Supplemental Materials and Methods

Growth of *S. griseus*

Growth of *S. griseus* strains in liquid medium was monitored by measuring the amount of intracellular proteins. Cells were collected by centrifugation and resuspended in 1 M NaOH. The cell suspension was boiled for 5 min, and the supernatant was collected by centrifugation. Protein concentration was determined by Bradford protein assay kit (Bio-Rad) using bovine serum albumin as a standard.

Primers

All PCR primers (except those described below) are shown in Supplementary Table 1. Chromosomal DNA was used as a template for PCR. For the construction of plasmids, nucleotide sequencing was used to ensure the absence of PCR errors in the amplified fragments.

Construction of plasmids for expression of polyhistidine-tagged AdpA

A 2-kb DNA fragment containing *adpA* and its 5’ upstream region was amplified by PCR using primers 5’-TATAAGCTTTGACGCTGGAGGGAGCAT-GCCCGA-3’ (HindIII site underlined) and 5’-TATGAATTCCTACGGGGCACTCCGCTGTCCCGG-3’ (EcoRI site underlined) and cloned between the HindIII and EcoRI sites of pTYM19, resulting in pTYM19-*adpA*. pTYM19-*Nhis12-adpA* was described previously.[1] To construct pTYM19-*adpA-Chis12*, a 2-kb DNA fragment containing *adpA* and its 5’ upstream region was amplified by PCR using primers 5’-TATAAGCTTTGACGCTGGAG-GGAGCATGCCCGA-3’ (HindIII site underlined) and 5’-TATGAATTCCTAGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGCGGGGCACTCCGCTGTCCCGG-3’ (EcoRI site underlined), and cloned between the HindIII and EcoRI sites of pTYM19. These plasmids were integrated into the chromosome of *S. griseus* mutant Δ*adpA* by site-specific recombination at the bacteriophage ϕC31 attachment site.[2]

Streptomycin assay

The amount of streptomycin produced was measured by a bioassay using *Bacillus subtilis* ATCC 6633 as an indicator.[3]

Preparation of total cellular protein from *S. griseus* and western blotting

For the extraction of total protein from mycelia in liquid culture, cells were harvested by centrifugation, washed twice, resuspended with native buffer (10 mM Tris-HCl, 150 mM NaCl, 10 mM EDTA, and 1 × protease inhibitor cocktail (Roche), pH 7.5), and disrupted with sonication at 4°C. The cell debris was removed by centrifugation. The procedure for extraction of total protein from mycelia on solid culture was as previously described.[1] Proteins were separated by 10% SDS-polyacrylamide gel electrophoresis (PAGE), and blotted onto a polyvinylidene fluoride (PVDF) membrane. His-tagged proteins were detected with penta-His HRP conjugate kit (QIAGEN) and a chemiluminescent kit (SuperSignal West Dura, Pierce).

Extraction of total RNA

Total RNA was isolated according to a previously described method.[1]

Microarray hybridization and data analysis

DNA microarray analysis was performed according to a previously described method.[3]

Co-purification of total RNA and genomic DNA

Two milliliter of cell culture was mixed with 4 ml of RNA protect (Qiagen) and incubated at room temperature for 5 min, then centrifuged. The cell pellet was resuspended in TE containing 20 mg/ml lysozyme and 2 mg/ml proteinase K, and incubated at room temperature for 5 min. Six hundred microliters of denaturing buffer (50 mM Tris-HCl (pH 8.0), 50 mM EDTA, 1% salcosyl and 5 M guanidine thiocyanate), 600 µl of phenol (pH 8.0) and 400 µl of zirconia/silica beads (ϕ 0.1 mm, Biospec) were added to the resuspended cells. Cells were disrupted by vigorously shaking for 2 min and incubation at 65°C for 10 min. Two hundred and eighty microliters of chloroform/isoamyl alcohol was then added and mixed. The liquid was centrifuged to collect the aqueous phase. Then, an equal volume of phenol/chloroform/isoamyl alcohol was added and mixed, and the liquid was centrifuged to collect the aqueous phase. After precipitation by isopropanol, the RNA and DNA pellets were suspended in cetyl trimethyl ammonium bromide (CTAB) buffer (50 mM Tris-HCl (pH 7.5), 10 mM EDTA, 0.8 M NaCl and 1% CTAB). The above-described chloroform/isoamyl alcohol treatment was repeated twice. After the final precipitation by isopropanol, the RNA and DNA pellets were suspended in water.

In silico prediction of AdpA-binding sites

AdpA-binding sites were predicted by MAST[4] motif search algorithm using the AdpA-binding motif built by MEME[4] from known *in vitro* AdpA-binding sequences.[5]

Competitive gel electrophoretic mobility shift assay (EMSA)

Competitor DNA fragments (130-200 bp) were prepared by PCR using appropriate primer sets. Recombinant AdpA protein with a His-tag at its C terminus was produced in *Escherichia coli* and purified on a Ni-NTA column (Qiagen), as described previously.[6] Two DNA fragments containing the AdpA-binding sites of *sgmA* and *sgiA* were labeled with digoxigenin (DIG) using a DIG DNA labeling kit (Roche) and used as probes.[7] Recombinant AdpA (500 ng) was incubated with DIG-labeled *sgmA*-P and *sgiA*-P (100 pg) in the presence of a competitor DNA fragment (500-fold excess), 1 µg poly(dI-dC)-(dI-dC), and 1 µg BSA for 30 min at room temperature in a buffer (10 µl) containing 50 mM NaH_2PO_4, 5 mM Tris·HCl (pH 8.0) and 10% (v/v) glycerol. The reaction mixture was then subjected to 6% PAGE at 4°C for 1 h at 120 V in the running buffer 0.5 × TBE. The DNA was electroblotted onto a Hybond-N+ nylon membrane (GE Healthcare) for 30 min at 100 mA in 0.5 × TBE buffer. For chemiluminescent detection, anti-DIG (Roche) and CDP-star (NEB) were used.

Supplemental Table S1. Primers used in this study.

	forward (5' to 3')	reverse (5' to 3')
[a]Competitive EMSA (130-200 bp)		
category-I genes		
sgmA_1	CTTCGTGCGCGACCTCCT	ATGACCGCCTGATGAGACA
sgmA_2	GTGACCACCCTGTGAATACG	GCAGATGACCGCACCTGT
amfR_1	GTCCTCGACGGCATCGAAC	GGCGTCGACGGGGTGGATT
amfR_2	ACATCCGAACGCCCCCTTCC	AAGGCGACGGGCTGTACG
adsA	AGCGTTATTCTCCTCAGACG	CAGGCCCGAGGCGTCAAC
sprB	ACCGGATCGACGCCTGAC	CAATCGCTGACCGGAGTATC
sprD	AGGCTCCCGGCGGACGAT	TTCCGATCGCGAACACTC
strR_1	GCTTTCATGTGGTGCTCCT	TGCCGAATACATGCAACTT
strR_2	GCGGGGTGGCCCTCCTATTT	GGGCTTTCACGGCGATAA
AdBS4_1	CGACTGGTTCCCGGTCGAGAG	ATCCCGCATGAGCAGCCACA
AdBS4_2	CGATCACAGGTGGTCAACAA	CTGCTTCCGGTGCGAGAC
AdBS4_3	TGACGGGGTGCGCTGAG	GCACGCCGGCGGTATCC
AsBS2_1	GGCCATATCCATACGACCAG	TCACCGAAGATGAGAATGTTT
AdBS2_2	CAGGGGCTCGGCGGATG	AATGAATGGCAATGCCCAAC
up-regulated by AdpA		
SGR1	GCAGGCGACTGTCAGTGT	ACGGGAGACCTTGTTGACC
SGR95_1	AGTTGCGCATGGCAATTTCT	TTTCGATGACAGTGCAGCTC
SGR95_2	ACGTTCGTGCGACCTGAG	GCGCTGATGTGTTCGGTTT
SGR110	AGTCTCTGCTGGGAGTCCTG	CGGTGAACGTCAGCCTCT
SGR179	GTACTGGCGGTCCGTGCT	GACGGCTTCCAGAATCTTCA
SGR180	CCTTCGGGCAGGGACAGC	CCGTCAGGAATCCACTGTTC
SGR262	GACCAACGCCACGACCAC	CGCTCTGGGCAGCTTCATA
SGR264	CCTGAGCGGATGCGAAAC	CGCTCCGCACCTCTCCCAAT
SGR299	GTGTCACACCCAGTGCCTTC	AGGGTGCGTGAGCCACCT
SGR381	TCCCGGCTCGCCGTGTC	TGGGTGGCGTGGTGGTG
SGR390	CCTTCTCCTCCATGCCTTCT	ATTGCCGCCAACCAGGAG
SGR452_1	GGGCGCCGGACTCCTCTC	CACCGGCAGCAGGTTGTT
SGR452_2	GAACCGGCACCGCGTGAG	GCTAGCGACCCTACCCATC
SGR462_1	TCTTCGTCGGTGTGTTTCC	ACACCCCGCGCCCACAG
SGR462_2	GTAGCGTCGCCGACAGATG	CCCGTACCTCTCAGCAGTAAA
SGR598_1	GGAACCCCTCCGCCAATAC	TAAGGGAGCAGAGGTTCGAT
SGR598_2	GGATGTGGCCGAAAGTCG	CGCTGTCGACGGTGTGGA
SGR681	CCATTGCTGCCCGCGTCTT	GGCCGTGGACGGCTGGTC
SGR692	CCCCCACCGCCCGATCC	CTGGTCGGAACGGAGACTTC
SGR695	ATGGGGGCCTCCTTCTCAG	CCCCCGTGTGGTGCATAC
SGR710_1	GCCGGGCCGATGAAGACC	GATCGCACCCGATTACCG
SGR710_2	CTTGGCGGCCGATCAGTAG	ACACGCTTGGCACCGAAAT
SGR731	GGCCGGGTTTTCGTTGTA	AGGACGGTCGGGGAACCT
SGR745	CTTGTGATCAGTCACTGTGCGGACCT	GGTGAGCGAGGCACGGTTG
SGR919	ATTCGGCCAGGCATCCTT	ACATGTGTCTGCAAGACCATAAA
SGR920	ATCACAGGCCGGAAATAGTC	CCAGAGCGTCACCACACC
SGR983	GGGCCGGGAGATTACTCATA	CCACCTTTCCTGCCATCAG
SGR1063_1	GCCGGTCACGAATCTGCAC	AAGGAGAAGCAGTCGAGGTC
SGR1063_2	CGCTCCTGGTGAATCAATTT	CAGAACAGTGCTTCGGCATA
SGR1175	GCTCCCCGGAGTCCTTTT	CAGCAGCGCCACACCTTC
SGR1176	AGCCGGCCTTGGTATCAG	ATCGGCCTGATCCGCTTC
SGR1225	ACCGACAGGGAACACCTCAC	GCGCTACCAGCTCCAAAG
SGR1270	GGGTGCTCTACCCTGTTCC	CTGCTGACATTAGCTCGATACG
SGR1279	CTACCTCAGCGTCGCGA	CCGCTCAGGGTAGGCCG
SGR1331	GGCGCGCTCGATGTCCTG	GTCGGCCCGAGGTCCAGAT
SGR1357	ATGGCGGTATGCGCCACATT	CTCCGGCCGATTGTGAAAT
SGR1360	CAGCCAGTCAAGCGATATGT	ACCCCCATGGCGTGCTCTT
SGR1477	GCCGTACGGTCGAGGAAC	CGCCTCCTGATTCCGTGA
SGR1521	GGGCCTCCCCCTTTTCTT	GCGACAGAGACGGCCGAAAC
SGR1599	GACCCGGCTCCTGGCTCTAC	CTGCGCTCCTGGCGGACT
SGR1699_1	CTGTCTGTTGCCGGTTGG	TTCGACGCATGAACCATTTA
SGR1699_2	GGCTCGCGGGGGTCAGAAC	ACCGAGAAGAAGTTTCGAAGAA
SGR1714	GCCGCGGAACCAACTGCT	GAGCGAGCAAGGGGCTTCAC
SGR1898	TACCGCCAAAAGGTGCATA	GACCAGGGCGATGACTACAG
SGR1940	CTGCTGAGCGCCGCGGC	TGAGCCGATCGCTCCCG

SGR1941	ACGTTTCCTCCTCCGACTG	GTGTCCTGACACCGGACCT
SGR1983	GGCATGTCTCGCAGCATC	CGAGGTCGTACTCCTTGGTC
SGR1984	AGGAAGTCCGACTAACTGTGGA	CGTACGCCGCAGGGGGTTA
SGR1994	GCCATGGCCCCCACCAG	AAACGGCCACCGGACGAT
SGR2001	CGGACGGTTGCGGCCGC	TGGGAGGCACTGGGGCG
SGR2020_1	CCTTCGAGACGCTTCCAC	ACCCGTCACCATCTGCTATT
SGR2020_2	CATTCGGGCAAGAGCTGTA	TCACAGCCGGCGGTGCC
SGR2064	AGGGTGGTCGTCGCGGTA	ACCCCTGCCCGACCGTTG
SGR2066_1	GTGTTCATCTGGTGCGGATA	CAGAAACCGGGCCGAGAG
SGR2066_2	GGAGCCGCCGGAGAAAC	GATGCGGACGACGGGTG
SGR2066_3	ACCTCCTCCACGTAAACACC	GTCCAGGACTCTGGGGCCTA
SGR2079_1	GGCGCGTCACCATGTGTAAT	GGTCCCGCGAGTGCACCA
SGR2079_2	CCTCGCGAGTTTCCGCCAGT	CCGGAACGCGTCGTTGATA
SGR2105	CCCGGTACGGGTGTTCTC	GACTGCGTCGTCTCACCTCT
SGR2115	GGCGTCAAGGAGTGCTTCTA	GAAGCGTCGCCGAAGGAC
SGR2148	TATTGGCCGGTTGTGTTCC	ATGGCCGGGGCCCTACG
SGR2179	AAGTCTGCAACCGACGTCTT	GGGTGTCGTGCCGGTTCC
SGR2185	CTCCGGCCGACCTACTCT	AGGCACTCGACACCATCG
SGR2186	GCTCAAAGTGCTCCTCACCG	TCGGGCGGAGTCCGAGG
SGR2197	CCCGAGAACACGCCATCC	ATTGTCGGACCCGTGGTG
SGR2214	GCTGCTCAGCGACTTGG	GAAAAGCGGCGCCTCAG
SGR2217	AGTCTGCACGAGCCCTTC	AAGTTCCGCTCCGCCTTT
SGR2336	GGTTCTTAACCACGGGAACG	TGGGTTTCGATGATGCTGAT
SGR2446_1	CCACCGGAACGATCATCT	CTCGGTGGCCGGGCAGTT
SGR2446_2	CTCCGCATAAGGAGGTGAAA	GTACATGGACGGCAAGACCT
SGR2446_3	CCAAATACACATGGCTGAGG	CGCTGTGGCCGTGCATAC
SGR2453	AGCTGGCTCTCCCTGGTTAG	CGCAGTATTCAGCACTACGG
SGR2479_1	GAAGCGCTTTTCGGCCAAC	CGTCCGCACGTCGAAGGT
SGR2479_2	GCGCGACCTCCGGTAATC	GCTACGGCTTCGCGAGGAT
SGR2484	CGGGGAGAACCGGTCGAG	GCCTACACCTCGCACCTC
SGR2493_1	GGTTGCGGCGATCATCC	ACTGGCGGCCCGATCCG
SGR2493_2	TCACCTCGTGGGGCGCTACT	CCCACCGCCGGAGAGGTC
SGR2519	ATCGATCGTCCAGAAGAACC	GTCTCACCCGGGGCCAAC
SGR2623	CTTCTGTTATTCGGCGCAAA	GAGCTCACGGAGCGATACC
SGR2648	GGAGAAACTCGATGGCTTCA	TTTGCGACAACCATGAGC
SGR2701	GCCGCAGGGGTCACACTT	CGGGACCGCGATCGAAAC
SGR2710	GGAGTTGGCCGACAATCG	TTTCCCTCTGGCGCTTCC
SGR2770	GAGTGCTAATCGCGGTCATA	CGGGGTTTAACAGTCTGTGG
SGR2783	CGACAGGGCGTCGGTAA	CTCGGGCGTCGGCATGG
SGR2820	CCCTCCTTTCATGCCGTAG	GCCGGGGTTTCCTGTATG
SGR2836	TAGGATTCCCGACTCGATTG	CCTGGGGGCCGACGAGTA
SGR2856	CTTCTCTGCCATTGCTCCTC	GTACTCGCGGTACGCGCTCA
SGR3143	TGTCCGGAACCCGTCACC	GCCAGTCGGCCCGAACAT
SGR3145	CCGCCCAGGTCACGTTTC	ACCGAGTTGGCGTGAGGT
SGR3149	ACGGTCGGGTCCGGAGG	ATGTCGGGCGGCCCGCC
SGR3168	ATTCGTGCCACCGTGGCC	TCGACTTCTCCCCGGCCG
SGR3226_1	GGGGCAATTCTGTATGGTTG	GGCACTTATGCCCCAAGAG
SGR3226_2	ATTCTCGTCCGATTGACCTG	CTTGCACGGGACCGCACT
SGR3307_1	GATCGCCGAGATCACTTCTG	GGACGACCACCCGAGAG
SGR3307_2	GTCCGGGACGGTGATTCT	AGGCCAGGGGACGGATCG
SGR3340_1	GACAGACGGAGAGGCCTTG	GTGAAGAACCATGCGGTTG
SGR3340_2	CAAGATTGGGCCCGAAGG	GCGCACTCCAGTCGGTTAC
SGR3370	GGGCTGCGTCTATGCGGTCA	CCCGTCAGGGTTGTACGC
SGR3379	CCGACCGGCCCGGAGAG	GAGTGCTCCTATACCTGACCA
SGR3399	CGAGTTGTCCTGTTTCTCCTC	CGCGGCCTCGACCAGGAT
SGR3428	TGATGCATCGCTTCTGTG	GAGAAGGCAACAGCAAGCAC
SGR3520	ACAGTCGTACCCCGGCGG	AACTGCGCGGGCGGCGC
SGR3532	ACCTGAACGGCTGAACAAAT	AGTCATCGAGCAGTGACGTG
SGR3552	ATGCCACCCCCTTGAGGT	CATGTCACTACAGCGTGTTGC
SGR3585	GTCCCGTGACACCGATTATT	CGAACGGTCACCTTCCTC
SGR3663	GTTCAGACGCCGGACCGG	GGCTCACCCGGCGCGGC
SGR3721	ATGCGTTGCCCGGCAGAT	CGGAGCTCACGGACTGAC
SGR3749	ATCGAGTCGCGGAGCGCG	CCGAGCTGGACGCCGAGC
SGR3768	GCAAATTCACCCGTTCAGTAA	GACGGTGACGCGATTGAT
SGR3777	GATACGTCCCCGCAGGTC	GTGCAGGCGGGGAAGGTGTT

SGR3840_1	TACGTTCACGCCGCGGG	GGTCTCCGCGCCGGAGC
SGR3840_2	CCCGGGTGAGTACAGACAAC	TTCCTCGTACTTCCGGCTTC
SGR3844	CCGAATATCCACAGATCTCTTTT	GAGACTAGTTGAGACCCTGCAA
SGR3901	GGGCAATCTGGACGCGG	CCGCAGCTCCGCCACGC
SGR3902_1	CGGAAACAGCGCCGATA	ACCGGTCCGGGAGGTGA
SGR3902_2	GCCCCTTAACGGTAGGGATA	GTACCGATGCCTCCCCAGGT
SGR3905	CTCCGCTCCCCGGCTGA	GCGTCCGCCGAGCTCAT
SGR3926	CACCTCATCTCTGCCGTCTT	GGGGGTGGGGTCGGTTG
SGR4011_1	CCGTACGGGCGTAACTGT	CCGGGTGATCAATTCTTCTG
SGR4011_2	CGTGATGGGGATAGACCAC	TTGTCAAGCCCCGAGATATG
SGR4021	ACACTCATCTAACCGAGTGATGG	CCGCACCCCGTCGATCC
SGR4052_1	CTCCATCGCTCGCACTCC	GACTTGAGTCACAGAGTCCATTT
SGR4052_2	GAGACCGGCGACGATTCC	GGAGTGCGAGCGATGGAG
SGR4070	GGTCCGACCCTCCCCATC	GGCAGTTTCGGAGCTTTCT
SGR4071	TACTGGTGGGCCAGTTCAT	GAAGACAGCCGGGATCTTCT
SGR4086	TCGGATGGGTGATTGGAG	AACACCCTCCCGACCAAG
SGR4191	CACGATGATCGGGTTGC	CTCGGCCCTGCGCCGGT
SGR4256	ACGAGTTGACGCGTCGG	AGATGGCCGTTCACTCGAC
SGR4279	GCCCTACGTTTTCACGAACC	GAGTCGGTCGAGGTGGTG
SGR4302	GTCGCGCTCACCACGAAG	GTCGGCTCGTCTTCCCGTA
SGR4304	CTTTTCTACAGAACTGGCCGAGA	ATTCGAATGGCAACTGTACTGC
SGR4396_1	ACCATCCCACTGACTGGTGT	AGCCGCGAAGCGGTGATG
SGR4396_2	CCCATTCCGTTCCGATGC	GCTTGTGCGGCGGATGAT
SGR4437	CGGATTCCGTGCCTGCTG	GCGTCAACTCTGTGACTTTCA
SGR4556	GGTTCACACCCGTCCCAGAC	GGCTTCTGAATAGCCGTCAA
SGR4619	CCCGTCTCTGATTGGTCACT	GCATACCGTCCGCATACC
SGR4671	GAGCGGGTAGCGTGAAATC	AACCCGGTTGATGGAATTTA
SGR4793	CCACGCCAGACCTGGTT	GGCCCGTCACGGTCAGC
SGR4807	GAACGGTTCCAGCCAACTAA	GCTCAGCAGTCCGATCTCTT
SGR4809	CTCGCGGGAGCCCTATTAAG	GGGAGTCGCCCCCATCTT
SGR4868	GTATCCGGGCACGTTGTG	GCTCGGCGGGTGTGTCACT
SGR4888	CCATGGCCGCGTCTGGTC	GGAGGCGAGTCAGGGACA
SGR4898	GTTGGCCGTATGTTCGTTTC	CAACTCCGCGATGGACAAG
SGR4899	CCCATCCCTTCCTTCTATCC	GCGCTCCAAAACGTGGTC
SGR4921	CCGGAAGCGTGCACCAC	GCGGAGGTGGGGCCGAC
SGR4958	GCTCATGCGCATACCGAAC	TACCGGCGCGTGGGTGAC
SGR4961	CTCCTGTGGTGTGTTGCTGT	GCCTCACCCCCTGAAACG
SGR5011	GGGTCGGCCTACGACTACAG	CACTGTTTACCCGTCATCG
SGR5013	CTTTGGCTGACCGCACGTC	TCGGGGTTCGGCCATATC
SGR5028	GGATTCGGTCGTCACAGG	TGGGCATCTAGACCGAGAAA
SGR5049_1	ATTCCTCGCGCGGCATTC	TGCGCCGACGACCGGACGT
SGR5049_2	AGCTGTACGGCGTCGGGTA	ATGGACCGCACCCGGCTTAC
SGR5049_3	CAGCCTGGACACATGGATAC	GAGCGGGGCGAGACCTTT
SGR5072	GTGGTCCGCGCCGAGCC	GAATTGCCGGACCCGGTC
SGR5085	CGTTTTCTTGACGGGTCCTT	GCGGGGGCAGATCCAGTC
SGR5226	GAACAAGCCATTACGTGACC	GTATGCGCATGCGGTGTT
SGR5399	CCGGTCGCCAGCAGGTCA	AAACGAGACAAAGTTGGTTGC
SGR5523_1	CGGCTGACCCCCACCAC	CTGTTGAGTGGCTCATGGAA
SGR5523_2	CAACAGCCACATCCACCC	TGTCGCCGTTCGGTGGCG
SGR5525	CTCCACAACCACCGCAAC	CATCGAGTAAATGTTCGAGTGAG
SGR5654	AATCCCCGATTCCGCAAG	GTCTCGTACTCCGGTGGTG
SGR5766_1	GGGTCTGTTTCCGGACATT	GAAGGCGTGTTTCGACTTTC
SGR5766_2	AGCACGAATTCGCGAAAGG	AGGAAGCTCAGCCGTGTCT
SGR5809	GAGCGTGGGCCCGACAAG	CACGGGCGAACCACTGTT
SGR5819	CAACTCCGTTCACTTTTAGGC	GAAGGGGCTGAGGGGTTC
SGR5856_1	GAACTGTTCAACACCCGTCA	CCGTACAGAGGTCCTGATCG
SGR5856_2	GGTTGATGTCGTCGTCGTG	CAAGGGTGAAGATCGGACAC
SGR5857	CAGCCGGGTCCGCGTGTTA	CAAGAAGGGTGAGCGGATCG
SGR5859	GCGTTTCCCTCCAGGTATG	CGAACATGTGGATCACTGC
SGR5909	CGACAGCCATCTTCCCGTAT	CCACCGGCGCACTCCTCT
SGR5914	CTCGCGCTTCCATGAGATAC	GATATCCGGGCCCTGGTCGAT
SGR5915	GAGGCGGAGCGAATTTCT	TACCGGACGCAGTCGAAC
SGR5922	CCGGGCATCGCTGACTCC	AAGGTGTTCGACCGAGGAA
SGR5933	GGCGGGTGCGGACACAC	GAGAGCAGGCGACCGGTG
SGR6006	ACACGGCGTTCGATGCAC	GTCGTTGGCCACCTGTCG

SGR6029	AGCGGGCTAGATAACACTCG	GTCCCACGCTCCTGCTGT
SGR6043	CGGAGAGGGGCTCCAACC	ACACCGCCCCGGCCCGGGA
SGR6054	ACCCACCAGGTGAGCGGAGA	GATATGTCGCGAAAATCCTG
SGR6126_1	GTCGATTCCGACACGCATC	ACCCCACCGTGCGTCTAC
SGR6126_2	TGCCCCCCGCCGCGCAC	GGGACGGCTGAAAATCATC
SGR6132	TCGACTTCCCGGTGCAC	AACCGAACACGCCCCTTT
SGR6153	CGACTCCCTCTCAAATCACC	ATCAACGCTCTGCCTCGTT
SGR6192	CCCCCGCGGGTCGTACCT	GTGGGCTGTGTGGGTGTG
SGR6286	TCCCTTTCCCGCCCTGGT	GTCCCGAATTCACCGCTTC
SGR6324	CCGGACCGGGACGAACAG	GTCGCCGGGATCCGAATA
SGR6363	GCCGTACCAGTTGGTGTTCT	GGATCCACTCGGATGTCAG
SGR6383_1	GTCCGCACGGCACCTTC	GCCCGCCGCACGGCATC
SGR6383_2	GGTTTGAACTTAATTTTACCTGAGC	CCGCGGATCACGCCGGC
SGR6548	TCCCCGGGAGGATCGTGAAC	GTGGGAGGATCGGCATGAG
SGR6629	CTCCTCACCGCCACACC	TCCGGAAGGGGGGCCGG
SGR6710_1	AGCCTAAGCTGGCCAACAA	AGGGATGGGCCGGGCAAGTA
SGR6710_2	ACTGCTGCTCGAAGAAGTGG	GTTCTTCCTGGCGACACAC
SGR6725	GGAATCAGGGGCACGGTA	GGCGTCGGCATGGTTGC
SGR6776_1	CGGAGGACAGGGATCAAC	CCTGTGCCCCGGTTCTG
SGR6776_2	TGTTCACACGTTTGTTCCACT	GGACGCGGCTGCCGCAC
SGR6776_3	AGATCGGTCGGTGCGGTGGT	CGTGGGCGCCTGCTGTTC
SGR6809	CTGCTGCGTACACCTGTCAT	CCGGACCCTCCGGACAGC
SGR6814	ACTTCGCCGCGGGCTGAT	GGCCGGAACGTGACGAAC
SGR6854	CTGACCGAAGGCGAGAGC	CGAATCCCGGAGGAACTAC
SGR6856	TAGCCGGCTCCCCGGTCG	TACCCGGGGCTTCCGCGC
down-regulated by AdpA		
SGR269	GCACCGTGCGGACACGAG	GAGGGGCGGGCCGAAGAT
SGR291	TTGCCCCCGTGCGACGGG	GAGCGGGCGGGCACTTT
SGR955	CGCAACCGATGGCTTGTT	CTTACCTGGTTCCCCCGCTCCT
SGR966	ACGGCAAGTAGGGCGATA	GCTGGAGATCTTCCGTCATT
SGR1311	GTGTTGCGGAGGGCGTTAG	CGTGCAGTGCGGGAGTGG
SGR1459	CGTTTCGGCAAGGGGGCTCT	GGCGCCCGTCGTTGTCAG
SGR1676_1	CAAGTTGCCCGGCGTGTC	ACTCGAACCGGCGGAGTC
SGR1676_2	ACTCCGCCGGTTCGAGTG	CACCGCGCGAGAACTTCG
SGR1869	TCGCCCGGCAGCAGACCTAT	TTGAACGAGTGGCATGTGGT
SGR1903	ACTTTCCGTCGACATCCATC	GCGCTTCTTCGTTCATGC
SGR1979	CAGACTGCTCCCGTGTCC	CTCGCGGGTGCGAGAGGT
SGR2045	ACAGTGTGGCCGGAACTC	ACCGCTCCCGGTCCTTTC
SGR2129	CGGACCGGGTCGGCCCCC	CAGCCGGTGCAGGGCGGAAG
SGR2195	CAGATGGGGCAGGATCAC	CCGATCACCGAGGTGGAG
SGR2322	TGGTCTTCCGGATCGTTAAT	AGCCCAACTCGCCCATATC
SGR2367	CGGCGGCCAGGCTATCAG	GTTCCCCGAGGGCGGAAAC
SGR2702_1	GCGCCGGGAAACCTCCAT	GGGGCGGAAAGGGCGTGT
SGR2702_2	CGCACCGGCTGCCGGAGA	GAAGGAGCCCGCGGTGG
SGR2730	TGGGGTGCCCGCGCGGGA	GCAGGCGGGGAGGGGGAAAT
SGR2910	GTTCGTACGGCCAGTCTGC	CGGTCTGAGCAGAGCACA
SGR2964	ATCCATAGCGGACCGGATAC	CGGTCTCGAGAGACTGGT
SGR3001	TCCAGAACCTGCAAACAAGTC	GAAGTGATCTTTCCCTCTACCG
SGR3022	GGGGAACGCCGCAGGAC	CACCGAAGTTGTCCACAGG
SGR3072	GCAGGGCCATCGCACGAC	CATGGGGACCACGCCTTC
SGR3165	TGAATCTGCTTTGGGTTGG	GGAGTCGACCGGAGCGGT
SGR3404	GCTATTGCGCCAGGGGCTTC	GGGCGGGGCATGTCCAAG
SGR3513	CCGCGATAGACATGACCTTG	ATCTGCACCTCTTCCGTCAC
SGR3524	CCCTGTTGCCGCCGCTG	GCTCAGCACGCTCACGGA
SGR3620_1	CTCCCAGTGTCGGCTAACTT	ACCGTTTACGTACCCAGCAT
SGR3620_2	TGGATCGATTCCAGCCACT	CGTGTACATGTGGATGCATTG
SGR3646	CGGGGCCCTTTGTGTGG	CCGATTACGGGAGGAACC
SGR3675	CCTCTGAGCTCCTGATTTCAA	ACACCCAACGCGGACGAT
SGR3701	GGGAACGTGGGTAAAGCTG	TTTTGTCCACCGGTCCTG
SGR3782	GCACAGCGCGCGTGAACT	GTACCCGGCCCGGCAACA
SGR3880	TGATCCGCCGCCGCCTGA	GGGGTGGTGTGCGTCTG
SGR3897	CCCTTGCGGAATTCGGCG	CCCCGCCCTGTTCGTTAAT
SGR3928	ATTCGGTCAGGCTGATGCTA	CCTGCCGGGTATATCGTAAC
SGR3960	GCGGAACTCATGTGGGTTAT	CATACGGCTTTCACACAGC

SGR3965	GACGCGGCACAGGTCTAC	CTTCCCCGTCTCGCATCAC
SGR4153	GGCCCGGACGGACTGGCTAT	CGGCGACCGAGGTCTTGC
SGR4276	ATTCACTTTCGCGATCATGC	GCCGGAGAGCCGCGAAG
SGR4380	CCGGGCACAACTCCTGA	CCCATGGCCGCCCGTCGG
SGR4383	GCGTCGTCGCAGGAGACC	GTGTATCTGGCGCTGCAC
SGR4443_1	GTGAGCCCCTTCACAAGGAT	AAGGGCCAAGGTCCAGCTC
SGR4443_2	CTTCTTCAGAATGCGACGAG	ATCCTTGTGAAGGGGCTCAC
SGR4455	CGAGACGCCAGGACAGAT	CAAGGTGAAATAAAGTGAAGTGGA
SGR4456	CTTGCTGGATCCGTCGTG	CTGTTGGGCTTCGGCTCT
SGR4462	CGTACGGGGCGGGGTCCT	GCATCACTGGCAGGACCTGTT
SGR4473	CTGTGATCCATGTCTCAAGTCC	CTCAGGAGCCGGCGGGAAC
SGR4482	ACCGTTAAGTAACTCAATTTTAGTCC	ATAGTCGGGGACCGGAAG
SGR4489	GGTCGGCTTGCCCGGAAT	GGCTGTTGCCAAGCTGAT
SGR4581_1	CACCGACCCGCCATGCTC	GGCGCACGGGAATCACTT
SGR4581_2	CCGTTGCCATGGCCGAGT	AAAGACGGCAGTCATTACCGGCTAC
SGR4623	CATCGGGACGTTCGATCT	AGTTCATGGCTGGGATGCTA
SGR4652	GAAAGTTCTCGCCAACGAAG	GCCTTGGCGGACTGGTTC
SGR4698	TGGCGTCTGCCGGTTTAC	ACATCGACGCCTGGAAGTC
SGR4724	CCGCGTACGGGATGTCC	GCCGATGACCGGTCGCG
SGR4803	GTCGGTATGGCGCCGGTAT	GTTCGGGGACGGTCCGAAG
SGR4919	CGCGATCTGCCCGTCGTC	CCGAGGTGGAGGCCATCG
SGR4930	CGACGATCTCGCCGATCA	GCCCCCGCACCCCTGTAAT
SGR4995_1	CTTCAGCCGGGAGAACAG	GTCCACGTCGAGGTGATGA
SGR4995_2	ATCGGTCAACTCGGAGGAC	CGCCCGTCGGTTCCCAAC
SGR5104	AGCGGCCTCGCGTCCGTA	GGCGGCTCCGGTACATTA
SGR5316	GCCACCGCCCCGGTTAACTT	GAGGGACGGGGTTGTGTAG
SGR5429	CCCGTACGGGCCCGTACA	GACGTTCTTCCGGCGGC
SGR5447	CCCCTTTTCCCGCTCAAC	ATCGCGACCACGACGAAG
SGR5467	CTCGTGCCCGCCATGAGT	CCTGACCCCACGCTCACCT
SGR5469	AGCACACTCACGCGAGCG	AACGACCGGGTCGGGCC
SGR5483	TACATGATGGGGCGCTTC	TCCCCGGGCGCCGATCGT
SGR5504	ACCGGCCCGGACCCGGACGT	GGTCCTGCACAGCCCGCA
SGR5533_1	GAGCGCGGCCTGCTAGGT	GGAACACCAGTTGTGCCGGAAT
SGR5533_2	GGACAGGCCGGAGAACACTA	GGCTCATCGTGCCCGTCGTT
SGR5674	CCTCCCCCGGTGGTGTC	GCCCATCGCCCACCACT
SGR5698	CAGCTCCAGTACATCGCTCA	CTAGGCAACGCCTGGGAAC
SGR5721	GGGCCTCGTGCGCTGTC	CGTGAAGTGACTGGGGTGAT
SGR5890	GGAGCGGTGCGGGTTCTTT	GCTCCGTCGCAGGTCAGT
SGR5904	GATCGGAGCCTCCACTTGT	ACGATAAGGCCAGGCCAC
SGR5977	GCGCATTCGACACATACAAC	ATCCAGCACTGTCCGCTATG
SGR6046	CTCACGGGACGGATCGTTA	TACGCAGCGTTACTTGGATG
SGR6069_1	AGGTCAGCCGGGTGATGTG	AGGTCCTGGAGCGCATCG
SGR6069_2	CCGGAGCTCTGGAGCAG	GGTCGACGCGCAACACT
SGR6089_1	ACGGGTCGCGGACTATAAC	CGCCAGGTTTTCTGTGACC
SGR6089_2	GACGACAGATAGAGCGGCTCAC	GGCGGGTCGTCATCGGTA
SGR6240	GCCGGGCGGCCCATCTAT	GCTGCTGGTAGGGATTCG
SGR6295	TCCCGCTGCGTCCGGAGT	CGTGCCCGGCGCTTCTC
SGR6342	AGCCGTCCAGGCAGTGAC	TCAATCATCGTCTCCCCTTG
SGR6353	GCGGACCTCGATCCGGC	TCAGCACTGTATGGGCCTTT
SGR6836	AGCCCCCGCCCGGCTGA	GAGGTTGCCCGGCCAGT
SGR6952	CGGGCACCGACCGGATAC	CATGGGTGGCCGTCCGAGT

Competitive EMSA (200-250 bp)
up-regulated by AdpA

SGR1357	CTGCGCATGAGCTGATCTT	GGATCGTCATCTGCTGTCGT
SGR1599	TCGGGAAGAAGCACTTTGAT	ATGATGCTCGTCGGGTTG
SGR1940	GCTGCCAGTGCTGCTGAG	CCAGGATGATTGGCCTGTT
SGR1983	CCTCGTCCGTATGGTGGAC	CGCGTCCGGGAGGGTGTC
SGR1984	CTCCACCGCTCTGACCTG	GGATCGGATTTCGAGGTG
SGR2020_2	GGGCAATAGCAGATGGTGAC	GCTCTCGGTCGGTTTCATT
SGR2197	CCGTAGGCATGCTCCATC	GTCACGGCACGAGGAAAG
SGR2493_1	GGTGTGGTGACTTGTGGTCA	GGACGGCTGGGAGCACTG
SGR2519	CGACGGCACCCGCAACAG	CGGGGAACTGCATGAAGAC
SGR2623	GGGTCTCCTATACCACTTGGA	TACGGTCACTTCGGAGGTCT

SGR3340_2	CGCATACGCATAGTCCGTTC	CAGTTCATCCGGATCGGTAG
SGR3370	GTTGTCGTATCCGACGATGA	CCACTGTGATGTCGAGAACC
SGR3379	ACGGACGCGTAGGGCTTC	CGGCGTGAGTGCTCCTATAC
SGR3428	AGGAACATGAATCAGCAGGAA	CCCTCAACGAGGTCAAGAAC
SGR3552	TCTTCGTGAGCGTGAGCA	GATTCGGCGCTGACTTGT
SGR3585	CCAGTGGTGACCTGAATGC	TTTAGCGAACTAAGCGTGGTC
SGR3663	CGCGGTCCTCGCAGAGAT	ATCGCCCTCGTCGCCGTCT
SGR3902_2	ACAACAATCCCGCCATCC	CCCTCGACACACAGACAGC
SGR3905	GTAACCCGTCGGGGTGT	ACGGCGTCCGCCGAGCTCAT
SGR4021	GCTCGTCGTACCGCGGCGTTCT	CACCGGCCCCCGCACCCCGTCGAT
SGR4556	GGGAATCGCCTCGGCAAG	CCGTTGCGGAGGACCTGT
SGR4793	AACTTATCGGGGCAACACAC	AGGGCTCGTACACGAAGATG
SGR4899	TGCGGATGTCTTCTTCTGTG	CTGACGAGTCACTCCAGCTC
SGR5011	GCTGCAGCACCAGACTCC	ACGGTGATTGACGAAATGGA
SGR5049_1	AACGACGCAATGTGCTCTG	GGGGGTGCCGCCGCTTC
SGR5049_2	GCCAGAAGTGAAAGGTCTCG	GCAAAGAAATTCGGGTGAC
SGR5085	CGCTACACGAACGGCTTT	ACAGCAGGCGTCCCTCCTC
SGR5399	GTCTTGGGAGCCCAGAACTC	GCATCTCGGGCATCTGTC
SGR5533_1	GAGAGACGCCTCGACAACC	GCCGTGCCGTAGTGTTCT
SGR5909	GTCGCGGCGAGCTCATGC	CCGACGCGTAACCGAGCAC
SGR5915	GCAAGCCACAGCAAGTACC	GTAACGCCCTCGGGTGAG
SGR5922	GTGCCGTGCTGCGCTTGG	AGCCGTACGCCACAGTCG
SGR5933	GCTCGACTCGGCAGTGCT	ACATATGCCCGAGCGAAG
SGR6006	CGGCGCACTGTCGCACAC	CGAGCCCTGGATCGGGATCTG
SGR6153	AAACACCGGCGAGTTTCG	GTGACGGGCGAGTCGTATC

down-regulated by AdpA

SGR1459	GTACGCCTCCGCCAGCTCGT	ACGGGCGCACAGGGACAG
SGR1676_2	ATCCGTGTGATGCCTTGACT	GAAGCACAACACGCATCAG
SGR1979	ACGACCGCATCCTGAGAC	ATCATCCCGCTTGCTCGT
SGR2702_2	CTCCCGTGCTCCGCCCTTC	AGGTAGTTGCCGAGGTGGAA
SGR2730	ATGCCCTCATGGGGTGTC	ATCCCGCAAGGCGCTGTT
SGR3675	ACCGCATCTGTCTCGATTGT	GTCGTGATGCGTAGTGCAAC
SGR3960	CGTGAGCAAGGGAACAGAA	CACTGCTTCGTACGTCATGC
SGR3965	CTCAGAAGGGGCGACAGA	GGGCAGGCTCGGGGAGTC
SGR4153	GAATCACCCGATTCACCATT	CCAGGAGGGCGGATTCGT
SGR4276	GTGAGTGCGGTCTCATGCT	CGATGGAAACAACGACTGG
SGR4443_1	CTCATGCCATCGAGTATCCA	GTTGCGGCCGTATGAAGG
SGR4443_2	GTGACGGTCGCCTCCCCGTA	CACGTGGGCGGCGAAGTGTAG
SGR4455	GTTCGTATGTTCGCGTTTCA	TGATCAGCGAACCTCAGTTG
SGR5467	AAATGATGACACCGGTCCAG	CCGAGGACCTGTGGAAGG
SGR5533_2	AGGGTCAATGCGCGAAGG	AGGTCCCGTGGATCTCTTG
SGR5698	GGAGACGTCGTCCACCAG	AGTCCTGAACGTGGTTCGAC
SGR5904	GAACGATGGGGACCGTC	GCTCATGCCCACACGATAAG
SGR5977	CAGGCTCGGTCTCGCTTC	CTTCGCGACAACCGGAAC
SGR6089_2	GGTTGACCAGGTGAGATTCC	GGGTCCTCCTGCCTCTTC
SGR6295	GTTCCCGTTCAACGAATTG	CAGATGGGAGGTGATCAGG
SGR6342	GGACGCGGTGACGGTGTG	GGAACAGCTGCCGCCTTG
SGR6836	CTTCGCCATGTGGCTGGT	AGACCGGCGCCGAGGTTG

RT-PCR

trn21	GGTAGAACATGAGCTTCCCAAG	CGGGTGACGAGAATCGAAC
trn50	GGCGTAGCTCAATGGTAGAG	GGCGACGGGAATCGAACC
trn27	GGGCCTTAGCTCAGTTGGTA	GAGATTCGAACTCCTGACATCTG
trn40	CAGTCTGGTAGCGCACCTC	GGACCTGTGGGGATTTGAAC
trn57	GGGTGCGTAGCTCAGGGGTA	GTTTCGAACCGCCGACAT
trn42	ACGTAGACACGGCGAGCTTA	CGGAGCCGGACTCGAACC
trn58	CCAGTACTCCAACTGGTTAGAGAGG	GATTCGAACCCACACTGTCC
trn26	TCAGTTGGTTAGAGCGCATCC	GGGCTAACAGGATTTGAACC
trn56	GCTCAGCCGGTTAGAGCAG	GGCGGGTGGGACTCGAAC
trn20	GGGTGTAGCGCAGCTTGG	GGATTTGAACCCACGACCT
trn51	GTGTGGCGCAGCTTGGTA	CGGATTCGAACCGACGAC
trn14	GCTCAATTGGTAGAGCACTGG	GGCCGGAGGGACTTGAAC
trn22	AGGAGCTCGCCTCGAAAG	GTAGCGGTGGGATTTGAACC

trn24	GTCTATGGCGCCGCACTG	GAGGGATTTGAACCCTCGAT
trn29	GGATTCGCCTAGTGGCCTA	TGGCGGAGGATACGAGATT
trn19	CCTTAGCTCAGTTGGCCAGAG	GGGATTCGAACCCGAGACCT
trn38	CTCAGTCCGGCCCAGAGC	GGATTCGAACCGACGACCT
trn54	TGTAGCTCAATTGGCAGAGC	GACTGGACTCGAACCAGTAACC
trn41	CATGGTGTAATCAGGCAGCA	CATCAGGATTTGAACCTGAACA
trn17	GTGCCCGAGTGGCCAAAG	CGAACCTGGGTAGGCTGA
trn36	GCCGTTAGCTCAATTGGTCA	GACTCGAACCCACAACCAA
trn23	CTCGTAGCTTAACGGATAGAGCA	GTGCACTCGGCAGGATTC
trn48	CTCAGCTGGCAGAGCACCT	GGGTGAGTAACGGGACTTGA

[a] Numbers are added after gene ID, when AdpA binds to two (or three) sites in a "putative regulatory region"; the farthest AdpA-binding site to its target gene is named 1.

Supplemental Table S2. AdpA-binding motifs with different affinities.

AdpA-binding sequence	affinities in vivo[a]	affinities in vitro
TGTCCGAAAA	343	1
	1094	4
	1647	5
TGGCCGGATT	903	2
	3957	4
	953	4
TGGCCGGAAC	185	1
	790	2
	293	4
TGGCCGGAAA	245	1
	1181	2
	504	4
TGGCCGAAAA	2724	1
	1988	3
TGGCCCGAAT	651	0
	705	3
CGGCTGGTTT	342	0
	191	4

[a] mean signal of ChIP-seq and ChAP-seq

Supplemental Table S3. List of genes that are probably activated directly by AdpA in both liquid and solid culture.

transcriptional unit	ID	description	memo[a]	identified previousl
SGR95t	SGR95t	putative regulatory protein		
SGR180-SGR179	SGR180	hypothetical protein		
	SGR179	hypothetical protein		
SGR264-SGR263	SGR264	putative cytochrome P450		
	SGR263	putative ferredoxin		
SGR299	SGR299	putative sporulation-control protein		2
SGR381	SGR381	hypothetical protein		
SGR598-SGR597	SGR598	hypothetical protein		2
	SGR597	hypothetical protein		
SGR681-SGR680	SGR681	hypothetical protein		
	SGR680	putative Hsp90-family heat shock protein		
SGR692-SGR691	SGR692	putative LacI-family transcriptional regulator		
	SGR691	hypothetical protein		
SGR695-SGR698	SGR695	putative glutamylcysteine synthetase		
	SGR696	conserved hypothetical protein		
	SGR697	conserved hypothetical protein		
	SGR698	conserved hypothetical protein		
SGR731	SGR731	hypothetical protein		
SGR745	SGR745	putative M23-family secreted peptidase	p	
SGR919-SGR916	SGR919	hypothetical protein		2
	SGR918	putative subtilisin-like serine protease	p	
	SGR917	hypothetical protein		
	SGR916	hypothetical protein		
SGR920	SGR920	hypothetical protein		
SGR1063-SGR1059	SGR1063	*rarA*	m, s	
	SGR1062	*rarB*	m, s	
	SGR1061	*rarC*	m, s	
	SGR1060	*rarD*	m, s	
	SGR1059	*rarE*	m, s	
SGR1175	SGR1175	putative phosphatidylserine decarboxylase		
SGR1176	SGR1176	putative phosphatidylserine synthase		
SGR1331-SGR1332	SGR1331	putative acetyltransferase		
	SGR1332	hypothetical protein		
SGR1357	SGR1357	conserved hypothetical protein		
SGR1360	SGR1360	putative transmembrane protein		
SGR1714	SGR1714	putative TerD-family protein		
SGR1898	SGR1898	putative signal recognition particle-docking protein FtsY		
SGR1983	SGR1983	putative 3-isopropylmalate dehydrogenase		
SGR2001-SGR1997	SGR2001	putative integral membrane phosphodiesterase		
	SGR2000	putative acetolactate synthase subunit large		
	SGR1999	putative acetolactate synthase subunit small		
	SGR1998	putative ketol-acid reductoisomerase		
	SGR1997	putative D-3-phosphoglycerate dehydrogenase		
SGR2066-SGR2069	SGR2066	putative phage tail sheath protein		2
	SGR2067	putative phage tail protein		
	SGR2068	hypothetical protein		
	SGR2069	hypothetical protein		
SGR2079	SGR2079	terpene cyclase (*gcoA*)	s	2
SGR2095	SGR2095	*sgmA*	p	1
SGR2105	SGR2105	hypothetical protein		
SGR2148	SGR2148	conserved hypothetical protein		2
SGR2217-SGR2214	SGR2217	putative sensor-like histidine kinase		
	SGR2216	conserved hypothetical protein		
	SGR2215	conserved hypothetical protein		
	SGR2214	putative ATP/GTP-binding protein		
SGR2393	SGR2393	*amfR*	m	1
SGR2446-SGR2447	SGR2446	tyrosinase co-factor protein (*melC1-2*)	s	2, 3
	SGR2447	tyrosinase (*melC2-2*)	s	

SGR2479	SGR2479	putative WhiB-family transcriptional regulator (*wblI*)			
SGR2710-SGR2708	SGR2710	hypothetical protein			
	SGR2709	hypothetical protein			s
	SGR2708	hypothetical protein			
SGR2770-SGR2769	SGR2770	putative GroES			
	SGR2769	putative GroEL1			
SGR2820-SGR2818	SGR2820	30S ribosomal protein S8			
	SGR2819	50S ribosomal protein L6			
	SGR2818	50S ribosomal protein L18			
SGR2836	SGR2836	hypothetical protein			
SGR3143-SGR3140	SGR3143	hypothetical protein			
	SGR3142	hypothetical protein			
	SGR3141	hypothetical protein			
	SGR3140	hypothetical protein			
SGR3226	SGR3226	putative cold shock protein		2	
SGR3307-SGR3306	SGR3307	anti-sigma factor antagonist (*bldG*)	m		
	SGR3306	putative anti-sigma factor			
SGR3340	SGR3340	putative WhiB-family transcriptional regulator (*wblA*)	m, s	2	
SGR3399-SGR3398	SGR3399	hypothetical protein		2	
	SGR3398	putative WD-repeat containing protein			
SGR3520	SGR3520	putative acetyltransferase			
SGR3663	SGR3663	conserved hypothetical protein			
SGR3768	SGR3768	putative D-alanyl-D-alanine carboxypeptidase			
SGR3840	SGR3840	conserved hypothetical protein		2, 3	
SGR3901	SGR3901	conserved hypothetical protein			
SGR3902	SGR3902	sporulation associated protein ORF1590	m	2	
SGR4011	SGR4011	putative CarD-like transcriptional regulator			
SGR4021	SGR4021	putative integral membrane protein			
SGR4086	SGR4086	conserved hypothetical protein			
SGR4151	SGR4151	*adsA*	m	1	
SGR4191	SGR4191	conserved hypothetical protein			
SGR4256	SGR4256	conserved hypothetical protein			
SGR4302	SGR4302	hypothetical protein			
SGR4396-SGR4392	SGR4396	putative sensor-like histidine kinase			
	SGR4395	conserved hypothetical protein			
	SGR4394	conserved hypothetical protein			
	SGR4393	putative ATP/GTP-binding protein			
	SGR4392	putative cytochrome P450			
SGR4807	SGR4807	putative LuxR-family transcriptional regulator			
SGR4809	SGR4809	putative lantibiotic modifying enzyme	s		
SGR4898-SGR4901	SGR4898	hypothetical protein			
	SGR4899	hypothetical protein			
	SGR4900	hypothetical protein			
	SGR4901	hypothetical protein			
SGR4921	SGR4921	conserved hypothetical protein			
SGR4961	SGR4961	conserved hypothetical protein			
SGR5028	SGR5028	hypothetical protein			
SGR5049	SGR5049	putative ArsR-family transcriptional regulator			
SGR5072-SGR5075	SGR5072	conserved hypothetical protein			
	SGR5073	conserved hypothetical protein			
	SGR5074	conserved hypothetical protein			
	SGR5075	hypothetical protein			
SGR5085	SGR5085	conserved hypothetical protein			
SGR5226	SGR5226	conserved hypothetical protein			
SGR5399	SGR5399	putative 5,10-methylenetetrahydrofolate reductase			
SGR5525	SGR5525	hypothetical protein			
SGR5762	SGR5762	*sprB*	p	1	
SGR5766	SGR5766	conserved hypothetical protein			
SGR5819	SGR5819	conserved hypothetical protein			
SGR5909	SGR5909	putative two-component system sensor kinase			
SGR5914	SGR5914	*strU*	s	2	

SGR5922-SGR5923	SGR5922	*stsB*	s	
	SGR5923	*stsA*	s	
SGR5931-SGR5932	SGR5931	*strR*	s	1, 2
	SGR5932	*aphD*	s	
SGR6043-SGR6044	SGR6043	putative elongation factor P		
	SGR6044	putative transcription termination protein		
SGR6071	SGR6071	putative LAL-subfamily transcriptional regulator (*AdBS4-orf1*)	s	1
SGR6126-SGR6129	SGR6126	putative sensor-like histidine kinase		2
	SGR6127	conserved hypothetical protein		
	SGR6128	conserved hypothetical protein		
	SGR6129	putative ATP/GTP-binding protein		
SGR6153	SGR6153	conserved hypothetical protein		2
SGR6286	SGR6286	putative regulatory protein		
SGR6383	SGR6383	gamma-butyrolactone-binding protein homologue		2
SGR6559-SGR6556	SGR6559	hypothetical protein (*AdBS2-orf1*)		1, 2
	SGR6558	hypothetical protein		
	SGR6557	hypothetical protein		
	SGR6556	putative permease of the major facilitator superfamily		
SGR6710	SGR6710	putative peptide monooxygenase		
SGR6725	SGR6725	hypothetical protein		
SGR6809	SGR6809	putative cyclic lipopeptide acylase		2, 3
SGR6814	SGR6814	putative phenylacetate:CoA ligase		
SGR6856-SGR6857	SGR6856	conserved hypothetical protein		2
	SGR6857	hypothetical protein		
trn42	trn42	*bldA*	m, s	1

[a] m: involved in moprhological differentiation, s: involved in secondary metabolism, p: extracellular protease

[b] 1: category-I target (see text), 2: target suggested by Hara *et al* . (reference 5 in the main text)

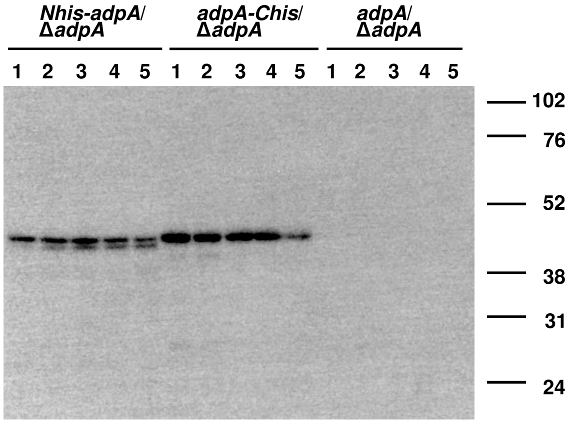
3: target suggested by Akanuma *et al* .(reference 6 in the main text)

SGR1270 (*eshA*), which should be included in the list by our criteria, is omitted, because we have revealed that AdpA indirectly activates this gene.[8]

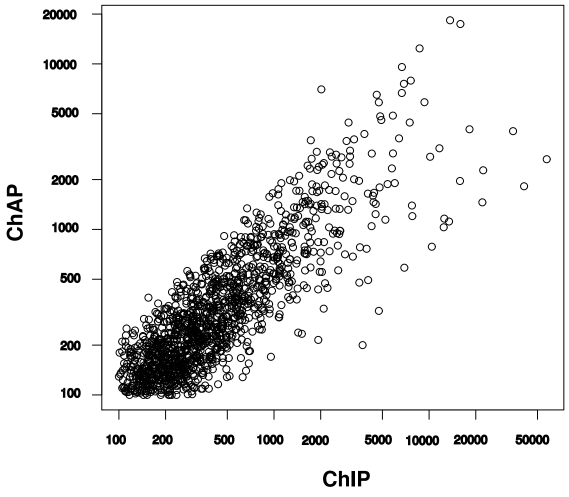
Supplemental Table S4. List of genes that are probably activated directly by AdpA, specifically in solid culture.

transcriptional unit	gene at the top of unit		identified previously[a]
	ID	description	
SGR13t	SGR13t	hypothetical protein	
SGR85t	SGR85t	hypothetical protein	
SGR96t	SGR96t	hypothetical protein	
SGR296-SGR295	SGR296	conserved hypothetical protein	2
SGR654	SGR654	putative MbtH-like protein	
SGR684	SGR684	hypothetical protein	
SGR815-SGR810	SGR815	conserved hypothetical protein (in putatuve NRPS-type-I PKS gene cluster)	
SGR977	SGR977	putative isopentenyl diphosphate isomerase	
SGR1067	SGR1067	conserved hypothetical protein	
SGR1227	SGR1227	hypothetical protein	
SGR1241	SGR1241	*sprT*	1
SGR1508	SGR1508	conserved hypothetical protein	
SGR1726	SGR1726	putative ppGpp synthetase/hydrolase (*relA2*)	
SGR1773	SGR1773	putative two-component system sensor kinase	
SGR1813	SGR1813	putative transcriptional termination/antitermination factor (*nusA*)	
SGR1818	SGR1818	putative proline tRNA synthetase	
SGR1999-SGR1997	SGR1999	putative acetolactate synthase subunit small	
SGR2097	SGR2097	putative glycogen phosphorylase	
SGR2107-SGR2108	SGR2107	putative two-component system sensor kinase	
SGR2318	SGR2318	conserved hypothetical protein	
SGR2344	SGR2344	conserved hypothetical protein	
SGR2403	SGR2403	conserved hypothetical protein	
SGR2456	SGR2456	conserved hypothetical protein	2
SGR2564	SGR2564	putative transcription elongation factor	
SGR3616	SGR3616	putative regulatory protein	
SGR3617	SGR3617	conserved hypothetical protein	
SGR3655	SGR3655	*ssgA*	1
SGR3841	SGR3841	hypothetical protein	
SGR3861	SGR3861	conserved hypothetical protein	
SGR3904	SGR3904	conserved hypothetical protein	
SGR3933	SGR3933	putative phosphate-binding protein precursor (*pstS*)	
SGR4170	SGR4170	hypothetical protein	
SGR4190	SGR4190	hypothetical protein	
SGR4618	SGR4618	conserved hypothetical protein (*AdBS3-orfA*)	1
SGR4706	SGR4706	hypothetical protein	
SGR4736-SGR4737	SGR4736	putative cellobiose ABC transporter permease protein	
SGR4983	SGR4983	putative 30S ribosomal protein S20	
SGR5348	SGR5348	hypothetical protein	
SGR5506	SGR5506	*sprU*	1
SGR5613	SGR5613	conserved hypothetical protein	
SGR5635-SGR5632	SGR5635	putative L-2,4-diaminobutyrate acetyltransferase (*ectA*)	
SGR5765	SGR5765	hypothetical protein	
SGR5767	SGR5767	hypothetical protein	
SGR5973	SGR5973	putative glycerophosphoryl diester phosphodiesterase	3
SGR6073-SGR6078	SGR6073	putative type-I PKS	
SGR6209-SGR6208	SGR6209	putative carbonic anhydrase	
SGR6257	SGR6257	conserved hypothetical protein	
SGR6451	SGR6451	conserved hypothetical protein	
SGR6586	SGR6586	putative carbonic anhydrase	
SGR6615-SGR6618	SGR6615	putative ABC-type Fe^{3+}-siderophore transporter substrate-binding protein	
SGR6691-SGR6693	SGR6691	putative DNA polymerase III alpha subunit	
SGR6806-SGR6805	SGR6806	conserved hypothetical protein	
SGR6807	SGR6807	hypothetical protein	
SGR7011	SGR7011	hypothetical protein	2

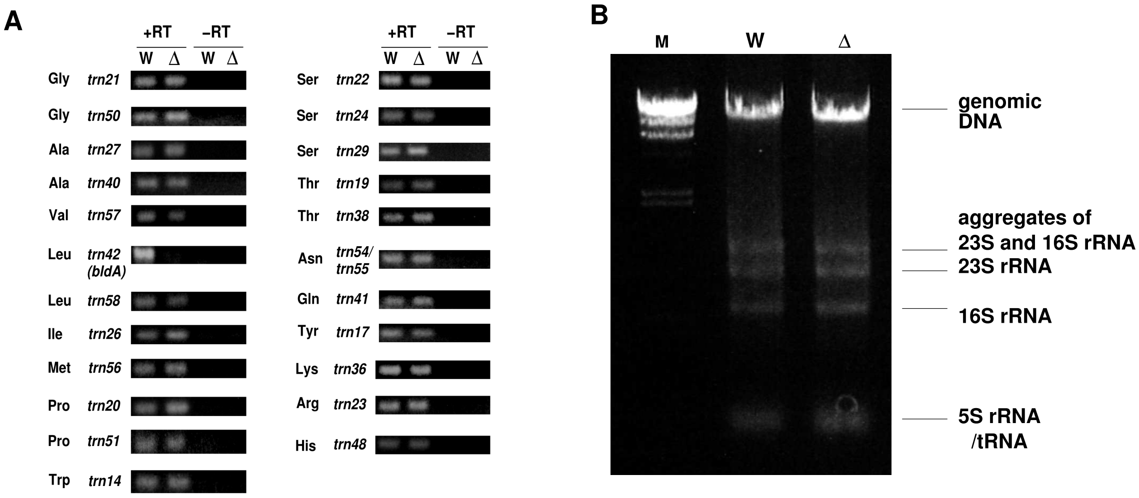
[a] 1: category-I target (see text), 2: target suggested by Hara *et al*. (reference 5 in the main text), 3: target suggested by Akanuma *et al.* (reference 6 in the main text)



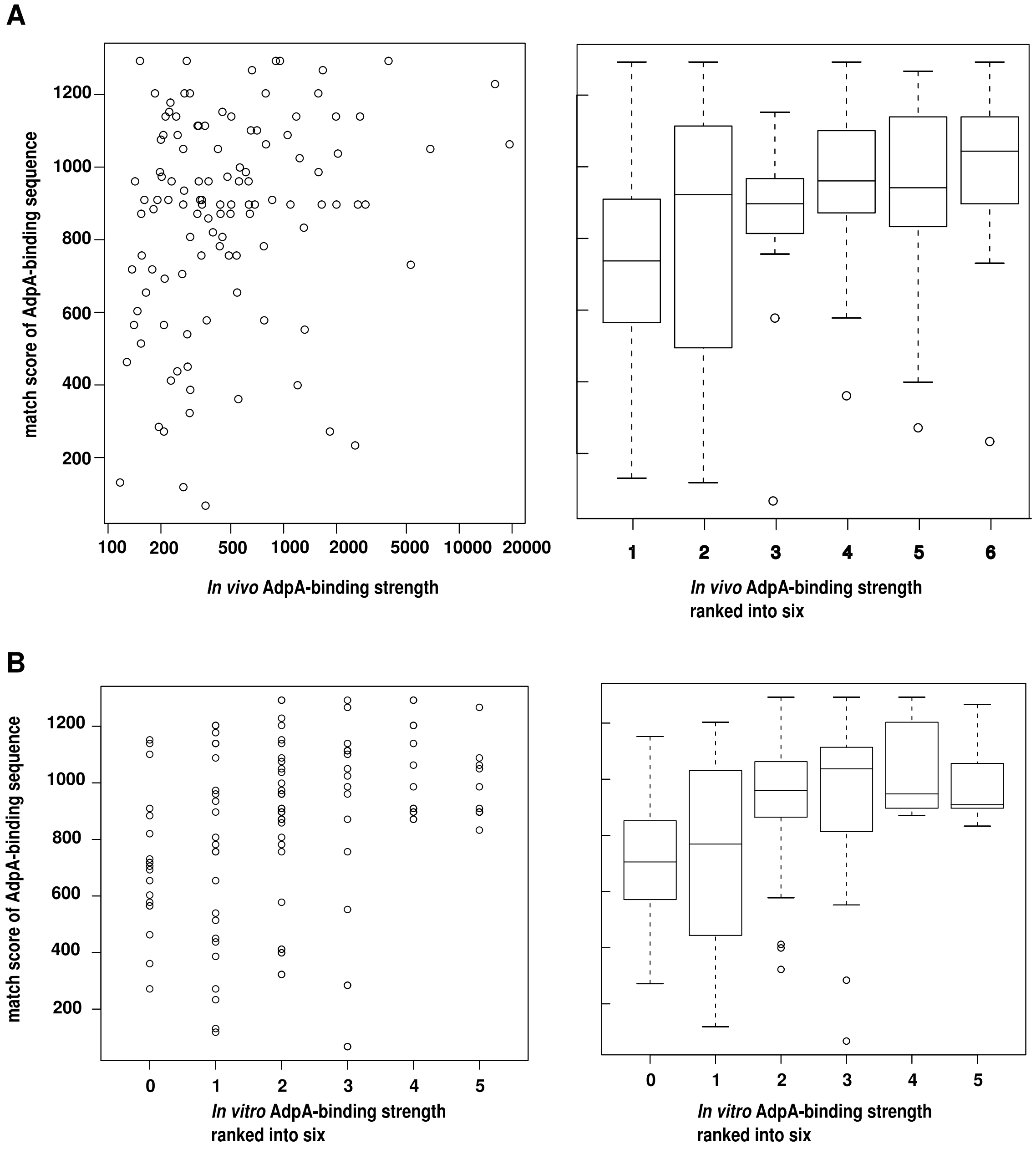
Supplemental Figure S1. **Changes in amount of polyHis-tagged AdpA in solid culture.** The strains were grown on YMPD agar. Total protein was extracted at 24 (lane 1), 36 (lane 2), 48 (lane 3), 60 (lane 4), and 72 (lane 5) h and 6 μg of each was electrophoresed and subjected to westeren blotting analysis with anti-polyHis-tag antibody.



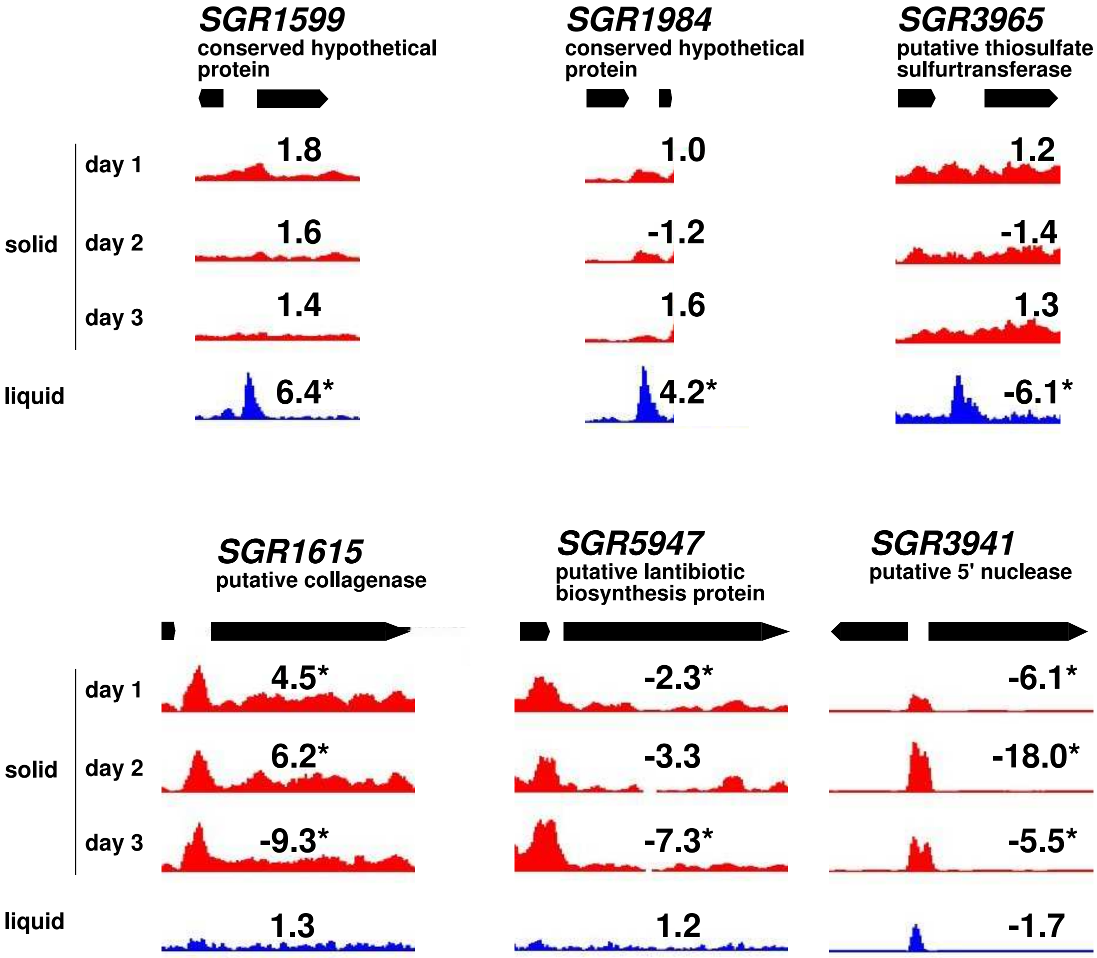
Supplemental Figure S2. **Comparison of signals of peaks between ChIP-seq and ChAP-seq.**



Supplemental Figure S3. Expression analysis of tRNA and rRNA genes in the mycelia grown for 18 h in liquid culture. (A) For tRNA genes that have one in vivo AdpA-binding site in their "putative regulatory region", expression levels were examined by semi quantitative RT-PCR in the N-His-AdpA-producing Δ*adpA* strain (*Nhis-adpA*/Δ*adpA*), as well as the control Δ*adpA* strain (*pTYM19*/Δ*adpA*). Control experiments with no reverse transcriptase (–RT) confirmed that the RNA samples contained no chromosomal DNA. Contrary to our expectation, 23 tRNA genes consisting of 22 transcriptional units were similarly expressed in both the strains, indicating that they were not regulated by AdpA. However, the expression level of *trn42* (*bldA*) was considerably higher in N-His-AdpA-producing strain than in the control Δ*adpA* strain. (B) All six rRNA operons (16S-23S-5S) have two AdpA-binding sites in each "putative regulatory region"; one is approximately 200 bp upstream from one of the transcriptional start points of the rRNA operon and the other is near the 5' end of the transcripts. Among six rRNA operons, the former regions are different from each other, while the latter regions are identical. We also compared the amount of rRNA between the N-His-AdpA-producing *adpA* strain and the control Δ*adpA* strain. To use the genomic DNA as an internal control, total RNA was extracted together with genomic DNA. The nucleic acid sample was subjected to agarose gel electrophoresis followed by ethidium bromide staining. No difference in the amount of rRNA between the strains was detected, indicating that these rRNA operons are not regulated by AdpA. W; NHis-AdpA producing Δ*adpA* strain (*Nhis-adpA*/Δ*adpA*), Δ; Δ*adpA* strain with the empty vector pTYM19 (*pTYM19*/Δ*adpA*), M; λ-HindIII molecular weight marker. [Additional Information] Seven small RNA genes also have one in vivo AdpA-binding site in their "putative regulatory region". Our previous study showed that two of them (*sgs3618* and *sgs5362*) were downregulated in the Δ*adpA* strain compared to the wild-type strain on solid medium. However, recombinant AdpA-C-His did not bind to the upstream regions of these two sRNA genes in vitro.[9] The AdpA-dependency of *sgs3618* and *sgs5362* remained to be confirmed. The remaining five sRNA genes were unlikely to be regulated by AdpA.[9]



Supplemental Figure S4. **Comparison of "match score" of AdpA-binding sequences to AdpA-binding strength *in vivo* (A) and *in vitro* (B).** Left graphs are scatter plots and right graphs are box plots (see the legend for Fig. 4). In the box plot (A), *in vivo* AdpA-binding strength is ranked into six categories; 1, ≤ 200; 2, ≤ 300; 3, ≤ 500; 4, ≤ 1000; 5, ≤ 2000; 6, > 2000.



Supplemental Figure S5. Six "relevant" AdpA-binding sites specifically bound in liquid (upper) or solid (lower) culture. Fold change in transcriptome analysis (*Nhis-adpA*/Δ*adpA* vs. pTYM19/Δ*adpA*) is also shown (data with a p-value by Student's *t*-test < 0.05 are indicated by *). The "apparently relevant" liquid culture-specific AdpA-binding sites seemed to be involved in the regulation of *SGR1599*, *SGR1984*, and *SGR3965*. On the other hand, the "apparently relevant" solid culture-specific AdpA-binding sites seemed to be involved in the regulation of *SGR1615*, *SGR5947*, and *SGR3941*. Biological significance of the liquid or solid culture-specific regulation of these genes by AdpA is unknown.

References

1. Higo, A., Horinouchi, S., and Ohnishi, Y. 2011, Strict regulation of morphological differentiation and secondary metabolism by a positive feedback loop between two global regulators AdpA and BldA in *Streptomyces griseus*, *Mol. Microbiol.,* **81**, 1607–1622.

2. Onaka, H., Taniguchi, S., Ikeda, H., Igarashi, Y., and Furumai, T. 2003, pTOYAMAcos, pTYM18, and pTYM19, actinomycete-*Escherichia coli* integrating vectors for heterologous gene expression, *J. Antibiot.,* **56**, 950–956.

3. Horinouchi, S., Kumada, Y., and Beppu, T. 1984, Unstable genetic determinant of A-factor biosynthesis in streptomycin-producing organisms: cloning and characterization, *J. Bacteriol.,* **158**, 481–487.

4. Bailey, T. L. and Gribskov, M. 1998, Methods and statistics for combining motif match scores, *J. Comput. Biol.,* **5**, 211–221.

5. Yamazaki, H., Tomono, A., Ohnishi, Y., and Horinouchi, S. 2004, DNA-binding specificity of AdpA, a transcriptional activator in the A-factor regulatory cascade in *Streptomyces griseus*, *Mol. Microbiol.,* **53**, 555–572.

6. Yamazaki, H., Ohnishi, Y., and Horinouchi, S. 2000, An A-factor-dependent extracytoplasmic function sigma factor (σ^{AdsA}) that is essential for morphological development in *Streptomyces griseus*, *J. Bacteriol.,* **182**, 4596–4605.

7. Hara, H., Ohnishi, Y., and Horinouchi, S. 2009, DNA microarray analysis of global gene regulation by A-factor in *Streptomyces griseus*, *Microbiology,* **155**, 2197–2210.

8. Tezuka, T., Ohnishi, Y., and Horinouchi, S. 2010, Conditional effect of the deletion

of *eshA* on streptomycin production in *Streptomyces griseus* IFO13350, *Actinomycetologica,* **24**, 45–50.

9. Tezuka, T., Hara, H., Ohnishi, Y., and Horinouchi, S. 2009, Identification and gene disruption of small noncoding RNAs in *Streptomyces griseus*, *J. Bacteriol.,* **191**, 4896–4904.