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Molecular basis of epigenetic inheritance

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Epigenetic marks, such as histone methylation, play a central role in gene expression, genome stability, cell differentiation and development. During DNA replication, chromatin undergoes a wave of disruption and reassembly. Little is known about how the epigenetic marks are faithfully inherited from one generation to the next. In fission yeast, the hallmark of heterochromatin, a condensed chromatin structure, is H3K9 methylation. The conserved epigenetic mark is mediated by small interference RNAs (siRNAs) in a cell cycle-dependent manner: at S phase, heterochromatin is briefly transcribed by RNA Polymerase II, and the transcripts are subsequently processed into siRNAs. The small RNAs, together with other key silencing factors, including Dos1/Clr8, Dos2/Clr7, and Rik1, mediate H3K9 methylation by a histone H3K9 methyltransferase, Clr4. Our resent findings indicate that the DNA polymerase components, such as the ε subunit, Cdc20, associates with Dos2-Rik1 complex, and is essential for H3K9 methylation and heterochromatin function. Moreover, our results show that Cdc20 regulates siRNA generation by promoting the RNA Pol II transcription in heterochromatin. These data suggest that DNA polymerase components may play a key role in inheritance of histone methylation by coordinating DNA replication, RNAi and histone methylation, and provide an explanation for previously observed cell cycle-regulated RNAi-dependent heterochromatin silencing. Based on these findings, we propose the model that at DNA replication forks, DNA polymerase subunits mediate recruitment of epigenetic factors required for RNAi and histone modification to heterochromatin to promote the faithful transmission of histone methylation

Biography

Fei Li received his Ph.D. from the University of Texas at Austin, and conducted his postdoctoral studies at University of Texas Southwestern Medical Center at Dallas and University of California at Berkeley. He currently is an assistant professor at Department of Biology at New York University. His research is focused on the study of epigenetic and chromatin regulation. He has published more than 10 peer-reviewed papers in reputed journals, including *Cell* and *Nature*, and is serving as an editorial board member of *Epigenetics & Genomics*

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