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Spermine-stabilized gold nanoparticles for SERS study of G-quadruplexes

Surface-enhanced Raman scattering (SERS) spectroscopy is a highly sensitive analytical technique in which Raman signals are strongly enhanced through the interaction of analyte molecules with roughened metal surfaces.[1] Colloidal metal nanoparticles are widely used as SERS substrates, where their surface chemistry, morphology, and aggregation behavior significantly influence the resulting spectra.[2]

G-quadruplexes (G4s) are non-canonical nucleic acid structures formed by guanine-rich DNA or RNA sequences.[3] Their structural polymorphism depends on sequence composition, strand orientation, loop arrangement, and the presence of stabilizing cations. G4-forming sequences are abundant in the human genome, particularly in telomeric regions and gene promoters. The formation of G4s within telomeric DNA inhibits telomerase - an enzyme highly active in most cancer cells - thereby preventing telomere elongation and suppressing tumor cell proliferation.[4] Human telomeric DNA, composed of tandem d(TTAGGG) repeats, can adopt several intramolecular G4 conformations, making it a suitable model for investigating nucleic acid structural polymorphism.

In this study, positively charged gold nanoparticles were evaluated as SERS substrates for the structural characterization of the human telomeric sequence Tel24, d[(TTAGGG)₄], in both its unfolded and G-quadruplex forms. Spherical gold nanoparticles stabilized with spermine, a positively charged polyamine commonly used to functionalize metal surfaces for interaction with negatively charged nucleic acids, were synthesized and characterized.[5] Additionally, star-shaped gold nanoparticles were prepared using HEPES buffer and subsequently functionalized with spermine.[6] The resulting positively charged colloidal substrates were assessed for their ability to generate characteristic SERS signals across different Tel24 conformational states.

The results demonstrate that nanoparticle morphology significantly impacts SERS signal generation and the spectroscopic characterization of oligonucleotides, even when employing identical surface modifiers. Both spermine-functionalized spherical and star-shaped nanoparticles enabled the detection of characteristic Tel24 vibrational features, highlighting the potential of positively charged colloidal gold substrates for differentiating between unfolded and G-quadruplex forms of human telomeric DNA.

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