# Chronicle / *Lab Book*

## Hangry? Here's Why

*Scientists unravel why feeling hungry can also mean feeling angry.*

LET'S BE HONEST; dieting is rough. Hunger can deflate a dieter's spirit and render friends and co-workers unbearable.

Still, hunger is evolutionarily beneficial, as it signals when our bodies need food. Eating activates reward systems in the brain, but scientists have puzzled for decades over why our mood turns bleak when hunger hits.

Scott Sternson, a group leader at Janelia Research Campus, decided to tackle that question in mice. His team started by looking at the brain's agouti-related peptide (AGRP) neurons, which, when activated in mice optogenetically, elicit voracious eating.

The researchers presented well-fed mice with two flavored gels; the mice showed no preference for one over the other, and neither had nutritional value. Whenever the mice nibbled at one of the gels, scientists activated their AGRP neurons. Surprisingly, the mice began avoiding that gel.

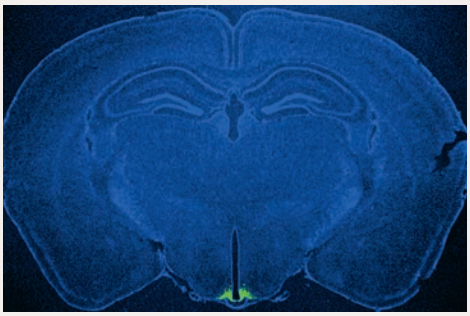
To further test the link, Sternson's team activated the AGRP neurons every time the mice went to a certain part of their cage. Sure enough, the mice began avoiding that area.

When the scientists peered into the rodents' brains, they observed that AGRP neurons are indeed active when the animals are hungry. But the neurons showed low activity during eating. In fact, they're inhibited as soon as food is sensed.

Thus, it appears that AGRP neurons encourage us to pursue food to avoid a state of physiological need for nutrients. Based on his team's findings, published April 27, 2015, in *Nature*, Sternson thinks the unpleasant feeling associated with AGRP activation prompts the drive to find food. This is important evolutionarily, as animals often face risks in seeking food. If hunger is unpleasant, animals are more likely to take that risk, ensuring their survival.

While that works for animals, it's tough on dieters. "When people try a weight-loss diet and find it to be unpleasant … it's pretty likely that the elevated activity of the AGRP neurons has something to do with it," Sternson says.

With that in mind, scientists are looking at how they might interfere with AGRP neuron activity. If the neurons behave similarly in humans, help in dropping those extra pounds may not be far off. *–Anzar Abbas*



***The brain's hunger-sensitive AGRP neurons (green) are responsible for the unpleasant feeling that drives us to snack.***

## IN BRIEF

### TEASING OUT NEURONAL FUNCTION

The brain holds a host of different kinds of neurons, each with its own job. Though you might think neuronal cells are highly organized, they are in fact intertwined in a colossal tangle. For scientists who want to study particular neuron types individually, teasing them apart is a major challenge.

Now, a team of researchers – led by HHMI Investigators Jeremy Nathans and Joseph Ecker, and Janelia Group Leader Sean Eddy – has devised a way to study individual cell types without getting mired in the tangle. Rather than trying to separate cells of a certain type from their neighbors, they've developed a way to isolate their nuclei. From there, they can study the cells' DNA, which provides information about the cells' activity and history.

"We weren't sure what to expect. This was an exploratory, discovery-level project," says Ecker of the study, published June 17, 2015, in *Neuron*.

But already, the method has revealed astonishing differences in cell types previously thought to be similar in function. "That means there's a lot of additional information here," says Ecker. Using the new technology, scientists will not only be able to delve even deeper into the secrets of the brain, but they might also gain greater understanding of other systems in the body as well.

### RADICAL VACCINE HAMPERS HERPES

The herpes simplex virus infects millions of people worldwide, yet the pathogen has for decades thwarted attempts to develop a vaccine.

Most efforts by scientists to create a herpes vaccine have focused on glycoprotein D (gD), a protein that triggers the production of protective antibodies. However, attempts to exploit gD in a vaccine have been futile.

"It was necessary to shake the field up and go another route," says virologist and infectious disease physician Betsy Herold. So she and HHMI Investigator William Jacobs, both at the Albert Einstein College of Medicine, joined forces to take a radically different approach.

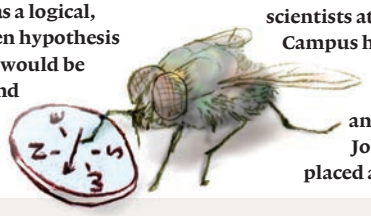
Instead of using gD, the researchers used a mutant strain of the virus lacking gD. "Once we had this mutant in our hands," says Herold, "it was a logical, scientifically driven hypothesis to say, 'This strain would be 100-percent safe and might elicit a very different immune response than the gD subunit vaccines that have been tried.'"

The study, published March 10, 2015, in *eLife*, tested the hypothesis in mice. The new vaccine completely protected the mice from the most common herpes infections, without any adverse effects.

If the vaccine works in humans as well as it does in mice, it could have a profound impact on the global prevalence of herpes.

### A COMPASS FOR FLIES

If you've ever made your way through a dark room, you've relied on neurons to help maintain your balance and bearings without vision. A fly's brain is much less complex than a human's, yet flies, too, can keep a sense of direction in the dark, scientists at Janelia Research Campus have found.



Group Leader Vivek Jayaraman and postdoc Johannes Seelig placed a tethered fly

Photo: Christopher Magnus, Illustration: Leif Parsons