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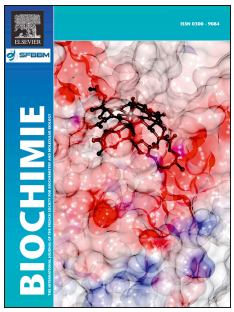

Dihydrodipicolinate synthase is absent in fungi

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ABSTRACT

The class I aldolase dihydrodipicolinate synthase (DHDPS) catalyzes the first committed step of the diaminopimelate (DAP) lysine biosynthesis pathway in bacteria, archaea and plants. Despite the existence, in databases, of numerous fungal sequences annotated as DHDPS, its presence in fungi has been the subject of contradictory claims. We report the characterization of DHDPS candidates from fungi. Firstly, the putative DHDPS from *Coccidioides immitis* (PDB ID: 3QFE) was shown to have negligible enzyme activity. Sequence analysis of 3QFE showed that three out of the seven amino acid residues critical for DHDPS activity are absent; however, exact matches to catalytic residues from two other class I aldolases, 2-keto-3-deoxygluconate aldolase (KDGA), and 4-hydroxy-2-oxoglutarate aldolase (HOGA), were identified. The presence of both KDGA and HOGA activity in 3QFE was confirmed *in vitro* using enzyme assays, the first report of such dual activity. Subsequent analyses of all publically available fungal sequences revealed that no entry contains all seven residues important for DHDPS function. The candidate with the highest number of identities (6 of 7), KIW77228 from *Fonsecaea pedrosoi*, was shown to have trace DHDPS activity *in vitro*, partially restored by substitution of the seventh critical residue, and to be incapable of complementing DHDPS-deficient *E. coli* cells. Combined with the presence of all seven sequences for the alternative α-aminoadipate (AAA) lysine biosynthesis pathway in *C. immitis* and *F. pedrosoi*, we believe that DHDPS and the DAP pathway are absent in fungi, and further, that robust informed methods for annotating genes need to be implemented.