Two proteins slow down the train of DNA replication in Drosophila

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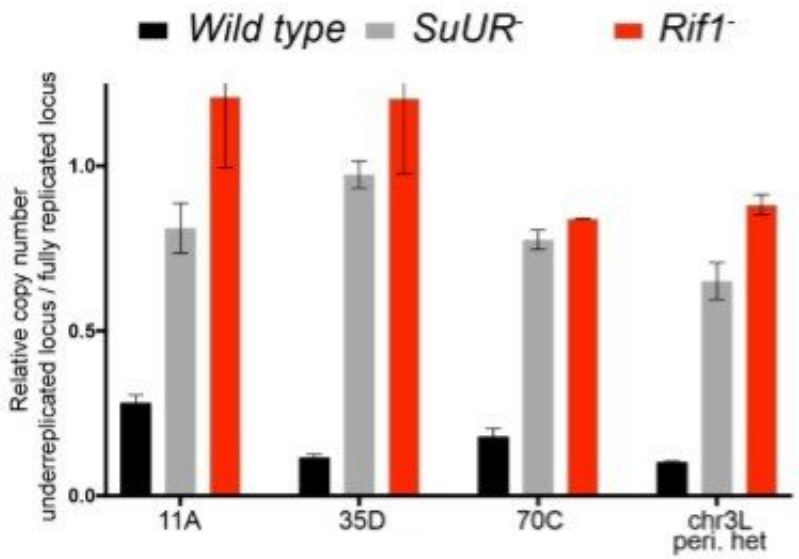

Quantitative droplet-digital PCR (ddPCR) copy number assay for multiple underreplicated regions. Each bar is the average enrichment relative to a fully replicated control region for three biological replicates. Credit: Jared Nordman

Two major factors matter when it comes to cells copying DNA: getting everything accurate in the sequence and how much of it is replicated. Mistakes can result in mutations, which can lead to diseases such as cancer.

Jared Nordman, assistant professor of biological sciences at Vanderbilt, said scientists already understood the amount of DNA replicated had to

do with where the duplication process started and ended – akin to a train carrying passengers from point A to point B. The train's starting point and destination are important, but so is its speed. When it comes to DNA replication, that area hasn't been explored as broadly.

"We knew that the Suppressor of Underreplication (SUUR) protein was involved in slowing down the replication machinery, but we didn't know how it worked," Nordman said. "In fruit flies, which have all the machinery necessary to copy DNA virtually identically to humans, the SUUR protein physically interacts with the Rif1 protein, bringing it to the train. Once there, Rif1 has the capacity to inhibit or slow down replication."

Rif1 controls how much DNA gets copied in human cells too, but nobody knows how it does this job. While humans don't have SUUR, they likely use another adaptive protein to help Rif1 slow down the replication machinery. This work was the foundation for a new National Science Foundation grant to interrogate how the Rif1 protein controls DNA replication, Nordman said.

His team's latest findings on the subject are outlined in a paper titled "Rif1 inhibits replication fork progression and controls DNA copy number in Drosophila," published Oct. 2 in the journal *eLife*.

More information: Alexander Munden et al. Rif1 inhibits replication fork progression and controls DNA copy number in Drosophila. Oct 2, 2018 doi.org/10.7554/eLife.39140.001

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