

Jumping After Mobile RNA

SCIENTISTS REVEAL THE STRUCTURE OF RNA THAT CAN LEAP AROUND THE GENOME.

Not all RNA is content to inactively remain in linear genetic fragments. Some bits of RNA can break away, or self-splice, and invade other areas of RNA and DNA, driving the evolution of new genes. Now a group of scientists, led by HHMI investigator Anna Marie Pyle of Yale University, has determined the structure of one of these feisty stretches of nucleotides.

Unlike DNA—typically found in basic double helices—RNA frequently adopts intricate structures, folding back on itself, making loops and hairpins and globs. Predicting how any given bit of RNA will arrange itself is exceedingly difficult given the possibilities. And studying this type of mobile RNA—known as group II introns—presents its own problems because the RNA is often reluctant to jump when it's not inside a cell.

Therefore, Pyle and her colleagues first had to find one that would cooperate in a test tube. After screening group II introns from a number of organisms—the jumping RNA exists in almost all bacteria, and in some plants, fungi, and animals—the group identified an intron from a deep-sea bacterium that readily self-spliced in the laboratory.

They isolated the intron—once it had already hopped out of its spot in the genome but before it had barged into a new gene—and used x-ray crystallography to generate a detailed picture of its

structure. The results appear in the April 4, 2008, issue of *Science*.

They found that the RNA folds into a globular shape, with the active parts of the molecule—needed for the splicing—nestled inside. These active parts, they noticed, bear striking similarity to substructures in the spliceosome—a complex of RNA and proteins that normally removes unneeded sections from a strand of RNA before it is used to code for a protein.

“I had high hopes that we would learn a lot from this molecule about the way RNA folds,” says Pyle. “And indeed, it really surprised us about the kind of structures that RNA can adapt. This was a treasure trove of structures.” ■ —SARAH C.P. WILLIAMS



The tertiary structure of the intron, with the active center of the molecule in red.

IN BRIEF

properties for a protein to gain entry into a compartment of a malaria parasite. The compartment—a plastid—is essential for the parasite's survival. Interfering with it could be a way to kill the parasite. The plastid is guarded by a cellular gatekeeper though, which lets only certain proteins inside.

Using a computer program, the researchers looked for similarities among the 500 or so proteins that the gatekeeper allows in. They found that all the proteins are at least 24 amino acids long, are positively charged, and include the two amino acids asparagine and lysine. So the researchers designed new proteins fitting this description. They reported in the March 25, 2008, online edition of the *Proceedings of the National Academy of Sciences* that, as long as the proteins fit the guidelines that the computer predicted, they were able to sneak into the malaria plastid.

“There is potential to use this relative lack of sophistication in the system as a way to confound [the parasite],” says McFadden.

HOW FLIES SENSE CARBON DIOXIDE

Carbon dioxide—an odorless, tasteless gas to humans—is an important messenger in the insect world. HHMI scientists have

uncovered hints as to how flies evolved specialized neurons for sensing carbon dioxide.

The researchers, led by Lawrence Zipursky, an HHMI investigator at the University of California, Los Angeles, were examining flies for an unrelated study when they noticed a peculiar fly under the microscope. Most fruit flies have carbon dioxide-sensing neurons only in their antennae, but this fly also had the neurons in the part of the nose called the maxillary palp.

Looking closer at the mutant fly, they found that the unusual neurons expressed both carbon dioxide-sensing receptors and another receptor for other odors typically detected by neurons in the maxillary palp. And following the path of the neurons revealed that they led to two areas in the brain—responsible for interpreting the two senses.

The researchers then found the genetic mutation responsible for the mixup. It codes for a short stretch of RNA—called a microRNA—that can regulate the translation of genes in neurons. Zipursky thinks the hybrid neuron they stumbled on, and the gene responsible for it, represents an evolutionary intermediate that could have preceded the fly's specialized carbon dioxide-sensing neurons.

“It really is an interesting issue from an evolutionary perspective,” he says. The research appears in the February 29, 2008, issue of *Science*.

DIVERSITY OF THE HUMAN GENOME REVEALED

By comparing nine human genomes, scientists have produced the first high-resolution map showing the structural variation between individual genomes. Much genetic research focuses on identifying small differences within single genes that can make a person more susceptible to a disease. But a team of researchers led by HHMI investigator Evan E. Eichler at the University of Washington was curious whether an approach could be developed to systematically discover and sequence larger structural differences between people's genomes: insertions, deletions, duplications, and inversions of large chunks of DNA.

Their comparison revealed that these larger differences are extremely common. In various parts of the genome, some people have segments that others don't. In other areas, large genetic regions may be flipped. Across the nine genomes, the researchers found 1,695 regions with these differences—all longer than 6,000 base pairs. In some locations, they report in the