Induction of DNA double strand break by environmental genotoxic and carcinogenic agents

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【Outline of survey】

DNA double strand break (DSB) presents serious DNA damage, which elicits cell lethal and genomic instability. Although ionizing radiation and ROS are known to generate DSB, recent technical evolution proved that it is also induced by exposure to ultra-violet and DNA inter-cross linkers, and moreover, to inhibitors of topoisomerase, whereas they do not directly bind to DNA but involved in DNA replication. Since carcinogenesis is promoted by ionizing radiation-induced DSB, it is pointed out that environmental genotoxic agents has potential DSB-mediated carcinogenicity. Therefore, to investigate the potential roles of DSB in environmental carcinogenic process, we planned here, 1) DSB generation by several environmental genotoxic agents in comaparison with ionizing radiation, 2) the underlying mechanisms, such as cell cycle checkpoints and DSB repair, against insults by their environmental agents.

【Expected results】

In modern life, peoples are suffered from exposure to environmental genotoxic agents or their daily uptakes; namely, topisomerase inhibitors and DNA inter-cross linkers observed in several constitutes in daily foods and Chinese medicines, DNA binding ability and genotoxicity in aromatic carbon with poly-benzene rings which have been reported in exhaust gas from diesel cars, and gneration of ROS by exposure to sun-light and asbestos, similarly to ionizing radiation. On the basis of generation of DSB, we evaluate their risks of individual genotoxic agents or their combined risks, and also study on initial step of carcinogenesis by environmental agents.

【References by the principal researcher】

- Antoccia A, Kobayashi J, et al.,Genome and Disease: Nijmegen breakage syndrome and functions of the responsible protein, NBS1、pp191-205, Basel, Karger, 2006 (review).
- Oba R, Komatsu K, Genome repair and carcinogenesis, Blood Oncology, 48:123-130,2004 (Japanese) (review).
- Nakamura A, Komatsu K, Phosphorylation of histone H2AX by DNA double strand break, Gene Medicine, 7:367-373, 2003 (Japansese) (review).
- Tauchi H, Kobayashi J, Morishima K, et al.,Nbs is essential for DNA repair by homologous recombination in higher vertebrate cells.Nature, 420:93-98, 2002

【Term of project】FY2006－2010

【Budget allocation】22,000,000 yen

【Homepage address】 http://www.rbc.kyoto-u.ac.jp/Genome/index.html