Sequencing and Analysis of the Resistome of *Streptomyces fradiae* ATCC19609 in Order to Develop a Test System for Screening of New Antimicrobial Agents

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Received November 3, 2015; in final form, November 6, 2015

Abstract—The paper provides the annotation and data on sequencing the antibiotic resistance genes in *Streptomyces fradiae* strain ATCC19609, highly sensitive to different antibiotics. Genome analysis revealed four groups of genes that determined the resistome of the tested strain. These included classical antibiotic resistance genes (nine aminoglycoside phosphotransferase genes, two beta-lactamase genes, and the genes of puromycin N-acetyltransferase, phosphinothricin N-acetyltransferase, and aminoglycoside acetyltransferase); the genes of ATP-dependent ABC transporters, involved in the efflux of antibiotics from the cell (MacB-2, BcrA, two-subunit MDR1); the genes of positive and negative regulation of transcription (*whiB* and *padR* families); and the genes of post-translational modification (serine-threonine protein kinases). A comparative characteristic of aminoglycoside phosphotransferase genes in *S. fradiae* ATCC19609, *S. lividans* TK24, and *S. albus* J1074, the causative agent of actinomycosis, is provided. The possibility of using the *S. fradiae* strain ATCC19609 as the test system for selection of the macrolide antibiotic oligomycin A derivatives with different levels of activity is demonstrated. Analysis of more than 20 semisynthetic oligomycin A derivatives made it possible to divide them into three groups according to the level of activity: inactive (>1 nmol/disk), 10 substances; with medium activity level (0.05–1 nmol/disk), 12 substances; and more active (0.01–0.05 nmol/disk), 2 substances. Important for the activity of semisynthetic derivatives is the change in the position of the 33rd carbon atom in the oligomycin A molecule.

Keywords: *Streptomyces fradiae*, antibiotic resistance genes, test system, oligomycin A

DOI: 10.1134/S1022795416060144