Institute colloquium

[Webinar] The establishment of sister chromatid cohesion is an aspect of the replisome unique to eukaryotic cells

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This Institute Colloquium is offered as a webinar. If you would like to attend this webinar, please register here.In addition to extruding long loops of DNA, cohesin topologically entraps within its SMC-kleisin ring (S-K) individual DNAs during G1 and sister DNAs during S-phase. Co-entrapment of sister DNAs is thought to be the mechanism by which cohesin holds sister chromatids together, a process crucial for mitotic and meiotic chromosome segregation. All three cohesin activities require two related hook-shaped proteins called Scc2 and Scc3. Using a combination of cysteine pair substitutions and thiol-specific crosslinking we provide a rigorous demonstration of entrapment activity in vitro. We show that Scc2 alone promotes entrapment of DNAs in the E-S and E-K compartments between ATP-bound engaged heads and the SMC hinge and associated kleisin respectively. This process does not require ATP hydrolysis nor is it accompanied by entrapment within S-K rings, which is a slower process that requires addition of Scc3 and is stimulated by ATP hydrolysis. Though cohesin can load onto chromosomes throughout the cell cycle, it normally only builds cohesion during S phase. A key question is whether cohesion is generated by conversion of cohesin complexes associated with un-replicated DNAs ahead of replication forks into cohesive structures behind them, or from nucleoplasmic cohesin that is loaded de novo onto nascent DNAs associated with forks, a process that would be dependent on cohesin's Scc2 subunit. We show here that in S. cerevisiae, both mechanisms exist and that each requires a different set of non-essential replisome-associated proteins. Cohesion produced by cohesin conversion requires Tof1/Csm3, Ctf4 and Chl1 (TCCC) but not Scc2 while that created by Scc2-dependent de novo loading at replication forks requires the Ctf18-RFC complex. Though inactivation of either pathway individually merely reduces the efficiency of cohesion establishment, simultaneous inactivation resembles the effect of cohesin ablation and is lethal. The association of specific replisome proteins with different types of cohesion establishment opens the way to a mechanistic understanding of an aspect of DNA replication unique to eukaryotic cells.

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Webinar

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