

Accepted Manuscript

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PII: S0960-894X(16)31302-6
DOI: <http://dx.doi.org/10.1016/j.bmcl.2016.12.035>
Reference: BMCL 24524

To appear in: *Bioorganic & Medicinal Chemistry Letters*

Received Date: 27 October 2016
Revised Date: 7 December 2016
Accepted Date: 10 December 2016

Please cite this article as: Del Prete, S., Vullo, D., di Fonzo, P., Osman, S.M., AlOthman, Z., Donald, W.A., Supuran, C.T., Capasso, C., Sulfonamide inhibition profile of the γ -carbonic anhydrase identified in the genome of the pathogenic bacterium *Burkholderia pseudomallei* the etiological agent responsible of melioidosis, *Bioorganic & Medicinal Chemistry Letters* (2016), doi: <http://dx.doi.org/10.1016/j.bmcl.2016.12.035>

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Sulfonamide inhibition profile of the γ -carbonic anhydrase identified in the genome of the pathogenic bacterium *Burkholderia pseudomallei* the etiological agent responsible of melioidosis

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Abstract. A new γ carbonic anhydrase (CA, EC 4.1.1.1) was cloned and characterized kinetically in the genome of the bacterial pathogen *Burkholderia pseudomallei*, the etiological agent of melioidosis, an endemic disease of tropical and sub-tropical regions of the world. The catalytic activity of this new enzyme, BpsCA γ is significant with a k_{cat} of $5.3 \times 10^5 \text{ s}^{-1}$ and k_{cat}/K_m of $2.5 \times 10^7 \text{ M}^{-1} \times \text{s}^{-1}$ for the physiologic CO_2 hydration reaction. The inhibition constant value for this enzyme for 39 sulfonamide inhibitors was obtained. Acetazolamide, benzolamide and metanilamide were the most effective (K_{IS} of 149-653 nM) inhibitors of BpsCA γ activity, whereas other sulfonamides/sulfamates such as ethoxzolamide, topiramate, sulpiride, indisulam, sulthiame and saccharin were active in the micromolar range (K_{IS} of 1.27 -9.56 μM). As *Burkholderia pseudomallei* is resistant to many classical antibiotics, identifying compounds that interfere with crucial enzymes in the *B. pseudomallei* life cycle may lead to antibiotics with novel mechanisms of action.

Keywords: carbonic anhydrase, γ class, inhibitor, sulfonamide, sulfamate, acetazolamide, drug resistance, *Burkholderia pseudomallei*.

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