

VID22 COUNTERACTS G-QUADRUPLEX-INDUCED GENOME INSTABILITY

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Genome instability is a pathological condition characterized by the accumulation of genetic alterations. It can cause cell death and, in higher eukaryotes, represents a hallmark of cancer cells. Using Synthetic Genetic Array (SGA) technology, we performed a yeast genetic screening to identify genes and pathways protecting from chronic DNA damage. Among the candidates, we focused on VID22, which encodes a putative transcription factor with an unclear role in the DSB repair pathway.

We found that *vid22Δ* cells show spontaneous genome instability and increased sensitivity to agents inducing replicative stress. Whole-genome sequencing of different *vid22Δ* mutants revealed an accumulation of gross chromosomal rearrangements, instability of repetitive sequences, and alterations at the rDNA locus. The affected regions are GC-rich and prone to form G-quadruplex (G4) structures. We demonstrated that Vid22 binds directly to G4 regions, protecting them from instability. Moreover, loss of Vid22 results in telomere length defects, characterized by enrichment of G4 motifs.

To dissect its function, we generated point mutants disrupting Vid22 homodimerization, DNA binding, or protein interactions. The characterization of these mutants will be also presented. Our data suggest that Vid22 is a novel regulator of G4 metabolism and genome integrity.