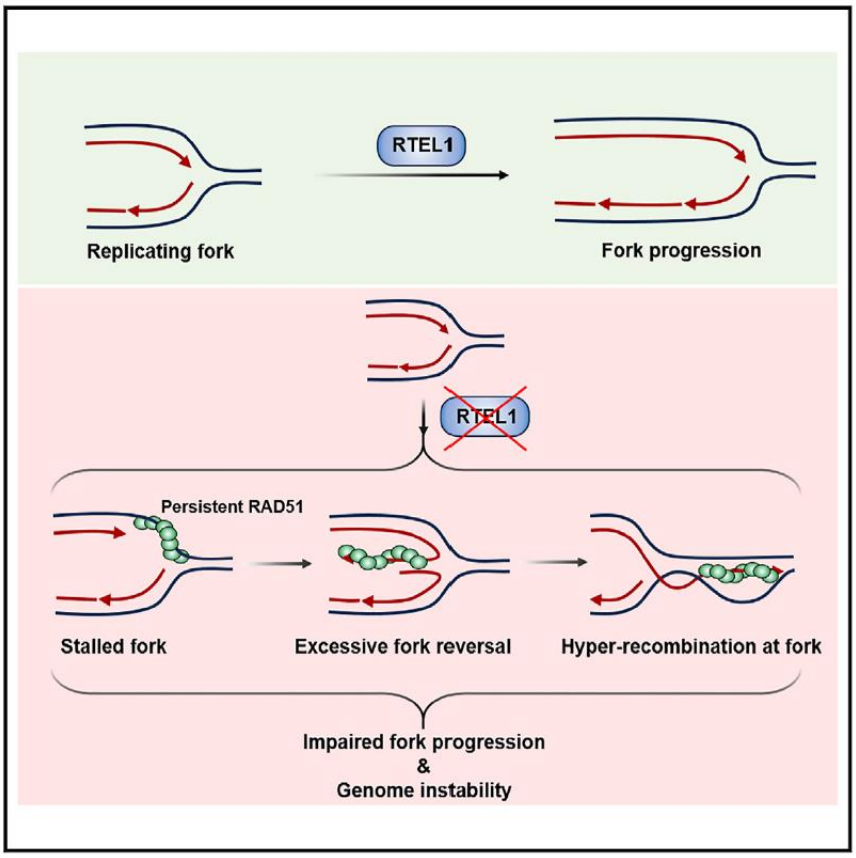
Details of Research Work

Dixit, S., Bhattacharya, D., Saxena, S., Sahoo, S., Nagraj, T., Chittela, R., Somyajit, K., and **Nagaraju, G.** (2024). RTEL1 helicase counteracts excessive homologous recombination to safeguard replicating genomes. ***Cell Reports*** **43:114594.**



Summary

Homologous recombination (HR) is an important pathway for the repair of DNA double-strand breaks, genome maintenance and tumor suppression. However, unregulated HR can lead to chromosomal rearrangements and genome instability. This work demonstrates the role of RTEL1 helicase in suppressing hyper-recombination during DNA replication and facilitating error-free genome duplication. The hyper-recombination and replication defects in RTEL1-depleted cells can be rescued by co-depletion of RAD51 and RAD51 paralogs. RTEL1 interaction with PCNA and its helicase activity is required for suppressing HR during DNA replication. Our data identify a novel role of RTEL1 helicase in restricting RAD51-mediated HR and fork reversal to facilitate error-free genome duplication. RTEL1 helicase mutations lead to Hoyeraal-Hreidarsson syndrome and Dyskeratosis congenita, characterized by developmental abnormalities, bone marrow failure and telomere dysfunction. In addition, individuals with mutations in *RTEL1* are also predisposed to high-grade glioma, astrocytomas, and glioblastomas. Our work provides insights into RTEL1 mutations leading to genetic diseases and cancer.

For complete details, please see the attached pdf of the published paper (*Cell Reports*, 2024)

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