indications that the ancestor of the group might have been an insect parasite are totally unexpected.

Comparative genomic analyses of microbial pathogens usually highlight differences between the pathogen and its close relatives. By contrast, the most remarkable feature of the *B. anthracis* genome is just how similar it is to *B. cereus*. With such a similar chromosomal content, the idiosyncratic virulence of each member of the *B. cereus* group is now attributed to differences in the mobile genetic elements of each species, as well as alterations at regulatory loci.

*Sheilagh Clarkson,*
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Nature Reviews Microbiology

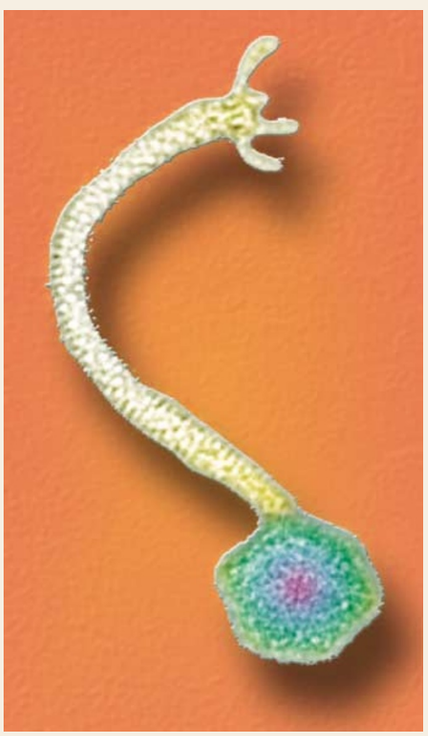

**References and links**

**ORIGINAL RESEARCH PAPERS** Read, T. D. *et al*. The genome sequence of *Bacillus anthracis* Ames and comparison to closely related bacteria. *Nature* **423**, 81–86 (2003) | Ivanova, N. *et al*. Genome sequence of *Bacillus cereus* and comparative analysis with *Bacillus anthracis*. *Nature* **423**, 87–91 (2003)

**WEB SITES**

**The Institute for Genomic Research (TIGR):** http://www.tigr.org

**Integrated Genomics**: http://www.integratedgenomics.com

Mycobacteriophage Cjw1, image courtesy of M. Pedulla, T. Harper and G. Hatfull.

MICROBIAL GENETICS

# Organ grinder not monkey?

**SpoOA, a transcriptional activator protein in *Bacillus subtilis*, is a well-established central player in sporulation. Now, a new study, published in *Genes and Development*, provides compelling evidence that SpoOA, rather than simply controlling the initiation of sporulation, is predominantly a cell-specific transcriptional regulator.**

***B. subtilis*** **is a well-characterized model system for differentiation and programmed cell-specific gene expression. During sporulation in *Bacillus*, two cell-types form: the mother cell and the forespore, which is destined to become a spore. Mutants that lack the SpoOA response regulator fail to enter the developmental pathway that leads to sporulation.**

**A complex phosphorelay integrates metabolic, environmental and cell-cycle cues to activate SpoOA. Phosphorylated SpoOA activates the transcription of sporulation genes, which tips the balance so that sporulation occurs. So, as in eukaryotes, the phosphorylation of key proteins regulates cell-cycle progression.**

**However, the situation is not as simple as it first seems. An operon in the mother cell controlled by SpoOA was transcribed after sporulation had initiated. This led Fujita and Losick to examine whether SpoOA controls gene expression following sporulation initiation. Surprisingly, by using GFP fusions to important SpoOA-regulated promoters, SpoOA was shown to be active throughout sporulation. Furthermore, it was active in a cell-specific fashion. SpoOA was shown to accumulate in the mother cell, and when a constitutively active SpoOA mutant was over-expressed in the forespore, sporulation efficiency was drastically reduced. Finally, expression in the mother cell of a truncated form of SpoOA, which competed with native SpoOA for phosphorylation, reduced sporulation efficiency. So, the location and activity of SpoOA is crucially important for development.**

**Viewed in this light, SpoOA is analogous to the related transcription factor CtrA in *Caulobacter crescentus*. Like SpoOA, CtrA is a master regulator that becomes a cell-specific transcription factor during the cell cycle of *Caulobacter*. CtrA activates or represses the expression of one-quarter of the *Caulobacter* cell-cycle-regulated genes, integrating DNA replication, morphogenesis and cell division. *Caulobacter* divides to produce two cell types: a stalked cell and a swarmer cell, which is a dispersal cell that swims until conditions allow renewed cell division.**

**CtrA binds to, and silences, the origin of replication in swarmer cells — initiation of chromosome replication depends on temporally controlled proteolysis of CtrA in the stalked cell. Why is SpoOA activity restricted to one cell type? When the wall is synthesized between mother cell and forespore, two-thirds of the forespore chromosome remains in the mother cell. Some genes are temporarily diploid in the mother cell and absent from the forespore. As the excluded chromosome is pumped into the forespore, certain genes are asymmetrically expressed. So, asymmetric expression of phosphorelay genes might result in SpoOA phosphorylation only in the mother cell. This could ultimately decide the fate of SpoOA, through targeted proteolysis of unphosphorylated SpoOA in the forespore. Comparisons between the parallel systems in *Caulobacter* and *Bacillus* will undoubtedly push forward our understanding of programmed cell-specific gene expression.**

***Susan Jones, Associate Editor,***
Nature Reviews Microbiology


**References and links**

**ORIGINAL RESEARCH PAPER** Fujita, M. & Losick, R. The master regulator for entry into sporulation in *Bacillus subtilis* becomes a cell-specific transcription factor after asymmetric division. *Genes Dev.* **17**, 1166–1174 (2003)

**FURTHER READING** Jensen, R. B. *et. al.* Dynamic localization of proteins and DNA during a bacterial cell cycle. *Nature Rev. Mol. Cell Biol.* **3**, 167–176 (2002)

**WEB SITE**

**Richard Losick's laboratory:** http://mcb.harvard.edu/losick

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