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Functional Significance of DNA in Animal Science

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Abstract

G-quadruplexes (G4s) are non-canonical structures that can be formed in DNA and RNA sequences which carry four short runs of guanines. They are distributed in the whole genome but are enriched in gene promoter regions, gene UTRs and chromosome telomeres. The entire spectrum of their functional functions is not yet completely explored, but there is clear evidence supporting their involvement in a variety of processes, including transcription control, replication, telomere organization, among others. There has been an increased interest in research for G4s over the last decade that has led to a deeper understanding of their function in many physiological and pathways. On the other hand, in plant species and animals of agricultural interest, these mechanisms are poorly studied. Here, we summarize the existing methods used to study G4s, analyze plant and farm animal studies, and address the benefits of a more rigorous inclusion of G4 research in the agricultural sciences.

Introduction

DNA occurs in non-canonical conformations such as triple-stranded DNA, cruciform DNA, supercoiled DNA, Z-DNA and G-quadruplexes except for the classical double helix structure. G-quadruplexes or G4s are four-stranded conformations that can be formed in the presence of monovalent cations on short stretches of G-tracts. The G4s' building blocks are planar G-tetramers that are stabilized and stacked one above the other by Hoogsten hydrogen bonds. Between each pair of tetramers, one monovalent cation is located and stabilizes the 3D-structure. Loops form the DNA sequences that bind the four G-tracts. This early study formed the basis for the current concept that within nucleic acids G4s can be formed. Later, in the 1980s, it was shown that G4 structures can be produced by telomeres, the regions at the ends of each chromosome that have repeated G-tracts. The folding of a single DNA strand, which gives rise to intramolecular or unimolecular G4s, may result in G4s. One sequence of consensus of this form of G4s is G3-5N1-7G3-5N1-7G3-5N1-7G3-5N1-7G3-55 (stricter or more flexible models have also been suggested). For the formation of intermolecular G4s, however, two or four strands may be combined, which are

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called bimolecular or tetramolecular respectively. G4s can be graded as parallel according to their strand orientation when both strands have the same orientation, antiparallel when two strands have the opposite orientation relative to the other two, and mixed when there is just one strand with the opposite orientation. They can be further characterized by the number and size of loops and by the appearance of bulges. The above features will affect the characteristics and the stability of the RNA molecules of the G4s. G4 structures are also present. RNA G4s are thermodynamically more stable than their DNA counterparts and only adopt parallel conformations. When sequences with the GGAGG motif are folded into a quadruplex structure with only two planar G-tetts, a special bimolecular topology for RNA G4s is adopted.

Conclusions

In the last decade, the scientific interest in G4s has grown significantly. As part of the scientific community's involvement with G4s, this has contributed to a better understanding of their role in many fundamental biological processes and their connection with several diseases, including cancer. Among the high number of G4-related scientific publications published each year, only a small proportion are published on plants and farm animals, removing any advantage that the newly known functions of G4s might benefit from research on these species. There are, indeed, only a handful of plants with genome-wide G4 motifs that have been identified. Efforts have been made to connect the G4s with certain biological processes for these animals, but they are still far from providing solid evidence. On the other hand, it is only the chicken genome that has been defined in terms of the distribution of G4 motifs among all farm animals. Efforts to characterize more farm animals in the genome will push the field to the level of the existing field of plant science. In order to reach from this stage to find practical positions for G4s that could support both animal and crop farming, there are many techniques that could then be pursued. First, metadata studies, for all characterized organisms, may

lead to more precise predictions of the G4s-associated pathways and processes. Secondly, based on experimental evidence to link G4s with functions and pathways of agricultural interest, the implementation of omics procedures using strategies and materials that have already been successfully implemented in human and mouse studies may be a further step. Finally, with the exception of solid proof, functional and mechanistic studies will also provide the necessary information.

The more systematic study of G4s could obtain great advantages from agricultural sciences. First of all, it will shed light on several genes' regulation of expression. Given the involvement of G4s in the recruitment of transcription factors, the facilitation/impairment and control of translation of RNA polymerase and their research could help to understand the mechanistic basis for the expression of several genes of a gene. Another important benefit that farm animals and plants could gain from the more intensive study of their G4s is that they could be used as human disease model organisms for which G4s are documented to play an important role. This will give the study of several agricultural species an extra boost by gaining additional funds.