Poster Presentation

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Structure of the homology domain of the DNA replication proteins Sld3/Treslin

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DNA replication in eukaryotic cells is tightly regulated so that each replication origin in chromosomal DNA fires just once in proper timing during a cell cycle. Activation of the replicative helicase at the origins is a key step of the regulation. This process is achieved by loading of Cdc45 and GINS onto the helicase core complex on the origins. Sld3 is a critical regulator for this process: Sld3 and Cdc45 form a complex, which associate with origins in a mutually dependent manner, and further phosphorylation of Sld3 by a cyclin-dependent kinase recruits GINS to the origins through the interaction with Dpb11. Sld3 is well conserved in fungi, and Treslin/Ticcr is identified as its functional counterpart in metazoans. Although Sld3 and Treslin do not show significant sequence similarity, recent bioinfomatic study showed that they share a homology region (Sld3/Treslin domain). Functional role of the domain has remained to be elusive, thus we set out for the structural study of the Sld3/Treslin domain of budding yeast Sld3. The crystal structure showed that the domain has rhombic shape, and there is a highly positively charged area on the molecular surface. Taken together with the preceding studies, the area is considered to be the interface to Cdc45. Shape and character of the interface were consistent with the structure model of Cdc45 proposed by SAXS and bioinfomatic studies. Our structural and functional analyses showed that the domain alone is enough to form stable complex with Cdc45, and the binding with Cdc45 is stabilized by structurally flexible arm. The arm was conserved, thus our binding model of Sld3 and Cdc45 was suggested to be common in Sld3 and Treslin.

Keywords: Sld3, Treslin, Ticrr, DNA replication, Crystal structure