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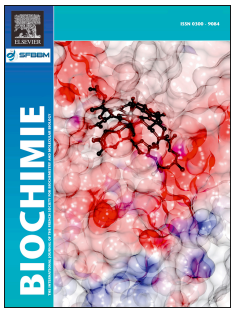

The revelation of selective sphingolipid pathway inhibition mechanism on fumonisin toxin binding to ceramide synthases in susceptible organisms and survival mechanism in resistant species

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Abstract

Fumonisin B1 toxin (FB1) is a well-known competitive inhibitor of ceramide synthase (CS) in yeast. However, FB1 is unable to obstruct CS from *Trichoderma* spp., which are well-known biocontrol agents. To explore the contrasting binding modes, a comparative structural analysis of complexes of FB1 with these two CS proteins was carried out. Formation of activation loop on the binding of substrates with the CS from yeast was observed but when inhibitor interacted with the activation loop, it transformed into helix leading to the potentially inactivated state of the enzyme. In yeast homologue of the enzyme, the inhibitor and substrates compete for the same binding site. Whereas, in the CS protein from *Trichoderma guizhouense*, no such competition for substrate binding site was observed and binding pocket of the enzyme could easily accommodate FB1 along with the interacting native substrates, which may lead to the successful catalysis.