New research illustrates how genome adapts to transposon invasion

December 22 2011

Small, mobile sequences of DNA left over from viruses, called transposons or "jumping genes" because of their ability to move around the genome, pose a significant threat to the genetic integrity and stability of an organism. Considered genetic parasites, these transposable elements are believed to comprise as much as 50 percent of the human genome. Because of the damage transposons can do to an organism's DNA, an immune-like response has evolved to turn off, or silence, these mobile genetic elements.

New research published in the journal *Cell* by the labs of William E. Theurkauf and Zhiping Weng at the University of Massachusetts Medical School sheds light on how the genome defends itself from these invading DNA parasites.

While it's known that specific small RNAs called Piwi-interacting RNAs (piRNAs) are responsible for silencing transposons, how this biologically critical system reacts to the introduction of a new transposon isn't fully understood. "The genome is littered with these transposons," said William E. Theurkauf, PhD, professor of molecular medicine at UMass Medical School and lead author of the study. "In Drosophila there are over 120 different forms of transposons and these are the active pathogen that we are looking at in this host-pathogen response. Meanwhile, piRNAs are produced from regions of the genome that contain bits and pieces of these transposons, and are the foundation for how these elements get silenced."

To understand how a genome responds to the introduction of a new transposon, Theurkauf and colleagues turned to a wild Drosophila, or fruit flies. Unlike standard lab-bred fruit flies, wild Drosophila contain a transposon called the P element that first began appearing in the population after scientists started breeding fruit flies to study genetic heredity in the early part of the 20th century. As a result, lab-bred fruit flies lack the P element transposon and the maternally inherited piRNA necessary to silence it. When these lab-bred females are crossed with the P element-carrying wild fruit flies, the off-spring are unable to silence the invading transposon and are sterile as a result.

Jaspreet Khurana, a PhD student in Theurkauf's lab, made the keen observation that as these flies aged the hybrids were gaining fertility. "Based on the observation that the flies recovered, it seemed likely that they were learning how to shut down transposons. We decided to use this system to look at the process of adaptation to a new transposable element," said Theurkauf.

Using a multi-disciplinary approach that included next generation sequencing, Theurkauf and colleagues were able to get complete genetic sequences of the sterile, hybrid flies at various stages of development. Jie Wang, PhD, a postdoc in the lab of Zhiping Weng, PhD, professor and director of the Program in Bioinformatics and Integrative Biology at UMass Medical School, analyzed the genetic information to see how the genome was responding to the introduction of the new transposon.

What they found was startling. In the hybrid off spring, the new transposon had triggered a response that disrupted the entire piRNA machinery. Not only was the newly introduced transposon jumping around the genome and causing a problem – which was expected – but most of the 120 plus transposons in the Drosophila genome had also become active. "This massive destabilization of the genome is probably why they're sterile," said Theurkauf.

As the hybrids aged, however, the new transposon and all the existing, resident transposons, got shut down and fertility was restored. "We found there were two mechanisms responsible for silencing the transposons," said Weng. "For P elements it turned out the flies learned to process the piRNA transcripts inherited from the father and turn them into mature piRNAs and silence the transposon. Resident transposons, by contrast, jump into piRNA clusters and alter the architecture in a way that makes new piRNAs that can silence the resident elements."

"The bottom line on our study is when you introduce a single, new transposon it leads to a genetic crisis that activates all the transposons in the genome and compromises fertility in these hybrids," said Theurkauf. "Remarkably, what emerges at the other end is an organism with an altered genome architecture that functionally recharges the piRNA clusters so they more effectively silence transposons."

Provided by University of Massachusetts