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BACTERIAL COMMUNICATION SYSTEMS

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It has known for a decade that bacteria can interact with each other via specific communication systems. These cell-to-cell communication mechanisms are used to regulate the expression of genes involved in diverse functions, such as bioluminescence, virulence, genetic competence, or the production of antimicrobial compounds. Modulation of the genes involved is done in a co-ordinated and cell density-dependent manner and has been termed quorum sensing. Quorum sensing systems are expected to evolve in high cell-density

ecosystems with many microbial interactions and a diffusion barrier, where they would enable bacterial populations to co-ordinate responses that might lead to competitive advantages, efficient adaptation and responses to changing environmental conditions, or co-ordination of interactions between bacteria and their abiotic or biotic environment.

A variety of physiological changes in bacterial populations have been shown to be dependent on specific cell densities and growth phases. This phenomenon of cell density-dependent gene expression has been termed quorum sensing, and was initially found to be involved in the regulation of bioluminescence in *Vibrio fischeri*. Since then, many other quorum sensing systems have been discovered in both Gram-negative and Gram-positive bacteria. Well-studied examples in Gram-negative bacteria include virulence and biofilm-formation in *Pseudomonas aeruginosa*, swarming motility of *Serratia liquefaciens* and root-nodule formation by *Rhizobium leguminosarum*. In Gram-positive bacteria quorum sensing regulation includes genetic competence in *Bacillus subtilis* and *Streptococcus pneumoniae*, virulence in *Staphylococcus aureus*, and the production of antimicrobial peptides, including bacteriocins and lantibiotics, in lactic acid bacteria. For regulation of these quorum sensing systems bacteria produce extracellular signalling molecules that are responsible for bacterial cell-to-cell communication. Several distinct families of signalling molecules have been identified so far, including N-acyl homoserine lactones, 4-quinolones, di-keto-piperazines, autoinducer-2 and peptides.

While many Gram-negative bacteria communicate via N-acyl- homoserine lactones, peptides are the most common and well-studied signalling molecules in Gram-positive bacteria, here referred to as autoinducing peptides (AIP). These signalling peptides show a variety of structures but share a small size, are ribosomally synthesised, and are in some cases subject to post-translational modifications that add to their stability and functionality. It has been suggested that genes for autoinducing peptides may also be present in Gram-negative bacteria, implying that peptide-based signalling is a general system in bacteria.

Autoinducer-2 (AI-2), which is a furanosyl-borate-diester, has been detected in both gram-negative and gram-positive bacteria and may therefore serve as an interspecies signalling molecule.

Operation of QS system is based on several key principles:

- The use of small signaling molecules - the QS system transfer signals from one cell to another by means of signaling molecules of different chemical nature.
- The presence of specific receptors - signaling molecules do not affect the expression of target genes directly. Activation of target genes occurs only after binding of signaling molecules with appropriate receptors.
- The influence of cell density - the launch of QS system occurs only when

cell density reaches a certain value, which correlates with the concentration of signaling molecules in the environment.

- Self control function - control the synthesis of new signaling molecules and receptors occurs as well as gene-targets in the absence of repression systems activation.
- The presence of selective mechanisms of negative regulation - there are both dependent and independent from QS negative regulation genes in the microorganism cells, which products are able to turn off selectively some chain of QS system or the whole system.

In the terms of structural and functional organization, there are two basic types of QS systems - autoinducing system and system of signal transduction.

The autoinducing system works in the following way. Signal molecules synthesized by I-protein, are taken out from the cells by diffusion and accumulate in the environment. When AHL molecules reach threshold concentration they enter inside the cells and bind with R-protein that leads to formation of AHL-R complexes. Multimeric complexes assume polymerase activity and cause target genes expression. n(AHL-R) complexes also induct expression of genes encoding I and R proteins and by this way cause accumulation of new AHL and their receptors i.e. inducing QS system function.

Signaling transduction system is typical for Gram-positive microorganisms. Peptides are used as signaling molecules in this system. Autoinducing peptides are processed during the export from the cell and in several cases they can be the subject to posttranslational modification before or after export. The modification reactions occur intracellularly on the precursor peptide and involve several modification enzymes encoded by the genes that are also the subject to autoregulation. The modified precursor peptides are exported by a dedicated ATP-depend ABC exporter. This transporter consists of three functional domains: domain A - is a channel through which polypeptide molecule passes; domain B - is ATP-ase which provides transporter function and domain C - is peptidase involved in polypeptide chains processing. In this way signaling peptide molecules accumulated in intracellular space. When the signaling peptide molecules reach threshold concentration they don't enter inside the cells but bind with specific receptors on the cell surface. This receptors are associated with sensor kinases (usually, histidine kinase) via transmembrane domain. Signaling peptides bind with the receptors lead to the activation of sensor kinase, which is phosphorylate peptide controller. After this, peptide controller acquires polymerase activity and activates target genes expression.