Supplemental Fig. S5. Local TOP2A Cleavage Site Base Preferences.

Hexanucleotides comprising positions -1 to +5 of cleavage sites relative to sense strand showing ≥2-fold enrichment relative to the frequency of the same hexanucleotides in the genome (top 10 of 445 total hexanucleotides for DMSO, and top 10 of 51 total hexanucleotides for VP16 are shown). DMSO represents native TOP2A hexanucleotide preferences. Hexanucleotides with ≥2-fold enrichment relative to the same hexanucleotides in the genome in TOP2 poison-treated but not DMSO-treated samples identify preferred hexanucleotides for TOP2A poisons. Underlined sequences denote palindromes. The data show C(-1) or G(+5) at 4 of the top 10 native TOP2A cleavage sites; C/T(-1) and/or G/A(+5) in all top 10 and 46/51 total (not shown) VP16-enriched hexanucleotides, as well as in 5/6 mitoxantrone-enriched hexanucleotides; and T(-1) or A(+5) at both genistein-enriched hexanucleotides, indicating consistency with known sequence preferences (Palumbo et al. 1994; Capranico and Binaschi 1998). The pBQ preference was C/G at -1 and +5. With DMSO also note CTAG preference at bases +1 to +4 suggesting dyad symmetry of overhangs, and two hexanucleotide palindromes. The fewer preferred genistein hexanucleotides may reflect cleavage complex instability (Bandele and Osheroff 2007). In agreement with prior studies (Capranico et al. 1993), the -1 and +5 bases of individual preferred hexanucleotides usually were not complementary to each other regardless of the treatment. Amplified samples; same treatments merged where applicable (Supplemental Table S1).