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Poster 8

NMR studies of p21Waf1/Cip1/Sdi1 C-terminal domain in the free and bound state

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Cyclin-dependent kinase(Cdk) inhibitor $p21^{Waf1/Cip1/Sdi1}$ is a multifunctional as well as tumor suppressor protein. The central role of $p21^{Waf1/Cip1/Sdi1}$ is to mediate G1/S arrest through inhibition of Cdks. Biological studies of CyclinD1/Cdk4 proposed that $p21^{Waf1/Cip1/Sdi1}$ C-terminal domain($p21^{CT}$) is a potent Cdk4 inhibitor. We report here structural differences of $p21^{CT}$ between the free and Cdk4 bound state using NMR spectroscopy and molecular modeling calculations. The solution structure of $p21^{CT}$ bound to Cdk4 suggested that Phe150-Tyr151 pair binds to Cdk4, which is similar to Phe87-Tyr88 pair within 310 helix of p27 inserts into the catalytic cleft of Cdk2 by mimicking the purin base of the ATP. Based on our studies, we observed that Phe159-Ser160 residues of $p21^{CT}$ complexed with Cdk4 had conformational transition for binding of Phe150-Tyr151 pair to Cdk4.