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Editorial

DPRE1 as a Promising Target for Tuberculosis Drug Discovery

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Tuberculosis is currently the infectious disease responsible for the largest number of deaths in the world according to WHO. Among the strategies recommended by WHO for disease eradication, the research and development of new drugs plays an important role [1]. The combination of validated target-based approaches with whole-cell screening appears to be a promising strategy to be explored for antitubercular drug discovery [2]. The drug candidate 6-chloro-2-ethyl-N-(4-(4-(4-(trifluoromethoxy)phenyl)piperidin-1-yl)benzyl) imidazo[1,2-a]pyridine-3-carboxamide (Q203) for instance, was initially discovered using whole-cell screening approaches and subsequently, its target was characterized as a component of the CytBC1 complex of the respiratory chain, namely QcrB [3]. Among the several molecular targets that have been discovered in recent years, the flavo-enzyme decaprenylphosphoryl-β-D-ribose oxidase (DprE1) has been shown to be a promising target for the discovery of new compounds [2,4]. DprE is a heterodimeric enzyme composed of two proteins: DprE1 and DprE2. Both proteins participate in the biosynthesis of decaprenylphosphoryl-β-D-arabinofuranose (DPA), a precursor of the mycobacterial cell wall component arabinan. Therefore, this enzyme plays an important role in the biosynthesis of components of the mycobacterial cell wall [5,6]. Recently, a number of compounds have been identified as inhibitors of the DprE1. For instance, in 2009, the nitro-benzothiazinone derivative 2-[2-methyl-1,4-dioxa-8-azaspiro[4.5]dec-8-yl]-8-nitro-6-(trifluoromethyl)-4H-1,3-benzothiazin-4-one (BTZ038) was reported as a potent antitubercular compounds with MIC_{90} of 2.3 nM against *Mycobacterium tuberculosis* $H_{37}Rv$ strains [7]. Christophe and collaborators also reported the discovery of another nitro derivative during a phenotypic screening program. The nitrobenzamide derivative N-(2-(4-methoxyphenoxy) ethyl)-3,5-dinitrobenzamide (DNB1) presented a MIC_{90} of 0.2 μM against intracellular and extracellular *M. tuberculosis* [8]. Landge and coworkers also reported a potent DprE1 inhibitor. The benzothiazole-N-oxide derivative 7-nitro-2-(piperidine-1-carbonyl)-5-(trifluoromethyl)benzo[d]thiazole 3-oxide showed MIC_{90} of 0.08 μM against *M. tuberculosis* $H_{37}Rv$ and IC_{50} of 0.09 μM against the enzyme DprE1 [9]. These potent antitubercular compounds represents the importance that the DprE1 enzyme plays for the survival of the *M. tuberculosis*.

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