indicating that virulent *P. syringae* also induces systemic susceptibility to *T. ni* herbivory but not via COR. In fact, it was found that COR induces systemic resistance to *T. ni*, consistent with its role as a JA mimic.

So, this work has revealed a role for COR in *P. syringae*-mediated manipulation of plant systemic defences and has also confirmed that the interactions involved in these defences are extremely complex. Future work will provide further details on the role of COR and its interactions with the SA- and JA-mediated pathways, as well as continuing to analyse the molecular mechanisms responsible for *P. syringae*-mediated susceptibility to insect herbivores.

Sheilagh Molloy

References and links

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BACTERIAL PHYSIOLOGY

A function for redundancy

The availability of genome sequences promises to enable researchers to understand the physiology of individual cells, but when there are two or more pathways for metabolism of a substrate — known as metabolic modules — it takes more than 'omics to probe which pathway is used and when. Marx *et al.* used flux analysis to show that methylobacteria metabolize formaldehyde by routing it through two different pathways, and report their findings in the latest issue of *PLoS Biology*.

Methylobacteria are facultative methylotrophs, meaning that these bacteria can grow on carbon compounds that have one or more carbon atoms. Methylotrophs can grow on methanol, which is important because plants produce methanol, and plant–bacterial associations might affect seed germination and plant development.

Growing on methanol presents methylotrophs with a problem — the central intermediate in methanol catabolism is formaldehyde, which is toxic. In methylotrophs, formaldehyde can be converted into serine, and shuttled into central metabolism by one of two routes that are found only in these bacteria — a direct route (green) or a long route (blue) (see figure). The direct route is a non-enzymatic reaction that combines formaldehyde with tetrahydrofolate to generate methylene-H_4F, whereas the long route consumes one molecule of ATP and involves several enzyme-catalysed steps. A third module found in many bacteria oxidizes formaldehyde to CO_2. Genetics indicate that both the direct and the long routes are required for growth on formaldehyde, but why does *Methylobacterium extorquens* have redundant metabolic modules? Marx *et al.* have tested this directly by monitoring the metabolism of methanol using stable-isotope and radioisotope-labelling approaches.

By growing *M. extorquens* on methanol labelled with deuterium (CD_3OD) they were able to unravel which module was used in different growth conditions, since the direct route incorporates 1 deuterium atom in each serine molecule, while the long route incorporates 2 deuterium atoms in each serine. By measuring the ratios of labelled serine produced they found that metabolism of formaldehyde by the long route dominated when succinate-grown cells were first fed methanol, but that after an acclimation period the direct route was favoured. Although both routes operate, they are used differentially dependent on the growth conditions.

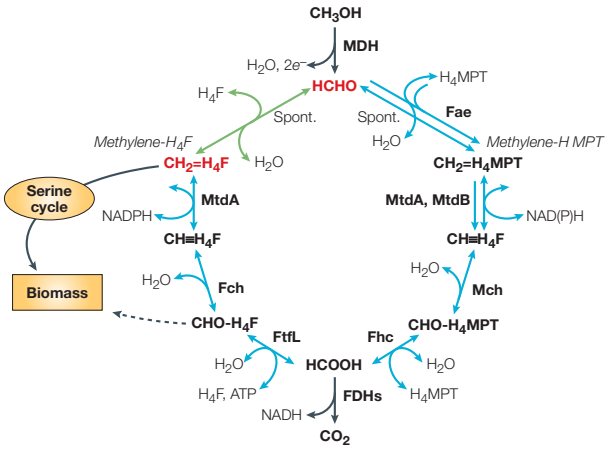

Image modified from Marx *et al.* *PLoS Biol.* (2005)

Flux of carbon through metabolism was also monitored using ^{14}C-labelled CH_3OH and by analysing the rates of methanol oxidation, assimilation of C1 units and CO_2 production. This analysis confirmed that the long route is initially used when cells are transferred to methanol, and that although the contribution of this route quickly declines, it is still considerable. A mathematical model produced using known kinetic parameters for the enzymes in formaldehyde metabolism was also devised. By simulating a switch from growth on succinate to methanol, the model predicted the same switch from the long to the direct route that was found using flux analysis. Marx *et al.* endeavoured to delete the *ftfL* gene, an intrinsic part of the long route, reasoning that if the long route is only necessary for acclimation to methanol growth, it might be possible to find mutants if the bacteria were already growing on methanol. The failure of this strategy indicates that both routes are needed, even when cells are continuously grown on methanol.

This research shows that biochemistry must go hand-in-hand with genomics to create useful models to understand cell physiology. Switching between different metabolic modes and metabolizing toxic intermediates isn't restricted to bacteria, so this research could represent a new paradigm for growth in toxic environments.

Susan Jones

References and links

ORIGINAL RESEARCH PAPER Marx, A. *et al.* Flux analysis uncovers key role of functional redundancy in formaldehyde metabolism. *PLoS Biol.* **3**, e16 (2005)

WEB SITE

Mary Lidstrom's laboratory:
http://www.hhmi.org/research/professors/lidstrom_bio.html