Regulation of gene expression during competence development in bacillus subtilis.

Sinderen, Douwe van

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
1994

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Summary and concluding remarks

The development of genetic competence in Bacillus subtilis represents a prokaryotic specialization process which has attracted much attention for several reasons. First, because B. subtilis is easily amenable to genetic analysis and is, therefore, the best-studied Gram positive prokaryote. In addition, B. subtilis is a non-pathogenic representative of an industrially important genus commonly used for fermentation processes. Furthermore, competence development is an example of a relatively simple cell-differentiation system and improved understanding of this process may facilitate further insight into the very complicated regulatory schemes underlying eukaryotic developmental programmes. Finally, from a scientific point of view the uptake of DNA is an intriguing transport process which is distinct from other transport systems since it requires unique adaptations to allow passage of the DNA macromolecule through the cell-envelope.

In recent years much has been learnt about the regulatory aspects of competence. Competence develops as a post-exponential response to nutrient deprivation and is under the control of a signal transduction system which monitors environmental and cytoplasmic changes. It has become apparent that the competence signal transduction pathway is embedded into a larger regulatory network controlling all known post-exponential adaptation responses.

Chapter I of this thesis reviews identified components of the competence signal transduction pathway, the signals they are responding to, their mutual interactions, and the means by which they effect synthesis of proteins involved in DNA binding, DNA uptake, and recombination.

Chapters II, III, and IV describe the cloning, sequence analysis and characterization of srfA, a large operon required for two different post-exponential processes, i.e. the non-ribosomal production of the peptide-antibiotic surfactin and competence development. srfA encodes a large multi-enzyme complex consisting of seven amino acid activation domains responsible for the activation and sequential addition of the seven amino acids which compose the surfactin molecule. It is shown that only the portion of srfA encoding the fourth, valine-activating domain plays a regulatory role in competence and functions as an assembly link between other regulatory components of the competence signal transduction pathway.

In chapter V it is demonstrated that the genetic determinant of the competence-required srfA region comprises a small open reading frame, comS, located within but translated in a frame different from that of srfA.

Chapter VI describes the cloning and characterization of comK, which, as reported in chapter VII, functions as competent. All regulators converge at the point of post-translational level. In competence transcriptional activation is required of the DNA-entry apparatus. Transcriptional effects are shown to be dependent on the target genes.

Chapters IX and X describe the cloning, sequence analysis and characterization of srfA, which are involved in the transcriptionally activated induction is shown to be used for the production of surfactin. Chapters XII describes the cloning and characterization of comK, which encodes an extracellular protein used for the production of surfactin.

Chapter XI describes the cloning and characterization of comK, which functions as a competence determinant. All regulatory genes converge at the point of transcriptional activation.

Chapters XI and XII describe the cloning and characterization of tlpC, which encodes chemotaxis proteins. This suggests the determination of the interglonal signal transduction pathway.

It has become evident that the signal transduction pathway responds to a variety of stimuli and conditions. During recent years many new and the actual sensory mechanisms and communication between B. subtilis will (continue to) competence regulation and
represents a prokaryotic cell for several reasons. First, it is, therefore, the best-choice is a non-pathogenic strain used for fermentation processes of a relatively simple process may facilitate the understanding of the underlying eukaryotic view the uptake of DNA transport systems since it is a non-pathogenic strain. Secondly, environmental and influence signal transduction controlling all known post-exponential steps and characterization of signal transduction processes, i.e. the non-pathogenic strain used for fermentation processes of a relatively simple process may facilitate the understanding of the underlying eukaryotic signal transduction processes. Secondly, environmental and influence signal transduction controlling all known post-exponential adaptation processes.

During recent years many components of this network have been identified and considerable progress has been made to elucidate the regulatory machinery involved. However, little is known about the nature of the environmental signals, their targets and the actual sensory mechanism involved in signal recognition. Active cooperation and communication between laboratories working on post-exponential regulation in *B. subtilis* will (continue to) be necessary to unravel the molecular basis underlying competence regulation and other post-exponential phenomena.

Chapter VII, functions as the final autoregulatory control switch before a cell becomes competent. All regulatory branches of the competence signal transduction pathway converge at the point of *comK* expression, both at the transcriptional as well as the post-translational level. In chapter VIII the gene product of *comK* is identified as the competence transcription factor (CTF), which is directly responsible for the transcriptional activation of the genes encoding components of the DNA uptake apparatus. Transcriptional activation of the latter genes as well as *comK* itself is shown to be dependent on the binding of ComK (CTF) to promoter-upstream regions of its target genes.

Chapters IX and X describe the finding that the *addAB* operon, *recA*, and *dinR*, genes which are involved in (the regulation of) recombination and DNA repair, are also transcriptionally activated during the development of competence. This transcriptional induction is shown to be dependent on CTF which binds to the (promoter-)upstream regions of these genes. The biological significance of the simultaneous synthesis of the DNA-entry apparatus and the induced expression of genes involved in recombination is evident: in this way it is guaranteed that the internalized single-stranded DNA will be used for the production of heteroduplex molecules.

Chapter XI describes the differential expression of two deoxyribonuclease (DNase)-encoding genes. The expression of *nucA* is under competence control and dependent on *comK*, although the DNase does not appear to play a role in competence. The *nucB* gene specifies an extracellular sporulation-specific DNase which seems to be expressed in a cell type-specific manner.

Chapter XII is included as an addendum and describes the sequence analysis and characterization of *tlpC*, a gene encoding a protein similar to methyl-accepting chemotaxis proteins. This gene was identified as a byproduct of the sequence determination of the intergenic region between *srfA* and *nucA*.

It has become evident that competence development is dependent on a multi-sensory signal transduction pathway as part of a regulatory network responsive to a wide variety of stimuli and controlling all known post-exponential adaptation processes. During recent years many components of this network have been identified and considerable progress has been made to elucidate the regulatory machinery involved. However, little is known about the nature of the environmental signals, their targets and the actual sensory mechanism involved in signal recognition. Active cooperation and communication between laboratories working on post-exponential regulation in *B. subtilis* will (continue to) be necessary to unravel the molecular basis underlying competence regulation and other post-exponential phenomena.