

## P051 Alteration of metal-mediated sequence-dependent DNA damage by catechol derivatization

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Catechols have been reported to exert the DNA damage with certain metal ions through the involvement of reactive oxygen species (ROS). The DNA damage induced by a certain metal is known to be sequence-dependent: e.g. copper ion preferentially oxidizes 5'-guanine (G) of consecutive Gs, which is explained by the HOMO theory. Here, we found that the damaging effect of catechols was abolished by ring acylation. The addition of copper ion and ROS-producible catechols drastically changed the CD spectrum of DNA and increased the G oxidation (8-oxodG), whereas no change was observed with acyl catechols. This CD change suggests the over-all structural change such as strand unwinding due to the unstable base pairing between cytosine and 8-oxodG. When copper ion was added into a DNA solution, cleavage by a certain restriction enzyme, BamHI (G|GATCC), not EcoRI (G|AATTC), was specifically inhibited. This indicates that copper ion binds to GG sequence of DNA. This sequence-dependent DNA damage can be attributed to the site-specific binding of copper ion chelated to catechols whose DNA-damaging effects are altered by the ring derivatization toward ROS-non-producible catechols.

### カテコールの誘導体化に伴う金属介在性塩基配列依存的DNA損傷の変動

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## P052 A possible involvement of bystander effects in the repression of spontaneous mutation induction

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It is important to elucidate the effects of ionizing radiation (IR) induced not in the cells directly hit by IR but in their neighboring cells, generally called as "bystander effect". When human lymphoblastoid cells (TK6) were incubated in the medium used for the cell irradiation (2 Gy of 135 MeV/u carbon-ion beam), the frequency of spontaneous thymidine kinase (TK) deficient mutations was lower than that observed with the normal un-irradiated medium. The reduction rate was only about 20% of the original level of total mutations, but such rate was considerably high as about 60% if restricted to those induced at relatively early period. The LOH (loss of heterozygosity) analysis for the isolated TK mutants demonstrated the repression of non LOH mutations, which were used to be induced earlier. The effects of irradiated medium are also under the examination whether the site-specific DSB in TK gene introduced by the expression of I-SceI restriction enzyme can be repaired more efficiently. Including this kind of approach, we are now elucidating the molecular mechanisms underlining the observed phenomenon, which might be classified as an adaptive bystander response,

### バイスタンダー効果が関与する可能性：放射線照射培地による自然突然変異誘発の抑制

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