The polyuridylic-polyadenylic sequence requirement for the formation of sticky DNA were evaluated in *Escherichia coli* plasmid systems to determine the potential occurrence of this conformation throughout biological systems. A mirror repeat, dinitucleotide tract of (GA(TC))$_{37}$, which is ubiquitous in eukaryotes, formed sticky DNA, but shorter sequences of 10 or 20 repeats were inert. (GGA(TCC))$_n$ inserts (where $n = 126, 159$, and $222$ bp) also formed sticky DNA. As shown previously, the control sequence (GA(TTC))$_{139}$ (450 bp) readily adopted the X-shaped sticky structure; however, this structure has never been found for the nonpathogenic (GAGGA(TC(TCTT))$_{65}$ of the same approximate length (390 bp). A sequence that is replete with polyuridylic-polyadenylic tracts that can form triplexes and slipped structures but lacks long repeating motifs (the 2.5-kbp intron 21 sequence from the polycystic kidney disease gene 1) was also inert. Interestingly, tracts of (GAA(TTC))$_n$ (where $n = 176$, or 80) readily formed sticky DNA with (GAGGA(TC(TCTT))$_{65}$ cloned into the same plasmid when the pair of inserts was in the direct, but not in the indirect (inverted), orientation. The stabilities of the triple base (Watson-Crick and Hoogsteen) interactions in the DNA/DNA associated triplexes and sticky DNA were reviewed in the companion paper (1). Because this novel DNA structure has never been found for the nonpathogenic (GAGGA(TC(TCTT))$_{65}$ of the same approximate length (390 bp). A sequence that is replete with polyuridylic-polyadenylic tracts that can form triplexes and slipped structures but lacks long repeating motifs (the 2.5-kbp intron 21 sequence from the polycystic kidney disease gene 1) was also inert. Interestingly, tracts of (GAA(TTC))$_n$ (where $n = 176$, or 80) readily formed sticky DNA with (GAGGA(TC(TCTT))$_{65}$ cloned into the same plasmid when the pair of inserts was in the direct, but not in the indirect (inverted), orientation. The stabilities of the triple base (Watson-Crick and Hoogsteen) interactions in the DNA/DNA associated triplex region of the sticky conformation account for these observations. Our results have significant chemical and biological implications for the structure and function of this unusual DNA conformation in Friedreich's ataxia.

The salient clinical and molecular biological features of Friedreich's ataxia (FRDA) as well as the properties of DNA three-stranded structures (triplexes) and sticky DNA were reviewed in the companion paper (1). Because this novel DNA structure was discovered (2) in the long GAA-TTC mutation in intron 1 of the frataxin gene, which is responsible for most cases of FRDA (3–7), we wished to determine the sequence requirements for its stabilization. Sticky DNA is a polypuridylic-polypurinemide (R-Y) triplex; hence, the features must include a mirror repeat sequence. However, the role of the distribution of purines and pyrimidines on the complementary strands has not been explored. Also, because a (GAA(TCT(TCTT))$_{65}$ tracts is present in the same intron, the significance of the DNA sequence on triplex and sticky DNA formation may have further relevance. At present, the function of this unusual repeating hexanucleotide tract is unclear, especially because it does not track through family pedigrees with the disease or inhibit transcription (2, 8–10).

The effect of GGA(TCC)-interrupted triplets in long GAA-TTC repeat tracts was investigated (10) to determine some of the sequence requirements for sticky DNA and to evaluate further the veracity of its long GAA-GATCTCC CAT triplex structure. Studies were conducted on a family of seven periodically substituted inserts (all ~130 repeats in length) which contain 0, 4, 7, 8, 11, 20, or 50% substitution of GATAATC with GATCTCC triplets. A relatively small amount of substitution (less than 11%) caused no inhibitory effects. However, higher levels of GATAATC interruptions reduced the formation of sticky DNA, alleviated transcription inhibition, and reduced genetic instabilities. We wished to further our studies with long DNA tracts with uniformly repeating polyuridylic-polyadenylic sequence motifs such as GATC, GGA(TCC), and GAGGA(TC(TCTT)).

Herein, we have evaluated the capacity of related types of long repeating R-Y sequences to form the sticky DNA structure, including GATC, GGA(TCC), and GAGGA(TC(TCTT)). Also, the ability of the FRDA GAA-TTC repeat to interact with each of these three repeat sequences was determined. These results provide important confirmatory evidence on the R-Y conformation of sticky DNA and give insights into possible DNA loop interactions in FRDA chromosomes.

A companion article (1) demonstrates that sticky DNA is only formed intramolecularly between a pair of GAA-TTC tracts in one DNA molecule.

**EXPERIMENTAL PROCEDURES**

**Preparation of Dimeric and Monomeric Plasmids—**Plasmid preparations after isolation from *Escherichia coli* contain monomeric as well as dimeric (and higher oligomeric) isomers of DNA. The typical biological dimer studied herein is shown in Fig. 1. Plasmids containing a single GATC tract (which are pUC9 derivatives) and plasmids containing one GATCC tract (which are pHCI9 derivatives) used in these studies are shown in Table I and have been described previously (11, 12). pBS4.0, which is a Bluescript KS derivative harboring the 2.5-kb R-Y tract from intron 21 of the frd1 gene, has also been described previously (13, 14). Plasmids with two R-Y tracts, which are pH222 derivatives, are shown in Fig. 2. The constructions of these DNAs are described below.

Mixtures of supercoiled dimeric and higher oligomeric forms of the pUC9 and pHCI9 derivatives were isolated after overnight growth in E. coli SURE strain, as described (1).

**Cloning of a Pair of R-Y Tracts into pBR322—**Fragments containing the (GAA(TCT(TCTT))$_{65}$ tracts and the (GAGGA(TC(TCTT))$_{65}$ tracts were prepared from pWS808 (15, 16) and pMPl93 (2), respectively, by BssHIII and HaeIII digestion (New England Biolabs, Inc.) following by filling in the recessed BssHIII 3’ termini with 0.1 unit of the Klenow fragment of *E. coli* DNA polymerase I (U. S. Biochemical Corp.) and dCTP plus dGTP (0.1 m each) (17). The repeating tracts are flanked by 34 and 54 bp of the human FRDA gene (3). The digested DNA was electrophoresed in a 7% polyacrylamide gel, stained with EtBr, and the band containing the triplet repeat fragment was excised. The DNA was eluted from the...
Fig. 1. RB formation by dimeric forms of the plasmids harboring RY inserts. A, generic structure of biological dimers of plasmids containing RY inserts. The inserts employed are shown in Table I. B, 1% agarose gel analyses of RB formation after HindIII cleavage of dimeric forms of pUC19 derivatives harboring (GAATC)n. C, 1% agarose gel analyses of RB formation after EcoRI cleavage of dimeric forms of pSPL3 derivatives harboring (GAAGGA/TCTTC)65 (left lane) and (GAATTC)176 (right lane), used as a point of reference for 0 and 100% RB formation.

Table I.

Amount of RB formed from plasmid dimers as a function of the sequence and length of the repeating tract

| Plasmid | Vector | Insert repeating sequence | RB formation |
|---------|--------|---------------------------|--------------|
| pGA10   | pUC9   | (GAATC)15                 | 0            |
| pGA20   | pUC9   | (GAATC)20                 | 23           |
| pGA37   | pUC9   | (GAATC)37                 | 23           |
| pRW3191 | pUC19  | (GAATTC)16                | 0            |
| pRW3193 | pUC19  | (GAATTC)20                | 0            |
| pRW3194 | pUC19  | (GAATTC)25                | 25           |
| pRW3195 | pUC19  | (GAATTC)44                | 44           |
| pRW3892 | pUC19NoI | (GAATTC)74          | 49           |
| pRW3892 | pSPL3  | (GAATTC)176              | 100          |
| pMP193  | pSPL3  | (GAAGGA/TCTTC)63         | 0            |
| pBS4.0  | pBluescript KS− | (GAAGGA/TCTTC)1000 | 0            |

excised band, purified by phenol-chloroform extraction, and precipitated with ethanol (15). Linearized pBR322 was ligated with the (GAAGGA/TCTTC)176-containing insert. The ligation and all subsequent cloning steps were performed as described earlier (17). Clones that included trinucleotide repeat sequence tracts, cloned into pUC19 site, were subsequently digested by EcoRI/HindIII, followed by filling in the recessed 3’ termini. Subsequent blunt end ligation of these DNAs with the insert harboring the (GAAGGA/TCTTC)63 tract enabled the construction of a set of plasmids (pRW5000–pRW5005) harboring the (GAAGGA/TCTTC)63 tract in the EcoRI site of pBR322 in both orientations and the (GAATTC)176 tract in the pUC19 site; the two inserts were oriented as direct repeats or inverted repeats (Fig. 2). pRW5001 and pRW5003, harboring (GAATTC)63, were isolated as deletion mutants of pRW5000 and pRW5002, respectively. From the other side, subsequent blunt end ligation of the above mentioned DNA, harboring the (GAATTC)176 tract in orientation 1, with the insert, harboring the (GAATTC)176 tract, enabled the construction of a pair of plasmids (pRW5086–pRW5087), harboring a pair of the (GAATTC)176 tracts both in direct and inverted orientations (Fig. 2).

For the preparation of the plasmid harboring two contiguous inserts, where two directly oriented (GAAGGA/TCTTC)63 are separated by 88 bp of human flanking sequence, a number of clones from (GAAGGA/TCTTC)63 blunt end ligation into the pUC19 site of pBR322 (1) were studied.

All plasmids were fully characterized by restriction mapping (to determine the orientation and length of the cloned trinucleotide repeat sequence) and dideoxy sequencing of both strands with Thermo Sequenase Radiolabeled Terminator Cycle Sequencing kit (U. S. Biochemical Corp.).

Detection of Retarded Band (RB) Formation—The presence of sticky DNA in a DNA preparation is determined routinely by the detection of a substantially RB on agarose gel electrophoresis after plasmid linearization as described (1).

RESULTS

Sticky DNA Formation by R-Y Sequences—Prior investigations (2, 8, 10) demonstrated that long tracts of GAATTC repeats readily form a new type of complex triplex called sticky DNA. However, a closely related repeating hexanucleotide sequence, GAAGGA/TCTTC, does not form sticky DNA under identical conditions (2, 8–10). Furthermore, studies on a family
of mutated GAA-TTC repeat tracts in plasmids containing various amount of GGA-TCC interruptions (ranging from 4 to 50%) revealed that GAA-TTC repeats with less than 20% interruptions form triplexes and/or sticky DNA similar to the uninterrupted repeat sequence (10).

To investigate further the sequence requirements for the formation of sticky DNA, we constructed and characterized families of recombinant plasmids containing all purines on one strand and all pyrimidines on the complementary strands of the inserts. \( (GA/CT)_n \) (where \( n = 10, 20, \) and 37) as well as \( (GGA/TCC)_n \) (where \( n = 16, 30, 42, 53, \) and 74) were prepared. Investigations were also conducted on a plasmid containing a 2.5-kbp R-Y tract that is present in intron 21 of the polycystic kidney disease 1 (\( PKD1 \)) gene (14). This sequence contains 23 perfect mirror repeats that can form DNA triplexes with stems of at least 10 bp and are clustered into three distinct regions of the 2.5-kbp tract. More than a thousand perfect tandem repeats, which will form slipped structures (18), are present. The dinucleotides TC and CT are the most common; however, they are excluded from the 5'-end where the mirror repeats predominate. The trinucleotide repeats are mostly CCT and are localized within one end of the tract. Pentanucleotide repeats include CTCCC, CTCTC, and CCCAT. These pentanucleotide repeats are also clustered within the R-Y tract. In summary, this \( PKD1 \) sequence shows the presence of many mirror and direct repeats that are localized within the sequence. This tract contains the highest density of unorthodox simple sequence repeat features (mirror, direct repeats, and R-Y strand bias) of any known sequence of this length (14).

To analyze the sequence requirements of the R-Y region for sticky DNA formation in the dimeric form, we isolated dimers from plasmid preparations grown in \( E. coli \) SURE cells. The accompanying paper (1) demonstrates that only dimeric and higher oligomeric, but not monomeric, forms of the plasmids will form sticky DNA. Thus, it was concluded (1) that two long tracts of R-Y must be present in one plasmid to generate sticky DNA. The plasmid monomeric forms of uninterrupted as well as periodically interrupted long GAA-TTC repeats will not form sticky DNA (1). Also, we would have liked to investigate the behaviors of long homopolymeric tracts of A-T as well as G-C. However, these investigations are precluded by the extreme genetic instability of these simple sequences (19, 20).

Studies were conducted to evaluate the capacity of the sequences described above and listed in Table I to form sticky DNA. Fig. 1A shows the generic structure of a biological dimer, obviously containing two identical tracts of the repeating se-
To compare the yield of RB formed from plasmids containing one (GAAGGA-TCCCTTC)$_n$ tract and one (GAA-TTC)$_n$ tract, we studied purified monomers (see "Experimental Procedures"). Yields of RB (in percent) were compared with the amount observed from purified monomers of pRW4886 (Fig. 2), harboring two (GAA-TTC)$_{176}$ tracts, both in orientation I, under the same conditions. All DNAs were cleaved simultaneously with EcoRI and EcoNI. All plasmids had the superhelical density as isolated from E. coli (\(\Delta \rho = 0.05\)) (25–27). RB formation was monitored as described under "Experimental Procedures."

| Plasmid     | Orientation of (GAAGGA-TCCCTTC)$_n$ | Orientation of (GAA-TTC)$_n$ | n | RB formation |
|-------------|-------------------------------------|-------------------------------|---|--------------|
| pRW4886     | NA                                  | NA                            | 176 | 100         |
| pRW4887     | NA                                  | NA                            | 176 | 0           |
| pRW5000     | I                                   | I                             | 176 | 89          |
| pRW5001     | I                                   | I                             | 80  | 53          |
| pRW5002     | I                                   | II                            | 176 | 0           |
| pRW5003     | I                                   | II                            | 80  | 0           |
| pRW5004     | II                                  | II                            | 176 | 88          |
| pRW5005     | II                                  | I                             | 176 | 0           |

* NA, not applicable.

Further gel electrophoretic analyses revealed that the RB found with GA-TC as well as with GGA-TCC inserts were, in fact, sticky DNA, by evaluating the lengths of the arms in the X-shaped structures formed after cleavage at different unique restriction sites. For the pUC19 derivatives, the DNAs were linearized with EcoRI or NdeI and for pUC9 derivatives, the plasmids were cleaved with EcoRI or HindIII. In all cases, the correlation described earlier (2) between the extent of retardation of the RB and the distance between the restriction enzyme cleavage site and the R-Y tract was observed (data not shown).

**Sticky DNA Formation by Two Nonhomologous Sequences in One Plasmid**—Further investigations on the role of DNA sequence on the capacity of two tracts of different types of R-Y sequence to form sticky DNA were conducted. Plasmids containing one tract of (GAAGGA-TCCCTTC)$_{80}$ and another block of (GAA-TTC)$_{176}$ were prepared and characterized (Fig. 2). Similar plasmids were also prepared in which the (GAA-TTC)$_{176}$ was replaced with (GAA-TTC)$_{80}$. Plasmids were characterized which contained the inserts in the direct repeat orientations as well as in the inverted repeat orientations (Fig. 2). Prior investigations (1) revealed that only plasmids containing inserts in the direct repeat orientation could form sticky DNA, and our current work confirms this conclusion (Table II).

Table II reveals that pRW4886, which contains two tracts of 176 repeats of GA-A-TTC in the direct repeat orientation (Fig. 2), readily forms sticky DNA (as described under "Experimental Procedures"). However, pRW4887, containing the same in-
The base oppositions are from the repeating triplet sequence. Thus, five of six (83%) of pairing in an antiparallel manner with the GAAGAA sequence is aligning and Hoogsteen. Accordingly, it is apparent that the GGAGAA tract from the of repeats are inverted in pRW5004 compared with pRW5000. Two plasmids are in the direct repeat orientation, but the pair

Inserts in the inverted orientation (pRW4887, 5002, 5003, and 5005) were devoid (2). Sticky DNA was stabilized by negative supercoiling as well as divalent metal ions. The long GAA-TTC repeats form R-Y triplexes at neutral pH (23). The companion article (1) demonstrates the necessity of two tracts of GAA-TTC in one molecule for the intramolecular formation of sticky DNA. Interestingly, a tract of (GAAGGA/TCTTC)$_{60}$ is also present in intron 1 of the frataxin gene (8). Thus, the stabilizing forces for sticky DNA generated by the fold-back of two GAA-TTC sequences that are proximal are sufficiently great to enable the formation of sticky DNA. Sharp bending of the 88-bp intervening sequence must have been caused by the stabilization and pairing of the GAA-TTC tracts. Because this 88 bp is shorter than the known persistence length of DNA, which is 450 Å or 130 bp (21, 22), we conclude that the interactive forces created by the pair of GAA-TTC tracts must be substantial.

DISCUSSION

Sticky DNA was described (2, 9, 10) as an X-shaped DNA molecule found in plasmids containing long tracts of GAA-TTC after linearization of the plasmid molecule. The lengths of GAA-TTC required for its formation correspond to the tracts found in intron 1 of the frataxin gene of FRDA patients (2). Sticky DNA was stabilized by negative supercoiling as well as divalent metal ions. The long GAA-TTC repeats form R-Y triplexes at neutral pH (23). The companion article (1) demonstrates the necessity of two tracts of GAA-TTC in one molecule for the intramolecular formation of sticky DNA. Interestingly, a tract of (GAAGGA/TCTTC)$_{60}$ is also present in intron 1 of the frataxin gene (8) but does not inhibit transcription (9, 12) nor track with the disease in family pedigrees; alternatively, sticky DNA effectively inhibits transcription (9).

We have evaluated some of the sequence requirements for the mirror repeat R-Y insert tracts to form sticky DNA. The following R-Y tracts were investigated: GA/TC, GAA-TTC, GGA-TCC, GAGGGA-TCTTC, and the 2.5-kbp R-Y tract from intron 21 of the polycystic kidney disease gene (24). However, expanded repeats of GGA-TCC have not been discovered to date in conjunction with a hereditary neurological disease (18). In plasmids containing a pair of tracts of the identical repeat sequences, we found that sufficiently long tracts of GA/TC, GGA-TCC, and GAA-TTC adopted the sticky conformation. Alternatively, neither the GGAAGA-TCTTC repeating hexanucleotide sequence nor the 2.5-kbp R-Y tract from the PKD1 gene adopted this unusual conformation. Because

![Diagram](image-url)
the two purine strands in the R-R-Y complex must be antiparallel (23), these results are readily explained from the known types of Hoogsteen bp schemes shown in Fig. 4; T-A-A and C-G-G are quite stable and favored structures, whereas T-A-G, C-G-A, and C-G-A+ are less favored. Accordingly, Fig. 5I demonstrates the facile triplex formation for GA/TC as well as GAA/TTC and Fig. 5II shows the stable bp interactions for GGA/TCC repeats.

Alternatively, Fig. 5III shows that for GAAGGA-TCCCTTC interacting with the identical sequence in an intramolecular reaction, only four of six (66%) of the triple base oppositions are stable, even in the optimal frame. This figure shows the potential pairing schemes in all six frames. Thus, this degree of stability is insufficient for the formation of sticky DNA (10) and provides a rational basis for the negative results shown in Table I for this sequence.

Studies were also conducted with plasmids containing GAAGGA-TCCCTTC and GAA-TC in the same plasmid in direct repeat orientations. These plasmids showed the formation of sticky DNA. Fig. 5IV shows that in the proper frames (a and d), five of six of the pairs are in stable Hoogsteen structures (Fig. 4A). This extent of pairing is sufficient to enable the formation of a stable triplex (10). Also, as expected, when two tracts of GAA-TC are present in the same plasmid (pRW4886) (Fig. 2), a stable sticky DNA structure was observed. In summary, the composite results demonstrate that the formation of sticky DNA requires the formation of at least 83% of acceptable Hoogsteen and Watson-Crick base oppositions. Accordingly, these data provide strong confirmatory evidence for the purine-purine antiparallel triplex structures proposed in Figs. 4 and 5.

Furthermore, our current results are in excellent agreement with prior studies (1), which showed that sticky DNA was an R-R-Y triplex with the purine strands in the antiparallel orientation. This investigation (1) with a family of inserts in recombinant plasmid dimers with varying extents of interruptions between the extremes of pure GAA-TC repeats (0% of GGA/TCC in the GAA/TT repeat sets) and the repeating hexanucleotide sequence GAAGGA-TCCCTTC (50% of GGA/TCC in the GAA/TT repeat sets) revealed that more than 20% interruption by GGA/TCC in the GAA/TT repeat sequence abolished the formation of sticky DNA. In summary, all of these results considered together provide important confirmatory evidence for sticky DNA as an R-R-Y triplex with the base pairing schemes shown in Fig. 4A with the two purine strands in the antiparallel arrangement.

The salient features of FRDA as well as its human and molecular genetic properties were reviewed in the Introduction to the companion paper (1). In patients, the expanded GAA/TT repeat (66–1,700 or more) may form sticky DNA and thereby inhibit transcription; prior investigations (9, 16) showed the efficiency of sticky DNA in transcription inhibition, which could explain the reduction of X25 mRNA in patients, which would result in a diminution of the amount of the frataxin protein, thus causing the disease pathology. The first intron of the frataxin gene also contains a (GAAGGA-TCCCTTC)65 tract, which is nonpathogenic (8). Unlike the GAA-TC repeat, this hexamer repeat does not form an antiparallel triplex and/or sticky DNA, does not inhibit transcription, and does not associate with the FRDA disease state (8–10). Because our investigations demonstrated the facility of formation of sticky DNA between long tracts of GAA-TC and this neighboring hexanucleotide repeat, it is possible that these two sequences interact to form a potent block for transcription in FRDA patients.

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REFERENCES
1. Vetcher, A. A., Napierala, M., Iyer, R., Chastain, P. D., Griffith, J. D., and Wells, R. D. (2002) J. Biol. Chem. 277, 39217–39227.
2. Sakamoto, N., Chastain, P. D., Parniewski, P., Ohshima, K., Pandolfo, M., Griffith, J. D., and Wells, R. D. (1999) Mol. Cell 3, 465–475.
3. Campuzano, V., Montermini, L., Moto, M. D., Pianese, L., Cossee, M., Cavalcanti, F., Monros, E., Rudiis, F., Dudol, F., Monticelli, A., Zara, F., Canizares, J., Koutnikova, H., Bidichandani, S. I., Geller, C., Brice, A., Tresuillas, P., De Michele, G., Fill, A., De Frutos, R., Palasu, F., Patel, P. I., De Donato, S., Mandel, J. L., Cucuzza, S., Koenig, M., and Pandolfo, M. (1996) Science 271, 1423–1427.
4. Durr, A., Cossee, M., Agid, Y., Campuzano, V., Mignard, C., Penet, C., Mandel, J. L., Brice, A., and Koenig, M. (1996) N. Engl. J. Med. 335, 1169–1175.
5. Montermini, L., Andermann, E., Labuda, M., Richter, A., Pandolfo, M., Cavalcanti, F., Pianese, L., Indice, L., Farina, G., Monticelli, A., Turano, M., Fill, A., De Michele, G., and Cucuzza, S. (1997) Hum. Mol. Genet. 6, 1261–1266.
6. Montermini, L., Kish, S. J., Jiralerspong, S., Lamarche, J. B., and Pandolfo, M. (1997) Neurology 49, 606–610.
7. Montermini, L., Richter, A., Morgan, K., Justice, C. M., Julien, D., Castellotti, B., Mercier, J., Pouier, J., Capozzi, F., Bouchard, J. P., Lemieux, B., Mathieu, J., Vanasse, M., Steni, M. H., Graham, G., Andermann, E., Andermann, F., Melancon, S. B., Keats, B. J., Di Donato, S., and Pandolfo, M. (1997) Ann. Neurol. 41, 675–682.
8. Ohshima, K., Sakamoto, N., Labuda, M., Pouier, J., Moseley, M. L., Montermini, L., Ranum, L. P., Wells, R. D., and Pandolfo, M. (1998) Neur-ology 53, 1854–1857.
9. Sakamoto, N., Ohshima, K., Montermini, L., Pandolfo, M., and Wells, R. D. (2001) J. Biol. Chem. 276, 27171–27177.
10. Sakamoto, N., Larson, J. E., Iyer, R. R., Montermini, L., Pandolfo, M., and Wells, R. D. (2001) J. Biol. Chem. 276, 27178–27187.
11. Collier, D. A., and Wells, R. D. (1990) J. Biol. Chem. 265, 10652–10658.
12. Ohshima, K., Kang, S., Larson, J. E., and Wells, R. D. (1996) J. Biol. Chem. 271, 16773–16783.
13. Van Raay, T. J., Burn, T. C., Connors, T. D., Petri, L. R., Germino, G. G., Klinger, K. W., and Landes, G. M. (1996) Microb. Comp. Genomics 1, 317–327.
14. Bacolla, A., Jaworski, A., Connors, T. D., and Wells, R. D. (2001) J. Biol. Chem. 276, 18597–18604.
15. Sambrook, J., and Russell, D. (2001) Molecular Cloning: A Laboratory Manual, 3rd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY.
16. Ohshima, K., Montermini, L., Wells, R. D., and Pandolfo, M. (1998) J. Biol. Chem. 273, 14588–14595.
17. Napierala, M., Parniewski, P., Pluciennik, A., and Wells, R. D. (2002) J. Biol. Chem. 277, 34087–34100.
18. Wells, R. D., and Warren, S. T. (eds) (1998) Genetic Instabilities and Hereditary Neurological Diseases, Academic Press, San Diego.
19. Klein, R. D., and Wells, R. D. (1982) J. Biol. Chem. 257, 12954–12961.
20. Klein, R. D., and Wells, R. D. (1982) J. Biol. Chem. 257, 12962–12969.
21. Gray, H. B., Jr., and Heare, J. E. (1968) J. Mol. Biol. 35, 111–129.
22. Hearst, J. E., and Steckmayer, W. H. (1962) J. Chem. Phys. 37, 1425–1433.
23. Le Dean, T., Perroault, L., Praseuth, D., Habhoub, N., Decout, J. L., Thuong, N. T., Lhomme, J., and Helene, C. (1987) Nucl. Acids Res. 15, 7749–7760.
24. Toth, G., Gaspari, Z., and Jurka, J. (2000) Genome Res. 10, 967–981.
25. Lilley, D. (1986) Nature 320, 14–15.
26. Bliska, J. B., and Cozzarelli, N. R. (1987) J. Mol. Biol. 194, 205–218.
27. Zacharias, W., Jaworski, A., Larson, J. E., and Wells, R. D. (1988) Proc. Natl. Acad. Sci. U. S. A. 85, 7069–7073.