第268回　化学コースコロキウムのご案内

「DDK-mediated regulation of the deSUMOylating enzyme Ulp2 facilitates DNA replication initiation」

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平成28年　11月21日（月曜日）16:00-17:00　11号館202室

要旨

Dbf4-dependent kinase Cdc7 (DDK) is crucial for chromosome replication initiation, in part by activating the replicative DNA helicase, MCM. Other means of DDK-dependent regulation of replication are less understood. Here, we uncover that the budding yeast deSUMOylating enzyme, Ulp2, is a DDK substrate that binds to replication origins and promotes their efficient firing. In DDK mutants and phosphodeficient Ulp2 variants, Ulp2 binding is deregulated, being less concentrated at origins and more diffused along chromosomes. Furthermore, in *ulp2* null and *ulp2* phosphodeficient mutants, origin firing-derived replication intermediates and BrdU incorporation efficiency are substantially decreased. Importantly, the replication initiation defects of *ulp2* cells can be rescued by removing the SUMO-targeted ubiquitin ligase, Slx5, indicating that Ulp2 is critical to protect SUMOylated replisome factors from proteasome-mediated degradation. We propose that DDK regulates Ulp2 distribution on chromosomes and concentration at firing origins to ensure a critical mass of SUMOylated replisome components poised for replication upon MCM activation.

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