A phospholipid pathway from plants to parasites

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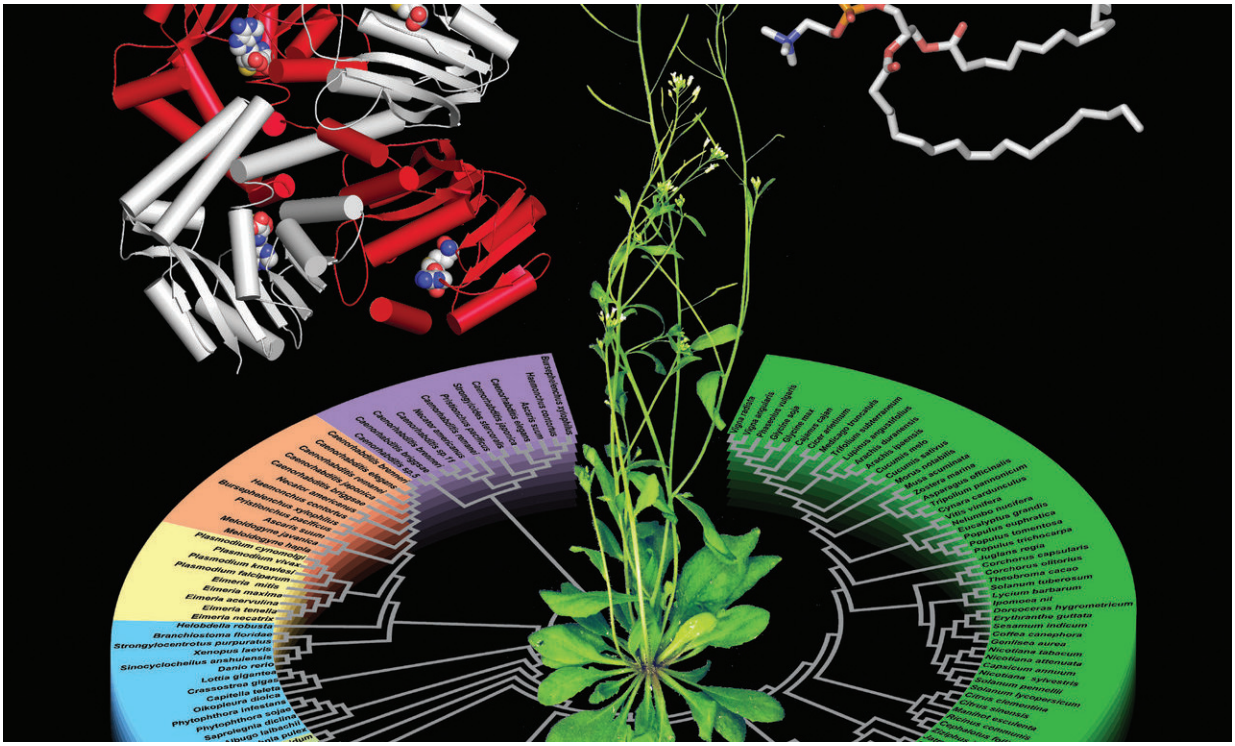

3-D structures of *Arabidopsis* phosphoethanolamine methyltransferase (PMT) and phosphatidylcholine, with evolutionary relationships of PMT sequences from different organisms. Credit: Soon Goo Lee and Joseph Jez

Recent findings by researchers at Washington University in St. Louis may aid in the development of therapies to treat parasitic infections, including malaria, and may help plant scientists one day produce hardier

crops. The research team's work is published in the Dec. 29 issue of the *Journal of Biological Chemistry*.

Choline is an essential nutrient that humans get from certain foods, including eggs, meat, leafy greens and nuts. The human body converts choline into phosphocholine (pCho), which it in turn converts into (among other essential building blocks) phosphatidylcholine (PtdCho), a component of cell membranes. Plants, however, can't acquire the nutrient from the environment and so must synthesize pCho from scratch. The biochemical pathway plants use to synthesize pCho is also found in nematodes and the malaria parasite *Plasmodium*.

In plants, the enzymatic reaction that produces pCho is essential for both normal function and for responding to stresses. Plant pCho is converted into PtdCho, which builds membranes that can adjust their rigidity in response to temperature changes. Plant pCho also gets converted into molecules that help the plant survive high salt. The enzymes that produce plant pCho are called called phosphoethanolamine methyltransferases (PMTs).

Soon Goo Lee, a postdoctoral research fellow at Washington University in the laboratory of Joseph Jez (who is also an associate editor of the *Journal of Biological Chemistry*), has been fascinated by PMTs in both plants and parasites for many years.

"Understanding the PMT enzyme is key to engineer plants with improved stress tolerance and enhanced nutrients," Lee said. Furthermore, since the PMT-catalyzed pathway is found in parasites but not humans, Lee and Jez's team is looking for inhibitors of this enzyme to treat diseases caused by these parasites.

The new study explains how PMTs of the model plant *Arabidopsis thaliana* share core features of parasite PMTs, with almost identical

structure at the active site. But the plant PMTs are roughly twice as large as the parasite ones, with large sections that can rearrange themselves to carry out multiple chemical reactions.

Furthermore, the three PMT types found in the plant - which were thought to carry out the same function - actually appear to play different roles depending on where they are found in the plant. Plant growth experiments showed that one type of PMT was essential for root development and salt tolerance, whereas the other two had no effect on roots and instead seemed to be found primarily in leaves.

In the long run, this big-picture view of PMTs in different organisms offers routes to precisely engineer enzymes with different functions.

"I love these kinds of stories, where I can look from the atomic [structure] to the physiological level to explain why these enzymes have different forms and how they work," Lee said.

More information: Soon Goo Lee et al, Conformational changes in the di-domain structure of Arabidopsis phosphoethanolamine methyltransferase leads to active site formation, *Journal of Biological Chemistry* (2017). DOI: 10.1074/jbc.RA117.000106

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