DNA TRIPLEX STRUCTURES IN HUMAN DISEASE

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Abstract :

It is now established that a small fraction of genomic DNA does adapt non-canonical B-DNA structure or “unusual” DNA structure. The Unusual DNA structures are represented as hotspots of chromosomal breaks, homologous recombination and gross chromosomal rearrangements since they are prone to the structural alterations. These structures, for example, DNA-hairpin, cruciform, Z-DNA, H-DNA (Triplex), tetraplex etc show different biophysical and biochemical properties. At least 30 human hereditary disorders are known to arise as a result of expansions of simple DNA repeats. Most of these disorders are caused by the triplet repeat expansion (TRE) like (CGG)*n*•(CCG)*n*, (CAG)*n*•(CTG)*n*, (GAA)*n*•(TTC)*n* and (GCN)*n*•(NGC)*n*.

Friedreich's ataxia, first autosomal recessive degenerative disorder of nervous and muscles tissue caused by the massive expansion of GAA repeats. GAA repeats occurs in the first intron of Frataxin gene X25 on chromosome 9q13-q21.1 and affects both male and female children which manifests itself before puberty and successively there is loss of voluntary muscle coordination. The GAA repeats form a H-DNA by folding back of the purine strand in a parallel fashion leading to parallel Pyrimidine * Purine •Pyrimidine (pY*R•Y) type of "DNA Triple Helix". The (R●R★Y) triplex further reduces the frataxin gene expression. Till date FRDA is the only disease known so far associated with DNA triplex. Biophysical studies on the DNA triplexes (containing GAA repeats) using UV melting, UV absorption, Fluorescence, Circular dichroic spectroscopy and EMSA will be presented. Genetic confirmation, circulating plasma DNA and MALDI -TOF proteomic data of FRDA patients (with $(\mathbf{GAA})_{900}$) repeats will be also discussed.