

Crystal Structure of human Tudor-SN and Implication of its Roles in RNA Interference

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The human Tudor-SN (also called p100) is a multiple function protein. So far Tudor-SN has been reported to function as a transcriptional co-activator, participate in RNA interference silencing complex assembling and hyper-edited microRNA cleavage. Although extensive functional studies have been carried out, the structure and domain arrangement of Tudor-SN is unknown. The structural based analysis of Tudor-SN is thus imperious for better understanding of the role of this protein in RNA interference and transcription activation.

We crystallized a stable 70-kD truncated form of human Tudor-SN and solved the structure by MAD method at a resolution of 1.9 Å. X-ray diffraction data were recorded at the Taiwan beamline BL-12B in SPring-8. The overall Tudor-SN structure contains three intact SN domains (SN3, SN4 and SN5) and one Tudor domain which is a insertion domain between second and third β -strands of SN5. Superposition of Tudor-SN with staphylococcal nuclease shows that some of the important active site residues of SN3 and SN4 domains are missing, indicating that some of the SN domains, including SN4, may not be active in RNA cleavage. Structural superposition of the OB fold in the SN domain of Tudor-SN with the OB-fold structure of Sac7d/DNA complex reveals a substrate binding cleft located between SN3 and SN4 interface. We suggest that SN3 domain is likely responsible for RNA cleavage and SN4 domain is likely involved in substrate binding but not in cleavage. These results are consistent with the activity assays for different truncated forms of Tudor-SN in RNA cleavage. In conclusion, the structural analysis of Tudor-SN suggests a coordination between two SN domains in RNA binding and cleavage and provides some clues for further functional investigations.