



BACTERIAL PHYSIOLOGY

Pinpointing the pathway

Researchers have identified a missing metabolic pathway that has turned out to be the most widely distributed acyltransferase system in bacteria, according to a recent report in *Molecular Cell*.

Phosphatidic acid is a key intermediate in the synthesis of membrane phospholipids. In the model Gram-negative organism *Escherichia coli*, the first step in the formation of phosphatidic acid is the acylation of glycerol-3-phosphate (G3P). This step is carried out by PlsB, a G3P acyltransferase that uses either acyl-ACP (ACP is an acyl-acyl carrier protein) or acyl-coenzyme A to add an acyl group to G3P. However, Gram-positive bacteria do not produce PlsB and in some Gram-negative organisms, *plsB* is non-essential, indicating that there must be another pathway capable of carrying out this key reaction.

Ying-Jie Lu and colleagues began investigating phosphatidic acid synthesis in the Gram-positive organism *Streptococcus pneumoniae*. Previous work in *E. coli* had identified another protein, PlsX, which it was thought might be involved in G3P metabolism. Biochemical analysis of the activity of *S. pneumoniae* PlsX showed that it had no intrinsic G3P-acyltransferase or fatty-acid kinase activity. Rather, it was found that *S. pneumoniae* PlsX is a soluble phosphotransacylase that catalyses the reversible conversion of the end product of type II fatty-acid biosynthesis, acyl-ACP, to a fatty-acyl phosphate, a new metabolic intermediate.

The authors then wondered whether there could be a second protein that used this activated fatty-acid intermediate to generate acylated G3P. They analysed the acyl-phosphate-dependent G3P-acylation activity in *S. pneumoniae* and found that, in contrast to *E. coli*, the main *S. pneumoniae* G3P acyltransferase activity requires an acyl-phosphate as the acyl donor. The protein responsible for this activity in *S. pneumoniae* was identified as the membrane-associated protein PlsY.

Analysis of the distribution of *plsX* and *plsY* revealed that the PlsX/Y pathway is widespread, with *plsX* and *plsY* present in 314 of the 395 complete and draft sequences examined. By contrast, *plsB* was only found in 102 of the 395 genomes examined, and was mainly confined to the γ -proteobacteria. So, it seems that Lu *et al.* have identified the main pathway responsible for the first step of phosphatidic acid biosynthesis in bacteria.

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ORIGINAL RESEARCH PAPER Lu, Y.-J. *et al.* Acyl-phosphates initiate membrane phospholipid synthesis in Gram-positive pathogens. *Mol. Cell* **23**, 765–772 (2006)

VIRUSES AND CANCER

Viral hijacking

Despite its association with tumours and unlike other DNA viruses, human cytomegalovirus (HCMV) does not transform cells, so how it exerts its oncogenic potential has been unclear. Martine Smit and colleagues now show that US28, an HCMV gene that encodes a G-protein-coupled receptor, is important for initiating angiogenesis in transformed cells.

The US28 receptor is a homologue of the human chemokine receptor CCR1 but, unlike its cellular counterpart, it signals in a constitutively active manner and has previously been shown to activate pathways that lead to cell proliferation and migration.

HCMV might use US28 to hijack several signalling networks within infected cells. In fact, this

viral receptor displays promiscuous G-protein coupling that causes the constitutive activation of different G proteins and potentiates the signalling of other cellular chemokine receptors.

Smit and colleagues found that when US28 is stably expressed in NIH-3T3 cells, the cells have an increased growth rate that results, at least in part, from the increased expression of cyclin D1. The US28-expressing cells also form foci *in vitro*, and after 5 days the cells express high levels of vascular endothelial growth factor (VEGF) compared with cells that express a mutant US28 that is unable to bind G proteins.

To further dissect the pathway activated by US28, the authors investigated the downstream signalling pathways and found that US28

PLANT DISEASE RESISTANCE

An open and shut case

A recent report in *Cell* has revealed that rather than being passive ports of entry, stomata have an active role in the innate immune response of plants to bacterial challenge, and that bacteria have evolved specific virulence factors to counteract this defence reaction.

Unlike fungal pathogens, bacterial pathogens cannot penetrate plant tissues directly. Instead, they rely on entry through wounds or natural openings in the plant surface. Stomata are microscopic pores in the plant epidermis that allow gaseous exchange and transpiration. Each stomatal pore is surrounded by two guard cells that control stomatal opening and closing in response to changing environmental conditions, such as light and humidity.

In this work, Maëli Melotto and colleagues studied the response of *Arabidopsis thaliana* stomata to challenge with the plant pathogen *Pseudomonas syringae* pv. *tomato*

DC300 (*Pst* DC300). After 1 hour of incubation with *Pst* DC300, the average width of the stomatal aperture decreased dramatically, and after 2 hours the number of open stomata was reduced by ~70%.

Is stomatal closure stimulated by a specific bacterial component, such as a PAMP (pathogen-associated molecular pattern)? Melotto *et al.* found that two well-known PAMPs — a flagellin-derived peptide and lipopolysaccharide — stimulated stomatal closure. In *A. thaliana*, the innate immune response can be either salicylic acid (SA)-dependent or SA-independent and the PAMP response was found to be part of the SA-dependent pathway. Stomatal closure is regulated by an abscisic acid (ABA) signalling pathway in guard cells, and Melotto *et al.* found that the PAMP-induced closure also involved ABA signalling.

The induction of stomatal closure was not restricted to *Pst* DC300 and was also observed with the human pathogen *Escherichia coli*