Findings: Understanding cancer

SHEILA PRAKASH

Two years ago, I had the pleasure of interviewing professor Randy Pausch for an alumni article about the Entertainment Technology Center. In the recent wake of his exuberant and downright remarkable approach to his pancreatic cancer diagnosis, I wanted to explain, to the best of my ability, what cancer is, and why it is so difficult to target.

An adult human body contains approximately 10 trillion cells. These cells grow and divide in an orderly manner. When old cells die, new cells proliferate to take their places.

This is an interesting point, and has important implications for cancer. The cells in the human body are in flux. They are constantly maturing, multiplying, and dying. To the naked eye, this turnover is undetectable because the body kills unnecessary cells and replaces missing ones so quickly that the body's overall cell count appears unchanging.

Imagine a company that hires and fires employees at a faster-than-normal rate. Within minutes of an employee being fired, another employee appears by the cubicle to take his spot. Over the course of a week, the staff number at the company is the same, but the employees are all new. The same applies to the cells in the human body.

In order for the body to maintain this perfect balance in cell number, the cell's life cycle has to be strictly regulated.

Going back to the company, imagine it loses its firing department to the flu. The firing department is sick, and cannot execute orders to fire employees, but the company is still hiring. Eventually, the building will be swamped with employees. Desperate for space, they crawl into the ventilation ducts, hang from the rafters, and occupy closets and bathrooms.

The hiring department is hiring out of control because there is no firing department to counterbalance it. The company has cancer, and if the problem is not fixed, employees will smash pipes, shatter windows, and break down walls until the building collapses.

The biological mechanism for this is fairly simple. The heart and soul of a cell is its DNA. A single piece of DNA contains all the information necessary to encode every single protein in the body.

In order for a cell to divide into two cells, it has to split this DNA into two copies — one for each cell. If the cell approaches its first checkpoint with faulty DNA, the birthday party is over.

It cannot proceed to the next phase in its life cycle until its DNA is repaired. Faulty DNA contains mutations, or errors, in the code.

As such, several proteins encoded by the DNA will also be faulty. This is bad, because some of these proteins are responsible for cell division.

There is one protein chiefly responsible for regulating cell cycle control. In 1993, it was named *Science* magazine's Protein of the Year. The protein is called p53, and it stops the cell containing faulty DNA from dividing. In addition, p53 also recruits the enzymes necessary to repair the DNA. If the damaged DNA is not fixed, p53 targets the cell for destruction.

Thus, p53 takes the role of the hiring and firing departments. As such, one of the most prevalent mutations leading to cancer is in the gene that makes p53. Because of its role in cell cycle regulation, p53 is called a proto-oncogene.

When proto-oncogenes contain a mutation, they become oncogenes.

Oncogenes cause cells to divide wildly and dangerously. If inherited, they can sometimes (but not always) give rise to cancer.

A second group of genes, tumor suppressor genes, is also important in cell-cycle control. Tumor suppressor genes code for proteins that inhibit cell growth.

Like proto-oncogenes, defects in tumor suppressor genes give rise to cancer.

Out of the roughly 35,000 genes in the body, only a small percentage of genes (the proto-oncogenes and the tumor suppressor genes) are related to cancer — p53 is a remarkable protein that functions as a tumor suppressor gene and a proto-oncogene.

Mutations in either set of genes can be inherited, or they can occur through environmental exposures to carcinogens.

A well-known oncogene is RAS, which is found on chromosome 11. Thirty percent of all tumors have a mutation in RAS. MYC is an oncogene associated with Burkitt's lymphoma, a cancer of the lymphatic system. Hereditary breast cancer results in inherited mutations in the tumor suppressor genes BRCA1 and BRCA2.

Sometimes, cells contain mutations. Almost all of the time, the mutations are repaired. In rare cases, particularly bad mutations (mutations in the cell cycle) pass on from cell to cell. These cells form a tumor.

Because cancerous cells can appear at any given time, and with no warning, the only current treatment of cancer is chemotherapy, which kills rapidly dividing cells. But cancer must exist as a clump of hundreds of cells exhibiting abnormal growth (a tumor) before it can be seen — making the individual targeting of cancerous cells impossible.

In the cancerous company, the employees will eventually die of starvation. The problem arises not when the employees are swarming the building, but when they are given food and water to survive. This is angiogenesis, and it is the process a tumor goes through to find nearby blood vessels to feed itself. Without this blood supply, the tumor cannot spread, or metastasize. It is benign.

Put another way, uncontrolled cell growth is only mildly bad until it hunts out blood vessels to sustain itself.

When a tumor recruits blood vessels, it comes to life. Now cells can slip off the tumor and into the blood stream.

From here, they can latch onto any tissue in the body and start the process anew. Cancer has entered the building — and it is not leaving anytime soon.

How Things Work: Nanotechnology

AKANKSHA VAIDYA

A college student might spend the night nursing a sore back because of carrying around volumes of books and a laptop all day. Given this, it is reasonable enough to wish for a scrap of paper which would have *everything* written on it. However, compared to particles that are one-billionth of a meter in each dimension, a scrap of paper is gigantic.

Thanks to the field of nanotechnology, the word "small" has a taken on a completely new definition. Nanotechnology deals with particles within the range of nanometers. (A nanometer is 10^{-9} meters.)

Although we can easily imagine such an idea today, it would have found its place in science fiction books some decades ago.

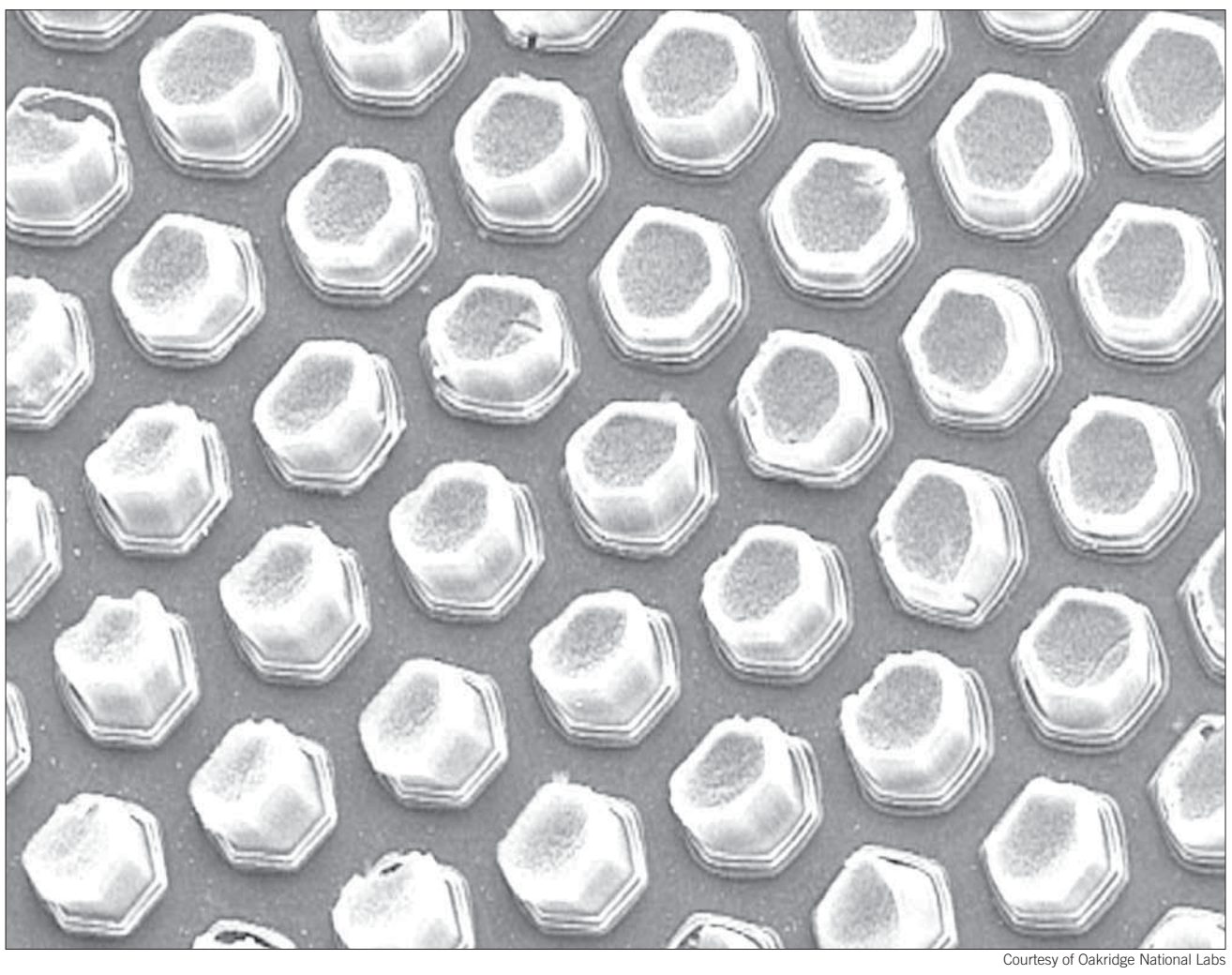
The concept of nanotechnology was proposed almost 50 years ago, when the bizarre idea of consolidating volumes of information onto a tiny surface was discussed by Nobel Prize-winner Richard Feynman. Feynman introduced nanotechnology in a talk called "There's Plenty of Room at the Bottom," delivered at the annual meeting of the American Physical Society at the California Institute of Technology (Caltech).

In the talk, given in 1959, Feynman asked, "Why cannot we write the entire 24 volumes of the *Encyclopedia Britannica* on the head of a pin?"

Feynman then explained his ideas for why putting an entire encyclopedia on a pin is possible and how it can be done. Although the talk probably raised a lot of eyebrows at that time, it got people thinking about nanotechnology and brought the field to where it stands today.

Nanotechnologists use devices like the scanning tunneling microscope, which takes images of the arrangement of atoms in a particular substance.

After knowing the arrangement of atoms in a substance, two different approaches can be used to create nano-devices.



Courtesy of Oakridge National Labs

A carbon nanotube pattern in the form of hexagons.

The first is the bottom-up approach, in which small particles are arranged in an orderly manner to form larger, complex objects.

The second approach is the top-down approach, where large objects are scaled down to a smaller size.

Depending on what device or technology is to be developed, either approach can be employed.

The applications of nanotechnology span a variety of different fields, ranging from quantum physics to medicine. Perhaps one of the most popular applications has been in the field of drug delivery.

Chemotherapy has been used to treat cancer since early 1940s. Traditional chemotherapy, which does not involve nanotechnology, has a number of side effects that make the treatment painful for the patient. The main reason for this is that chemotherapy affects all types of cells and does not specifically target the cancerous cells.

New technology now enables scientists to attach RNA molecules to nanoparticles filled with chemotherapy drugs. The RNA molecules are synthesized such that they specifically target cancerous cells. Therefore, the drugs are delivered only to cancerous cells, leaving the other cells of the body unharmed.

Another application is the creation of extremely strong materials. Carbon nanotubes consist of allotropes, or different forms of carbon. These have astonishing properties; one of which is strength, making them useful in devices like bulletproof jackets.

Nanotechnology is also being applied to produce different kinds of fabrics. Clothes can now be coated with zinc oxide nanoparticles, which act as protection from the ultraviolet rays of the sun. Some clothes also have little hair-like nanoparticles on them, which can repel water and dirt particles to make the clothes stain free. Stain-resistant clothing and pain-free chemotherapy are definitely useful innovations, but the best is yet to come.

Researchers now believe that using nanotechnology, virtually *any* object can be manufactured out of thin air.

These materials will actually be built out of atoms, since atoms and molecules can stick together because of magnetic and electrical properties.

If the particles are carefully manipulated, they can be ordered into a regular structure. Scientists hope to accomplish this using nanomachines called "assemblers," which can be programmed to organize the particles into ordered structures as complex as computers. This technology, known as "molecular manufacturing," may soon become a reality.

While nanotechnology has some people dreaming of a futuristic world, it comes with its drawbacks.

Particles have very different properties when they are in bulk or in a large cluster compared to when they are separated into nano-sized particles.

Scientists fear that some molecules which we know to be harmless may actually be harmful when they are nano-sized. Making clothing or drug delivery devices out of such materials may therefore be extremely dangerous.

Another concern is that since nanoparticles can have atomic physical and chemical properties, they may be used to create potentially disastrous weapons.

If used in the right way, though, nanotechnology can definitely prove to be an asset to mankind. As for college students, what was once a dead weight on their shoulders may eventually be merely tiny lumps in their pockets.

Health Talk: Sleeping foot

CLAIRE MORGENSTERN

Have you ever tried to get up and take a step after sitting in a strange position, only to find that one of your feet has "fallen asleep"?

Yet, after a tingling or burning sensation in the affected limb subsides, the foot returns to normal. However, the process is more complicated than that; "sleeping foot," or "paresthesia," is actually caused by blocked nerve pathways or arteries, preventing the regular flow of electrochemical impulses from reaching the brain.

Electrochemical impulses are transmitted by the body's neurons, cells in the nervous system that are responsible for transmitting information. This process allows for rapid communication between different parts of the body.

When pressure is exerted on a foot, arm, or leg over a sustained period of time, it can compress arteries in that area, which means that the arteries lose the ability to transport nutrients like oxygen and glucose to the tissues and nerve cells in the affected area, which they need to function normally.

Once the limb is moved, nutrient-fortified blood returns to the area, which results in the familiar "pins and needles" feeling.

The sensation is caused by an abnormal transmission of signals to the brain. Nerve pathways become blocked, and the body can no longer send electrochemical impulses to the brain.

As a result, the nerves begin to behave erratically, sending "mixed signals" to the brain. These signals result in a tingling sensation in the affected area.

Once the body changes position, the electrochemical impulses begin to flow properly. However, from the time that the body changes position until the time when the exchange of electrochemical impulses is completely restored, the intensity of the tingling increases, causing the "pins and needles" feeling.

The "pins and needles" sensation may dissolve into an uncomfortable burning feeling before the affected area of the body feels normal. The nerve fibers that regulate pain, temperature, and motor control are thin, allowing the victim to move the affected limb before regaining feeling in it, and to feel the tingling sensation rather quickly.

The burning, however, is caused by separate thicker nerve fibers that may take longer to begin transmitting electrochemical impulses again.

Certain areas of the body are more prone to this sensation than others. Specifically, nerves that are close to the body's surface and near a bone are more susceptible to paresthesia, such as the median nerve in the wrist, which causes Carpal Tunnel Syndrome if damaged.

Other common conditions of this type include Ulnar Nerve Palsy, which occurs from repeatedly hitting the nerve close to the elbow, or "funny bone"; Peroneal Nerve Palsy, also called "foot-drop," which is damage to the nerve at the lower part of the knee and results in inability to flex one's foot upward; and Radial Nerve Palsy, prolonged pressure on the nerve on the underside of the upper arm.

Radial Nerve Palsy is also called "Saturday Night Palsy" because it often occurs in people who sleep soundly after drinking heavily.

Although uncomfortable, paresthesia can actually be beneficial, as the sensation alerts an individual to change his or her position to restore blood flow.

If the blood flow is restricted and nerves are compressed for several hours, the victim could suffer permanent nerve damage, called mononeuropathy.

This results more often from prolonged pressure on a nerve that occurs during sleep or from staying in a crouched position for a sustained period of time.

However, mononeuropathy can also result from accidents, extreme cold or heat, radiation therapy for some types of cancer, and having a cast or crutches that do not fit correctly.

"Sleeping foot" is considered a temporary mononeuropathy, which can be cured by resting, not putting pressure on the area, or applying heat to the site of the discomfort.

More serious cases of prolonged nerve compression, however, may require physical therapy or surgery.

Such cases can usually be diagnosed via physical examination by a medical professional.

Zachary Wallnau/Art Staff