



	Experiment title: London Cancer Group BAG - Quadruplexes	Experiment number: LS-1950
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Report:

Linear eukaryotic chromosomes have specialised ends called telomeres. Due to the basic asymmetry of the semi-conservative DNA replication, the ends of chromosomes cannot be replicated by the cells normal replication machinery. These 3' guanine rich telomere sequences can form unusual four-stranded structures called G-quartets from one, two or four stands.

These structures have shown to inhibit telomerase and thus G-quadruplex based inhibitors of telomerase may have a potential in anti-cancer therapy. Structural insights have been useful in studying the interactions of the quadruplex. Thus we hope to further our studies by studying the DNA-drug interactions that would give an insight of how these drugs interact with these targets.

We have solved the quadruplex structure formed by the oxytricha telomeric sequence d(G₄T₄G₄) in the trigonal space group at a 1.6Å. The three-dimensional structure forms hairpins, which joins to make a four-stranded helical DNA structure, with thymine containing loops at either ends. The guanine residues form the quartets. The quartets are characterised by cyclic Hoogsteen hydrogen bonding of four guanines in a coplanar arrangement. A metal cation is located in between the quartets. 4 quartets are observed in the structure.

