February 17, 2021

Plant Biology

How a mint turned into catmint

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doi.org/10.25250/thescbr.brk475

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This Break was edited by Akira Ohkubo, Scientific Editor - TheScienceBreaker

The plant catmint can send your cat into a state of frenzy. It generates a cat-tempting chemical, unlike other members of the mint family. This study has investigated how this unique plant evolved the ability to make the cat attractant.

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The plant catmint, also known as catnip, is named after its notorious effect on cats. When cats sniff or rub against catmint, it drives them to act strangely: rolling over, pawing and rubbing. Its scientific name is also feline-inspired: *Nepeta cataria*.

The cause of the cats' behavior is a molecule catmint produces called nepetalactone, a type of molecule known as an iridoid. Iridoids are found in various flowering plants. However, we don't think that catmint makes nepetalactone to get cats high, but rather to repel plant-eating insects. In fact, nepetalactone is known as efficient at repelling some insects as the common synthetic repellent DEET.

Catmint species are part of the mint family, which includes common herbs such as oregano, thyme and, of course, mint. Whilst iridoids are found in many plants in the mint family, they are absent in plants very closely related to catmint. This indicates that during the evolution of the mint family over many millions of years, the ability to make iridoids was lost and then regained.

Unlike animals, plants cannot "move" to change their environment to avoid plant-eaters. Instead, they can adapt to the environment by making functional molecules such as poisons and pigments. We thought that catmint would make a great case study to investigate how plants evolve to make these adaptative molecules. Firstly, nepetalactone is a relatively simple molecule, so we didn't have to investigate too many steps. Secondly, we had already discovered that enzymes—a group of proteins, molecular machinery of life, acting as biocatalysts—called iridoid synthase (ISY) and nepetalactol-related short chain dehydrogenases (NEPS) play roles in nepetalactone production in catmint. Finally, we were working in a large international collaborative team of scientists with lots of expertise in the mint family. So we set out to understand how catmint evolved to make nepetalactone.

We used different methods to investigate catmint evolution. The first step was uncovering the genomes of catmint species. A genome is a set of all genes in a given species, wherein each gene is a recipe for generating a specific protein. Obtaining genomic data enabled us to identify the location of all the genes involved in nepetalactone production. By creating the evolutionary trees of different genes, we could estimate when a particular gene loss or appearance happened in evolution. More remarkably, these evolutionary trees let us resurrect an 'ancestral' enzyme based on its genetic information. We can make it and test its function in the lab: a little like Jurassic Park but with a single catmint enzyme instead of whole dinosaurs. By using this variety of methods, we were able to build a picture of how catmint evolved to make nepetalactone.

We focused on the key genes involved in iridoid production in the plant: the recipes for generating ISY and NEPS enzymes. An evolutionary tree of ISY genes allowed us to find that ISYs from catmint differed from those found in other iridoid-producing species. Plus, there were no ISY genes at all in the genomes of species closely related to catmint. This suggested that an ancestral ISY gene was lost and then had to re-evolve to enable catmint to make iridoids.

Then we looked at the location of the ISY gene in the catmint genomes, and we found they locate close to NEPS genes. When genes with related functions are close to each other in the genome, they are referred to as gene clusters. We thus discovered a nepetalactone gene cluster!

To investigate further the relationship between the evolution of genes and the formation of gene clusters, we tracked the evolution of ISY gene in catmint. We found that, around 20 million years ago, ISY gene evolved its ability to generate the iridoid-producing enzyme whilst located at one place on the genome and sometime later moved next to the NEPS to form the gene cluster. This result indicates that gene evolution precedes gene cluster formation.

In this study, we discovered how a mint turned into catmint: how a plant gained the ability to make nepetalactone, the cat-attracting molecule. Our discovery provides general lessons for how new chemistry evolves in plants, providing them with a strategy to survive in a local environment. This knowledge could help us discover new molecules made by plants that could be beneficial to human health.