Reduce and Recycle
EXERCISE PROMPTS CELLS TO TURN UNWANTED PROTEINS AND CELLULAR JUNK INTO ENERGY.

Exercise is clearly beneficial, and now there’s scientific evidence that explains why time in the gym can help fend off diabetes—and potentially other diseases. According to HHMI investigator Beth Levine, cells break down cellular junk to get extra energy, thereby cleaning house while you exercise.

Cells use a process called autophagy to recycle unwanted proteins and cellular structures. During this process, a double membrane forms around the cellular garbage. An organelle called a lysosome then fuses with the membrane and its enzymes rush in to break up the unwanted cargo, yielding raw materials for producing new proteins or energy for the cell.

Scientists have long known that stress can trigger a boost in autophagy, as the process helps cells adapt to changing nutritional and energy demands. Levine, a physician at the University of Texas Southwestern Medical Center, suspected that exercise might have a similar effect because it also increases cells’ energy demands. To test this idea, she and her colleagues used transgenic mice whose cells produce a green glowing signal when autophagy occurs. After 30 minutes of running on treadmills, the mice showed increased autophagy in their heart and skeletal muscle cells as well as in their liver and pancreatic cells.

Next, the scientists created mice that could experience autophagy under normal conditions but were unable to ramp it up during exercise or starvation. In a paper published January 18, 2012, in Nature, the researchers report that these mice were unable to increase their muscle glucose uptake and had decreased endurance. And, unlike normal mice, exercise did not protect them against diabetes induced by a high-fat diet. During exertion in normal mice, an enzyme called AMP kinase helps cells take in more sugar from the bloodstream. However, this enzyme wasn’t activated in Levine’s mice. Several oral drugs used to treat type 2 diabetes work by activating AMP kinase, and it appears that autophagy induced by exercise does the same thing.

These findings suggest that increased autophagy may be the reason exercise protects against type 2 diabetes and other metabolic disorders. Levine also thinks it’s possible that activation of autophagy may contribute to other health benefits of exercise, including protection against cancer, neurodegenerative diseases, and aging.

In Brief
WHY YOU CAN’T CLONE A HUMAN
HHMI scientists recently discovered why a cloning technique called somatic cell nuclear transfer works in animals but not in humans. The study, done at the Harvard Stem Cell Institute, brings scientists closer to using stem cells to study disease and create healthy tissue.

Somatic cell nuclear transfer is a form of cloning in which the nucleus of an adult cell is transferred into another cell—usually an unfertilized egg—whose nucleus has been removed. When the recipient cell divides, it creates daughter cells that are genetically identical to the donor. To date, the technique has not successfully been used in human cells.

HHMI early career scientist Kevin Eggan and HHMI investigator Doug Melton attempted to tackle this problem using single-celled embryos donated by couples undergoing fertility treatment, rather than unfertilized eggs. When they transferred DNA into the embryos, development continued though its early stages but came to a halt after four days. The same technique in mouse embryos produced stem cells within hours. The reason for this difference, the scientists report in the October 4, 2011, issue of Nature Communications, is that the human cells failed to turn on the genes in the transferred nucleus. It’s not clear what prevents this essential activity from occurring in the human cells, but Eggan says his team’s finding could eventually help make nuclear transfer a viable option.

PATTERNING FLIGHT FOR FOOD
When a fruit fly gets a whiff of a rotting banana, it abandons its normal random flight pattern and assumes a more directed trajectory toward the food. According to HHMI early career scientist Mark Frye, this switch is coordinated by a particular area of the brain that integrates smell and visual information.

Frye and his colleagues at the University of California, Los Angeles, showed that a fly normally has some variability in its flight path, ignoring the visual world to an extent. When it smells food, however, the fly switches to a visual path that will quickly take it to its next meal. But, as they report in the October 19, 2011, issue of the Journal of Neuroscience, when a region in the brain called the mushroom body is blocked, the flies no longer change their visual flight patterns in response to food odors.

The mushroom body has been implicated in smell processing in other organisms. But it’s most commonly been associated with learning and remembering smells. Flies, which don’t return to where they were born or to a home base, have less need for this type of learning. So it’s not surprising, Frye says, that the mushroom body has more diverse functions in flies.

ACTIVATING EMBRYONIC DEVELOPMENT
In nearly all animals, the newly fertilized egg initially relies on proteins and RNA from its mother to get through the first stages of development. Within a few hours, however, the embryo’s own genome kicks in and the process of development begins in earnest. New research by HHMI investigator Michael Eisen and colleagues suggests that a single protein called Zelda is largely responsible for driving this maternal-to-zygotic transition in the fruit fly.

Eisen and his colleagues at the University of California, Berkeley, knew that Zelda controlled the activation of a few genes expressed just before the maternal-