BACTERIAL PHYSIOLOGY

From start to finish for *Streptomyces*

Antibiotic production is coordinated with the developmental programme of *Streptomyces* spp., but little has been known about the cues that switch on secondary metabolism and tie it to morphological development. In a new paper in *EMBO reports*, Sébastien Rigali, Fritz Titgemeyer, Gilles van Wezel and colleagues now describe a complete *Streptomyces* signalling cascade, from nutrient sensing to antibiotic production.

N-acetylglucosamine (GlcNAc) is known to cause developmental arrest of *Streptomyces coelicolor* on rich media, and so Rigali *et al*. began by analysing the effect of GlcNAc on the production of two antibiotics, undecylprodigiosin (Red) and actinorhodin (Act). A high concentration of GlcNAc blocked antibiotic production and sporulation during growth on rich media and triggered antibiotic production and sporulation during growth on minimal media. This effect was common to many *Streptomyces* spp., and so the accumulation of GlcNAc seems to be an important checkpoint for the induction of secondary metabolism. This was reinforced by the finding that antibiotic production in several streptomycetes was induced by addition of GlcNAc to the medium, probably through the up-regulation of some of the many 'sleeping' antibiotic gene clusters in their genomes.

The GlcNAc regulon is under the control of the DasR global transcriptional regulator, and so Rigali *et al*. went on to probe the role of DasR in antibiotic production. DasR-binding sites were found upstream of the transcriptional activators of the *red* and *act* gene clusters, and DasR binding to these regions was confirmed by gel-shift analysis. Further investigations showed that in a *dasR* mutant, expression of the *act* and *red* gene clusters was upregulated. Finally, the authors investigated the origins of the GlcNAc signal. Previously, they had noted that chitin, the natural polymeric form of GlcNAc, had no effect on development or antibiotic production, and that chitinase genes and a cell-wall aminopeptidase gene are part of the DasR regulon. In a *dasR* mutant grown on minimal medium, expression of the aminopeptidase was increased but there was no induction of the chitinase genes.

The authors end by presenting a detailed model to explain these observations in which *Streptomyces* spp. use GlcNAc as a signal for the nutritional status of the environment and the global regulator DasR as the master switch that responds to this signal.

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ORIGINAL RESEARCH PAPER Rigali, S. *et al*. Feast or famine: the global regulator DasR links nutrient stress to antibiotic production by *Streptomyces*. *EMBO Rep*. 30 May 2008 (doi:10.1038/embor.2008.83)