

The critical roles of G-quadruplexes in neuronal developmental stages through chromatin conformational changes.

Norifumi Shioda, Yasushi Yabuki, Sefan Asamitsu

Dept. Genomic Neurology., IMEG., Kumamoto Univ.

Guanine-rich DNA and RNA can form a four-stranded structure, termed G-quadruplexes (G4) in cells. The formation of G4 is implicated in many physiological events, such as gene transcription, translation, and epigenetics. However, the presence of G4 has not been revealed in the brain. Here, we demonstrate the localization of G4 in the mouse brain by immunohistochemical analysis. In cultured mouse forebrain neurons, numerous punctate G4 immunoreactivities (G4-IR) were observed in nuclei as well as in cytoplasmic areas, including axons, dendrites, and postsynapses. Interestingly, the G4-IR in nuclei show more co-localizations with the bright spots of DAPI-positive heterochromatin clusters in cultured mature compared to immature neurons. In slices from adult mouse brain, the G4-IR were distributed throughout the brain but were particularly prominent in the hippocampus, olfactory bulb, and cerebellum. In the hippocampus, G4-IR were strongly expressed in neurons and weak in astrocytes. Consistent with the results in cultured neurons, the nuclear G4-IR were co-localized with heterochromatin in calbindin-positive mature granule cells but less in doublecortin-positive neuronal progenitor cells in the dentate gyrus. Electron microscopic immunolabeling revealed G4-IR on nucleolus-associated chromosomal domains (NADs) and cytoplasm in the adult mouse hippocampal CA1 region. These observations demonstrate the critical roles of G4 in neuronal developmental stages through chromatin conformational changes and in the cytoplasmic metabolism of RNA.