

## **S1-4**

### **RPA-governed Endonuclease Switching during Eukaryotic Okazaki Fragment Processing.**

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At the eukaryotic replication fork, discontinuous synthesis of lagging strand DNA gives rise to Okazaki fragments carrying ribonucleotides derived from the primer RNA at their 5' ends. Efficient removal of these ribonucleotides is vital for maintaining genome integrity. In this report we show that the endonucleases Dna2 and Fen1 act sequentially to facilitate the complete removal of the primer RNA. The sequential action of these enzymes is governed by the single-stranded DNA binding protein, RPA. Our results demonstrate that the processing of Okazaki fragments in eukaryotes differs significantly from and is more complicated than that occurring in prokaryotes. We propose a novel biochemical mechanism for the maturation of eukaryotic Okazaki fragments.