A little over a decade ago, two important cancer biologists published a paper in Cell that has become a seminal work in the field. It describes the six biological hallmarks of cancer. The fact that most or all of these factors are present in just about all of the different kinds of cancers highlights how many checks and balances are present in normal biology, that there are very consistent themes in cancer biology, and also explains why cancer is largely correlated with increasing age: it usually takes decades for a confluence of all of these derangements to occur in the same cell, then grow to become detectable. Here’s the list:

1) Self-sufficiency of growth signals: Normal cells require signals to specify when they should grow and divide. Cancer cells no longer require external signals to be stimulated to grow, often having on-off switches that are stuck in the on position.

2) Insensitivity to anti-growth signals: It’s not enough to be triggered to grow and divide, because the biological systems are balanced with brakes to inhibit excessive cell growth. Cancer cells have lost this function.

3) Evading apoptosis: Apoptosis is a biological self-destruct program that cells have. It’s a normal part of development that leads to things like the space between fingers and toes (cells there are programmed to die at a particular point in normal development), and it’s also built into other cells when the growth is careening out of control. This automated self-destruct mechanism is turned off in cancer cells.

4) Limitless replicative potential: Though self-sufficiency of growth systems, insensitivity to anti-growth signals, and elimination of the self-destruct program should theoretically be enough to produce ongoing cancer cell growth and division, most cells also automatically stop growing
beyond a certain point. Cancer cells continue to grow without any inhibition.

5) Sustained angiogenesis: Cancer cells without a new blood supply can’t grow beyond about 1-3 mm without outpacing their blood supply. If that happens, they have no way to receive nutrients and eliminate waste necessary to survive. Cancer cells put out molecular signals that attract new blood vessels to the cancer from outside, providing a new mechanism for the support needed to grow. Several agents targeting these angiogenic signals, such as Avastin (bevacizumab) have been studied and proven to improve survival in several types of cancer.

6) Tissue invasion and metastasis: The definition of malignant vs. benign is based largely on the potential of a malignancy (cancer) to invade into surrounding tissues and spread to other parts of the body.

Though these general principles have been defined, there is still much we need to learn about the details. But just as Avastin provides an example of a mechanism of treating cancer by attacking one of these key elements, each of the other hallmarks provides a line of attack for new therapeutics in development.