New insights on non-canonical DNA structures: G-Quadruplex folding of RPGR exon ORF15 might impair photoreceptor vesicular trafficking and ciliogenesis

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Abstract

During last years it has becoming evident that non-Watson–Crick base pairing, resulting in the assembly of alternative DNA secondary structures, also occurs in the genome. Such noncanonical structures, called non-B form DNA, include the G-quadruplexes, stacked nucleic acid structures that form within G-rich DNA or RNA sequences. Dysregulation of DNA-G4 is associated with human disorders, including neurological dysfunction and accelerated ageing, even if its role in neurophysiology/neuropathology has not yet been fully elucidated. We present results coming from our recent experiments on X-linked retinitis pigmentosa (OMIM 26800), a group of hereditary disorders that can lead to blindness because of photoreceptor degenerations. The most frequently mutated X-linked retinitis pigmentosa genes is RPGR (RP3), and codes for a protein with a series of six RCC1-like domains (RLDs), involved in ciliogenesis, microtubule organization and regulation of transport in primary cilia. RPGR presents a splicing variant, called exon ORF15, which constitutes a mutational hot spot in a huge number of patients. The most challenge peculiarity of exon ORF15 is its repetitive nature, particularly of guanine (G)-rich sequences, that makes it very difficult to screen. Thus, we investigated the possible molecular causes that determine such difficulties by a multiple in-silico approach, evaluating the possibility that, due to its nature, exon ORF15 could show a G-quadruplex structure. All exploited algorithms confirmed the possibility that several G-quadruplex could be folded in RPGR exon ORF15, providing new insights towards a better sequencing approach to RPGR screening and Xlinked retinitis pigmentosa diagnosis.

Biography:-

Luigi Donato, PhD in “Applied Biology and Experimental Medicine”, frequents the Labs of Molecular Genetics of University of Messina, Italy. He is a researcher of the IEMEST institute in Palermo, Italy, too. He published more than 50 papers in reputed journals and participated in more than 30 national and international congresses, also being in the Organizing Committee in several of them. He was a member of ARVO and he is a member of AIBG. He joined the Editorial Board of several journals, such as “Cell Cycle”, “BMC Bioinformatics”, also acting as Guest Editor for “Antioxidants” and “Frontiers in Genetics”. His main research fields are retinal dystrophies and omics approaches.

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