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Selectivity of Spermine Homologs on Triplex DNA Stabilization

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We synthesized seven homologs of spermine ($H_2N(CH_2)_3NH(CH_2)nNH(CH_2)_3NH_2$, where n=2-9; n=4 for spermine) and studied their effects on melting temperature (T_{m1}), conformation, and precipitation of poly(dA).2poly(dT). The triplex DNA melting temprerature, T_{m1} was 34.4℃ in the presence of 150mM KCl. Addition of spermine homologs increased T_{m1} in a concentration-dependent and structure-dependent manner, with 3-6-3 (n=6) exerting optimal stabilization. The dT_{m1}/dlog[polyamine] values were 9-24 for these compounds. The duplex melting temperature, T_{m2} was insensitive to homolog concentration and structure, suggesting their ability to stabilize triplex DNA without altering the stability of the underlying duplex. Circular dichroism spectral studies revealed ψ-DNA formation in concentration-dependent and structure-dependent manner. Phase diagrams were constructed showing the critical ionic/polyamine concentrations stabilizing different structures. These compounds also exerted structural specificity effects on precipitating triplex DNA. These data provide new insights into the ionic/structural determinants affecting triplex DNA stability and indicate that 3-6-3 is an excellent ligand to stabilize poly(dA).2poly(dT) triplex DNA under physiologic ionic conditions for antigene therapeutics.