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z naslovom:

Genomic G-quadruplexes as Drug Targets

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Abstract:

While most of the DNA in the human genome exists in the classical double-helical form first proposed by Watson and Crick, specific sequences can, and do, adopt unusual alternate structures. Among these are G-quadruplexes, which are four-stranded structures that feature stacked G-quartets, a novel planar arrangement of four hydrogen bonded guanine bases. This lecture will briefly review the discovery and history of G-quadruplex structures, and exciting recent discoveries that suggest the existence of such structures *in vivo*. The possible functional roles of G-quadruplexes in telomere biology and in the control of gene expression will be considered. Most drugs act by interfering with the function of specific protein targets, but there is a pressing need to cultivate non-protein drug targets as the number for "druggable" protein targets seems to be shrinking. Why G-quadruplexes are attractive drug targets will be considered. Finally, I will describe an integrated drug discovery platform developed in our laboratory for finding small molecules that bind selectively to G-quadruplexes. This platform uses virtual screening to discover compounds that bind to selected receptor sites within quadruplex structures, followed by experimental validation of these hits by high-throughput biophysical testing. Some promising initial results will be shown.

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