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Fundamental understanding of DNA damage by low energy electron collision

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Low energy electron (LEE) interactions with biomolecules have been relevant for significant scientific and technological applications in the fields of plasma medicine, radiation damage and biofuel technologies. It is well known and widely accepted that LEEs (especially below 15 eV) can generate DNA damage such as base release, single- and double-strand breaks and structural alterations via energy resonance process named dissociative electron attachment (DEA) [1-2]. We have investigated biological effects induced by LEE collision and some adducts in order to increase LEE response sensitivity and selectivity. We have especially focused on the synergistic effect (or combined effect) of DNA damage caused by the combination of LEEs, metal ion and flavonoid actions. The recent studies with metal ion adducts have shown the possibility of damage control through synergistic and reductive effects on LEE-induced DNA damage [3].

We have experimentally studied the biological effect of LEE collision with model plasmid DNA, pBR322 (4,321 bp, double-stranded supercoiled). Figure 1 shows experimental setup for LEE electron collision on the solid phase DNA film [3]. It mainly consists of electron gun, faraday cup, sample holder and vacuum system. It is possible to independently irradiate lyophilized DNA films with monochromatic electrons. We have analysed DNA damage using 1% agarose gel electrophoresis (GE healthcare) after electron irradiation and DNA sample recovery. This technique allows the obvious separation of each DNA damage (linear-, circular- and supercoiled DNA) corresponding to double strand break, single strand break and non-break, respectively. After that, each type of DNA damage can be quantified and compared in each experimental condition.

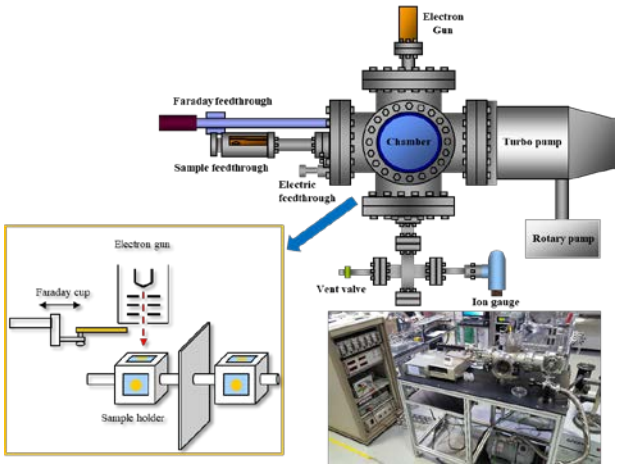

Figure 1. Experimental setup for electron collision with solid state biomolecules. It consists of electron gun, faraday cup, sample holder, and vacuum system.

We have observed that LEEs can indirectly generate DNA damage through DEA resonant process. When the transition metal ion attached on two adjacent guanines, the yields of DNA damage were dramatically increased than that of LEE single collision effect. This phenomenon might be related to Fenton-like reaction by metal ion. In an attempt to increase sensitivity of LEE collision effect on DNA damage, quercetin adduct also showed some meaningful increasing results. Most of data showed DNA damage by the combined effect were higher than that of each single effect. That is, low energy electron-induced DNA damage in the presence of Cu^{2+} ion and flavonoid quercetin is much sensitive to the incoming LEE due to higher temporary negative ion (TNI) formation sites and structural modification. Figure 2 shows the principal mechanism of LEE-induced DNA damage on the left side and the schematic diagram of other possible mechanisms on the right side. Interestingly, some results showed the opposite biological effect on DNA damage at some certain combinations between metal ion and quercetin.

In conclusion, we have investigated and compared biological effect on DNA damage by LEE collision, metal ion and flavonoid quercetin. The combined effect made much higher DNA damage than that from independent single effect. It may be originated from DEA, structural alteration, Fenton-like reaction and electron/energy transfer processes. Definitely, further investigations are required to clarify the exact and precise mechanisms on it.

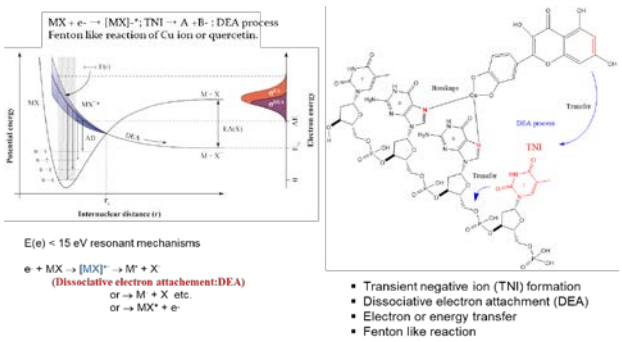

Figure 2. A schematic representation of DEA process and the possible mechanisms of LEE-induced DNA damage.

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References

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