A subfamily of MalT-related ATP-dependent regulators in the LuxR family

The hallmark of the bacterial regulatory proteins belonging to the LuxR family is a conserved helix-turn-helix motif (Prosite motif PS00017) located in their C-terminal DNA-binding domain (the Pfam database provides an alignment of the corresponding domains; http://www.sanger.ac.uk/software/Pfam/browse.shtml). Members of this rapidly expanding family include regulators of two-component sensory transduction systems as well as ATP-binding regulators of the LuxR family. The features distinguishing MalT from other LuxR family members (size, N-terminal ATP-binding site) have been identified in AlkS, a regulator of the acetoin dehydrogenase operon in Klebsiella pneumoniae (8). In the DNA region upstream of thcF, encoding the thiocarbamate herbicide-inducible non-haem haloperoxidase from the actinomycete Rhodococcus erythropolis (4), we have identified a gene encoding another LuxR family member of unusual size (ThcG, 927 aa) with an ATP-binding motif close to the N-terminal end (unpublished data). By scrutinizing the protein databases for proteins combining these features, a sub-family of regulators emerged for which the acronym LAL (Large ATP-binding regulators of the LuxR family) is proposed.

An overview of currently known LAL proteins is provided in Table 1. They range in molecular mass from 88 kDa (Rv0339c) to 125 kDa (Rv1358). Among regulators from Gram-negative bacteria, AlkS from Pseudomonas oleovorans (regulator of alkanete metabolism; 13) and OrfV from Pseudomonas alcaligenes (clustered with xcp genes; 5) conform to the requirements set for LAL regulators. However, the subfamily seems to be dominated by regulatory proteins from Actinomycetes. The Mycobacterium tuberculosis genome (2) apparently encodes five such regulators and several representatives are also found in Streptomyces species, but in most cases their function is not yet known. LipK is involved in production of an extracellular lipase by Streptomyces exfoliatu (11). As inferred from the associated genes, the other Streptomyces proteins may be involved in polyketide synthesis (6, 10, 12) or sterol metabolism (7). Apart from the N- and C-terminal regions, sequence conservation between LAL proteins is very low. The motif discovery tools MEME (http://www.sds. edu/meme/meme/website/mast.html) and BLOCKMAKER (http://blocks.f McLRC/OB/ blocks/blockmk/ make_blocks.html) readily identified the conserved regions with the Walker A and B motifs and with the helix-turn-helix domain but no additional conserved region common to all these LAL proteins was apparent. A database search for additional proteins combining the three MEME-based motifs using MAST (http://www.sds.edu/ meme/meme/website/mast.html) revealed no other LAL-like proteins.

The conservation of the nucleotide-binding and DNA-binding domains among LAL proteins points to a common mechanism of ATP-dependent transcriptional activation different from the activity of the majority of LuxR family members. Probably, the large non-homologous central part of a LAL regulator allows for a complex modulation of its activity by interaction with multiple effectors.

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Species Protein Size (aa) ATP-binding site* HTH† Function (cluster)† Accession no.

**γ-Proteobacteria**


*Klebsiella pneumoniae* AcO 921 64–71/153–157 874–901 Acetoain dehydrogenase U10533

*Pseudomonas syringae* MalT 877 36–43/123–127 832–859 (xcp operons) AF092918

*Pseudomonas oleovorans* AlcS 882 51–58/138–142 818–845 Alkane oxidation X52935

*Actinomycetes*


*Rv0366c* 1085 221–228/291–295 1041–1068 – AL0211931

*Rv0890c* 882 15–22/84/88 835–862 – Z73101


*Streptomyces coelicolor* LipR 941 41–48/95–99 873–900 (Extracellular lipase) AF009336

*SC1A7.02c* 892 61–68/144–148 846–873 – AL031155

*Streptomyces exfoliatus* LipR 934 7–95–995 868–895 Extracellular lipase M86351

*Streptomyces hygroscopicus* Orf6 948 16–23/159–163 900–927 (Polyketide synthesis) AF071011

*Streptomyces venezuelae* OrfH 872 16–23/106–110 834–861 (Polyketide synthesis) X86780

*Streptomyces sp.* PikD 928 32–39/134–138 880–907 (Polyketide synthesis) AF079139

*Rhodococcus erythropolis* ThcG 927 44–51/142–146 875–902 (Non-haem chloroperoxidase) U95170

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*Preceding entries in the table are numbered sequentially.*

*Position of LuxR-type helix–turn–helix motif (HTH, DNA binding site; Prosite PS00622).*  
†If the actual regulatory function has not yet been identified, the function of adjacent genes, if known, is indicated in parentheses.

†§The *S. exfoliatus* LipR displays the Walker B motif but lacks the Walker A motif (11). The occurrence of a correctly positioned Walker A motif in a different reading frame suggests a possible frame-shift in the reported sequence. The LipR homologues from *S. coelicolor* (this table) and *S. albus* (partial sequence for N-terminal fragment; 3) contain both motifs.

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