An arms-race with mutual benefits

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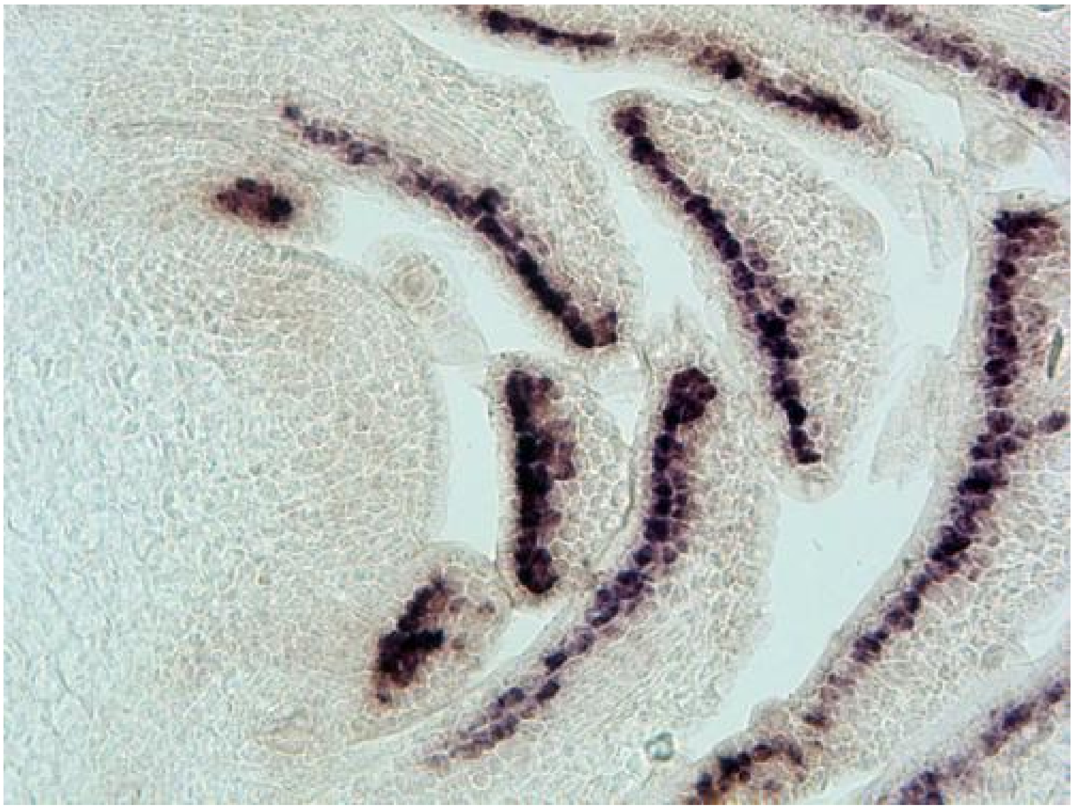

Section of plant tissue with staining of Evadé RNA (dark blue) as an indicator of its multiplication in only one specific cell-type. Credit: Arturo Marí-Ordóñez / ETH Zürich

When you hear the word "mutations", you probably think of something negative like heritable diseases. But mutations also mean genetic diversity and are at the centre of evolution. Researchers have now uncovered a surprisingly sophisticated system that balances protection from harmful mutations and genetic diversification in a plant.

Large parts of the genome – from plants to animals and humans – consist of stretches of ancient viral DNA that used to be able to "copy and paste" themselves to any other place in the genome. As these so called retrotransposons can insert themselves into and thus interrupt genes that are vital to keep intact, organisms have evolved ways to lock these pieces of foreign DNA in their place in the genome. Only under special circumstances can retrotransposons "break free", for instance under conditions of stress.

Olivier Voinnet, professor of RNA Biology, and his doctorate student Arturo Marí-Ordóñez discovered a remarkably sophisticated system that evolved to control the balance between multiplication and "locking" of a retrotransposon in the plant Arabidopsis thaliana. The special relationship between the plant and the retrotransposon has several aspects: by allowing the retrotransposon to multiply to a certain degree, the plant genetically diversifies its offspring. At the same time, the plant developed a fail-safe mechanism to stop the retrotransposon from multiplying too much.

Diverse offspring

The researchers found that the retrotransposon, called Evadé (French for "escapee"), multiplies in the plant only in one specific cell type, the one that the plant uses to produce seed and therefore offspring. By restricting its multiplication to only one type of cells Evadé avoids harming its host plant in the process of "copying and pasting", which could cause abnormalities that compromise the plant's fitness.

However, Evadé does multiply and by doing so in the female tissue that generates the egg and - after fertilization - the seed, it diversifies the plant's offspring. This allows new versions of the plant to grow that may be better adapted to the environmental conditions at hand. Those eggs that are compromised due to Evadé inserting into an essential gene do not get fertilized and abort.

An arms-race

In this context, Voinnet, Marí-Ordóñez and their colleagues discovered that the relationship between Evadé and the plant is an arms-race, one the plant eventually wins: The retrotransposon developed a trick to evade the first of the two waves of counter-attack the plant mounts against its multiplication. Yet, it falls prey to the second, which ultimately restricts the amount of Evadé copies in the plant genome to approximately 40. Both waves of attack make use of the intermediate of Evadé's "copy-and-paste" process: The "copying" involves transcription of the Evadé DNA to RNA, the "pasting" a reverse transcription of Evadé RNA to DNA coupled to the insertion of this new DNA into a random site in the plant genome.

For the first wave of attack, the plant uses a few copies of the Evadé RNA as a template to produce a sort of homing device: a specific kind of very short RNA molecules that complement perfectly the Evadé RNA. These homing devices guide a set of molecular scissors to Evadé's RNA which would subsequently be cut into harmless pieces unable to invade further the plant genome. Yet, Evadé evades this attack by shielding its RNA from being cut by the scissors with a protective coat of small proteins. Thus, the scissors bind Evadé's RNA to no avail, the RNA cannot be cut into pieces and can still "paste" itself into another place in the genome.

As Evadé escapes the first wave of attack, multiplies, and therefore more and more copies of its DNA are transcribed to RNA, there comes a point when there are more copies of retrotransposon RNA than molecular scissors. This saturation of the plant's "scissor system" triggers the second wave of attack, the one Evadé cannot escape: The plant cells start producing another kind of homing device from the Evadé RNA. These do not guide molecular scissors but a certain protein complex to all the copies of Evadé's DNA inserted in the plant genome. There, this protein complex chemically modifies the Evadé DNA in such a way that the it can no longer be transcribed into RNA. By nipping the "copy and paste" process in the bud, the plant stops Evadé from multiplying further and effectively locks it in its place.

A riddle with many layers

To study the relationship between Arabidposis and Evadé Voinnet and Marí-Ordóñez used a genetic trick to awaken the sleeping retrotransposon: they specifically removed the chemical modifications that stop its transcription to RNA. "It was astonishing to see that Evadé became completely locked in place again exactly by the 14th plant generation after we had freed it", says Voinnet. "That is when there are so many copies of it that the plant's response tips from the first to the second strategy of attack."

Figuring out the complex relationship between Arabidopsis and Evadé was a riddle with many layers, according to the researchers. The results of their investigation have recently been published in *Nature Genetics*. "A study of this kind has never been conducted before in plants or any other organism," emphasises Voinnet. For the first time, the researchers were able to experimentally reconstruct and analyse the events underlying the awakening, multiplication and eventual demise of a retrotransposon.

More information: Marí-Ordóñez A, et al. Reconstructing de novo silencing of an active plant retrotransposon. *Nature Genetics*, 2013, Epub ahead of print, DOI: 10.1038/ng.2703

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