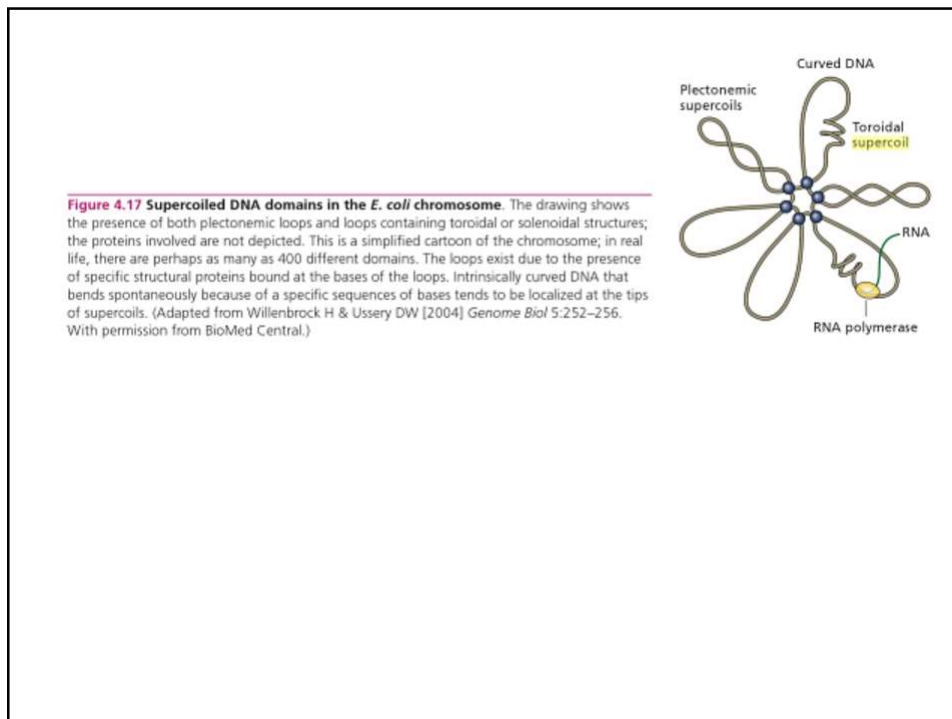
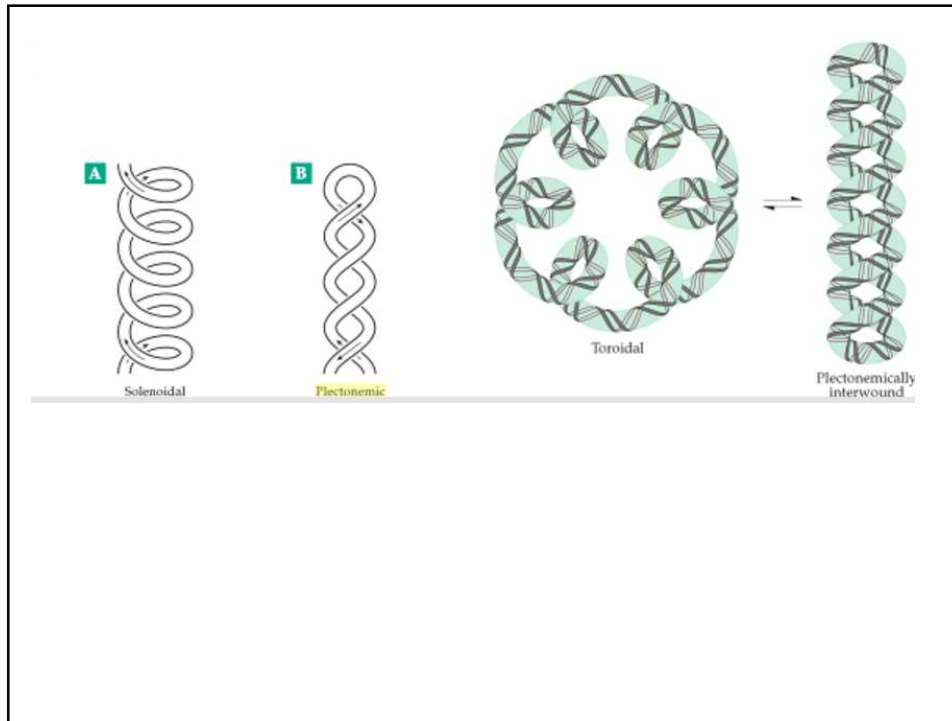
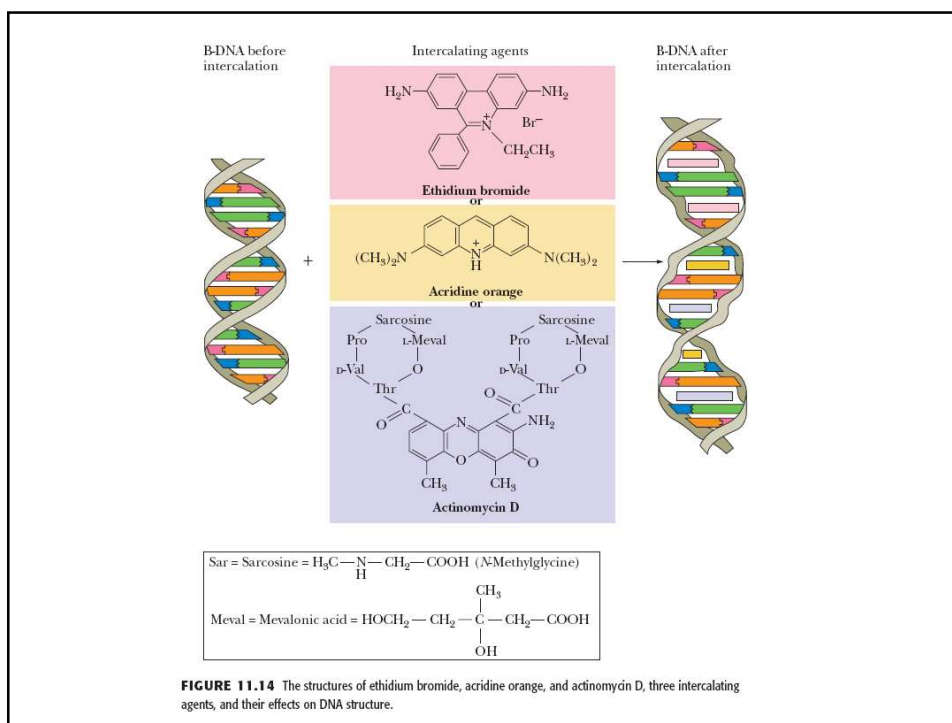
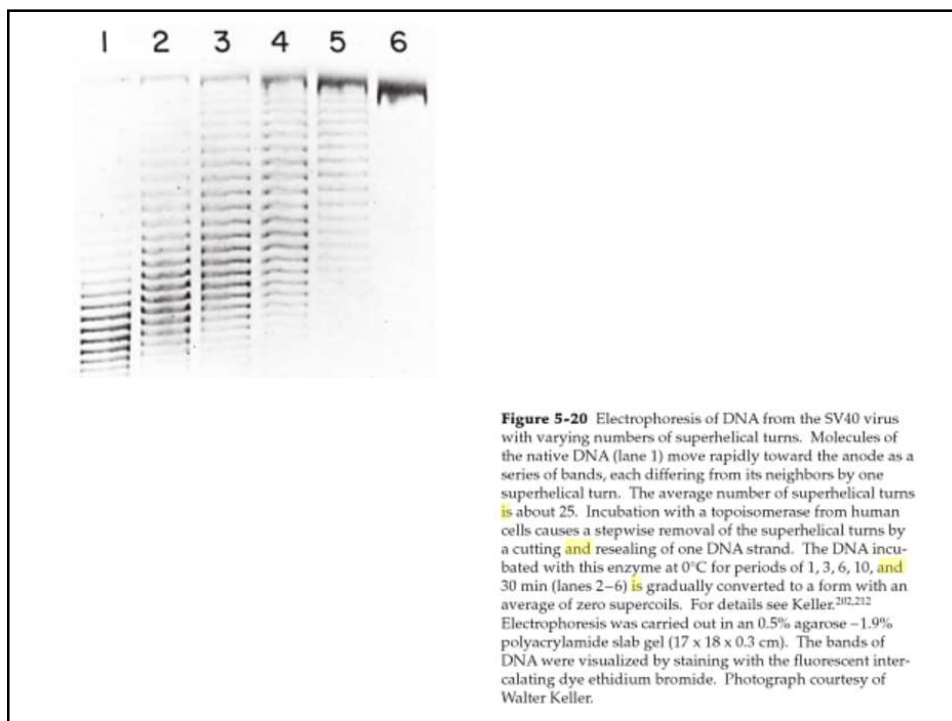
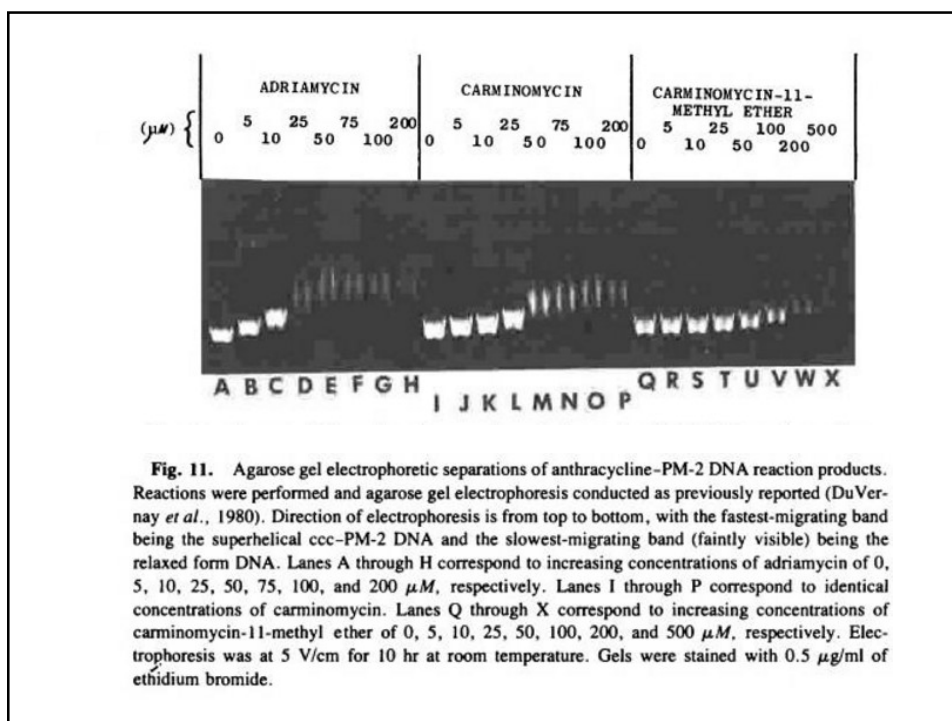
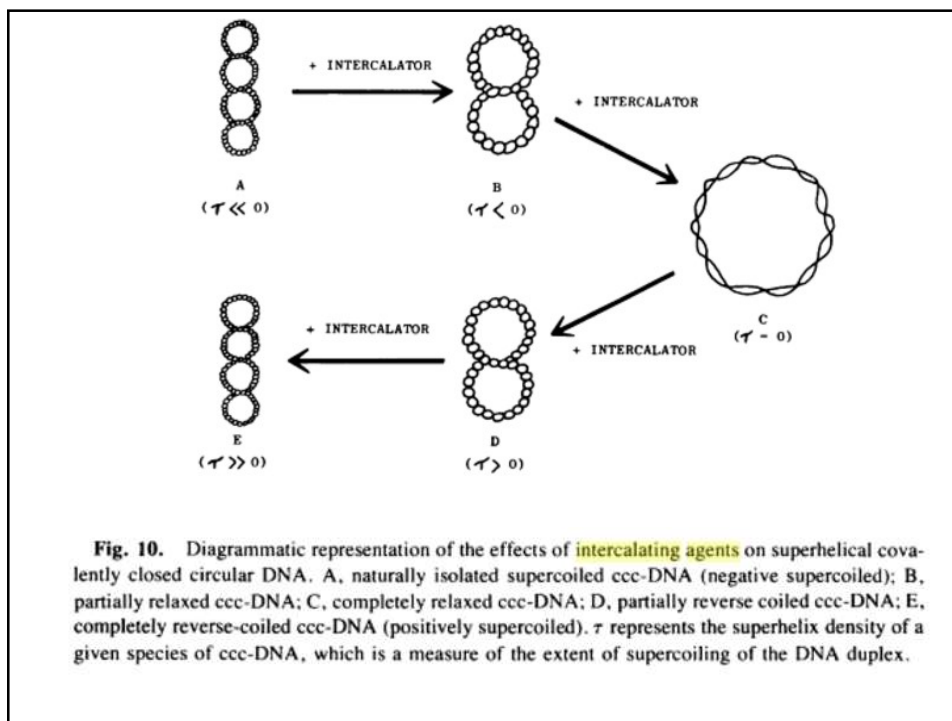


FIGURE 11.26 A 400-bp circular DNA molecule in different topological states: (a) relaxed, (b) negative supercoils distributed over the entire length, and (c) negative supercoils creating a localized single-stranded region.







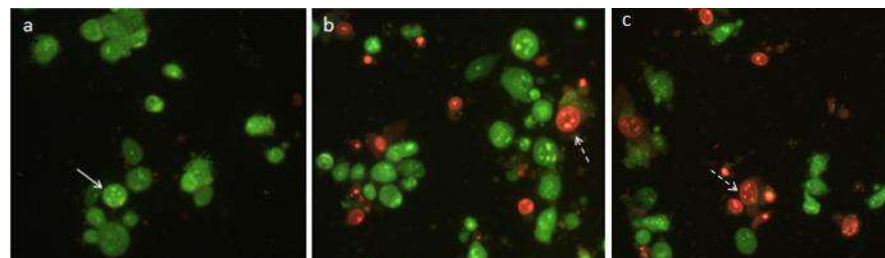
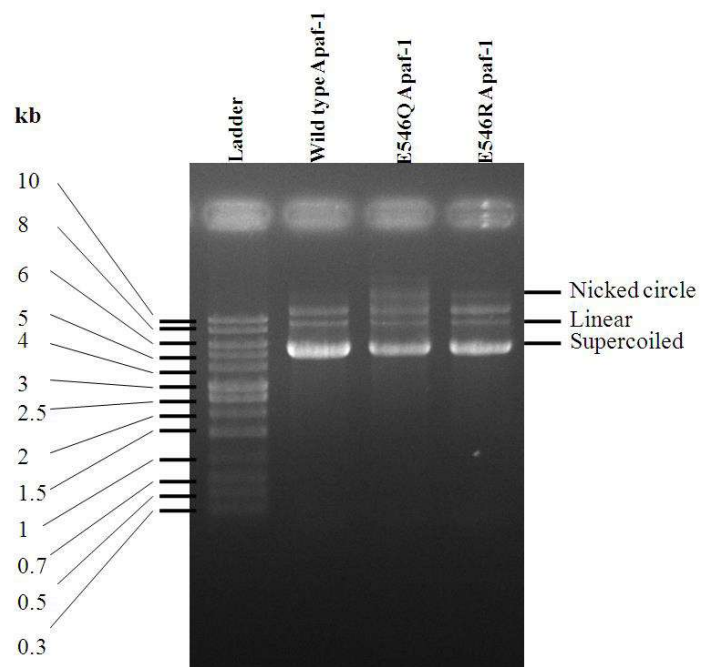
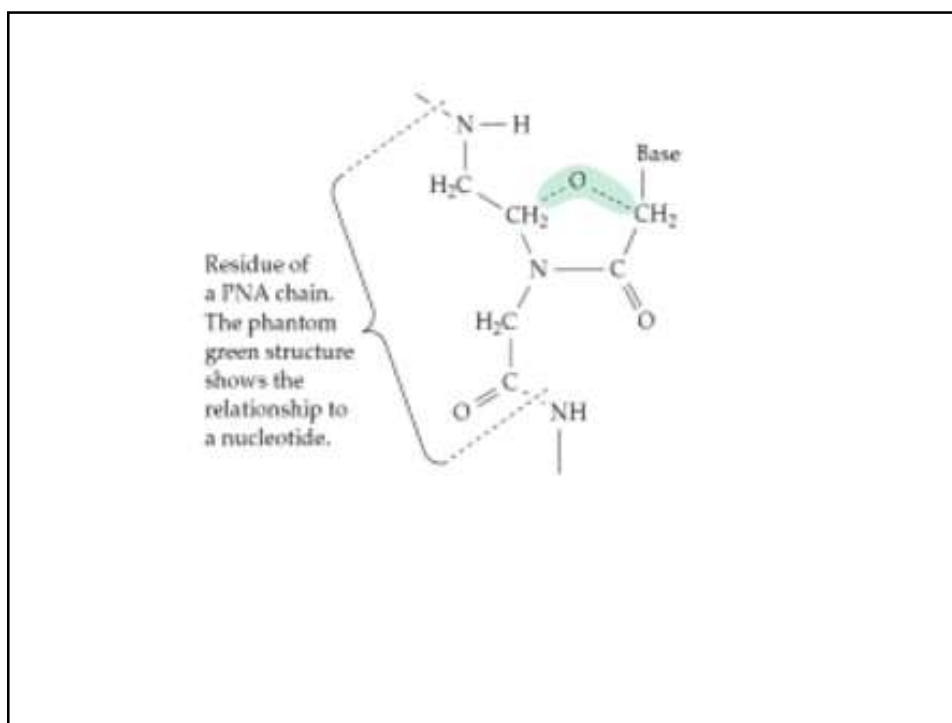
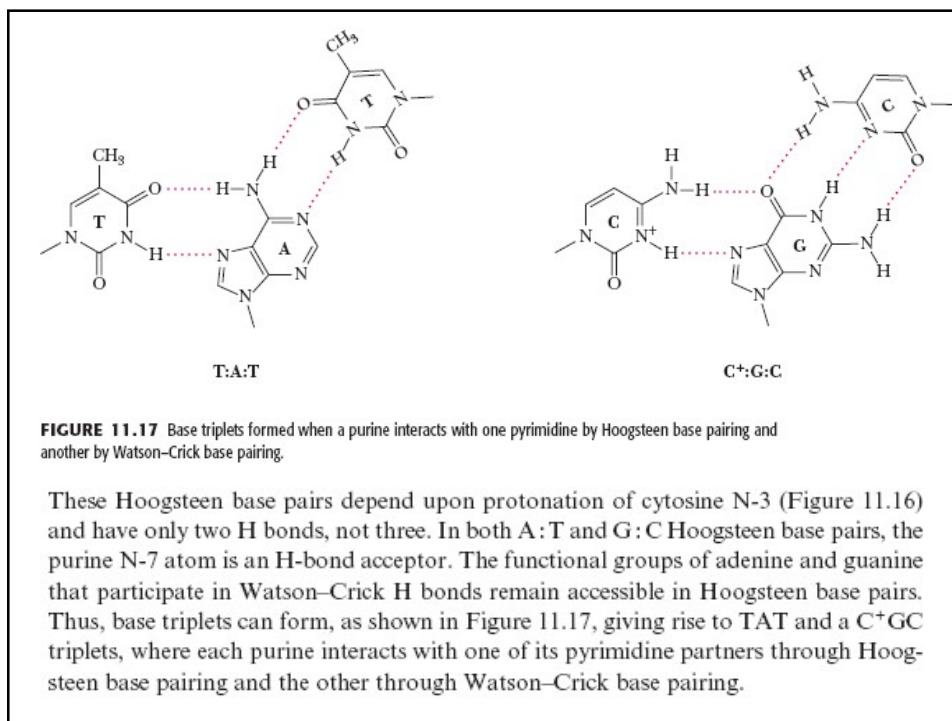
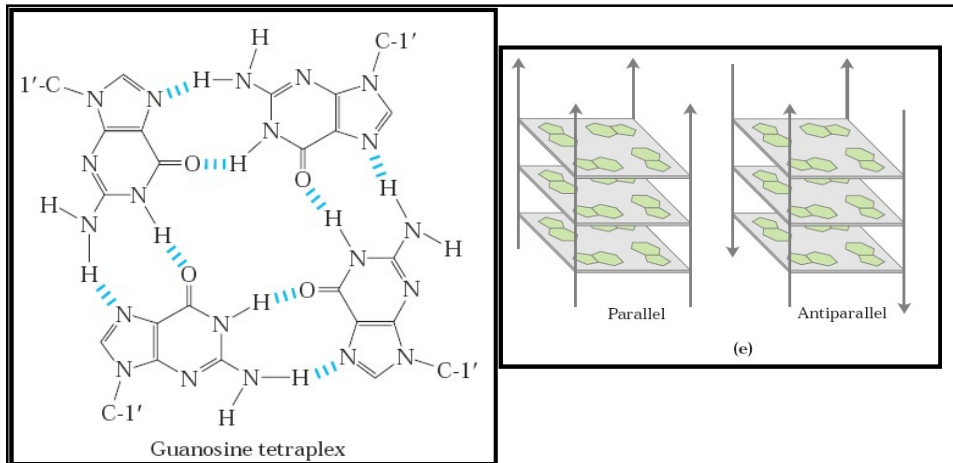


Figure 5. Acridine orange/ethidium bromide fluorescent staining of MDA-MB-231 cells for determine apoptosis: (a) DMSO 1% as control; (b) cells treated with IC_{50} concentration of compound **4a** (c) cells treated with IC_{50} concentration of etoposide as positive control for 24 hr. White arrow indicates live cells and dashed arrow indicates apoptotic cells. The images of cells were taken with a fluorescence microscope at 400 \times

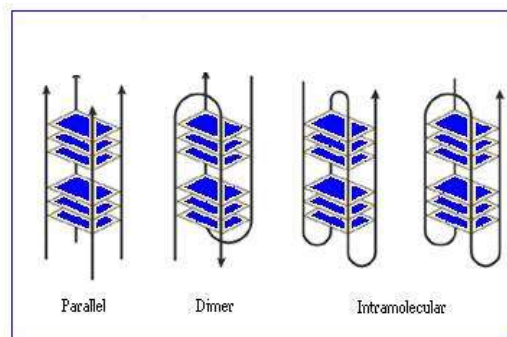
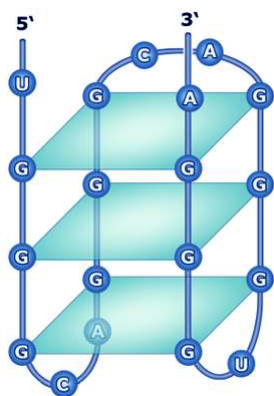






Four DNA strands can also pair to form a tetraplex (quadruplex), but this occurs readily only for DNA sequences with a very high proportion of guanosine residues.

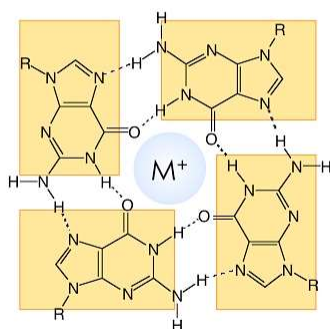
Quadruplexes can be formed from one, two or four separate strands of DNA (or RNA) and can display a wide variety of topologies.



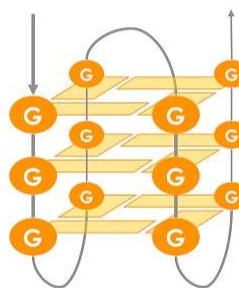
G-quartets are stabilized by a monovalent cation (Na^+ or K^+) localized in the center of the structure

Telomeric DNA

5' -...TTA**GGGTTAGGGTTAGGGTTAGGG**...-3'



G-quartet



G-quadruplex (G4)

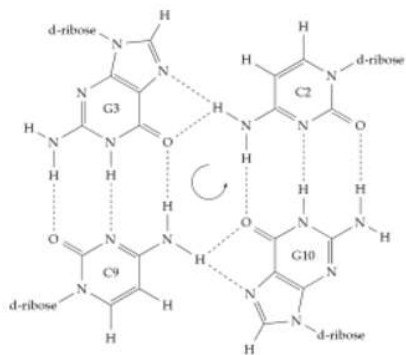
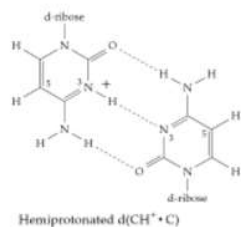
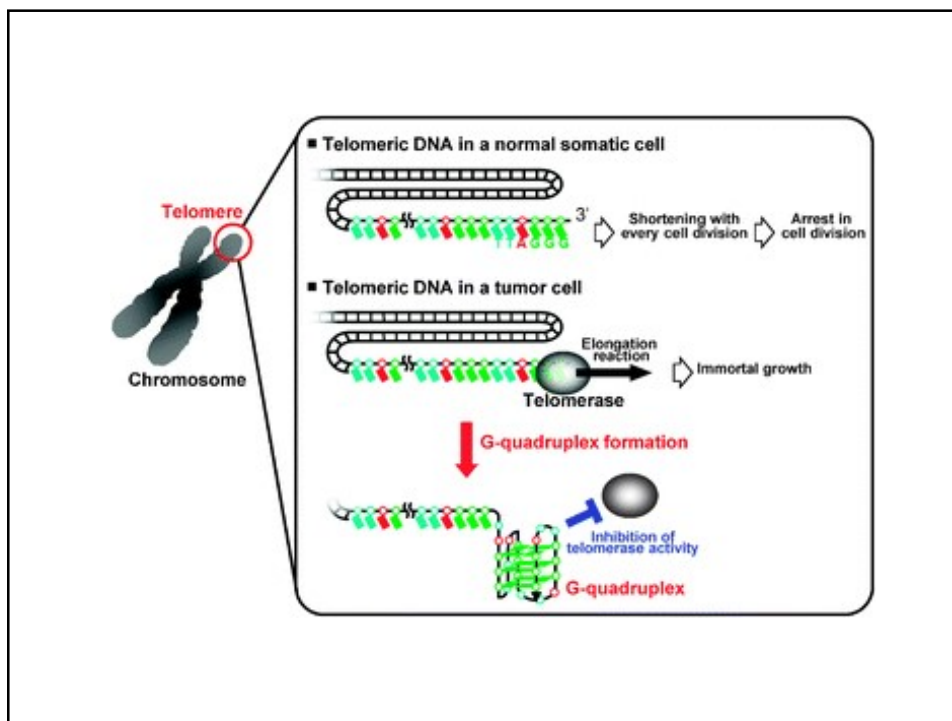


Figure 5-26 Structure of a $\text{G}\cdot\text{C}^+\cdot\text{G}\cdot\text{C}^+$ tetrad present in a quadruplex structure formed by the oligonucleotide d(GCCCTTTGGCG) in Na^+ -containing solution. See Kettani *et al.*²⁷⁶



Bioinformatics and molecular sequence analysis indicates that G-quadruplexes are over-represented in specific regions of the genome with key biological contexts. This includes DNA telomere ends and promoter regions (translation start sites) of several important oncogenes [21,33,38,39]. It has been shown that the formation of quadruplexes inhibits the telomere extension by the telomerase enzyme, which is up-regulated in cancer cells, as well as negatively regulating oncogene's transcription [40,41]. Because of its biological significance and antitumor potential, the G-quadruplex has attracted intense interest as an important target for drug design and development and there is a huge interest in design and development of small molecules to target these structures. A large number of so-called G-quadruplex ligands, displaying varying degrees of affinity and more importantly selectivity, have been reported [42,43].

Table 4. Sequences in cancer-related genes that have been identified as forming quadruplex structures

Gene	Sequence	Ref
<i>c-myc</i>	<i>Pu27</i>	88
	T T A T G G G A G G G T G G G A G G G T G G G A A G G	
	<i>Myc-2345</i>	88
	T G A G G G T G G G A G G G T G G G A A	
	<i>Myc-1245</i>	
	T G G G A G G G T T T T A G G G T G G G A	
	<i>Myc-22</i>	89
	T G A G G G T G G G T A G G G T G G G T A A	
	<i>Pu241</i>	90
	T G A G G G T G G I G A G G G T G G G A A G G	
<i>c-kit</i>	<i>kit1</i>	91
	C A G A G G G A G G C G C T G G G A G G A G G G C T G	
	<i>kit2</i>	92
	C C C G G G C G G G C G C G A G G G A G G G A G G C	
<i>VEGF</i>		96
	C C C G G G C G G G C C G G G G C G G G G T C C C G G C G G G C G G A G	
<i>HIF-1α</i>		95
	G C G A G G G C G G G G A G A G G G A G G G C G C G	
<i>hcf-2</i>		93
	G T C G G G C G A G G G C G G G G A A G G A G G G C G C G G G C G G G A	
<i>k-ras</i>		97
	G G G A G G G A G G G A A G G A G G G A G G G A G G G A	
<i>Rb</i>		98
	C G G G G G T T T T G G G C G G C	

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SURVEY AND SUMMARY

Quadruplex DNA: sequence, topology and structure

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ABSTRACT

G-quadruplexes are higher-order DNA and RNA structures formed from G-rich sequences that are

that short G-rich sequences at the ends of telomeric DNA in eukaryotic chromosomes can associate together in physiological ionic conditions to form discrete four-stranded structures (variously termed quadruplexes, tetraplexes or G4