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Dynamic functional regulation of Pro-isomerase by intrinsically disordered region, IDR

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Many proteins have a structure in which some domains are connected by the linker. The region that doesn't have specific structure was thought that it was a simple string to tie between domains, and it was rarely thought about the detailed functions. We study a role of the linker which is intrinsically disordered region (IDR).

Pin1 is a phosphorylation-specific peptidyl prolyl *cis/trans* isomerase (PPIase). Pin1 is composed of two independently moving domains connected by the unstructured linker, intrinsically disordered region: the phosphor-peptide binding WW domain and the catalytic PPIase domain. It has been known that the WW domain connected by the linker is indispensable for cell-survival even though the isolated PPIase domain shows the isomerase activity. Recent studies demonstrated that the transient inter-domain interaction between the WW and PPIase domains mediated by the linker is strongly engaged in the regulation of the Pin1 isomerase activity. However, the correct role of the flexible linker in this regulatory-mechanism is still unclear. In this study, we introduced a mutation, I28A where is known to be the center of the inter-domain contacting-region, and investigated the effect on the substrate-binding-affinity and the Pin1-isomerase-activity by the less-inter-domain interaction mutation.

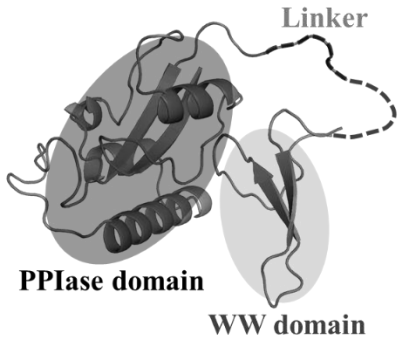

Fig. 1 Ternary structure of Pin1

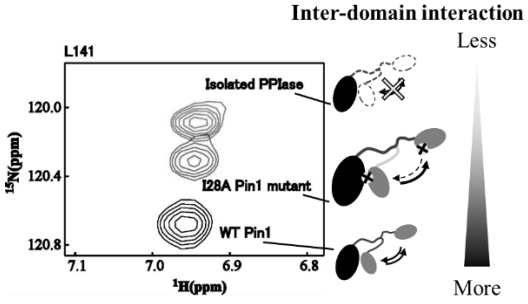

Fig. 2 The chemical shift changes of the inter-domain residue (L141) for a series Pin1 mutants.

References

[1] Wilson, K.A., Bouchard, J.J., and Peng, J.W. (2013) Interdomain Interactions Support Interdomain Communication in Human Pin1. Biochemistry 52, 6968–6981.