Complementary function of AP endonucleases and AP lyases during Base Excision Repair: an unsolved question

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Abasic (apurinic/apyrimidinic, AP) sites arise frequently in DNA by cleavage of the N-glycosylic bond between the nitrogenous base and deoxyribose. Such cleavage may occur by spontaneous hydrolysis or by the catalytic activity of DNA glycosylases on damaged or modified bases. AP sites may be processed either by AP endonucleases or AP lyases, but the relative roles of these two classes of enzymes are not well understood. An unresolved question is whether the sequence flanking the AP site and/or the orphan base on the opposite DNA strand influence the probability of processing either by an AP endonuclease or an AP lyase. AP sites opposite G are common intermediates during repair of deaminated cytosines, whereas AP sites opposite C arise during repair of oxidized guanines. We have analyzed the activity of plant and human AP endonucleases and AP lyases on DNA substrates containing an abasic site opposite either G or C in different sequence contexts. In all contexts the major *Arabidopsis* AP endonuclease (ARP) exhibited a significantly higher activity on AP sites opposite G. In contrast, the main plant AP lyase (FPG) showed a greater preference for AP sites opposite C. The major human AP endonuclease (APE1) preferred G as the orphan base, but only in some sequence contexts. No preference for the orphan base was observed in the AP lyase activity detected in human cells extracts. We propose that plant AP endonucleases and AP lyases play complementary repair functions on abasic sites arising at C:G pairs, neutralizing the potential mutagenic consequences of C deamination and G oxidation, respectively.