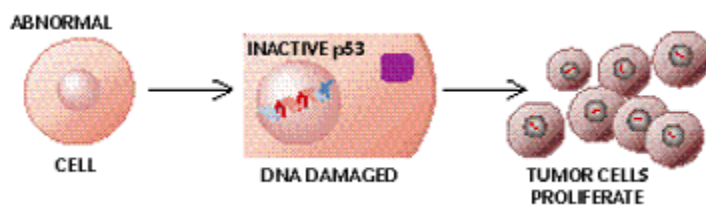


## Angiogenesis: Cancer's Lifeline

### Understanding Cancer

Cancer, abnormal division of the body's cells, has long been the nemesis of medical science. While years of toils by researchers have slowed the spread of cancer and even alleviated the symptoms, there is no known cure for the deadly disease. However, a drug currently under development offers new hope that humans may finally have prevailed in the fight against the second leading killer in the world.

To understand **angiostatins**, the revolutionary new drug, it is vital to comprehend the root cause of cancer. Cancer begins when **DNA**, the carrier of all genetic information,

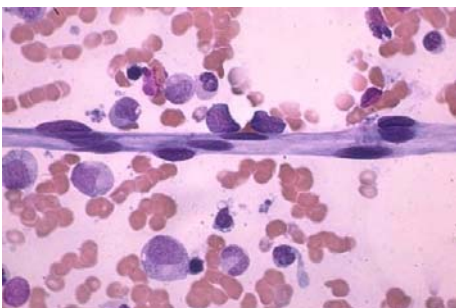


**Figure 1: Tumor Cells.** Damaged DNA results in the creation of a tumor, a clump of cells growing abnormally. Tumor cells reproduce rapidly.

is damaged, causing the formation of a **tumor**, a clump of cells growing rapidly (See Figure 1). The tumor relies on blood vessels, though, to achieve

its rapid rate of growth. The blood vessels bring nutrients to feed and nurture damaged cells (locations around the tumor), to assist in destroying healthy **tissue**, or a group of cells, and to serve as the “highway” for tumor cells to spread.

### Angiogenesis: Creation of New Blood Vessels

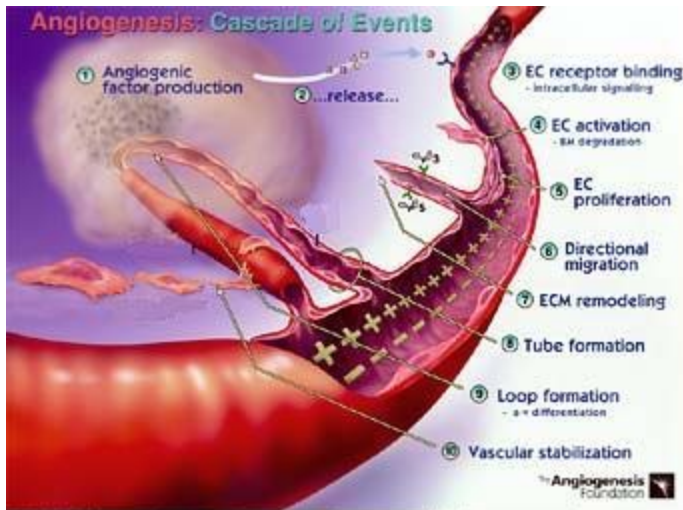


**Figure 2: Endothelial cells.** A strand of EC cells in the bone marrow magnified 100X.

As tumors begin to grow, blood vessels become scarce; the tumor has exceeded the capacity provided by the current number of blood vessels.

However, the tumor then produces a specific

enzyme, called an **angiogenic growth factor**, which stimulates the creation of new blood vessels in a process called **angiogenesis**. After the growth factors have been secreted, **endothelial cells (EC)**, the cells responsible for the growth of blood vessels, begin to



**Figure 3: Angiogenesis.** The process of angiogenesis, the creation of new blood vessels. Note the tumor represented as (1); it secretes the angiogenic growth factor (2), which binds to the epithelial cells (EC) (3) and activates them (4). The EC proliferate (5) and create new blood vessels (6-10).

proliferate. Finally, the EC dissolve holes in current blood vessels and expand the vessels toward the source of the secretion, in this case the tumor. Two types of blood vessels are formed: **tubes**, a standard vessel which spans from one point to another

point, and **loops**, vessels which start and end in the same proximity, helping circulate

blood. Finally, the new blood vessels are stabilized and structurally supported by additional cells in a process called **vascular stabilization**. While angiogenesis, a naturally occurring process, occurs in healing injuries and reproduction, if the body loses control of it, cancer and other **angiogenesis-dependent diseases** will develop.

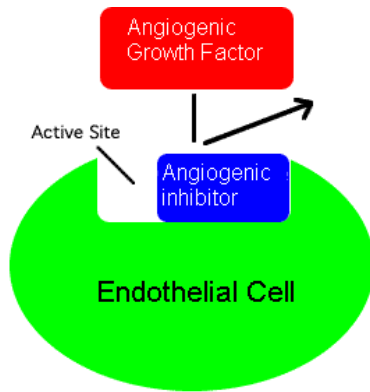
### Angiostatsins: Targeting the lifelines

In the past, researchers targeted the tumor, focusing their attention on such methods as **radiation** and **chemotherapy** (See Figure 4), both which attempt to

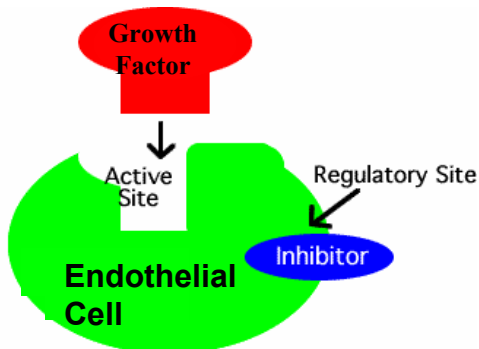
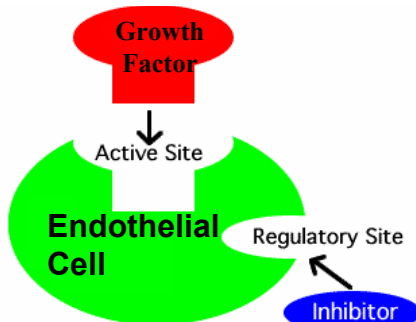


**Figure 4: Radiation therapy.** Traditional methods attempt to kill the tumor.

kill the tumor. However, researchers at Bristol-Myers Squibb recently began testing revolutionary new drugs called **angiostatins**, and their close relatives, **endostatins**. Both



An angiogenic inhibitor binds to the active site, blocking the growth factor from attaching.



**Figure 6: Noncompetitive inhibition.** An angiogenic inhibitor binds to the allosteric (regulatory) site (top), changing the shape of the cell. The growth factor can no longer attach to the active site (bottom).

angiostatins and endostatins work in a similar manner; they only differ slightly in their physical and chemical composition.

Angiostatins work by secreting a protein called an **angiogenic inhibitor**, which block the production of angiogenic growth factors (See

Figure 5). While there are two types of inhibition, they work in essential the same manner. By

binding either to the endothelial cell protein's

**active site**, the location where the growth factor normally binds, or the **allosteric site**, another site

separate from the active site, the angiogenic

inhibitor prohibits the growth factor from attaching

to the EC. In **competitive inhibition**, the

angiogenic inhibitor binds to the active site,

blocking the growth factor from attaching. Thus,

the inhibitor competes with the growth factor,

leading to the name of the process. The other

type of inhibition is **noncompetitive inhibition**,

where the inhibitor binds to another site in the cell's

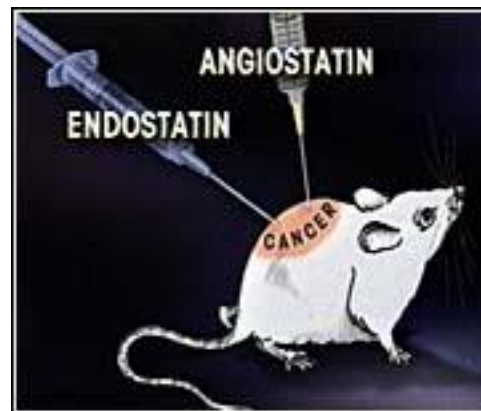
protein, called the **allosteric site**, sometimes

referred to as the **regulatory site**. The inhibitor causes the cell to change its conformation; the active site is transformed, and the growth factor can no longer attach to the cell. (See Figure 6) Thus, the EC cannot be activated; because the growth factor cannot stimulate angiogenesis and create new blood vessels, the tumor is literally starved out of the required nutrients. As a result, the tumor cannot expand, and cancer is effectively checked. While these drugs are still several years away from being available to the general public, the preliminary results are encouraging. In clinical trials around the nation, researchers have stopped cancer in various organisms, including mice, after the injection of angiostatins and endostatins (see Figure 7). More tests of angiostatins and endostatins are currently being performed, and human testing could begin in less than a decade.

### The Future of Angiostatins

While more extensive work and research needs to be conducted, angiostatins offer the best hope for a cure of cancer in over three centuries. In fact, some studies show that angiostatins, when combined with traditional treatments such as chemotherapy, may extend a

cancer patient's life by up to 30 percent and significantly reduce the growth of the tumor. With each promising clinical trial, scientists are closer than ever to unlocking the key against cancer. Perhaps mankind has gained the advantage in the fight against cancer with the help of angiostatins halting the process of angiogenesis and starving cancer of its required nutrients and blood supply.



**Figure 7: Injection of drugs.** In clinical trials, mice with cancer have been injected with both angiostatins and endostatins; the results are promising.

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**Figure 3:** Angiogenesis Foundation, Understanding Angiogenesis  
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**Figure 4:** Skull Valley Goshutes Research Facility, Scientific Project  
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**Figures 5 and 6:** Gresham High School, Science Department  
<<http://ghs.gresham.k12.or.us/science/ps/sci/ibbio/chem/notes/chpt8/>>

**Figure 7:** Access Excellence, National Health Museum  
<<http://www.accessexcellence.org/WN/SUA12/angio598.html>>