Cell–cell signaling pathway activating a developmental transcription factor in *Bacillus subtilis*

J.-Arturo Londoño-Vallejo and Patrick Stragier

Institut de Biologie Physico-Chimique, 75005 Paris, France

Transcription in the mother cell at early stages of sporulation in *Bacillus subtilis* is controlled by σ^E , a σ factor that is synthesized in the predivisional cell as an inactive larger precursor, pro- σ^E . Activation of σ^E depends on σ^F , the factor that governs transcription in the forespore. Genetic experiments have indicated that transduction of the activation signal from the forespore to the mother cell requires the products of some genes belonging to the σ^F -controlled regulon. We have identified and characterized a σ^F -dependent gene, *csfX*, encoding a protein necessary and sufficient for triggering processing of pro- σ^E . The CsfX protein contains a typical amino-terminal signal sequence suggesting that, although synthesized in the forespore, it may act across the septum to activate the membrane-bound enzyme that is responsible for pro- σ^E processing in the mother cell.

[Key Words: Sporulation; *Bacillus subtilis*; σ factor; secreted protein]

Received December 9, 1994; revised version accepted January 18, 1995.

Early during sporulation in *Bacillus subtilis* an asymmetric division event generates two cells with different but coordinated developmental fates (Losick and Stragier 1992; Errington 1993). Differential gene expression in these two cells is largely governed by new transcription factors. It is initiated by activation of the σ^F factor in the smaller cell, the forespore (Margolis et al. 1991; Partridge et al. 1991), which is required for subsequent activation of the σ^E factor in the larger cell, the mother cell (Driks and Losick 1991; Losick and Stragier 1992). σ^E is synthesized in the predivisional cell (Gholamhosseinian and Piggot 1989) as an inactive larger precursor, pro- σ^E (LaBell et al. 1987) the product of the *spoIIGB* gene (Stragier et al. 1984; Trempey et al. 1985a), which is cotranscribed with *spoIIGA*, the gene encoding the putative pro- σ^E processing enzyme (Stragier et al. 1988). SpoIIGA is predicted to be a membrane-bound protein (Stragier et al. 1988; Peters and Haldenwang 1991) and is also synthesized before septation, suggesting that it is present on both sides of the septum. It has been hypothesized that σ^F is involved in generating the signal that triggers pro- σ^E processing, by inducing transcription of a gene, *X*, whose product acts vectorially from the forespore to the mother cell (Losick and Stragier 1992). Further support of the idea that pro- σ^E processing is regulated by the products of some genes belonging to the σ^F -controlled regulon has been obtained recently (Shazand et al. 1995). To start elucidating the molecular basis of this transduction pathway between the forespore and the mother cell, we have searched for genes controlled by σ^F (collectively designated by the *csf* acronym). This strategy has led to

the identification and characterization of *csfX*, a σ^F -controlled gene encoding a protein necessary and sufficient for triggering processing of pro- σ^E .

Results

The screening rationale

We have searched for σ^F -dependent genes by screening a plasmid library creating *lacZ* transcriptional fusions after integration into the *B. subtilis* chromosome through a single homologous recombination event (O'Reilly et al. 1994). To allow easy identification of the *csf-lacZ* fusions, the plasmid library was introduced into a strain in which σ^F activity was dependent on the presence of xylose (by placing the regulatory gene *spoIIE* (Margolis et al. 1991) under the control of a xylose-inducible promoter). In such a strain the presence of xylose in sporulation agar plates leads to σ^F activity appearing at the normal time and being correctly compartmentalized (F. Arigoni and P. Stragier, unpubl.). Because σ^F activation induces the whole sporulation cascade (Losick and Stragier 1992), a null mutation was introduced in *spoIIGB*, the gene encoding σ^E , to avoid expression of *spo-lacZ* fusions controlled by σ factors other than σ^F . Furthermore, because pro- σ^E processing occurs in a *spoIIIE36* mutant, in which only 30% of the chromosome around the replication origin is segregated into the forespore (Wu and Errington 1994), we inferred that the *csf* genes required for activating σ^E were present in the chromosome segment that enters the forespore. There-

fore, we introduced this additional mutation in our recipient strain to focus our search on that region of the chromosome.

Of 47 *lacZ* fusions identified as being dependent on xylose on sporulation agar plates, 33 were found to be inactive in a strain carrying a null mutation in *spoIIAC*, the gene encoding σ^F , and thus to be actually dependent on σ^F and not on xylose itself. DNA adjacent to the *lacZ* fusions was cloned for each candidate, and restriction and nucleotide sequence analyses revealed the presence of nine distinct families. Various deletions and disruptions were created in the immediate vicinity of the original fusion points. We checked the effect of these mutations on sporulation and σ^E activity on solid media, by introducing them into a wild-type strain containing a fusion of *lacZ* to the σ^E -controlled *spoIID* promoter (Rong et al. 1986).

The CsfX protein is required for pro- σ^E processing

One locus was found to be essential for sporulation and for expression of *spoIID-lacZ*. Sequence comparison indicated that the gene initially fused to *lacZ*, and now called *csfX* (Fig. 1), lies in a region sequenced in the frame of the *Bacillus* Genome Sequencing Project (accession no. Z38002) and that it is identical to the *ipc-27d* open reading frame located at 327° on the chromosome. The CsfX protein is predicted to contain 224 residues with a typical signal sequence, followed by a potential cleavage site after residue 23, and a carboxy-terminal region extremely rich in charged residues, especially glutamic acid.

The availability of a large sequence from that region allowed us to refine our inactivation procedure and to disrupt precisely either *csfX* or the genes located immediately upstream or downstream of *csfX* (Fig. 1). The latter mutations had no obvious phenotype, whereas inactivation of *csfX* blocked sporulation and prevented σ^E activity, on plate and in liquid media (Fig. 2). Immunoblot analysis using a monoclonal antibody directed against σ^E showed that the defect in σ^E activity was attributable to the absence of the processing of its precursor (Fig. 2). When grown in sporulation conditions and examined by phase-contrast microscopy, the *csfX* mutant was found to accumulate disporic forms, a feature characteristic of the absence of σ^E activity (Lewis et al. 1994; not shown). Mutations in the same locus have been obtained independently by screening for clones displaying σ^F but no σ^E activity (Karow et al. 1995).

Figure 1. Schematic representation of the *csfX* locus and its neighboring genes. Thick arrows indicate the orientation of transcription and, in the case of *csfX*, the putative transcription start. The location of the original fusion point with the *Escherichia coli lacZ* gene is shown. The position and size (in bp) of the various deletions created by insertion of a kanamycin-resistance cassette are indicated with the corresponding sporulation phenotype.

Figure 2. Blockage of pro- σ^E processing in a *csfX* mutant. (Top) The time course expression of a transcriptional fusion (integrated at the *amyE* locus) of the *lacZ* gene to the σ^E -dependent *spoIID* promoter in a wild-type (●) and in a *csfX* strain (○). Time indicates hours in sporulation. (Bottom) An immunoblot analysis of pro- σ^E processing in the same set of strains, samples being harvested at the hours indicated.

csfX is controlled exclusively by σ^F

The *csfX* open reading frame is preceded immediately by a sequence similar to that found in other σ^F -dependent promoters (Sun et al. 1991). A DNA fragment containing the *csfX* gene and only 82 bp of sequence upstream of its putative transcription start was able to fully complement in *trans* the sporulation defect of the *csfX* mutant, indicating that all the signals required for correct expression of *csfX* are located in that short interval.

To follow the expression of *csfX* we used the original *csfX-lacZ* fusion, which was moved to the ectopic *amyE* locus. In a wild-type strain containing this fusion, β -galactosidase synthesis starts 1 hr after the onset of sporulation and continues for the next hour (Fig. 3A). It is reduced to the background level in a *spoIIAC* mutant (no σ^F), it is not affected by a *spoIIIG* mutation (no σ^G), and it doubles in a *spoIIGB* mutant (no σ^E), as already de-

Figure 3. Dependence of *csfX* transcription on σ^F . (A) Time course expression of a transcriptional *csfX-lacZ* fusion integrated at the *amyE* locus in a wild-type strain (●), as compared to strains disrupted for the genes encoding the sporulation σ factors σ^F (*spoIIAC*, ○), σ^E (*spoIIIGB*, ◆), and σ^G (*spoIIIG*, □). The background level of β -galactosidase activity observed in the absence of *lacZ* fusion has been subtracted. Time indicates hours in sporulation. (B) Time course expression of the same *csfX-lacZ* fusion in a wild-type strain (●), as compared with strains carrying the *spoIIAC561* (altered σ^F , ○) or the *spoIIIE36* (chromosome segregation defect, ◆) mutation. Note the difference in scale. Time indicates hours in sporulation. (C) Time course expression of the same *csfX-lacZ* fusion during exponential growth in cells engineered to produce either σ^F (●), or σ^G (◆), or σ^B (□), in response to isopropyl β -D-thiogalactoside (IPTG). Time indicates hours after addition of IPTG. No β -galactosidase was accumulated in the absence of IPTG.

scribed for another *csf* gene (Lewis et al. 1994). Interestingly, *csfX-lacZ* is overexpressed in a *spoIIAC561* mutant that synthesizes an altered form of σ^F that allows pro- σ^E processing (Illing and Errington 1991) (Fig. 3B). Finally, *csfX-lacZ* is expressed at a very high level in a *spoIIIE36* background (Fig. 3B), an unexplained phenomenon that certainly contributed to the detection of the original *csfX-lacZ* fusion, as this fusion is expressed at an almost undetectable level in a wild-type strain.

These genetic dependencies are in perfect accordance with the assumption that *csfX* is controlled by σ^F . Conclusive evidence for this regulation is provided by experiments in which expression of *csfX-lacZ* can be induced very efficiently during exponential growth by the sole presence of σ^F but not by the related factors σ^G and σ^B (Fig. 3C).

The *CsfX* protein is sufficient for pro- σ^E processing

We wondered whether genes other than *csfX* were required for activation of pro- σ^E processing. It has been shown previously that expression of the whole σ^F -dependent regulon during exponential growth activates SpoIIIGA-mediated processing of pro- σ^E (Shazand et al. 1995). A similar experiment in which only the *csfX* gene was artificially expressed during growth, together with the *spoIIIG* operon encoding SpoIIIGA and pro- σ^E , indicated that the CsfX protein is sufficient for activation of pro- σ^E processing and expression of a σ^E -dependent *lacZ* fusion (Fig. 4). Moreover, expression of *csfX* independent

of σ^F early during sporulation (by placing the *csfX* gene under the control of the *spoIIIG* promoter) allows pro- σ^E processing to occur in the complete absence of σ^F (Fig. 5). Altogether, these results demonstrate that *csfX* is the only gene controlled by σ^F required for activation of σ^E .

Discussion

The early forespore-mother cell transduction pathway

The whole sporulation cascade of gene expression has been proposed to be controlled by a crisscross mechanism in which signals flow from one cell to the other where they induce the next developmental step by activating a new σ factor. Three such transduction pathways have been postulated, between σ^F and σ^E , between σ^E and σ^G , and between σ^G and σ^K (Losick and Stragier 1992). Until now, the latter case was the best understood at the genetic level, but it has not yet been possible to find conditions allowing activation of σ^K under artificial conditions, a prerequisite for analyzing the role of the various partners in the pathway.

Because such conditions have already been defined for σ^E , by inducing simultaneously σ^F , SpoIIIGA, and pro- σ^E during exponential growth (Shazand et al. 1995), the identification of the *csfX* gene has allowed us to unravel the complete transduction pathway leading from σ^F to σ^E . The *csfX* gene is controlled exclusively by σ^F and is therefore presumably transcribed only in the forespore (Margolis et al. 1991). As expected from the existence of

Figure 4. Activation of SpoIIIGA-mediated pro- σ^E processing by CsfX during exponential growth. (Top) The time course expression of a transcriptional fusion of the *lacZ* gene to the σ^E -dependent *spoIID* promoter (integrated at the *amyE* locus) in cells engineered to produce pro- σ^E , as well as SpoIIIGA ($\blacklozenge$), CsfX ($\square$), or both ($\bullet$), in response to IPTG. Time indicates hours after addition of IPTG. No β -galactosidase was accumulated in the absence of IPTG. (Bottom) An immunoblot analysis of pro- σ^E processing after addition of IPTG, in the same set of strains and the same samples.

pro- σ^E processing in a *spoIIIE36* mutant, the *csfX* gene is located in the region of the chromosome that belongs to the 30% closest to the replication origin. It should be noted that the very high level of *csfX* transcription observed in this background was completely abolished by inactivating *spoIIAC*, or by moving the *csfX-lacZ* fusion from the *amyE* locus (which segregates into the forespore in this mutant) to *thrC* (which does not), indicating that the overexpression observed is still dependent on σ^F and is forespore compartmentalized (not shown).

Inducing *csfX* together with *spoIIIGA* and *spoIIGB* during exponential growth is sufficient to get efficient pro- σ^E processing and expression of a σ^E -dependent *lacZ* fusion. In addition to confirming that SpoIIIGA is the pro- σ^E processing enzyme as suggested originally (Stragier et al. 1988), these experiments indicate that no other *csf* gene is involved in the pathway, as demonstrated further by the bypass of σ^F for pro- σ^E processing observed when *csfX* is expressed through an early sporulation promoter independent of σ^F . The *PspoIIG-csfX* construct has no negative effect on sporulation of a wild-type strain and

fully complements the sporulation defect of a *csfX* mutant, suggesting that the σ^E molecules processed before asymmetric septation (if any) do not interfere with the sporulation process.

The role of CsfX

The sequence of the CsfX protein does not give any clue about its function. However, it is very likely that CsfX plays a catalytical role because experiments in which *csfX* was under the control of the inducible *spac* promoter have shown that the background level of *csfX* expression in the absence of inducer is sufficient for production of 5% of the wild-type level of heat-resistant spores (not shown). The presence of a signal sequence indicates that CsfX is presumably translocated outside of the forespore cytoplasm where it could act, directly or indirectly, on the SpoIIIGA molecules embedded in the septum membrane on the mother cell side (Fig. 6). Previous experiments have shown that the septum is not absolutely required for transducing the CsfX signal to SpoIIIGA and that conditions can be found where σ^E is

Figure 5. Bypass of σ^F for activation of σ^E by CsfX during early sporulation. (Top) The time course expression of a *spoIID-lacZ* fusion (integrated at the *thrC* locus) in cells containing a second copy of the *csfX* gene under the control of the *spoIIG* promoter (integrated at the *amyE* locus), and in which *spoIIAC* (the gene encoding σ^F) is either intact ($\bullet$) or disrupted ($\circ$). Time indicates hours in sporulation. (Bottom) An immunoblot analysis of pro- σ^E processing in the same set of strains, with samples being harvested at the hours indicated.

Figure 6. Signaling pathway coupling mother cell-specific gene expression to forespore development. A portion of the sporulation septum is schematized, with the forespore on the left and the mother cell on the right. It consists of the cytoplasmic membranes of the two cells (shown as lipidic bilayers) bracketing a thin peptidoglycan cell wall (shown as a weaved layer). Cell-specific activation of σ^F after septation leads to *csfX* being expressed only in the forespore. Its

signal sequence should allow the Csfx protein to be exported outside of the forespore and to be released in the innerseptal space. There, it could either contact the membrane-bound SpoIIIGA protein directly or modify some septum feature sensed by SpoIIIGA and trigger processing of pro- σ^E in the mother cell. The potential processing activity of SpoIIIGA in the forespore (?) remains to be investigated.

processed in the same cell where Csfx is synthesized (Shazand et al. 1995). Therefore, the action of Csfx on the SpoIIIGA molecules present in the forespore membrane remains a matter of speculation. Csfx appears to generate a short-range signal, as we have not been able to observe any extracellular complementation when mixing *csfX* and *spoIIIG* clones. Interestingly, these experiments allowed us to detect a pigmentation difference between these two classes of mutants, which are both devoid of active σ^E . This suggests that Csfx might modify some feature of the bacterial envelope, including the septal space, which, in turn, would activate SpoIIIGA processing activity. Such a signal transduction pathway is reminiscent of the coupling of σ^K activation in the mother cell to *spoIVB* expression directed by σ^G in forespore at late stages of sporulation (Cutting et al. 1991). The homologous roles played by Csfx and SpoIVB at different stages of development might reflect related enzymatic functions. Presumably both proteins synthesized in the forespore are involved in remodeling of the peptidoglycan present in the space between the forespore and the mother cell. In addition, or as a mere consequence of their enzymatic function, they activate a membrane-bound protease that triggers a new transcription program in the mother cell.

Materials and methods

Cloning of *csfX*

The integrative plasmid library (O'Reilly et al. 1994) was introduced in the recipient strain MO1809 [*trpC2 phe-1 xylAΔtet spoIIIEΔkan spoIIIGBΔerm spoIIIE36 amyE::[P_{xylA}-spoIIIE spc]*, and the transformants selected on sporulation agar plates, in the presence of chloramphenicol (5 μ g/ml), xylose (2.5 mM), and 5-bromo-4-chloro-3-indolyl- β -D-galactopyranoside (100 μ g/ml). Blue colonies were purified and checked for their color in the absence of xylose. The selected strains were grown in the presence of 50 μ g/ml of chloramphenicol to amplify the integrated *lacZ* plasmids, which were rescued by restricting chromosomal DNA with *EcoRI*, followed by ligation and transformation of *Escherichia coli* (Perego 1993). In the case of the *csfX* locus, a 2.5-kb fragment was recovered that corresponds to the initial *Sau3A* fragment cloned upstream of *lacZ* in pJM783 (O'Reilly et al. 1994). Partial nucleotide sequence was obtained using a primer hybridizing just downstream of the fusion point. DNA extending 2.7 kb farther downstream was cloned by a similar

procedure after restricting nonamplified chromosomal DNA with *PvuII*.

lacZ fusions

The original fusion between *csfX* and *lacZ* was recovered as a *SphI*-*Clal* fragment that contained 354 bp upstream of the putative transcription start of *csfX* as well as the junction with *lacZ* at a *Sau3A* site located at codon 40 in *csfX*. This fusion was cloned in the pDG268 vector (Antoniewski et al. 1990) and introduced into the chromosome at the *amyE* locus (Shimotsu and Henner 1986). The *spoIID-lacZ* transcriptional fusion integrated at the *amyE* locus has been described previously as well as the conditions of culture and β -galactosidase assay (Stragier et al. 1988). All of the strains used are derivatives of strain JH642. β -Galactosidase activity is expressed as nanomoles of 2-nitrophenyl- β -D-galactopyranoside hydrolyzed per minute per milligram of protein.

Induction of σ factors during growth

Conditions of induction of the *spac* promoter (Yansura and Henner 1984) by IPTG during exponential growth have been described previously (Frandsen and Stragier 1995). The genes encoding the various sporulation σ factors were cloned downstream of the *spac* promoter on a multicopy plasmid providing resistance to erythromycin. To avoid interferences attributable to autoregulation, competition, or inhibition, the strains carried chromosomal disruptions of *spoIIIG* (the gene encoding σ^G), when inducing σ^F or σ^C , or of both *sigB* and *rsbW* (the genes encoding σ^B and its inhibitor), when inducing σ^B .

Heterochronic expression of *csfX*

The *csfX*-coding sequence was cloned as a *BfaI*-*XhoI* fragment downstream of the *spac* promoter, in a plasmid allowing integration by marker exchange at the chromosomal *thrC* locus (a gift of A.-M. Guérout-Fleury, Institut de Biologie Physico-Chimique, Paris, France). The *BfaI* site overlaps the putative *csfX* transcription start, and the *XhoI* site is located 120 bp downstream of the *csfX* reading frame. The *Pspac-csfX* construct fully complements the sporulation defect of a *csfX* mutant when grown in the presence of 1 mM IPTG. The multicopy plasmids carrying various parts of the *spoIIIG* operon (encoding SpoIIIGA and pro- σ^E) under the control of the *spac* promoter have been described previously (Stragier et al. 1988). The *BfaI*-*XhoI* fragment carrying the *csfX*-coding sequence was also cloned downstream of the *spoIIIG* promoter [which is activated shortly after the onset of sporulation (Kenney and Moran 1987)],

in a plasmid allowing integration by marker exchange at the chromosomal *amyE* locus.

Immunoblot analysis

Clarified crude extracts prepared by ultrasonication were analyzed by polyacrylamide gel electrophoresis (PAGE; 12.5% acrylamide) in the presence of SDS. Proteins were detected by immunoblotting (Sambrook et al. 1989), using a monoclonal antibody directed against σ^E (Trempy et al. 1985b) and a secondary antibody conjugated to alkaline phosphatase (Hyclone).

Acknowledgments

We thank K. Devine for the *lacZ* plasmid library, F. Arigoni for the *xyl-spoII*E strain, P. Glaser for sequence data, B. Haldenwang for the anti- σ^E antibody, and M. Karow and P. Piggot for unpublished results. This work was supported by grants from Centre National de la Recherche Scientifique (URA1139), Institut de la Santé et de la Recherche Médicale (CRE930111), and the Human Frontier Science Program.

The publication costs of this article were defrayed in part by payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 USC section 1734 solely to indicate this fact.

References

- Antoniewski, C., B. Savelli, and P. Stragier. 1990. The *spoII* gene, which regulates early developmental steps in *Bacillus subtilis*, belongs to a class of environmentally responsive genes. *J. Bacteriol.* **172**: 86–93.
- Cutting, S., A. Driks, R. Schmidt, B. Kunkel, and R. Losick. 1991. Forespore-specific transcription of a gene in the signal transduction pathway that governs pro- σ^K processing in *Bacillus subtilis*. *Genes & Dev.* **5**: 456–466.
- Driks, A. and R. Losick. 1991. Compartmentalized expression of a gene under the control of sporulation transcription factor σ^E in *Bacillus subtilis*. *Proc. Natl. Acad. Sci.* **88**: 9934–9938.
- Errington, J. 1993. Sporulation in *Bacillus subtilis*: Regulation of gene expression and control of morphogenesis. *Microbiol. Rev.* **57**: 1–33.
- Frandsen, N. and P. Stragier. 1995. Identification and characterization of the *Bacillus subtilis* *spoIIP* locus. *J. Bacteriol.* **177**: 716–722.
- Gholamhoseinian, A. and P.J. Piggot. 1989. Timing of *spoII* gene expression relative to septum formation during sporulation of *Bacillus subtilis*. *J. Bacteriol.* **171**: 5747–5749.
- Illing, N. and J. Errington. 1991. Genetic regulation of morphogenesis in *Bacillus subtilis*: Roles of σ^E and σ^F in prespore engulfment. *J. Bacteriol.* **173**: 3159–3169.
- Karow, M.L., P. Glaser, and P.J. Piggot. 1995. Identification of a gene, *spoIIR*, which links the activation of σ^E to the transcriptional activity of σ^F during sporulation in *Bacillus subtilis*. *Proc. Natl. Acad. Sci.* (in press).
- Kenney, T.J. and C.P. Moran Jr. 1987. Organization and regulation of an operon that encodes a sporulation-essential sigma factor in *Bacillus subtilis*. *J. Bacteriol.* **169**: 3329–3339.
- LaBell, T.L., J.E. Trempy, and W.G. Haldenwang. 1987. Sporulation-specific σ factor σ^{29} of *Bacillus subtilis* is synthesized from a precursor protein, P³¹. *Proc. Natl. Acad. Sci.* **84**: 1784–1788.
- Lewis, P.J., S.R. Partridge, and J. Errington. 1994. σ factors, asymmetry, and the determination of cell fate in *Bacillus subtilis*. *Proc. Natl. Acad. Sci.* **91**: 3849–3853.
- Losick, R. and P. Stragier. 1992. Crisscross regulation of cell-type specific gene expression during development in *Bacillus subtilis*. *Nature* **355**: 601–604.
- Margolis, P., A. Driks, and R. Losick. 1991. Establishment of cell type by compartmentalized activation of a transcription factor. *Science* **254**: 562–565.
- O'Reilly, M., K. Woodson, B.C.A. Dowds, and K.M. Devine. 1994. The citrulline biosynthetic operon, *argC-F*, and a ribose transport operon, *rbs*, from *Bacillus subtilis* are negatively regulated by Spo0A. *Mol. Microbiol.* **11**: 87–98.
- Partridge, S.R., D. Foulger, and J. Errington. 1991. The role of σ^F in prespore-specific transcription in *Bacillus subtilis*. *Mol. Microbiol.* **5**: 757–767.
- Perego, M. 1993. Integrational vectors for genetic manipulation in *Bacillus subtilis*. In *Bacillus subtilis and other Gram-positive bacteria: Biochemistry, physiology, and molecular biology* (ed. A.L. Sonenshein, J.A. Hoch, and R. Losick), pp. 615–624. American Society for Microbiology, Washington, D.C.
- Peters, H.K. III and W.G. Haldenwang. 1991. Synthesis and fractionation properties of SpoIIGA, a protein essential for pro- σ^E processing in *Bacillus subtilis*. *J. Bacteriol.* **173**: 7821–7827.
- Rong, S., M.S. Rosenkrantz, and A.L. Sonenshein. 1986. Transcriptional control of the *Bacillus subtilis* *spoIID* gene. *J. Bacteriol.* **165**: 771–779.
- Sambrook, J., E.F. Fritsch, and T. Maniatis. 1989. *Molecular cloning: A laboratory manual*, 2nd ed. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York.
- Shazand, K., N. Frandsen, and P. Stragier. 1995. Cell-type specificity during development in *Bacillus subtilis*: The molecular and morphological requirements for σ^E activation. *EMBO J.* (in press).
- Shimotsu, H. and D.J. Henner. 1986. Construction of a single-copy integration vector and its use in analysis of regulation of the *trp* operon of *Bacillus subtilis*. *Gene* **43**: 85–94.
- Stragier, P., J. Bouvier, C. Bonamy, and J. Szulmajster. 1984. A developmental gene product of *Bacillus subtilis* homologous to the sigma factor of *Escherichia coli*. *Nature* **312**: 376–378.
- Stragier, P., C. Bonamy, and C. Karmazyn-Campelli. 1988. Processing of a sporulation sigma factor in *Bacillus subtilis*: How morphological structure could control gene expression. *Cell* **52**: 697–704.
- Sun, D., P. Fajardo-Cavazos, M.D. Sussman, F. Tovar-Rojo, R.M. Cabrera-Martinez, and P. Setlow. 1991. Effect of chromosome location of *Bacillus subtilis* forespore genes on their *spo* gene dependence and transcription by σ^F : Identification of features of good σ^F -dependent promoters. *J. Bacteriol.* **173**: 7867–7874.
- Trempy, J.E., C. Bonamy, J. Szulmajster, and W.G. Haldenwang. 1985a. *Bacillus subtilis* sigma factor, σ^{29} , is the product of the sporulation-essential gene *spoIIG*. *Proc. Natl. Acad. Sci.* **82**: 4189–4192.
- Trempy, J.E., J. Morrison-Plummer, and W.G. Haldenwang. 1985b. Synthesis of σ^{29} , an RNA polymerase specificity determinant, is a developmentally regulated event in *Bacillus subtilis*. *J. Bacteriol.* **161**: 340–346.
- Wu, L.J. and J. Errington. 1994. *Bacillus subtilis* SpoIIIE protein required for DNA segregation during asymmetric cell division. *Science* **264**: 572–575.
- Yansura, D.G. and D.J. Henner. 1984. Use of the *Escherichia coli* *lac* repressor and operator to control gene expression in *Bacillus subtilis*. *Proc. Natl. Acad. Sci.* **81**: 439–443.

Cell-cell signaling pathway activating a developmental transcription factor in *Bacillus subtilis*.

J A Londoño-Vallejo and P Stragier

Genes Dev. 1995, **9**:

Access the most recent version at doi:[10.1101/gad.9.4.503](https://doi.org/10.1101/gad.9.4.503)

References

This article cites 24 articles, 18 of which can be accessed free at:
<http://genesdev.cshlp.org/content/9/4/503.full.html#ref-list-1>

License

Email Alerting Service

Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article or [click here](#).