Cleavage enhancement of specific chemical bonds in DNA-Cisplatin complexes induced by X-rays

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Synopsis The chemical bond transformation of cisplatin-DNA complexes can be probed efficiently by XPS which provides a concomitant X-ray irradiation source as well. The presence to Pt could considerably increase formation of the SE induced by X-ray and that the further interaction of these LEE with DNA leads to the enhancement of bond cleavages.

The interaction between cisplatin and DNA constitutes the basis of its chemotherapeutic mechanism and plays the key role in chemoradiation therapy.[1] However, the molecular mechanism of increased DNA radiosensitivity from the binding of Pt-based antitumor drugs remains a controversial debate, since fundamental information on the detailed chemical bond transformation of DNA during high energy irradiation is not yet available.

We harness X-ray photoelectron spectroscopy (XPS) as an in-situ efficient characterization technique for monitoring chemical bond transformation in DNA and cisplatin-DNA complexes under synergic X-ray irradiation. By analyzing the variation of relative peak area of core elements of DNA as a function of irradiation time, the most vulnerable scission sites in DNA are found to be those containing phosphate and glycosidic bonds. (Fig.1) Compared to DNA, the effective rate constants of the corresponding phosphodiester and glycosidic bond cleavages for cisplatin-DNA complexes are 1.8 and 1.9 folds larger. These damages and their enhancements are similar to those induced by low energy electrons (LEE). Consistently, the magnitude of the secondary electron distribution produced by the X-rays on the cisplatin-DNA complexes is considerably increased compared to that of pristine DNA.

The data suggest that DNA radiosensization by cisplatin results not only from the sensitization of DNA to the action of LEE, but also from an increase the production of LEE at the site of binding of the cisplatin.[2] The results provide new insights into the mechanisms of cisplatin-induced sensitization of DNA under X-ray irradiation, which could be helpful in the design of new cisplatin-based antitumor drugs. Financial support for this work was provided by the NNSF of China (20973039).

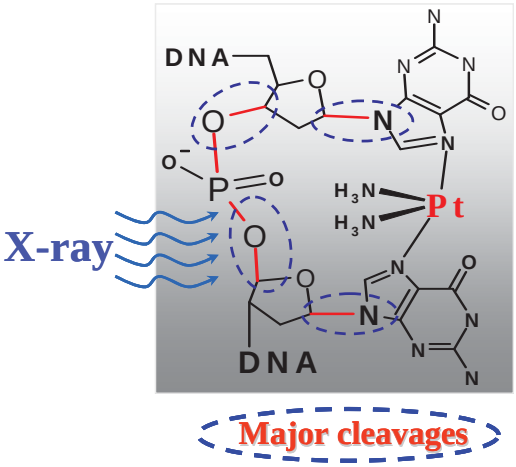

Figure 1. The schematic major cleavages of cisplatin-DNA complexes induced by X-rays.

References

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