

Electronic states of Br-incorporated DNA related molecules : Mechanism of radio-sensitization of biological effects

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1 Introduction

Cells with DNA incorporating Br-dUMP as a thymidine monophosphate (dTMP) analog are known to be highly sensitive to ionizing radiation. To clarify physicochemical mechanism of the bromine-radiosensitization, the electronic state of the Br-DNA related molecules was investigated applying X-ray photoelectron spectroscopy (XPS). In terms of “radiation effect”, total yield of low-energy secondary electrons, generated by inelastic scattering of photo- or Auger electrons in the bulk of sample, were also quantified using the XPS apparatus.

2 Experiment

Brominated or non-brominated nucleobases (5-bromouracil and thymine), nucleosides (5-bromodeoxyuridine; BrdU and thymidine; dT), and nucleotides (Br-dUMP and dTMP) were chosen as sample molecules. Pellets or thin films of the sample molecules were prepared for XPS measurements performed at BL27A according to our previous paper [1]. In this study, we particularly focused to obtain XPS spectra of the valence electrons. The yields of inelastic scattering secondary electrons from the sample surface arising in a low energy region between 6 to 50 eV were also gained as integrated signal of the XPS spectra.

3 Results and Discussion

Peaks observed in the photoelectron spectra showed that binding energies of core level (K-shell) electrons for the C, N, O and P atoms did not significantly depend on bromination. Binding energies of valence electrons for the brominated molecules, on the other hand, were almost 0 eV from a vacuum level. These were 1.0 to 1.8 eV higher than those of non-brominated molecules as shown in Figure 1. The results suggest that the presence of Br may not significantly affect the electronic states of inner shell, but narrow an energy gap between HOMO and LUMO. This electronic property would facilitates charge transfer leading to DNA damage, particularly through reaction with low energy secondary electrons, such as thermally hydrated electrons. Interestingly, the energy gap of dTMP was significantly smaller than those of thymine or dT. The

phosphates might play a role of steppingstones that boost the charge transfer along “a molecular wire” of DNA.

In addition, low-energy electron yield measurements revealed that BrU and BrdU showed three times higher efficiency in generating these electrons by 2 or 3 keV X-ray exposure than those for correspondent non-brominated molecules. For both Br-dUMP and dTMP, on the other hand, the yields were significantly (4-10 times) larger than those for nucleobases or nucleosides, so that the enhancement of electron yields by bromination might be obscured by their overwhelming yields. The phosphate could also narrow energy gap and facilitate the electron emission. These results suggest that the low energy electrons are preferentially emitted around the Br atom as well as phosphate group. Certain fractions of low energy electrons would cause dissociative electron attachment resulting in free-radical formation to finally induce debromination or strand breaks.

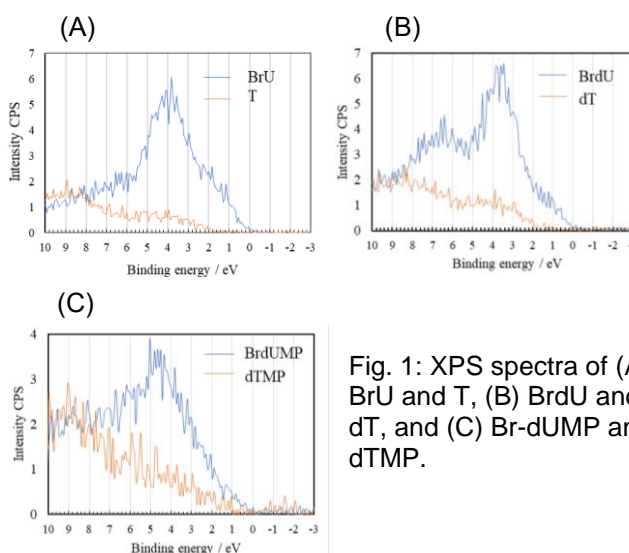


Fig. 1: XPS spectra of (A) BrU and T, (B) BrdU and dT, and (C) Br-dUMP and dTMP.

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References

[1] M. Hirato *et al.*, *Int. J. Radiat. Biol.* Published online (2020).

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