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ARTICLE-A-DAY

Genes and Cells

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Healing Wounds

The text is from the U.S. National Institute of General Medical Sciences.

The coverings for all your body parts (your skin, the linings of your organs, and your mouth) are made up primarily of epithelial cells. You might think that of all the cell types, these would be the ones staying put. Actually, researchers are learning that epithelial cells are also good at snapping into action when the situation calls for them to get moving.

Say you get a nasty gash on your foot. Blood seeps out, and your flesh is exposed to air, dirt, and bacteria that could cause an infection. Platelets stick together, helping to form a clot that stops the bleeding. At the same time, your skin cells rapidly grow a new layer of healed skin over the wound.

Researchers have learned that epithelial cells have the wondrous ability to move around in clumps. These clumped cells help clean up an injured area quickly by squeezing together and pushing away debris from dead cells.

All organisms get wounds, so some researchers are studying the wound-healing process using model systems. For example, William Bement of the University of Wisconsin, Madison, examines wounded membranes of frog oocytes. He chose these cells because they are large, easy to see into, and readily available. Looking through a specialized microscope, Bement watches what happens when wounds of different shapes and sizes start to heal.

Bement learned that just as with human epithelial cells, the wounds in frog oocytes gradually heal by forming structures called contractile rings, which surround the wound hole, coaxing it into a specific shape before gradually shrinking it. He is now identifying which molecules regulate this process. His research may help find better ways to treat injuries in people and animals. . . .

Growing It Back

The text is from the U.S. National Institute of General Medical Sciences.

If scientists could figure out how salamanders regrow their legs and tails, they might be a step closer to helping people who have lost limbs.

If a salamander or newt loses a limb, the creature can simply grow a new one. The process is complicated-cells must multiply, morph into all the different cell types present in a mature limb (such as skin, muscle, bone, blood vessel, and nerve), and migrate to the right location. Scientists know that special growth factors and hormones are involved, but no one knows exactly how regeneration happens. Some believe that understanding how amphibians regenerate their tissues might one day enable doctors to restore human limbs that have been amputated or seriously injured.

It may seem a distant goal, but researchers like Alejandro Sánchez Alvarado are fascinated with this challenge. Several years ago, Sánchez Alvarado, a biologist at the University of Utah School of Medicine in Salt Lake City, set out to find a way to help solve the regeneration mystery. After reading scientific texts about this centuries-old biological riddle, Sánchez Alvarado chose to study the problem using a type of flatworm called a planarian. This animal, the size of toenail clippings, is truly amazing. You can slice off a piece only 1/300th the size of the original animal, and it will grow into a whole new worm.

To understand the molecular signals that can make this feat possible, Sánchez Alvarado is reading the worm's genetic code. So far, he and his coworkers have used DNA sequencing machines and computers to read the spellings of over 4,000 of the worm's genes.

To focus in on the genes that enable planarians to regenerate, Sánchez Alvarado and his coworkers are using RNA interference (RNAi). . . . RNAi is a natural process that organisms use to silence

certain genes. Sánchez Alvarado's group harnesses RNAi to intentionally interfere with the function of selected genes.

The researchers hope that by shutting down genes in a systematic way, they'll be able to identify which genes are responsible for regeneration. The researchers are hoping that their work in planarians will provide genetic clues to help explain how amphibians regenerate limbs after an injury. Finding the crucial genes and understanding how they allow regeneration in planarians and amphibians could take us closer to potentially promoting regeneration in humans.

Tuning Cells

The text and image are from the U.S. National Institute of General Medical Sciences.

Liver cells look almost nothing like nerve cells. Muscle cells bear little physical resemblance to white blood cells. Yet every cell (with just a few exceptions) is encased in a membrane, contains a nucleus full of genes, and has ribosomes, mitochondria, [endoplasmic reticulum], and Golgi [apparatus]. How can cells be so similar, yet so different?

Despite decades of hard work, cell biologists still don't fully understand how developing cells turn into all the different types in your body. But they do know that this process, called differentiation, is governed by genes. Your body "tunes" the genes of each cell type differently. Depending on where in the body it is located, a given gene can be turned off, weakly on, or strongly on. For example, the gene for globin, which composes hemoglobin, is strongly on in cells that will mature into red blood cells and off in every other cell type.

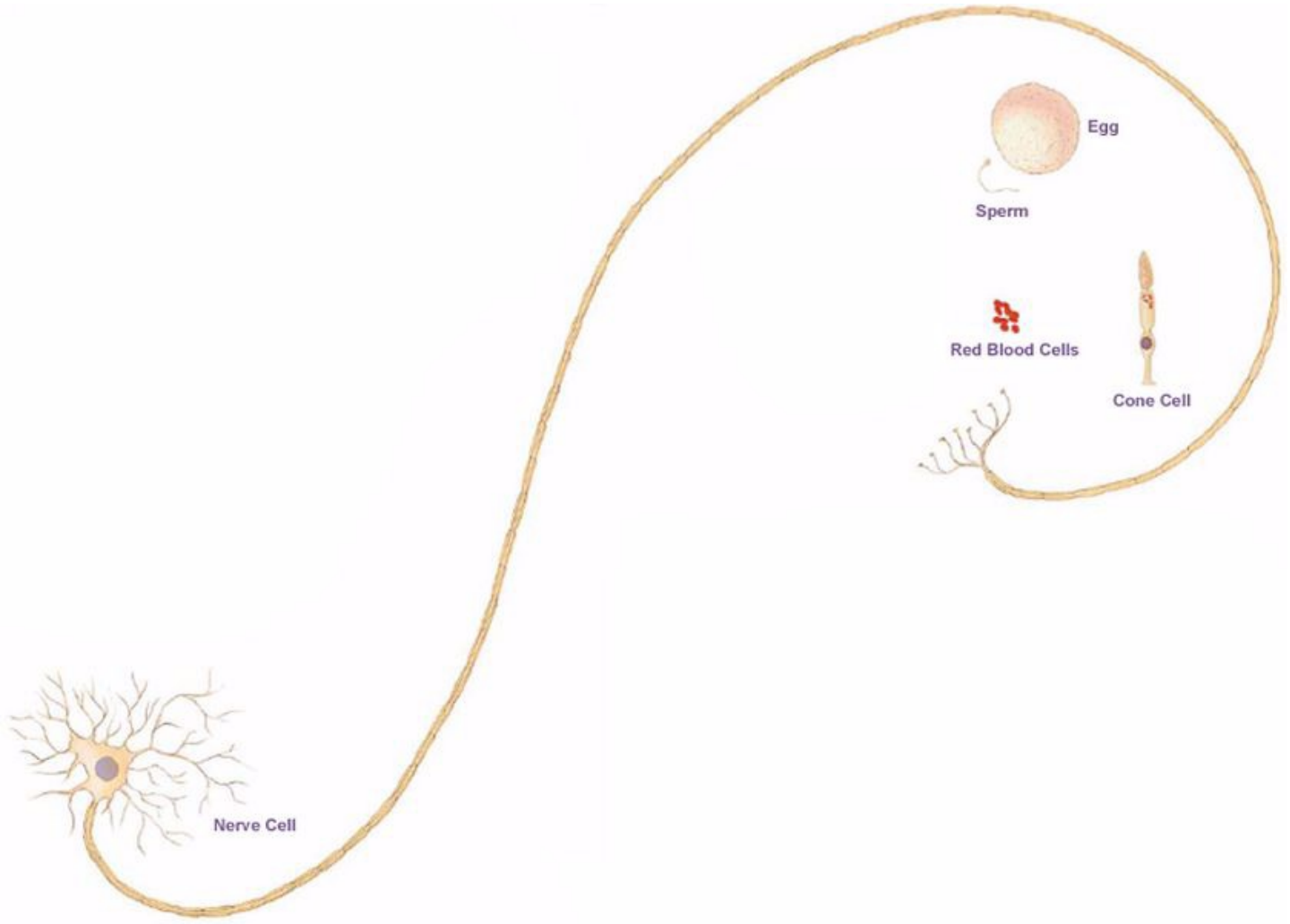
Cells control the tuning, or expression, of genes by keeping a tight rein on RNA polymerase. For genes that are strongly on, cells use special molecular tags to lure in RNA polymerase and to ensure that the machine works overtime transcribing those genes. For genes that are off, cells use different tags to repel RNA polymerase.

Fit for the Job

The tuning of a cell's genes determines which products it can make. Liver cells make loads of enzymes to break down drugs and toxins. Certain immune cells produce antibodies to help fight infections. Cells in a variety of organs-including the pancreas, brain, ovary, and testes-whip up hormones that are secreted into the bloodstream. Many of these substances are produced throughout life in response to the body's need for them. Others are made only at specific times, like the milk proteins produced in a woman's breasts after she gives birth.

The pattern of gene expression also determines a cell's shape, allowing it to perform its job. For example, cells lining your small intestine have hundreds of miniature extensions (microvilli) used to absorb nutrients. Each sperm cell turns on genes needed to develop its wagging flagellum. Rod and cone cells in your eye express genes needed to form their characteristic shapes ([cylindrical] and cone-shaped respectively).

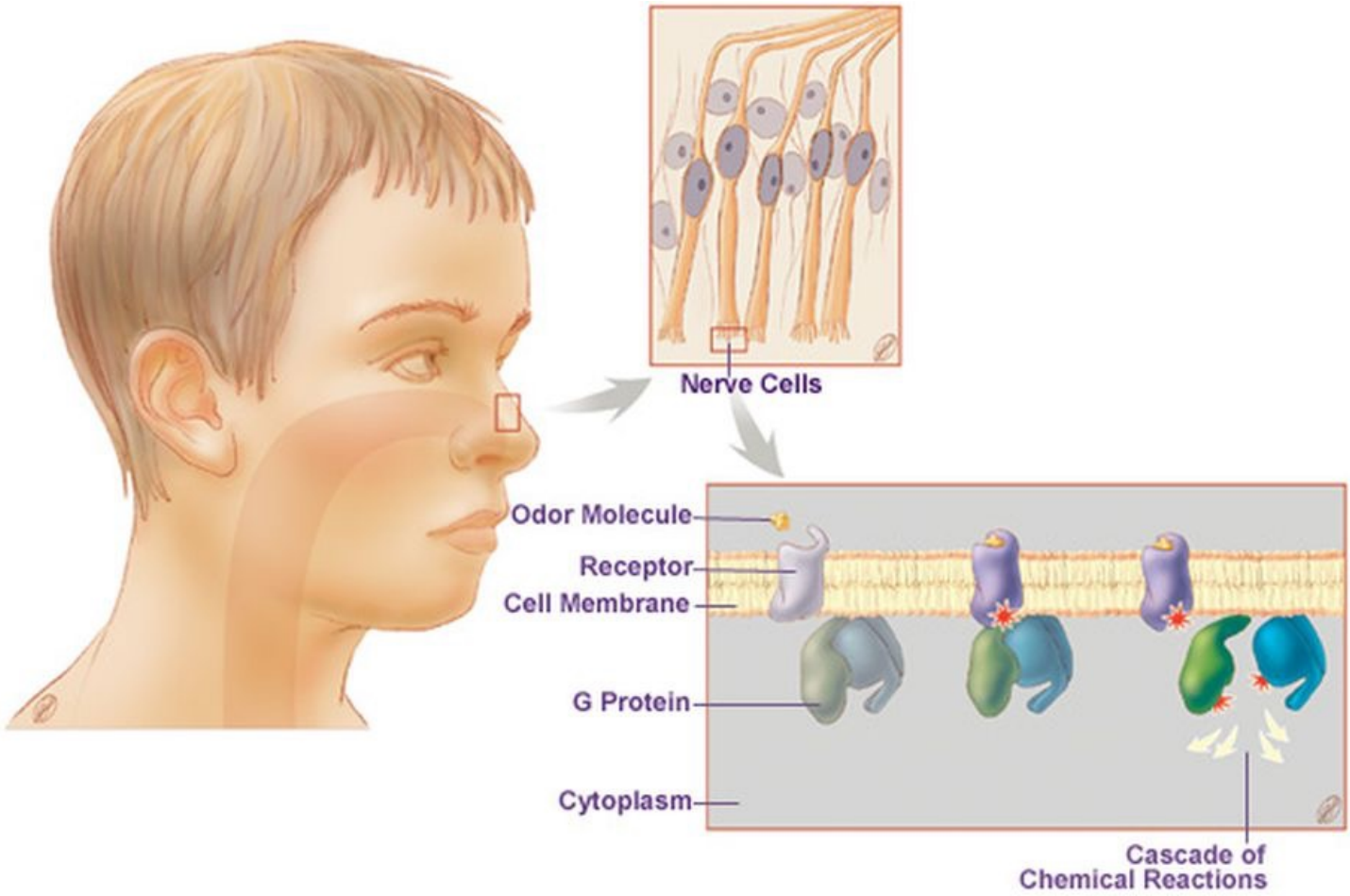
The body even alters the balance of organelles in different tissues. Take your heart, for example. This incredibly durable machine is designed to produce the extraordinary amount of ATP energy required for nonstop pumping-it pumps 100,000 times a day, every day, for your whole life. To do this, it is made up of specialized muscle cells jam-packed with mitochondria. A human heart cell contains several thousand mitochondria-around 25 percent of the cell's volume. Cells that don't need much energy, like skin cells, contain only a few hundred mitochondria.



Each cell is genetically customized to do its unique job in the body. Red blood cells are shaped like lozenges, so they can float easily through the bloodstream. Nerve cells have long, invisibly thin fibers that carry electrical impulses throughout the body. Some of these fibers extend about 3 feet-from the spinal cord to the toes! Also shown here, sized proportionately, are a human egg cell, sperm cell, and cone cell of the eye (which allows you to see in color).

The Science of Senses

The text and image are from the U.S. National Institute of General Medical Sciences.



Each [sensory organ] has cells equipped for detecting signals from the environment, such as sound waves, odors, and tastes.

. . . Each of [your sensory organs such as your ears, nose, and tongue] has cells equipped for detecting signals from the environment, such as sound waves, odors, and tastes. You can hear the phone ring because sound waves vibrate hairlike projections (called stereocilia) that extend from cells in your inner ear. This sends a message to your brain that says, "The phone is ringing." Researchers have discovered that what's sending that signal is a channel protein jutting through a cell membrane, through which charged particles (primarily potassium ions) pass, triggering the release of neurotransmitters. The message is then communicated through the nervous system.

Similarly, for you to see and smell the world around you and taste its variety of flavors, your body must convey molecular signals from the environment into your sensory cells. Highly specialized molecules called G proteins are key players in this transmission process.

Imagine yourself walking down a sidewalk and catching the whiff of something delicious. When odor molecules hit the inside of your nose, they are received by receptor molecules on the surfaces of nerve cells. The odor message fits into a specially shaped site on the receptors, nudging the

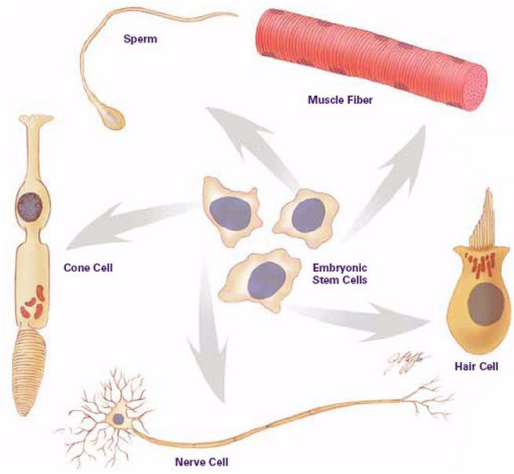
receptors to interact with G proteins on the inner surface of the nerve cell membrane. The G proteins then change their own shape and split in two, which sets off a cascade of chemical reactions inside the cell. This results in an electrical message that travels from your nose to your brain, and evokes your response-"Yummm . . ."

Figuring out the molecular details of this process led to the 2004 Nobel Prize in physiology or medicine for two researchers, Richard Axel of Columbia University in New York, and Linda B. Buck of the Fred Hutchinson Cancer Research Center and the University of Washington in Seattle.

All-In-One Stem Cells

The text and image are from the U.S. National Institute of General Medical Sciences.

There is only one type of cell that is completely generic-its gene expression is tuned so broadly that it has unlimited career potential to become any kind of cell in the body. These undifferentiated cells cease to exist a few days after conception. They are embryonic stem cells.



These undifferentiated cells cease to exist a few days after conception. They are embryonic stem cells.

Each of us was once a hollow ball of 100 or so identical embryonic stem cells. Then, as dozens of hormones, sugars, growth-promoting substances, and other unknown chemical cues washed over us, we began to change. Certain cells grew long and thin, forming nerve cells. Others flattened into skin cells. Still others balled up into blood cells or bunched together to create internal organs.

Now, long after our embryonic stem cells have differentiated, we all still harbor other types of multitalented cells, called adult stem cells. These cells are found throughout the body, including in bone marrow, brain, muscle, skin, and liver. They are a source of new cells that replace tissue damaged by disease, injury, or age. Researchers believe that adult stem cells lie dormant and largely undifferentiated until the body sends signals that they are needed. Then selected cells morph into just the type of cells required. Pretty cool, huh?

Like embryonic stem cells, adult stem cells have the capacity to make identical copies of themselves, a property known as self-renewal. But they differ from embryonic stem cells in a few important ways. For one, adult stem cells are quite rare. For example, only 1 in 10,000 to 15,000 cells in bone marrow is capable of becoming a new blood cell. In addition, adult stem cells appear to be slightly more "educated" than their embryonic predecessors, and as such, they do not appear to be quite as flexible in their fate. However, adult stem cells already play a key role in therapies for certain cancers of the blood, such as lymphoma and leukemia. Doctors can isolate from a patient's blood the stem cells that will mature into immune cells and can grow these to maturity in a laboratory. After the patient undergoes high-dose chemotherapy, doctors can transplant the new infection-fighting white blood cells back into the patient, helping to replace those wiped out by the treatment.

Although researchers have been studying stem cells from mouse embryos for more than 20 years, only recently have they been able to isolate stem cells from human embryos and grow them in a laboratory. In 1998, James A. Thomson of the University of Wisconsin, Madison, became the first scientist to do this. He is now at the forefront of stem cell research, searching for answers to the most basic questions about what makes these remarkable cells so versatile. Although scientists envision many possible future uses of stem cells for treating Parkinson's disease, heart disease, and many other disorders affected by damaged or dying cells, Thomson predicts that the earliest fruits of stem cell research will be the development of powerful model systems for finding and testing new medicines, as well as for unlocking the deepest secrets of what keeps us healthy and makes us sick.

Cells on the Move

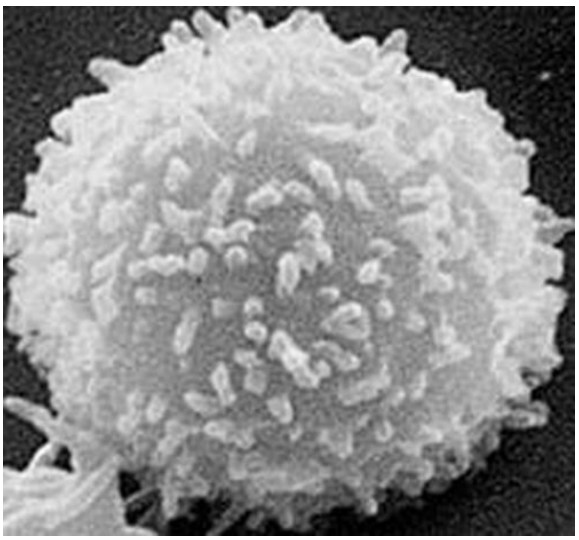
The text is from the U.S. National Institute of General Medical Sciences.

Although many types of cells move in some way, the most well-traveled ones are blood cells. Every drop of blood contains millions of cells-red blood cells, which carry oxygen to your tissues; platelets, which are cell fragments that control clotting; and a variety of different types of white blood cells. Red blood cells, which get their deep color from rich stores of iron . . ., are carried along passively by . . . the bloodstream. In contrast, other blood cells can move quickly out of the bloodstream when they're needed to help heal an injury or fight an infection.

Infection Protectors

White blood cells serve many functions, but their primary job is protecting the body from infection. Therefore, they need to move quickly to an injury or infection site. These soldiers of the immune system fight infection in many ways: producing antibodies, engulfing bacteria, or waging chemical warfare on invaders. In fact, feeling sick is often the result of chemicals spilt by white blood cells as they are defending you. Likewise, the pain of inflammation, like that caused by sunburn or a sprained ankle, is a consequence of white cells moving into injured tissue.

How do white blood cells rush to heal a wound? Remarkably, they use the same basic process that primitive organisms, such as [amoebae], use to move around.



White blood cells protect us from viruses, bacteria, and other invaders.

Shape-Shifting Amoebae

In a remarkable example of cell movement, single-celled organisms called amoebae inch toward a food source in a process called chemotaxis. Because they live, eat, and die so fast, amoebae are excellent model systems for studying cell movement. . . .

Peter Devreotes of Johns Hopkins University School of Medicine in Baltimore, Maryland, studies the molecular triggers for chemotaxis using bacteria-eating amoebae named Dictyostelia that undergo dramatic changes over the course of their short lifespans.

Individual Dictyostelia gorge themselves on bacteria, and then, when the food is all eaten up, an amazing thing happens. Tens of thousands of them come together to build a tower called a fruiting body, which looks sort of like a bean sprout stuck in a small mound of clay.

Devreotes and other biologists have learned that Dictyostelia move by first stretching out a piece of themselves, sort of like a little foot. This "pseudopod" then senses its environment for the highest concentration of a local chemical attractant-for the amoebae this is often food, and for the white blood cell, it is the scent of an invader. The pseudopod, followed by the entire cell, moves toward the attractant by alternately sticking and unsticking to the surface along which it moves. . . . Devreotes is hopeful that by clarifying the basics of chemotaxis, he will uncover new ways to design treatments for many diseases in which cell movement is abnormal. Some of these health problems include asthma, arthritis, cancer, and artery-clogging atherosclerosis.

Usman Bashir (CC BY-SA 4.0)

Dictyostelia can completely transform themselves from individual cells into a multicellular organism. Studies of these unique creatures are teaching scientists important lessons about development, cell movement, and cell division.

You've Got Nerve(s)!

The text is from the U.S. National Institute of General Medical Sciences.

What happens when you walk barefoot from the swimming pool onto a section of sun-baked pavement? Ouch! The soles of your feet burn, and you might start to hop up and down and then quickly scamper away to a cooler, shaded spot of ground. What happened?

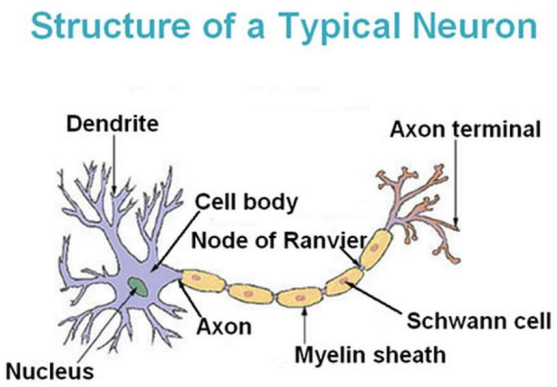


illustration of a neuron

Thank specialized cells . . . . Networks of connected cells called neurons make up your body's electrical, or nervous, system. This system works to communicate messages, such as, "Quick, move off the hot pavement!" Cells of the nervous system (specifically neurons) possess special features and a unique shape, both of which suit them for their job in communication. Or, as scientists like to put it, structure determines function.

Neurons have long, spindly extensions called axons that carry electrical and chemical messages. These messages convey information to your brain-"The ground is burning hot!"-and responses back from the brain-"Pick up your foot!"

To transmit these messages, charged particles (primarily sodium ions), jet across a nerve cell membrane, creating an electrical impulse that speeds down the axon. When the electrical impulse reaches the end of the axon, it triggers the neuron to release a chemical messenger (called a neurotransmitter) that passes the signal to a neighboring nerve cell. This continues until the message reaches its destination, usually in the brain, spinal cord, or muscle.

Most neurons can convey messages very fast because they are electrically insulated with a fatty covering called myelin. Myelin is formed by Schwann cells-one of the many types of glial cells that supply support and nutrition to nerve cells.

Nerves coated with myelin transmit messages at a speed of about 250 miles per hour, plenty of time for the message to get to your brain to warn you to lift your foot before it burns.

One reason young children are at a higher risk for burning themselves is because the neurons in children's bodies do not become fully coated with myelin until they are about 10 years old. That means it takes dangerously long for a message like, "The stove is hot!" to reach a young children's brains to tell them to pull their hands away.

Myelin formation (and consequently the conduction of nervous system messages) can be disrupted by certain diseases, such as multiple sclerosis. Symptoms such as numbness, double vision, and muscle paralysis all result from faulty nerve conduction that ultimately impairs muscle cell function.

Rise Up

by Stephen Fraser

A treatment enabled a paralyzed man to stand and take steps again.

It was an evening in July 2006. The Beavers, Oregon State University's baseball team, had recently won the College World Series. One of the team's pitchers, Rob Summers, 20, was retrieving his gym bag from his parked car when another car hit him. "The car then drove off, leaving me there with no help," says Summers.

Courtesy Rob Summers

The impact rendered Summers *paraplegic*-unable to move his lower body. His doctors told him he'd never walk again-hard news for an active young man to hear.

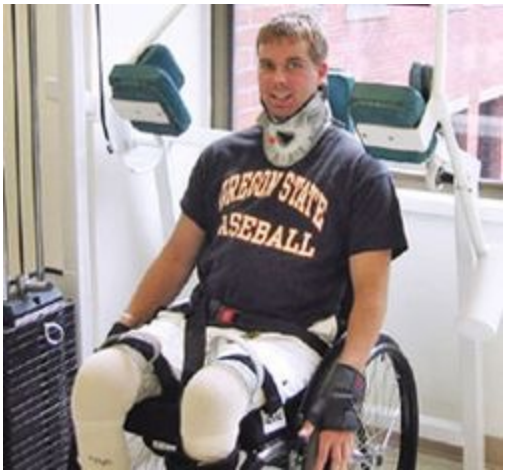
"They told me that I had no hope," says Summers. "My comment was, 'You don't know me very well. I'm going to fight until I get well again.'"

Five years later, Summers regained the ability to stand and could take steps on a treadmill. His recovery "remains unprecedented," European researchers commented in the British medical journal *The Lancet.* "We are entering a new era."

Information Highway

The car that hit Summers seriously injured the lower part of his *spinal cord*-the column of nervous tissue that runs through the backbone. It carries messages to and from the brain, the body's central

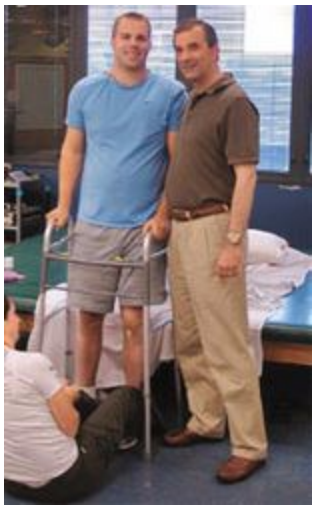
organ. Radiating outward from the spinal cord is a web of *motor neurons,* which govern movement. The damage done to Summers's spinal cord stopped the brain's messages from reaching many of the motor neurons in his lower body, preventing him from standing or walking.



Courtesy Rob Summers

Rob Summers after the accident that rendered him a paraplegic.

After the accident, Summers underwent two years of standard therapy-muscle massages, lessons in how to use a wheelchair, and the like. Before then, little more could be done for paraplegic patients. Summers had the good fortune, though, to be chosen for an experimental research project. "Rob was an ideal candidate," says one of the project's researchers, Susan Harkema, a professor of neurosurgery at the University of Louisville in Kentucky. "He was young and in otherwise good health. He's also a very determined, disciplined person -an extraordinary young man."



Courtesy Rob Summers

Summers stood with his father, Mike Summers.

In a four-and-a-half-hour operation, the research team implanted electrodes in Summers's spinal cord. The electrodes were then wired to a pulse generator that was implanted in his back. The pulse generator is remotely controlled by a device outside the body.

Body's Wiring

After the surgery, Harkema and her team began the treatment. They switched on the pulse generator for two hours a day, electrically stimulating the nerves in his spinal cord. Nerves can respond to electrical stimulation because the messages they carry take the form of electric signals. Nerves are the body's "wiring."

On the third day of electrical stimulation, Summers was able to stand with assistance. "It was unbelievable," he says. "There was so much going through my head at that point. I was amazed; I was in shock."

By 2012, Summers could not only stand but also could walk slowly on a treadmill with the aid of an assistant and a supporting harness. He was able move his hips, knees, ankles, and toes voluntarily. The exercise had enabled his leg muscles to regain some of their former mass.

Sensory Signals

The brain does more than just control movement. It receives messages from all parts of the body. Many of the messages come from the eyes, ears, nose, skin, and muscles. Those messages travel by way of the *sensory neurons.* Summers's spinal cord wasn't totally damaged. It could still receive limited sensory signals from the muscles in his lower body.

That residual feeling in his lower body might be what enabled the experimental treatment to succeed, says Harkema. Sensory messages from the legs might have been traveling to Summers's electrically stimulated spinal cord, prompting it to send signals along the motor neurons and make the legs move.

"Our big finding is that the spinal cord is as sophisticated as the brain," says Harkema. "It has a memory. When you walk, it remembers that you are on two legs or one. The spinal cord basically takes information from the brain and then handles all the details. We didn't know that before."

Patients who don't have some physical sensation, as Summers does, may not be helped by the treatment, says Harkema.

Body Control

Spinal cord damage can do more than impair limb function. Victims can lose bladder and bowel control. Those functions are regulated by another part of the nervous system-the *autonomic nervous system*-that

radiates from the spinal column. It controls automatic processes in the body, such as heart rate, blood pressure, sweating, and salivation. Summers has regained function in his bladder and bowels. He also has been able to discontinue a variety of expensive medications prescribed to alleviate pain and prevent heart disease.

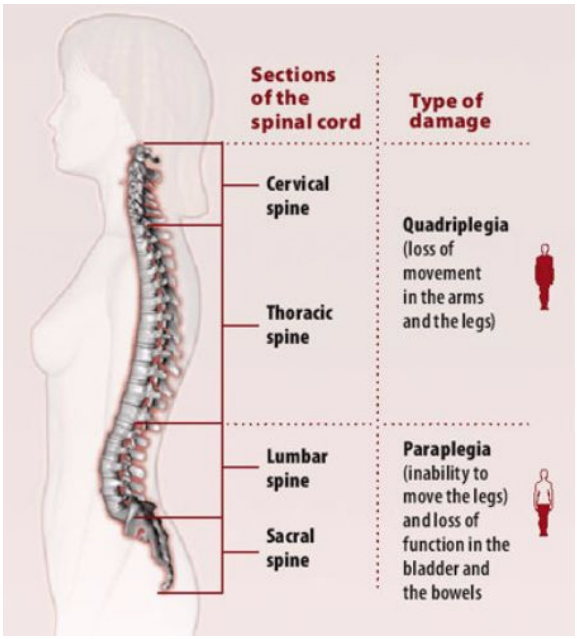
"Now I can stand," says Summers. "I've gotten my confidence back to just go out in public." His goal is to stand and walk completely normally. "I'm working toward that every day."

Frazier Rehab Institute; Courtesy Rob Summers

Monitoring Summers' Leg Movements Right: Neurosurgeon Susan Harkema

Broken Cord

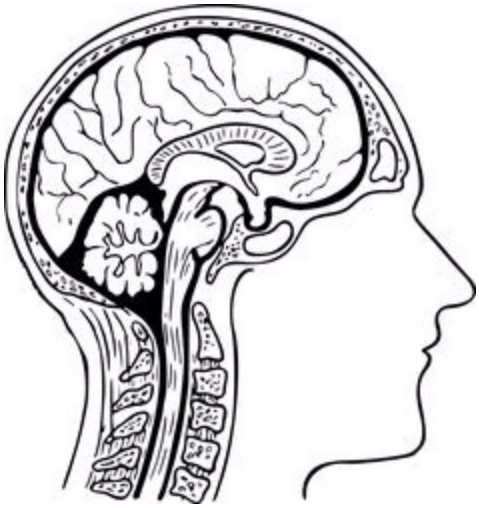
The spinal cord carries nervous signals back and forth between the brain and the rest of the body. An injury to it can cause a complete or partial loss of function depending on the severity of the damage.



KRT/Newscom

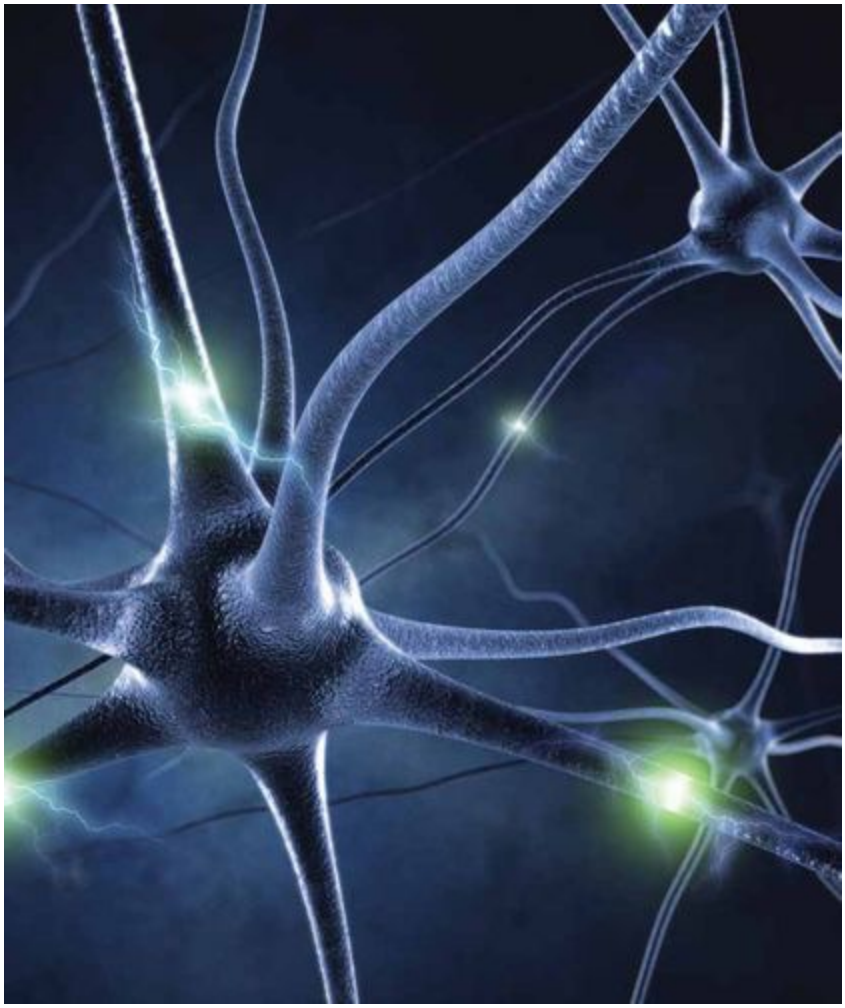
Neurologists

by ReadWorks



Head anatomy

The brain is a complex and important organ with many different jobs. The brain controls every other organ in the body. For example, the heart pumps and the lungs breathe because the brain tells them to. The brain also stores memories. The brain allows people to remember things that happened to them in their past, like special events. It also helps people build muscle memory. An example of building muscle memory is practicing an instrument. If a piano player practices the piano every day, her finger muscles will remember the movements in the future. The brain is the organ behind that muscle memory!



Core Knowledge

Representation of neuron

The brain also changes all the time. Neurons are the cells of the nervous system and there are around 100 billion neurons in the human brain. The brain changes as its neurons create new connections. When a person is learning a new skill, his or her brain's neurons connect with each other. These connections get stronger with time and practice. Reading, writing, and speaking are all possible because of connections between neurons. Do you remember when you first learned to read? It was much harder to read. Your brain's connections were not strong yet. Now, reading is much easier because you have strengthened those connections with practice. Every time you read a word, you are exercising your brain!

Photograph of girl reading a book

Neurologists make sure that the brain's connections are working properly. Neurologists are brain doctors, and they use machines to see what is happening inside of the brain. Neurologists can see which connections in the brain are working and when. If a patient is speaking, certain connections will be working. If a patient is moving his or her leg, different connections will be working. Neurologists can also see if connections are not working. This helps them to figure out what is wrong with a patient.