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COMMUNICATIONS

Published on Web 08/22/2002

Long-Range Charge Transport in Duplex DNA: Anthraquinone Sensitization Results Are Independent of Terminal Ionic Distribution

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Received May 16, 2002

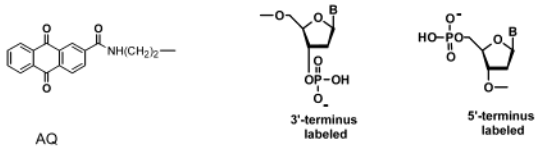
Soon after the famous double helical structure of DNA was proposed and understood, the suggestion was made that its regularly ordered array of aromatic bases might provide a path for the conduction of electrical charge.[1] This possibility has fostered an intensive investigation of the chemistry and physics of a variety of DNA structures under a broad range of environmental conditions.[2−7] Most thoroughly examined is the capacity of radical cations ("holes") to migrate through relatively short (15−50 base pairs) duplex DNA oligonucleotides in solution.[2,4,6−8] This investigation has led to the generally accepted view that holes do migrate in DNA, but specific aspects of the mechanism are still uncertain. In particular, the suggestion that DNA oligonucleotides in solution behave like "molecular wires"[9−12] has been replaced by the view that charge transport proceeds primarily by a series of thermally activated hops.[4,13−18] DNA is a polyanion, and it has been shown that hole delocalization and migration are affected by the motions of its sodium counterions and solvating water molecules, which modulate the ionization potential of the constituent bases.[19] Very recently, Barton and Williams proposed an additional effect of ion distribution on long-range hole transport in DNA.[20] By consideration of anomalous patterns of reaction at susceptible GG sites, they propose that oxidation potentials of remote guanines are influenced by the charge at the termini of DNA oligonucleotides. We repeated these experiments using the precise DNA sequence used by Barton and Williams, but we replaced the rhodium metallointercalator they used as the charge injector with a covalently linked anthraquinone derivative (AQ). In our experiments, the pattern of reaction at GG steps is consistent with the vast body of existing work, and there is no significant effect caused by variation of charge at the DNA termini. These findings show that the baffling results obtained with rhodium metallointercalators are caused by phenomena unrelated to the mechanism of long-range charge transport in DNA.

Irradiation of a sensitizer, an AQ or a rhodium metallointercalator, for example, that is linked to DNA causes the one-electron oxidation of an adjacent base to form its radical cation. The radical cation can migrate through the DNA, and it can be trapped by reaction with H_2O, which occurs primarily at the 5′-G of GG steps.[21,22] Proximal GG steps are located closer to the sensitizer, and distal GG steps are farther away. These experiments are usually carried out under "single-hit conditions", and the pattern of guanine reaction is presumed to reflect the effects of distance and base sequence on radical cation transport. In the vast majority of cases examined, the amount of reaction decreases as the distance to the guanine increases, which yields a proximal-to-distal ratio of reactivity that is greater than 1.

We prepared the AQ-containing oligonucleotide shown in Chart 1; its complementary strand, which contains two GG steps, was

Chart 1

5′-**AQ** -	A	C	G	A	G	C		C	G	T	T	T	T	T	G	C		C	G	T	A	T - 3′
DNA(1) 3′-	T	G	C	T	C	**G_p**		**G_p**	C	A	A	A	A	A	A	C		**G_d**	**G_d**	C	A	T	A - ^{32}P
DNA(2) ^{32}P-	T	G	C	T	C	**G_p**		**G_p**	C	A	A	A	A	A	A	C		**G_d**	**G_d**	C	A	T	A - 5′



labeled with ^{32}P at either its 3′ or its 5′ end. These structures were confirmed by Maxim/Gilbert sequencing and by mass spectroscopy.[23] In these experiments, reaction at guanine is usually detected by treating the irradiated samples with piperidine, which causes strand breaks at the damaged bases, followed by electrophoresis and autoradiography. Labeling of the oligonucleotide at its 3′ or 5′-terminus causes the structural differences that are also shown in Chart 1. In particular, the negative charge associated with the phosphate group moves from one end of the oligomer to the other with the label. Until the recent report of Williams and Barton,[20,24] it has not been expected or observed[25] that the position of the label would affect the pattern of guanine reaction.

Samples of the duplexes AQ-DNA/DNA(1) and AQ-DNA/DNA-(2) were irradiated at 350 nm, where only the AQ absorbs, under identical conditions (5 μM DNA, 10 mM sodium phosphate, pH = 7.0, ca. 30 °C) and then treated with piperidine at 90 °C for 30 min. The irradiated DNA samples were analyzed by electrophoresis on a denaturing polyacrylamide gel (PAGE), visualized by autoradiography, and quantified by phosphorimagery; the results are shown in Figure 1.

Inspection of Figure 1 shows that for both DNA(1) and DNA-(2) there is more reaction at the 5′-G of the proximal GG step than there is at the distal GG step. Quantification of the PAGE reveals that the proximal to distal reaction ratio is 10 ± 1 independent of whether the ^{32}P label is at the 3′- or 5′-terminus of the oligomer. This is in contrast to the findings of Williams and Barton who report a distal-to-proximal ratio of 0.4 ± 0.1 when the labeled phosphate is at the 3′-terminus and a value of 5.2 ± 0.4 when the sample is 5′-labeled.

It is not possible to be definite about why systems that contain rhodium metallointercalators or anthraquinone derivatives as one-electron oxidants (charge injectors) give different results. A related finding was reported for the comparison of rhodium metallointercalator[26,27] and AQ-sensitized[28] repair of thymine dimers, where it was suggested that low quantum efficiencies for reaction of the rhodium metallointercalator might play a role.[29] That seems less likely in the present case. However, it is clear that the interpretation of long-range charge transport experiments that employ linked

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10.1021/ja026932f CCC: $22.00

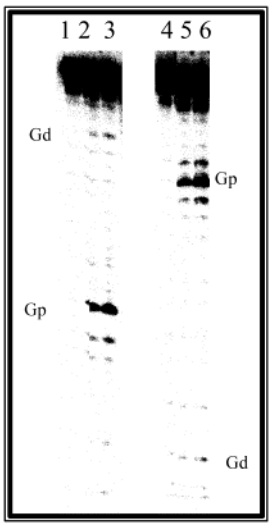

Figure 1. Autoradiogram showing strand cleavage of DNA(1) and DNA-(2) following irradiation (350 nm) of their duplexes with the AQ-containing strand, piperidine treatment, and PAGE. Each sample contained 5 μM duplex DNA that was labeled with ^{32}P (each lane contains 3000 cpm) at the 3′-terminus or the 5′-terminus of the non-AQ strand. Lanes 1−3 correspond to 0, 20, and 30 min of irradiation of DNA(2), and lanes 4−6 correspond to 0, 20, and 30 min of irradiation of DNA(1).

rhodium metallointercalators as the charge injector in DNA may be unique, and the results should be assessed by using other sensitizers.

Acknowledgment. This work was supported by a grant from the National Science Foundation, for which we are grateful. Dr. S. Kanvah assisted in the preparation and analysis of DNA samples.

Supporting Information Available: Experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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JA026932F