

Crystal Structures of Apo-Cyclophilin from *Moniliophthora perniciosa* and Its complex with Cyclosporin A.

Monzani, P.S.¹, Pereira, H.M.², Meirelles, F. V.³, Oliva, G.², Cascardo, J.C.M¹

¹ Departamento de Ciências Biológicas, UESC, Bahia, Brazil; ² Instituto de Física de São Carlos, USP, São Paulo, Brazil; ³ Departamento de Ciências Básicas, USP, Pirassununga, Brazil.

Moniliophthora perniciosa is the causal agent of witches' broom in the cacao culture. Cyclophilins have been implicated in a wide variety of cellular processes, including the response to environmental stresses, cell cycle control, regulation of calcium signaling and the control of transcription. Involvement of cyclophilins in pathogenicity was pointed out both in fungi pathogenic toward animals or plants. In Yeast, calcineurin and cyclophilin are involved in fungal morphogenesis and virulence, and there is evidence that cyclophilin interacts with calcineurin in the absence of cyclosporin. It has been proposed that cyclosporin acts by interfering with the interaction between cyclophilin and calcineurin. We have cloned the cyclophilin gene in the vector pET28a, expressed, purified, concentrated at 6 mg/mL and crystallized. Apo form was crystallized in 30% PEG400 and 0.1 M CAPS pH 10.5, while bound form in 1.8 M (NH₄)₂SO₄, 0.1 M TRIS pH 8.5 and 3 times more cyclosporin than protein. The structures were solved by molecular replacement with the Phaser program using yeast cyclophilin as a search model and refinement was carried out with PHENIX and COOT programs. Models present R_{work} 0.17 and R_{free} 0.20 to apo and bound forms and good stereochemistry checked by PROCHECK program. Structures obtained are similar to the others structures deposited. Cyclosporin A was well defined in the electronic density. Previous analysis shows that cyclosporin inhibits fungi germination and this cyclophilin isoform present absent or low peptidyl prolyl *cis-trans* isomerase activity.

Keywords: Cyclophilin, *Moniliophthora perniciosa*, Witches' broom.
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