Papers of the Week

Lipid Synthesis Story Now Complete ♦

Phosphatidate phosphatase catalyzes the dephosphorylation of phosphatidate (PA) to yield diacylglycerol and P_i. There are two different types of PA phosphatase, Mg^{2+}-dependent or Mg^{2+}-independent, based on the cofactor requirement. Mg^{2+}-dependent PA phosphatase is thought to be mainly involved in the *de novo* synthesis of triacylglycerol and phospholipids, but this has not been proven because the gene encoding the enzyme has yet to be found. This has changed, however, with the publication of this Paper of the Week by Gil-Soo Han and colleagues.

Using a reverse genetic approach, Han *et al*. identified *PAH1* as the gene encoding an Mg^{2+}-dependent PA phosphatase enzyme in *Saccharomyces cerevisiae*. Overexpression of the *PAH1* gene in *S. cerevisiae* resulted in elevated levels of Mg^{2+}-dependent PA phosphatase activity, and deletion of the gene resulted in the reduction of enzyme activity. Characterization of the Mg^{2+}-dependent PA phosphatase activity resulting from the heterologous expression of *PAH1* in *Escherichia coli* confirmed the gene-enzyme relationship. Additionally, cells containing a *pah1*Δ mutation accumulated PA and had reduced amounts of diacylglycerol and triacylglycerol. Interestingly, this gene turns out to be a homolog of the *LPIN1* gene identified in mammalian cells as controlling adipogenesis. Because Mg^{2+}-dependent PA phosphatase has been the only remaining enzyme in the pathway for glycerolipid synthesis whose molecular description is missing in reviews and textbooks, this work fills in a major gap currently present in our knowledge of lipid synthesis.

♦ See referenced article, *J. Biol. Chem.* 2006, **281,** 9210–9218