# Protein serine/threonine kinases in signal transduction for secondary metabolism and morphogenesis in Streptomyces

## Abstract

A number of proteins in the Gram-positive bacterial genus Streptomyces are phosphorylated on their serine/threonine and tyrosine residues in response to developmental phases. AfsR is one of these proteins and acts as a transcriptional factor in both the regulation of secondary metabolism in Streptomyces coelicolor A3(2) and morphological differentiation in Streptomyces griseus. In S. coelicolor A3(2), AfsR is phosphorylated on its serine and threonine residues by more than three protein kinases whose kinase activity is enhanced by means of autophosphorylation on their serine and threonine residues. The degree of autophosphorylation of AfsK is regulated by KbpA which, by binding directly to the kinase domain of AfsK, inhibits its autophosphorylation. Phosphorylation of AfsR enhances its DNA-binding activity and causes it to bind the promoter elements, including –35, of afsS, thus resulting in activation of afsS transcription. ATPase activity of AfsR is essential for this transcriptional activation, probably because the energy available from ATP hydrolysis is required for the isomerization of the closed complex between AfsR and RNA polymerase to a transcriptionally competent open complex. afsS, encoding a 63-aminoacid protein, then activates transcription of actII-ORF4, a pathway-specific transcriptional activator in the actinorhodin biosynthetic gene cluster, in an as yet unknown way. Distribution of the afsK-afsR systems in a wide variety of Streptomyces species and the presence of many phosphorylated proteins in a given Streptomyces strain suggest that the signal transduction via not only two-component regulatory systems but also serine/ threonine kinases generally regulates secondary metabolism and morphogenesis in this genus.