GENOMICS OF DNA REPAIR

- STUDENTS / UNIVERSITIES

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PURE PROGRAM FOR UNDERGRADUATE RESEARCH

ABSTRACT

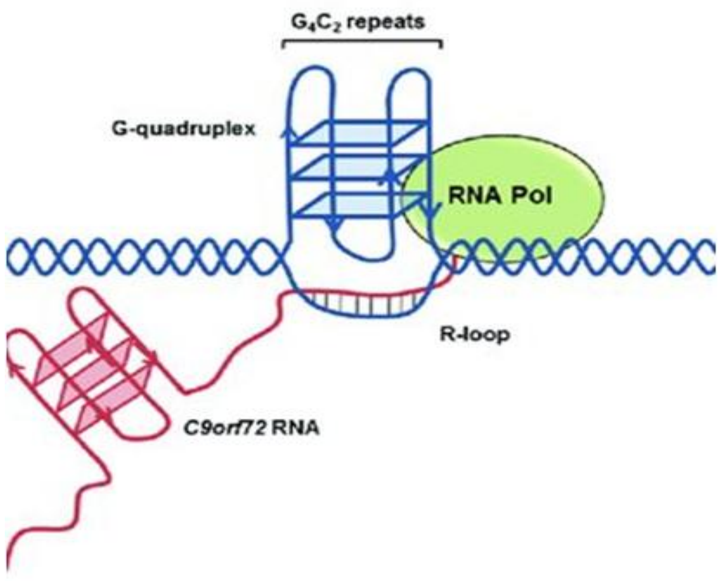

Figure 1: G-quadruplex and R-loop structures on DNA transcript (Barker, H. et al. 2017)

DNA damage can be repaired under physiological conditions by Nucleotide Excision Repair (NER) which is affected by 3D structure of DNA. R-loops and G-quadruplexes (G4s) are noncanonical 3D DNA structures which are mostly found at regulatory sites such as oncogene promoters, replication origins and telomeres. In this work, we focus on the effect of these noncanonical DNA structures on NER. XR-seq data constructed by Li, W. et al. (2018) for *S. Cerevisiae* was used to generate a repair data by using genome wide mapping of G4s (Marsico, G. et al. 2018) and R-loops (Castellano-Pozo, M. et.al. 2013) . Putative G-Quadruplex Sequences (PQS) were used as control for G4 repair. G4, R-loop and PQS repair data were compared with shuffled repair data of each, for extensive control. Our analysis shows that NER decreases at the sites of G4 structures when R-loop structures do not show any significant difference. As the results were derived from the repair data only, it cannot be concluded whether these results correlate with the damage ratio. Further work can be done to analyze the repair of G4 and R-loop damage sites particularly and draw conclusions accordingly.

XR-seq | excision repair | R-loop | G4 | PQS

OBJECTIVES

Understanding the effects of G-quadruplex and R-loop 3D DNA structures on Nucleotide Excision Repair (NER) by using bioinformatic analysis.

PROJECT DETAILS

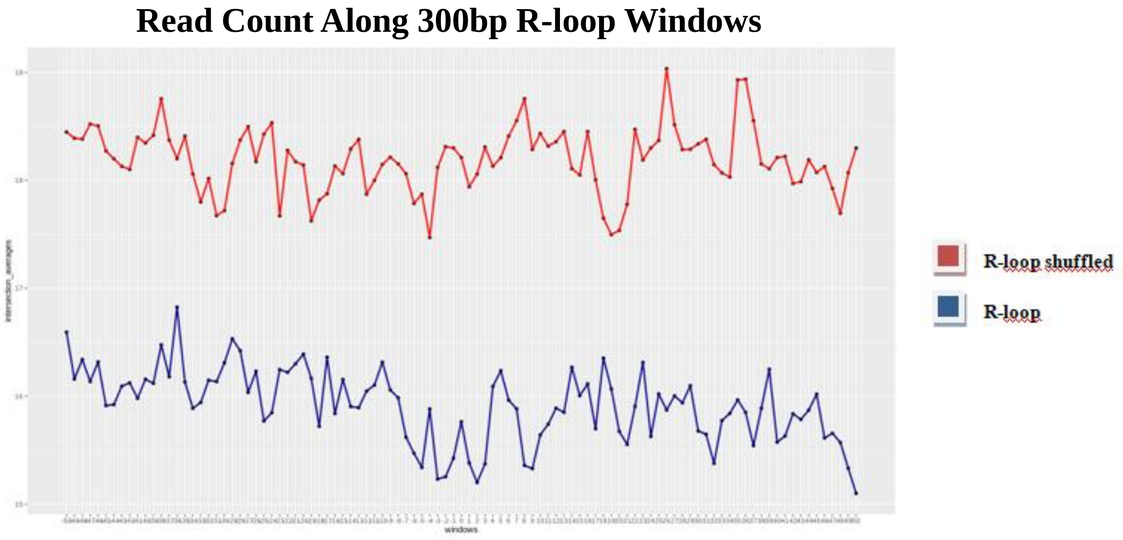

Figure 2: Line plot for average read counts of each window for R-loop and R-loop shuffled data.

The plot was constructed by ggplot2 package on R. 300bp R-loop fragments were created and randomly distributed over yeast genome by using *bedtools shuffle* and 101-piece windows were made by *bedtools makewindows*. Repair counts were obtained by *bedtools intersect*. The plot shows that R-loop shuffled counts are more than R-loop counts although they do not show a significant difference around window 0 where R-loop structures are accumulated.

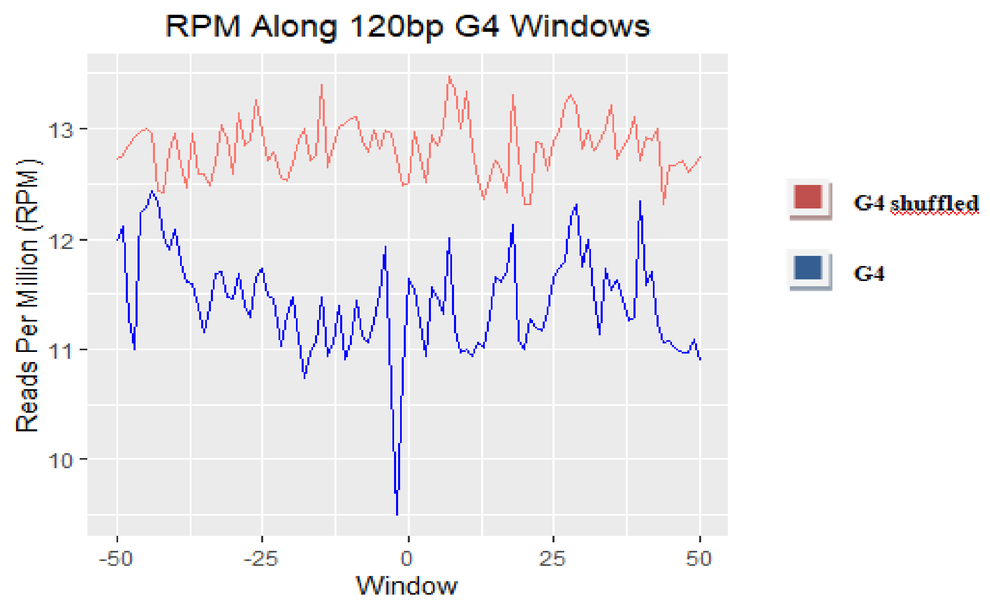

Figure 3: Line plot of RPM counts for G4 and G4 shuffled data.

The plot was constructed by ggplot2 package on R. 120bp G4 fragments were created and randomly distributed over yeast genome by using *bedtools shuffle* and 101-piece windows were made by *bedtools makewindows*. Repair counts were obtained by *bedtools intersect* and read counts per million (RPM) were calculated. The plot shows that shuffled data has greater repair counts than G4 data. G4 repair counts drop significantly around window 0 where G4 structures are accumulated.

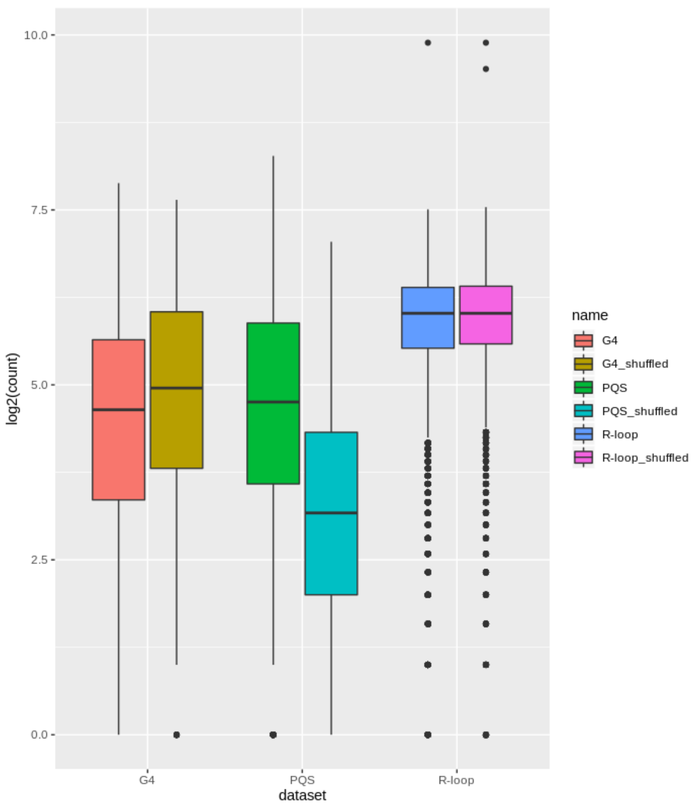

Figure 4: Box plot created for G4, PQS, R-loop and shuffled data of each by using ggplot2 package on R.

Plot shows a subtle decrease for R-loop data compared to shuffled data counts when the counts for G4 data decreases significantly when compared to shuffled data. PQS data was used as control for G4 data.

CONCLUSIONS

Formation of R-loop structures does not have a significant effect on NER, when formation of G4 structures decreases NER. Further research can be done to explain the relation of PQS to NER. Damage-seq can be applied to data for observation of the damage sites on G4 and R-loop structures and results related to the repair of these damage sites can be obtained.

REFERENCES

Figure 1: Barker, H. et al. (2017) RNA Misprocessing in C9orf72-Linked Neurodegeneration. Frontiers in Cellular Neuroscience, 11.

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Li, W., Adebali, O., Yang, Y., Selby, C. P., & Sancar, A. (2018). Single-nucleotide resolution dynamic repair maps of UV damage in Saccharomyces cerevisiae genome. Proceedings of the National Academy of Sciences,115(15), E3408-E3415. doi:10.1073/pnas.1801687115

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