DNA STRAND BREAKAGE BY ^{125}I-DECAY IN OLIGODNA

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Abstract

A double-stranded oligodeoxynucleotide containing ^{125}I-dC in a defined location, with 5'- or 3'-^{32}P-end-labelling of either strand, was used to investigate DNA strand breakage resulting from ^{125}I decay. Samples of the ^{32}P-end-labelled and ^{125}I-dC containing oligoDNA were incubated in 20 mM phosphate buffer (PB), or PB + 2 M dimethylsulphoxide (DMSO) at 4°C during 18-20 days. The ^{32}P-end-labelled DNA fragments produced by ^{125}I decays were separated on denaturing polyacrylamide gels, and the ^{32}P activity in each fragment was determined by scintillation counting after elution from the gel. The fragment size distribution was then converted to a distribution of single stranded break probabilities at each nucleotide position. The results indicate that each ^{125}I decay event produces at least one break in the ^{125}I-dC containing strand, and causes breakage of the opposite strand in 75-80% of events. Thus, the double stranded break is produced by ^{125}I decay with probability ~0.8. Most of single stranded breaks (around 90%) occurred within 5-6 nucleotides of the ^{125}I-dC, however DNA breaks were detected up to 18-20 nucleotides from the decay site. The average numbers of single stranded breaks per decay are 3.7 (PB) and 3.3 (PB+DMSO) in ^{125}I-dC containing strand, and 1.5 (PB) and 1.3 (PB+DMSO) in the opposite strand. Deconvolution of strand break probabilities as a function of separation from the ^{125}I, in terms of both distance (to target deoxyribosyl carbon atoms, in B-DNA) and nucleotide number, show that the latter is an important parameter for the shorter-range damage. This could indicate a role for attenuation/dissipation of damage through the stacked bases. In summary, the results represent a much more extensive set of data than available from earlier experiments on DNA breakage from ^{125}I-decay, and may provide new mechanistic insights.