EFFECT OF G-QUADRUPLEX FORMATION ON UV-INDUCED DAMAGE AND NUCLEOTIDE EXCISION REPAIR

Cem Azgari¹ and Ogün Adebali¹

¹Faculty of Engineering and Natural Sciences, Molecular Biology, Genetics and Bioengineering, Sabancı University Orhanlı, Tuzla, 34956, Istanbul

G-quadruplexes (G4s) are non-B DNA structures formed by four or more guanine tetrads stabilized by a charged ion. The formation and cellular functions of G4s are widely studied. G4s are known to localize at telomeres and promoters with a range of functions including maintaining genome integrity at telomeres and suppressing or initiating transcription. Moreover, G4s can cause mutagenesis if they stay persistent during replication [1]. Although thermodynamically stable G4s are linked to double-strand breaks and genome instability, their effect on UV-induced damages and the interplay between nucleotide excision repair and G4 formation are unclear. Aiming to uncover this relationship, we have obtained genome-wide G4 maps in HeLa cells using G4P-ChIP-seq data and motif finder algorithms Quadron [2] and G4-Miner [3]. Then, we applied Damage-seq and XR-seq methods on HeLa cells, which maps UV-induced damages [(6-4)PPs and CPDs] and nucleotide excision repair of these damages, respectively [4]. Profiles of (6-4)PP and CPD damage around G4 regions suggest that the damage formation on the G4s was lower than in the neighboring regions. On the contrary, we observed higher relative repair on G4s compared to the flanking regions. We are currently working on understanding the reasons behind these profiles that will provide insights into co-occurrence of G4s and UV-induced damage and the response of nucleotide excision repair in these sites.

Keywords: G-quadruplex; Nucleotide excision repair; UV damage; (6-4)PPs; CPDs; XR-seq; Damage-seq

References

[1] Ui, A., Chiba, N., & Yasui, A. (2020). Relationship among DNA double-strand break (DSB), DSB repair, and transcription prevents genome instability and cancer. Cancer science, 111(5), 1443-1451.

[2] Sahakyan, A. B., Chambers, V. S., Marsico, G., Santner, T., Di Antonio, M., & Balasubramanian, S. (2017). Machine learning model for sequence-driven DNA G-quadruplex formation. Scientific reports, 7(1), 1-11.

[3] Tu, J., Duan, M., Liu, W., Lu, N., Zhou, Y., Sun, X., & Lu, Z. (2021). Direct genome-wide identification of G-quadruplex structures by whole-genome resequencing. Nature communications, 12(1), 1-9.

[4] Hu, J., Adebali, O., Adar, S., & Sancar, A. (2017). Dynamic maps of UV damage formation and repair for the human genome. Proceedings of the National Academy of Sciences, 114(26), 6758-6763.

Corresponding author's address

To whom correspondence may be addressed: Sabancı University, Faculty of Engineering and Natural Sciences, Tuzla, Istanbul, 34956 Turkey Tel.: 216-568-7043; E-mail: oadebali@sabanciuniv.edu.