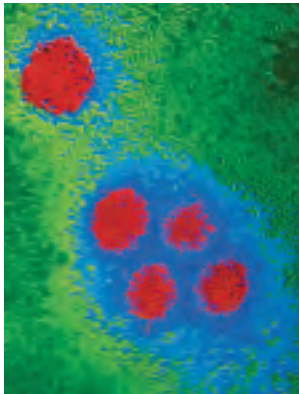


Viral Takeover

SCIENTISTS UNCOVER HOW SOME MOSQUITO-BORNE VIRUSES HIJACK CELLS TO REPRODUCE.

Dengue virus commandeers fat droplets inside cells in order to replicate and spread, new research shows. Using an anti-obesity drug that reduces the number of these fat droplets slows the spread of the virus, according to work by HHMI international research scholar Andrea V. Gamarnik and her colleagues.



Dengue virus particles (red) infect a cell (blue) in this electron micrograph.

Dengue virus contains a single RNA strand, which is replicated inside infected cells and then packaged into new viral particles. To figure out how the virus commands infected cells to do the packaging, the scientists tagged capsid proteins—found in the viral particles—with fluorescent labels. Under the microscope, the capsid proteins encircled fat droplets—sacs involved in producing and storing lipids.

Gamarnik’s lab group then mutated different parts of the capsid protein to determine which section was attracted to the fat droplets. When they mutated the middle region, the capsid proteins could no longer bind to the fat droplets and the virus’s spread slowed drastically.

To find a mimic for this viral slowdown, the researchers turned to a drug designed for treating obesity that decreases the number of fat droplets per cell. The drug worked to slow dengue—the number of new viral particles per cell dropped more than 100-fold.

“This is an interesting and new example of how a virus uses a specific organelle in the cell for its own purpose,” says Gamarnik. “It opens the door for new ways to think about antiviral strategies.”

Published in the October 2009 issue of *PLoS Pathogens*, the work also shows that dengue virus spurs the cell into making more fat droplets for it to use. Since other members of the mosquito-borne *Flavivirus* genus—including West Nile virus and yellow fever—share with dengue the use of capsid-encased particles to spread, Gamarnik thinks these other viruses may use the same mechanism.

■ —SARAH C. P. WILLIAMS

IN BRIEF

made incorrectly or not at all, and most disease-causing mutations are found in these regions.

Within hours of receiving the data, a postdoctoral fellow in Lifton’s lab had pinpointed a mutation known to cause congenital diarrhea. Doctors were able to tailor their treatment of the infant to this disease.

As sequencing genes becomes faster and cheaper, Lifton expects this approach will become more widely used. His techniques are described in the November 10, 2009, issue of the *Proceedings of the National Academy of Sciences*.

HEADS OR TAILS

Cut off the head of a planarian—a tiny flatworm—and it grows back within days. Remove its tail and a new one grows. Understanding the cellular pathways involved in the planarian *Schmidtea mediterranea*’s remarkable regeneration could lead to ways to regrow or repair damaged organs in humans. HHMI investigator Alejandro Sánchez-Alvarado has now uncovered a signaling pathway vital to planarian regeneration.

Sánchez-Alvarado’s team at the University of Utah decided to see what role the Hedgehog signaling pathway played

in planaria—in humans, the pathway is vital for ensuring proper placement of body parts during development. A search through the planarian genome found that, unlike in other worms, such as the commonly studied *Caenorhabditis elegans*, most components of the human Hedgehog signaling pathway also exist in planaria. So Sánchez-Alvarado and his colleagues used RNAi—which can selectively turn off genes—to silence planaria’s Hedgehog pathway. The planaria without Hedgehog, the researchers discovered, could regrow their heads but not their tails. Moreover, planaria with extra Hedgehog signaling grew tails in place of heads after the heads were amputated.

The results, published December 4, 2009, in *Science*, show that Hedgehog’s role in planarian regeneration is in establishing orientation along the head-tail axis. Further work could reveal what signaling pathways establish other lines of orientation.

THE TASTE OF CARBONATION

Drink from a bottle of sparkling water, and your taste buds immediately sense the carbonation. It’s not just the fizzy feeling on your tongue but a slightly sour taste that sets it apart from flat water. Researchers led by HHMI investigator Charles S. Zuker

have now identified the taste receptor cells, molecules, and neurons that recognize carbon dioxide.

Zuker and his collaborators had previously identified receptors for four of the five tastes: sweet, sour, bitter, and umami (savory taste). To study the taste of carbonation, they recorded activity from a major nerve in the tongues of mice as the animals ingested club soda, gaseous carbon dioxide, or carbon dioxide dissolved in a neutral solution. The taste system showed activity, confirming that the taste buds can sense carbonation.

To pinpoint which taste buds were at work, the researchers used mice engineered to lack different classes of taste cells. Mice lacking sour-sensing receptors couldn’t sense carbonation, they found. Testing various molecules within sour-sensing cells, the team homed in on the receptor necessary to taste carbon dioxide: a membrane-tethered enzyme called carbonic anhydrase (Car4). Mice without Car4 can’t taste carbon dioxide.

The findings, reported in *Science* on October 16, 2009, also explain why drugs for altitude sickness inhibit the ability to taste carbonation, a phenomenon known as “champagne blues.” The drugs block Car4.