

Researchers discover novel 'gene toggles' in world's top food crop

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Blake Meyers, associate professor of plant and soil sciences at UD, a collaborator on the research, is working to determine when the newly discovered microRNA in rice first evolved. Credit: Kathy F. Atkinson/University of Delaware

University of Delaware researchers, in collaboration with U.S. and international colleagues, have found a new type of molecule--a kind of “micro-switch”--that can turn off genes in rice, which is the primary source of food for more than half the world's population. The discovery is reported in the March 25 issue of the *Proceedings of the National Academy of Sciences of the United States of America*.

Composed of short lengths of ribonucleic acids (RNAs), on the order of about 20 nucleotides long, these novel molecules, called natural antisense microRNAs (nat-miRNAs), target the genes sitting directly across from

them on the opposite strand of DNA in a rice cell.

In addition to uncovering a new genetic switch and gaining insight about its pathways and evolution, which are important to the health of a grain that feeds most of the world, the research also may help scientists locate this type of novel gene regulator in other organisms, including humans. MicroRNAs regulate 30 percent of human genes and thus are critical to human health and development.

The research was led by Pamela Green, the Crawford Greenewalt Chair of Plant Sciences at UD, and Blake Meyers, associate professor of plant and soil sciences, and their laboratory groups at the Delaware Biotechnology Institute, including associate scientist Cheng Lu, postdoctoral researchers Dong-Hoon Jeong and Kan Nobuta, graduate students Karthik Kulkarni, Manoj Pillay, and Shawn Thatcher and research associate Rana German.

Scientists at Cold Spring Harbor Laboratory and at the Chinese Academy of Sciences collaborated on the project.

MicroRNAs are small RNA molecules that play a key role in regulating cellular processes, including a cell's development and its responses to stress. These micro-molecules bind to specific messenger RNA molecules, which carry instructions to the cells to make particular proteins. This binding typically causes the messenger RNAs to be degraded in plant cells.

“We were using a deep-sequencing approach to identify new microRNAs when we found these novel examples,” said Green. “These tiny RNA molecules are a special type of microRNA that have an antisense configuration relative to their targets. It's an exciting finding. We believe they could be present in many organisms,” she noted.

Some 240 microRNAs previously had been annotated in rice. Using a high-throughput gene-sequencing technique known as Massively Parallel Signature Sequencing (MPSS), the UD research team analyzed over 4 million small RNAs from 6 rice samples, which yielded 24 new microRNAs, including the unique new group of molecules called natural antisense microRNAs.

When a gene is ready to produce a protein, its two strands of DNA unravel. The first strand, called the “sense” transcript, produces messenger RNA, which carries the recipe for making a specific protein. However, the other strand of DNA may produce a complementary antisense RNA molecule, which sometimes can block production of the protein, thus turning off, or “silencing,” the gene.

In the newly discovered case, the sense messenger RNA and antisense RNA operate differently, and different pieces are spliced out of each. These splicing differences limit the pairing ability between the sense and the antisense to a small region that includes the microRNA. In addition, splicing of the precursor of natural antisense microRNAs allows a hairpin to form, and hairpins are a requirement for any microRNA to be made.

Green noted that such microRNAs are not present in the common research plant *Arabidopsis*, which is a dicotyledon, a plant group that has two seed leaves (cotyledons) when it first sprouts. However, the UD team has identified the novel microRNAs in monocotyledons--plants that have solitary seed leaves--such as rice, corn and other grains.

“The novel microRNAs, target sites, and sense-antisense transcript arrangement that we discovered are conserved among monocots, indicating that this pathway is at least 50 million years old,” Meyers noted.

The next step in the research, Green said, will be to try to understand how microRNAs help rice plants respond to adverse environmental conditions, such as drought or limited nutrient availability.

In addition, the UD group currently is analyzing small RNAs in a diverse set of plant species to determine if this new class of microRNA may be present in a broader set of monocots or other plants.

“Comparative genomics is an important method for understanding microRNA evolution and diversity and has the potential to tell us when this type of natural antisense-microRNA might have first evolved,” Meyers said.

Source: University of Delaware

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