Getting around gene loss

October 29 2010

Credit: Andrea Piacquadio from Pexels

Genes ‘knocked out’ experimentally in metabolic networks of the model plant species, *Arabidopsis thaliana* (Fig. 1), are compensated for by duplicate genes or alternative synthetic pathways, according to research led by Kousuke Hanada of the RIKEN Plant Science Center, Yokohama.

Gene knockouts often have no obvious effects on an organism's biological characteristics or 'phenotype', because their function is compensated for by duplicate genes or alternative pathways allow the effects of gene loss to be circumvented.

For metabolic products, studies on these mechanisms have been limited to yeast. Hanada's team therefore assessed the relative importance of these mechanisms in Arabidopsis. "*Arabidopsis* suited our purposes beautifully because many gene knockout mutants have been generated and many of its metabolic networks are known," explains Hanada.

To study the robustness of *Arabidopsis* metabolic networks to gene loss the researchers knocked out individually some 2,000 highly expressed genes and then quantified 35 metabolic products in the seeds of the mutant plants by high-throughput analysis.

They compared what happened to production of metabolites when genes with and without duplicates were knocked out. The metabolites assessed included 17 essential amino acids (primary metabolites) found in all organisms, and 18 secondary metabolites called glucosinolates produced specifically by *Arabidopsis* and its relatives.

Knocking out either single-copy genes or genes with only distantly related 'duplicates' tended to have larger metabolic effects than those caused by knocking out genes having closer copies resulting from more recent gene duplication events. "Only recently duplicated genes appear to play a significant role in functional compensation of metabolites in *Arabidopsis*," says Hanada.

By analyzing the structure of the *Arabidopsis* metabolic network, the researchers found that primary metabolites are more often synthesized by alternative biochemical pathways than are secondary metabolites.

Primary metabolites are more likely than secondary metabolites to be essential for plant survival. Surprisingly, however, the researchers found that duplicate genes more often compensated functionally for experimentally induced gene loss in the synthesis of secondary metabolites than in that of primary metabolites. This contrasted with their previous work that showed that, in general, more severe phenotypic effects in Arabidopsis tend to be better compensated for by gene duplication than less severe effects.

Hanada suggests that the existence of multiple alternative pathways for synthesizing primary metabolites makes these particular *Arabidopsis* networks highly robust to the loss of individual genes.

“Our findings shed valuable new light on the gene–phenotype relationship, laying the groundwork for new theoretical models in systems biology,” says Hanada.

More information:

Hanada, K., et al. Functional compensation of primary and secondary metabolites by duplicate genes in *Arabidopsis thaliana*. *Molecular Biology and Evolution Advance Access*, published 24 August 2010, doi:10.1093/molbev/msq204

Hanada, K., et al. Evolutionary persistence of functional compensation by duplicate genes in *Arabidopsis. Genome Biology and Evolution* 1, 409–414 (2009) article .

Provided by RIKEN