

Cryo-EM structure of the SAH-riboswitch involved in the virulence and survival of *Pseudomonas aeruginosa*

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Infections caused by *Pseudomonas aeruginosa* are common medical problems in hospitals and are particularly dangerous for immunocompromised patients Pang Z et al. (2019) *Biotechnol Adv* 37, 177-192. In *P. aeruginosa* strains, *S*-adenosyl-*l*-homocysteine (SAH)-responsive riboswitch (SAH-RS) is located at the 5'UTR of the mRNA that encodes five enzymes involved in different vital and virulent processes. The structural changes of the SAH-RS, upon ligand binding, activate the expression of downstream genes Wang JX et al. (2008) *Mol Cell* 29, 691-702. The genes within this operon encode crucial elements of bacterial metabolism: (1) SAH hydrolase (SAHase), regulating SAH concentration and, consequently, methylation reactions, (2) methylenetetrahydrofolate reductase, involved in *l*-homocysteine removal after SAH decomposition and methionine synthesis, (3) an alarmone hydrolase, responsible for a degradation of the guanosine-based second messenger ppGpp - a key participant in the stress response by inhibiting RNA synthesis, (4) a glycosyltransferase involved in a biofilm formation and (5) ATP-dependent RNA helicase, which play a crucial role in DNA replication and repair processes. The expression of this operon is tightly controlled by the concentration of SAH in the bacterial cells. The prevention of binding SAH to the riboswitch would disrupt the methylation reactions and the biosynthesis of five crucial proteins involved in *P. aeruginosa* metabolism at once. This aim requires structural studies of this riboswitch. Using single-particle cryo-EM analysis, we determined the native 3D structures of SAH-free RS (5.7 Å). These data will serve as the basis for future studies on developing innovative antimicrobial agents targeting SAH-RS. This project is supported in part by National Science Centre (Poland) 2018/30/E/NZ1/00729. Cryo-EM sample preparation and data collection took place at the SOLARIS National Synchrotron Radiation Centre (Poland), at the Cryo-EM facility infrastructure.