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Proceeding Paper

Production of Beta-Carbonic Anhydrases from *Pseudomonas aeruginosa* and Biothermodynamical Analysis of Their Interaction With Potential Inhibitors †

Rimvydė Čepaitė *, Vaida Juozapaitienė * and Daumantas Matulis *

Vilnius University, Institute of Biotechnology, Department of Biothermodynamics and Drug Design

* Correspondence: rimvyde318@gmail.com (R.C.), vaida.jogaite@bti.vu.lt (V.J.); daumantas.matulis@bti.vu.lt (D.M.)

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Abstract: *Pseudomonas aeruginosa* is one of the most commonly isolated opportunistic pathogens and is globally recognized as a serious threat because of its immunity to nearly all known antibiotics. The genome of this human pathogen, causing life-threatening infections, contains three genes, PAO102, PA2053, and PA4676, encoding for putative beta-carbonic anhydrases (β-CAs) psCA1, psCA2, and psCA3, respectively. β-CAs are zinc metalloenzymes that catalyze reversible CO_2 hydration to bicarbonate. By performing their function β-CAs maintain the intracellular balance of CO_2 and bicarbonate inside the cell. This chemical equilibrium is needed for most of the intercellular biosynthetic reactions and is vitally important for the survival of the pathogen. Therefore, the importance of the β-CAs in bacterial physiology makes these metalloenzymes a promising group of antimicrobial drug targets. In this study β-CAs of *P. aeruginosa* were cloned, heterologously expressed, and purified. The protein stability and catalytic activity analysis has confirmed that the recombinantly expressed his-tagged *P. aeruginosa* β-CAs demonstrate identical properties and catalytic activity to native β-CAs, therefore they can be used for potential inhibitor screening. A library of commercially available CA inhibitors was tested using recombinant proteins to determine the ability of these ligands to bind β-CAs of *P. aeruginosa*. None of the investigated molecules were able to bind psCA1 and psCA2, nevertheless, four of them were able to bind psCA3. The dissociation constants of ligands that can bind β-CAs were found to vary mostly in the micromolar range under different binding conditions, therefore these molecules appear to be promising inhibitors of psCA3.

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