New Data Science in Nucleic Acids Chemistry (20): G-quadruplex DNA formations depending on the environments in the mitochondrial matrix

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Molecular crowding alters the physicochemical properties of the solution and affects profoundly the stabilities of canonical and non-canonical nucleic acid structures.[1] Intracellular crowding environment varies spatio-temporally within the cell. In particular, macromolecular crowding in the mitochondrial matrix has been suggested to be much higher than that of the nucleus and cytosol.[2] Mitochondrial DNA houses potential quadruplex-forming sequences (PQS) that participate in regulatory functions of mitochondria.[3] Prediction of the G4 formation in mitochondrial environment is important for understanding the role of G4 in mitochondrial functions. In this study, the level of G4 formation was measured in the large and small cosolutes such as polyethylene glycol (PEG) 8000, PEG 200, and 1,3-propanediol. Mitochondria-like crowding environment was simulated using various concentrations of the cosolutes based on the intra-mitochondria viscosity data.[2] Spectroscopic methods and fluorescence-based assays were employed to quantify the G4 formation *in vitro*. In accordance with the stability of duplexes predicted by our nearest-neighbor parameters,[4] the G-rich duplex was effectively destabilized, inducing higher level of G4 formation in mitochondrion-like conditions compared to the nucleus-like conditions. The effect of G4 formation on cellular mitochondrial gene expression was also investigated using peptide-based mitochondria-targeting plasmid carrier, where the formation of G4 stalls transcription of the GFP gene in the plasmid. Compared to the nucleus, GFP expression was repressed in the mitochondria, indicating relatively preferential formation of G4 in the mitochondria. To investigate the role of mitochondrial G4 formation in diseases, the level of GFP expression was also compared between cancerous and non-cancerous cells. The findings of this study provide useful insights for the prediction of the behaviour of nucleic acids in mitochondria.

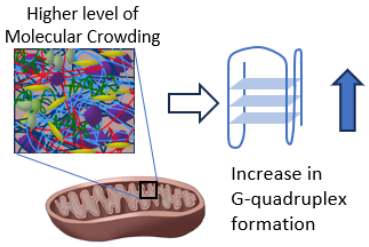

Figure 1. Enhancement of G-quadruplex formation in mitochondria

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