Biotechnology is spending time and money on trying to figure out why kids and adults are heavier, on average, than previous generations. Heavy teens often become heavy adults, and those who weigh 40 percent more than their ideal weight are prone to health problems, making health officials and policymakers anxious. To help combat obesity, biotech researchers are figuring out what parts of the human genome control weight, developing ways to control weight, and searching for treatments to deal with obesity-related illnesses, such as diabetes.

In this issue of Your World, we take a closer look at biotechnology’s involvement in the complex issue of obesity. Keep in mind these main points:

- Obesity has genetic components.
- Biotechnology is exploring the human genome for ways to control weight.
- Nutrigenomics might help us choose our diets based on genetic makeup.
- Regardless of your genes, eating and exercising carry a lot of weight in how heavy you’ll be as an adult.

As always, we hope you enjoy the magazine. We also hope it inspires you to choose a career in the exciting world of biotechnology.

**ADIPOSE TISSUE (FAT CELLS)**

Fat plays important roles within our bodies. We store energy in the form of fat, which acts as a nutritional reserve. Fat also absorbs shocks to protect internal organs, insulates our bodies against cold, and in some cases, produces heat.

**HOW FAT IS PROCESSED FROM FOOD**

1. **Food containing fat enters the stomach.** Stomach acid helps prepare food for the digestive process that takes place in the intestines. Most fat in food exists as triglycerides.

2. **Once in the intestines, bile salts from the gallbladder help break up large droplets of fat into smaller particles.**

3. **The fat particles are broken down further by special pancreatic enzymes called lipases.** The resulting fat cell component—glycerol and fatty acids—are small enough to be absorbed by intestinal cells.

4. **In the intestinal cells, triglycerides are formed and coated by a protein. These are called chylomicrons. The coating helps them dissolve faster in water. Too big to pass through capillaries, the chylomicrons enter the lymphatic system, where veins provide access to the bloodstream.**
we each crave, and how each body responds to exercise and diet.

Our understanding of how genes affect weight gain is still in its infancy. The first fat-regulating gene, leptin, was discovered only 11 years ago. Today, researchers estimate that up to 340 different genes are involved in determining weight. Differences in these genes may account for 50 to 70 percent of the variations in obesity among the people around us.

THE SIZE OF THE PROBLEM

The number of obese Americans has doubled over the past 20 years to nearly one out of every three adults. While there is no accepted definition for obesity in adolescents, about one out of seven American adolescents is considered overweight. Researchers have been trying to figure out why so many people are now heavier.

The most common measure of obesity for adults is the body mass index (BMI), the ratio of weight divided by height squared. (To find your BMI, multiply your weight in pounds by 704.5 and divide by your height in inches squared.)

A BMI above 25 is defined as overweight, above 30 as obese, and above 40 severely obese. A man 5 feet, 6 inches tall, for example, would be overweight at 155 pounds, obese at 186 pounds, and severely obese at 247 pounds.

Bmi FOR CHILDREN AND TEENS:
http://www.cdc.gov/nccdphp/dnpa/bmi/bmi-for-age.htm

Health officials have long linked BMIs above 30 with increased chances of high blood pressure (which may cause a stroke), heart disease, diabetes, and even some relatively rare types of cancer.

Yet some of these links are being rethought today. While few doubt severe obesity leads to illness, medication and exercise allow many obese people to live healthy lives. In fact, recent surveys suggest that adults who are moderately overweight are likely to live longer than those in the “healthy” weight category. Claims in a report from the Centers for Disease Control and Prevention that 300,000 Americans die prematurely from obesity in 2005 are now thought to be an underestimate; and women’s necks are less than 34 cm (13.4 inches) around.

Researchers are turning to biotechnology to understand the genetic mechanisms that cause obesity and affect health. Genetics is a powerful tool for tracing how the parts of the metabolic system interact with one another. By mapping these mechanisms, researchers hope to one day explain how people like Danielle Alvarado remain thin on diets that fatten the rest of us—and develop treatments for obesity-related diseases and perhaps even obesity itself. Keep reading this issue of Your World to find out more details! —Alan Brown
What makes people obese?
The simple answer is that our bodies are wired to put on fat. When humans had to hunt and forage for food, daily meals were never a sure thing. Our bodies evolved to consume rich foods high in calories and store the excess energy as fat. When food was scarce, we burned fat for energy. Today, where daily meals are a given and high-calorie foods are plentiful, our bodies still behave as they did thousands of years ago: they tell us to eat rich foods and store the excess calories as fat.

So why don’t we just keep getting fatter?
It turns out that every body has a target weight range and will regulate itself to remain there. Obesity researchers typically find their subjects have difficulty losing or gaining weight. When they eat more calories, their metabolism speeds up and they burn more calories; when they eat less, their bodies turn down the heat.

This regulatory system works so well, adults in the Western world gain only about 0.5 to 1.0 pound annually. This is equivalent to eating one more Ritz cracker per day than the body can metabolize.

Yet some people remain thin and others grow obese. This has to do with their genetic programming: some people are genetically disposed to store fat more easily than others.

Scientists know this because they found a way to separate the influence of genes from such environmental factors as eating and exercise habits. They investigated identical twins adopted by different families. Since the twins had identical genes, only their environment differed. In terms of obesity, the twins more closely resembled each other than the families that brought them up. These studies suggest that 40 to 70 percent of their obesity was inherited.

Unfortunately, our understanding of the genetics that regulate obesity is still sketchy. Only in the past decade, starting with the identification of the gene that makes the hormone leptin, have scientists begun to unravel how the body regulates fat storage. While hundreds of genes play a part in this complex process, only a few of the chemicals they make have major roles.

Insulin is one of them. The pancreas makes insulin when it detects the presence of the sugar glucose from food. The body treats glucose as pure fuel, and insulin regulates how fast its cells burn or store that fuel.

A second hormone, leptin, is produced in fat cells. It signals that the body has stored
energy as fat. When leptin levels rise high enough, they suppress appetite. They also work with insulin to regulate metabolism. Babies born without the ability to make leptin are constantly hungry and become severely obese.

Scientists are currently investigating about 60 chemicals that help control weight gain. Ghrelin, for example, is the most prominent of more than 20 chemical agents that make us hungry. Ghrelin rises between meals and declines when insulin and leptin levels rise.

Evidence suggests that imbalanced diets may interfere with chemical processes that tell us when we’ve had enough to eat or possibly even what to eat. Eating fat, for example, does not reduce ghrelin levels—and appetite—as fast or as much as eating protein or sugar. Fructose, a sugar commonly used to sweeten soda and baked goods, does not suppress hunger as well as glucose, a product of bread and starch digestion. Rats fed fatty diets grow less sensitive to leptin over time.

The more scientists dig, the more metabolic mysteries they unearth. They have found that obese people lose their sensitivity to leptin, but cannot explain why. They know that many obese people fail to produce enough insulin and become diabetic, yet cannot explain how this happens.

Clearly, we are genetically programmed to put on fat. Yet we are years away from understanding why one person gains weight on the same diet that leaves another slim.

—Alan Brown

**Mighty Mouse**

Scientists believe that 100 or more genes make agents that control obesity. Each one interacts with other body chemicals in countless ways. The only way to unravel those mechanisms is to eliminate one gene at a time and observe what happens.

Since 1987, scientists have been able to do this by “knocking out” genes in mice. The results have given us new insights into obesity. In 1999, Canadian researchers knocked out the gene that makes the enzyme PTP-1B. The modified mice resisted weight gain even when fed a very high-calorie, high-fat diet.

The same proved true when University of Wisconsin scientists knocked out the gene that produces SCD, an enzyme that helps mice make body fat. The change also boosted mouse metabolic rates.

In 2005, Washington University researchers modified the ability of skeletal muscle to metabolize fat and created mice that can grow fat but resist diabetes.

In each case, scientists hope to develop drugs that target these enzymes in order to fight diabetes and obesity.

—A.B.
Hold the soda! It may taste good now, but soda pop is one of the biggest contributors of calories—as sugar—to the average American diet. And too much of it increases the risk of gaining weight and developing diabetes later in life, according to a study of 91,000 nurses out of the Harvard School of Public Health.

Sugar itself is not bad. In fact, it’s the basic source of energy for your body. Without it, your cells would not produce energy. Sugar in the bloodstream stimulates particular cells, called beta cells, to produce insulin, which increases the flow of sugar from the bloodstream to muscles and other cells to be used as fuel. Insulin also tells the liver to take sugar out of the bloodstream to store for later use. When sugar levels fall, insulin levels fall and levels of something called glucagon rise, signaling the liver to release sugar.

Types of Diabetes

In type 1 diabetes, the body’s immune system destroys the insulin-producing beta cells in the pancreas. With type 1 diabetes, people get insulin through shots or a pump so they can process sugar.

In type 2 diabetes, the body produces insulin, but not enough or the cells can’t use it well. Of people with diabetes, 90 to 95 percent have this type. Type 2 has been more common among people over 50, but is now occurring more often in younger people. Obesity and lack of exercise are major risk factors for this type of diabetes. Genetic factors may also play a role.

Diabetes can be controlled, but even well-controlled diabetes has consequences. Diabetes affects blood glucose levels, making them too high or too low. When this happens, you might feel sleepy, dizzy, confused, or have blurred vision.

This may not be serious when you’re listening in class, but it could be fatal when you’re driving. If your blood glucose level is too low, you might make bad choices, not focus on your driving, or lose control of your car. Long-term complications can lead to blindness, heart disease, kidney disease, and even amputation.

Biotech Possibilities

Researchers in Chicago believe the scientific community knows enough now to treat most diabetes patients with therapies that involve changing cells themselves, cell-based therapy. They have formed an international project focused on a cure for diabetes in five years.

Factoid

About 18.2 million Americans, or 6.3 percent of the population, had diabetes in 2002, and the numbers are rising. Lifestyle patterns you’re setting now, as well as genetics, may lead to or lower the risk you’ll get diabetes.

Making Transplants Easier

A current but very difficult treatment for diabetes is to transplant a pancreas or its beta cells. Beta cells are part of the endocrine system and produce insulin. The transplant attempts to replace cells destroyed by the immune system. The beta cells can sometimes be injected so they lodge in the liver and produce insulin. But it is difficult to keep the immune system from continuing to destroy the new beta cells, too. In April 2005 for the first time doctors transplanted beta cells from a live donor, a mother to her daughter. Biotechnologists are developing immunosuppressive drugs to prevent the body from destroying its own beta cells. Gene therapy genetically modifies beta cells before transplantation to protect them from the immune system. — L.V.
Cell-based therapies being researched include manipulating different kinds of cells to produce insulin. This is possible because every cell has the same genetic information as all other cells; each cell “turns on” a different part according to the kind of cell it is. Currently, advanced medical treatments can sometimes transplant insulin-producing cells into the body, but many of these cells die or are rejected. Other gene therapy includes modifying these cells before transplantation so fewer die.

In type 1 diabetes, the immune system destroys many components of the insulin-producing beta cells in the pancreas. An arm of biotechnology called immunogenetics concentrates on interfering with the processes that destroy these cells. Genetic studies are testing members of families with diabetes for genes that increase susceptibility or that protect against diabetes. This type of screening led to the discovery of insulin-producing cells in the thymus, where insulin might be used to help train or screen maturing immune system cells to recognize “self” versus “other,” a critical area of malfunction in autoimmune diseases. These cells have also, unexpectedly, been found in fat and bone marrow cells.

In other areas of biotech, molecular biologists are studying how to interfere with the signaling proteins on islet cell surfaces that make them susceptible to attack by the immune system.

In bioinformatics, researchers are using computers to manipulate complex genomic information to model a non-obese diabetic mouse in researching type 1 diabetes.

Researchers in biotherapeutics are developing such treatments as
- antibodies that protect insulin-producing cells from immune system attack;
- drugs that stop the immune system from destroying cells or make cells more receptive to insulin;
- a new drug modeled on the saliva of a Gila monster that stimulates insulin production.

Biotechnologists have isolated the active compounds in plants that help the body process glucose, a type of sugar. Drug makers are even developing insulin powder that people would inhale rather than inject. Bioengineering applies engineering principles to sensors for administering insulin or monitoring blood sugar levels.

Bioengineering is also applied to treating complications from the disease such as blindness. Tiny electrode arrays on a thin sheet of silicon make artificial retinas for diabetics who are blind.

People working in biotechnology are among those trying to prevent and treat diabetes, a disease that is an increasing concern as more people get too heavy.

—Linda Voss

Insulin Production in a Beta Cell in the Pancreas. Mitochondria (which provide cells with energy) are green, and the nucleus is purple. The folded membrane below the nucleus is the endoplasmic reticulum, which divides the cell into compartments. Insulin made in the cell is packaged in secretory granules (blue balls in pink saucers). These migrate through the cell and are secreted directly into a blood capillary (bottom, containing red blood cells).
People come in all weights and sizes. Some eat but never gain a pound and others seem to gain weight by looking at a piece of pizza. So what causes some people to be overweight?

Researchers are looking in many directions—at brain chemicals that make us hungry or crave food, at gut chemicals that regulate digestion or feelings of fullness, at ways to make our bodies burn more fat as energy, or how to prevent the body from absorbing fat.

Most available weight-loss medications suppress appetite by altering chemical processes in the brain to block feelings of hunger. One prevents the stomach and small intestine from absorbing some of the fats eaten. Unfortunately, these medications are limited to very overweight or obese people; some carry the risk of addiction or other unhealthy side effects or diarrhea, flatulence, and other intestinal problems; and all but one are meant for only short-term use.

The quest for new anti-obesity drugs marches on. Scientists developed a drug, now in late-stage testing, to block the action of certain brain cell molecules—cannabinoid receptors—that cause people to crave food. Overweight people who took this cannabinoid-1 (CB-1) receptor antagonist during clinical trials lost more weight than people not taking it. The drug may be available in 2006.

Another compound in late-stage testing is ciliary neurotropic factor (CNTF). This genetically engineered version of a human
Eating Disorders

Obsessing about weight may cause bad habits such as eating too little and exercising too much (anorexia nervosa), or throwing up after meals (bulimia). Doctors treat eating disorders by changing how patients look at themselves, fixing their eating habits, prescribing antidepressants, or some combination. Biotech scientists are even experimenting with reactivating parts of the human growth hormone molecule associated with burning fat.

While studies continue in people, laboratory scientists study genes associated with obesity and fat cells in mice to try to understand how genes and fat cells work in people.

One thing is sure: healthy eating habits and regular exercise control weight gain. Only continuing research will identify the most beneficial medications to help people who cannot control their weight through diet and exercise.

—Joene Hendry
How is biotech addressing the “diet” part of living healthfully?

Any two humans, no matter how far removed geographically, have about 99.9 percent of their DNA in common. This close relatedness is what makes us a single species—a species, after all, is just a group of organisms that can reproduce with one another. Yet, the tiny fraction of our DNA that varies from one person to the next can determine a lot—everything from physical features such as height and skin color to less obvious characteristics, such as how well each body uses the vast array of substances present in food for energy.

The science of sorting out what each of us should and should not eat is known as **nutrigenomics**, or nutritional genomics. This kind of personalized nutrition seeks to provide a molecular understanding for how what we eat (i.e., nutrition) affects health by changing an individual’s genes, what the genes produce (express), or both. Scientists who do research in this field have discovered, perhaps not surprisingly, that there is no one-size-fits-all diet. While the field is still young, it’s possible that some day a test will screen a child for hundreds of possible gene variants and that this information will help her choose what she will eat for the rest of her life.

Before that day arrives, scientists have a lot of work to do to discover all the genes that might be relevant to a person’s diet. Some of these traits we have known about since long before genetic tests were invented. For example, nine out of 10 adult Asian Americans will get sick if they drink milk. That’s because members of this population lose their ability to produce lactase, the enzyme that digests lactose, a sugar present in milk, soon after they reach the age at which they would typically be weaned from their mothers’ milk. Now, a test can tell us which people will get sick—without making them drink any milk.

Other traits, such as how individuals respond to fat and cholesterol in their diets, have only recently been linked to specific genes. Heart disease is the biggest killer in the United States, so any advance that can help us understand why some individuals can tolerate a given amount of fat in their diet while others cannot could help save millions of lives.

Scientists will also need to gain a better understanding of the reciprocal relationship between food and genes—that is, not just how genes affect what we should eat, but also how what we eat affects our genes. While good examples of this phenomenon are hard to come by in humans, studies in mice suggest that mothers who don’t consume enough nutrients can change the methylation of their own DNA. **Methylation** is a chemical change that adds a methyl group (a carbon and three hydrogen atoms) to a specific place on your DNA, and methylation is one of the ways our bodies turn on and off genes during the course of our lifetime. Intriguingly, these changes may even be passed on to a mouse’s offspring.

A handful of companies have already begun offering genetic screens for gene variants known to be linked to everything from heart disease to...
Bioengineering Healthier Food

Fish are rich in omega-3 fatty acids, which are increasingly recognized as a “superfood” that appears to boost everything from heart health to mood. Unfortunately, many of the fish rich in omega-3s are either quickly disappearing from the oceans or contain worrisome levels of mercury, or both. Enter a Harvard research team led by Dr. Jing Kang, who has figured out how to use genetic engineering to insert a gene for an enzyme found in C. elegans into mammalian cells that lack the enzyme to convert omega-6 fatty acids into omega-3 fatty acids. They have created transgenic mice expressing the omega-3 enzyme (desaturase). The technique might some day be applied to livestock, yielding heart-healthy steaks and, perhaps more importantly, adding to the handful of natural sources of this valuable nutrient. —C.M.

C. elegans. The Caenorhabditis elegans nematode worm is a soil-dwelling bisexual organism. One of its enzymes can help mammals produce healthful omega-3 fatty acids.

SINCLAIR STAMMERS/SCIENCE PHOTO LIBRARY
How Low Should You Go?

You can’t watch television these days without seeing news about childhood or adult obesity. Schools throughout the nation are banning junk foods and sodas high in sugar to reinforce good health and diet practices. The federal government even has sent researchers to West Virginia to try to understand why its residents have such a high obesity rate. Nutritionists and doctors continue to champion better nutrition and more exercise for today’s overweight youth and adults. To help in the struggle to lose excess weight, the biotechnology and pharmaceutical industries also are busy developing anti-obesity drugs. The stated goal is to avert the adverse health consequences, such as heart disease and diabetes, that can occur with extra weight and poor diet. But when might it be appropriate to use diet and exercise only or anti-obesity drugs that are available—or both—in people? And in a culture fixated on the pursuit of being as skinny as models and TV stars, some people might use drugs to meet artificial standards of weight rather than health goals. Here are some cases to consider as you think about which interventions might best be used.

Case 1

John G. is 7 years old and has Prader-Willi syndrome, a condition that causes him to be overweight. Characterized by compulsive eating and an obsession with food, the disorder often begins before age 6. Problems in the hypothalamus, part of the brain that regulates appetite and satiety, are believed to cause the disease. His parents must strictly supervise his eating and even lock the kitchen and food storage areas at home. Weekly, John sees a child psychiatrist to help him cope.

Question 1

What if a drug could be developed that would curb John’s appetite, allowing him to live a life not subject to continual food monitoring by his parents and other adults? Should he get it?
Mary H. is 11 years old and 25 pounds overweight. Her mother, father, and brother also are overweight. No one in the family eats healthfully. The parents give their children money for breakfast at fast-food restaurants. At school, the fare also is high in carbohydrates and fat. For dinner, the family often orders pizza. Family time is spent watching television eating! The cupboards are filled with potato chips and cookies. They eat very few fruits or vegetables. Mary, near puberty, has decided she wants to lose weight and hopes to help her family do so, too. She has tried to eat salads and exercise, but it is hard for her to keep weight off when others in her family have not changed their eating styles.

Frank W. is 14 years old. He is athletic, handsome, and a good student. Unlike others at his school, he understands proper nutrition and physical exercise in maintaining his weight. Most of the time, he is careful about what he eats and works out to keep in shape. On some weekends, though, Frank likes to indulge in eating frenzies, wolfing down cheeseburgers, fries, ice cream, and candy. By Monday, he often has gained some weight. To lose the extra pounds, during the rest of the week, he cuts back heavily on calories, sometimes to the point of not eating enough food and feeling faint.

Frank finds out a new anti-obesity drug might make it easier for him to quickly lose the extra weight he gains on those overindulgent weekends. He tells his parents he wants to see a doctor to get a prescription for the medication because he is afraid he will get fat. Should the doctor give it to him?

—Robin Eisner

What if Mary can convince her family to see a physician so they all can start a prescription regimen for a new anti-obesity drug? Should they all start on a drug or should a diet and exercise program be the goal?
The mice in Jeffrey Friedman’s laboratory aren’t your ordinary rodents. They’re superfat, three times larger and five times fatter than other mice. And it’s a good thing they’re big, because Friedman’s career rests upon their shoulders.

Friedman attracted worldwide attention in 1994 when he figured out why this strain of mouse is so fat. By analyzing their DNA, he discovered that these mice lack a gene responsible for encoding a hormone that normally zips through the bloodstream and tells the brain, “Stop eating.” Friedman later found that another strain of obese mice lack the receptor in the brain designed to receive the “I’m full” message.

As a kid in suburban Long Island, Friedman wasn’t thinking, “I want to be a fat-mouse specialist when I grow up!” He wanted to become a doctor, like most of the scientifically minded kids in his neighborhood. So he did. After graduating from high school at 16, he earned a medical degree at 22. But while Friedman enjoyed caring for patients, he sensed a medical career would leave him intellectually hungry.

He spent the year 1980 working in a research lab, where he first encountered the obese mice. “They captured my imagination,” he says. “And I enjoyed science so much I decided to go back to school and get a Ph.D.” By 1986, he had a doctorate in molecular biology and his own lab at Rockefeller University.

Thanks to his discoveries, he now has the chance to help more people than any one physician ever could.

“There’s a popular view that obesity results from a lack of willpower or [from] fast food,” Friedman says. “While these things are clearly relevant, the evidence shows that obesity is highly genetic—almost as inheritable as height.” The discovery of a powerful biological system operating under the conscious mind’s radar screen could help destigmatize obesity, he says.

His discoveries could also lead to an obesity treatment. Mice injected with the missing hormone —called leptin—lose weight like mad. They also recover from diabetes. These findings have sent the biotechnology industry scrambling to come up with an obesity drug that would do the same for people.

In the meantime, Friedman has extended his own research to humans. He’s made three visits to a far Pacific island called Kosrae to study human obesity. Adapting the techniques he once used on mice, he is exploring the link between differences in DNA and differences in weight among these isolated islanders.

On a typical day, however, Friedman is in his New York lab. He spends most of his time writing and talking with people. Rather than conducting experiments himself, he oversees a lab consisting of the mice, 15 scientists, and a constantly rotating cast of high school, college, and postgraduate students.

Will Friedman’s seven-year-old twins follow in his footsteps? He says it’s too early to tell, although the girls enjoy visiting the mice. “What I do has some attraction for them,” he says with a laugh, “but it’s partly because they like the fact I’m boss.”

—Rebecca A. Clay
Leptin to the Rescue?

To complete this activity, a “Green Fluorescent Protein (GFP) Purification Kit” needs to be ordered.* A UV lamp with long wavelength is needed to see the green fluorescence.

A system of genes, proteins, and neurotransmitters controls how our bodies store fat—and this regulates what we weigh. This system tells our brains not only when we should eat, but also when we should stop eating. One of the proteins responsible is called leptin. Produced in our fat cells, leptin helps to send signals to the brain that we are full. Some researchers have hypothesized that leptin, discovered in 1997, may help us treat obesity.

Because obese mice injected with leptin lose weight, this protein looked like an easy treatment for obesity. However, scientists discovered that leptin made in the human body does not last very long. It would take leptin injections or leptin pills every hour to produce in humans the same results as in mice, making it very expensive and inconvenient!

To solve the problem, scientists are investigating the idea of genetically modifying leptin so that it will last many hours, or even days, in the human body. This involves genetically engineering bacteria to produce a new kind of leptin with amino acid differences that slow its breakdown in our bodies.

A Question about Leptin

Researchers have found that some obese individuals have high levels of leptin, while some other obese individuals have low levels of leptin. Based on what you know about this protein, how do you think both of these situations could result in obesity? An Internet or literature search can help you find additional answers.

Research a Cure

With the necessary kit, you can explore what it is like to be a researcher producing long-lasting leptin. Hydrophobic interaction column chromatography (HIC), a technique used in biotechnology to separate and purify proteins, will enable you to isolate a simulated modified leptin from an extract of bacterial proteins. HIC takes advantage of the fact that some proteins are more hydrophobic (“water hating”) than others; they bind to the chromatography gel and thus wash out of the HIC column less easily. As you lower the salt content of your solution, you will observe that the simulated modified leptin, which is more hydrophobic than the other bacterial proteins in your extract, remains in the HIC column longer than the less hydrophobic proteins.

First, your teacher will help you grow bacteria containing a simulated modified leptin, which has been tagged with a green fluorescent marker to make it easier for you to see. Now you are ready to follow these steps:

- In a microtube, centrifuge the enzyme-digested bacteria containing the simulated modified leptin for 10 minutes.
- While centrifuging, prepare your HIC column by adding 2 mL of equilibration buffer. Drain the buffer until 1 mL is left above the top of the gel matrix.
- After centrifuging, view the tube with UV light and note your observations on your data sheet.
- Transfer 250 uL of supernatant to a new microtube and label it “Modified Leptin.” Transfer 250 uL of binding buffer to the “Modified Leptin” microtube and then mix.
- Label three collection tubes 1, 2, and 3. Place the HIC column on top of Tube 1. In this tube, collect the 1 mL of buffer that is on top of the gel. Examine the column using UV light and note your observations.
- Take 250 uL of the solution from the tube labeled “Modified Leptin” and load it on the top of the column. Let this solution drip into Tube 1. Examine the column using UV light and note your observations.
- Transfer the column to Tube 2. Add 250 uL of wash buffer to the column and let it flow through the column into Tube 2. Examine with UV light and note observations.
- Transfer the column to Tube 3. Add 750 uL of TE (modified leptin elution) buffer to the column. Let the solution pass through the column and collect in Tube 3. Examine with UV light and note your observations.
- On your data sheet, note any differences in color among the three tubes and column at each of the three. Report whether you were successful in isolating your simulated modified leptin from the bacterial extract.

Investigate Leptin

- Design a study to determine if a genetically modified, long-lasting leptin could help obese individuals.
- What is your hypothesis?
- What control and experimental groups would you use to test your hypothesis?
- What variables would you need to control?
- What experimental results would you predict?

*See Teacher’s Guide online at <www.biotechinstitute.org>.
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