Three-dimensional Structure of Human FKBP52

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FKBP family proteins are immunophilins which process peptidyl-prolyl isomerase (PPIase) domain and they can all bind FK506, a macrolide immunosuppressant. FKBP52 is a FKBP protein, which can be separated into four domains. The first (FK1) and the second (FK2) domains are similar with FKBP12. The third domain includes three tetratricopeptide repeat (TPR) motives and the forth domain contains calmodulin binding-site.

We have overexpressed and purified FKBP52 full-length and three segments of FKBP52, including FKBP52-FK1, N(1-260) and C(145-459). The crystals of FKBP52-FK1, N(1-260), C(145-459) have been obtained, as well as the complex of C(145-459) and a C-terminal pentapeptide MEEVD from Hsp90. The three dimensional structure of FKBP52 has been defined based on the crystal structures of N(1-260) and C(145-459). The structures have indicated the pattern of natural substrates binding to the active site of PPIase and the reason why the FKBP52-FK506 complex is not able to inhibit calcineurin activity, and has interpreted why FK2 has no PPIase activity. The functional differences between FKBP52 and FKBP51 have been clarified by comparing their structures. A hormone-signaling model based on FKBPs / Hsp90 / hormone receptor complex assembly has been proposed and FKBP51 is regarded as a negative feedback factor of FKBP52 in hormone signaling.

Keywords: FKBP52, PPIase, hormone receptor complex