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Oral presentation

Induction of 8-oxoguanine DNA Glycosylase 1 Gene Expression by HIV-1 Tat

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In order to identify the cellular gene target for Tat, we have performed gene expression profile analysis and found that Tat upregulates the expression of 8-oxoguanine DNA glycosylase (OGG1) gene, encoding an enzyme responsible for repairing the oxidatively damaged guanine, 7,8-dihydro-8-oxoguanine (8-oxo-dG). We observed that Tat induces OGG1 gene expression by enhancing its promoter activity without changing the mRNA stability. We found that the upstream AP-4 site within the OGG1 promoter is responsible and that Tat interacts with AP-4 and removes AP-4 from OGG1 promoter by *in vivo* chromatin immunoprecipitation assay. Thus, Tat appears to activate OGG1 expression by sequestrating AP-4. Interestingly, although Tat induces oxidative stress known to generate 8-oxo-dG that causes the G:C to T:A transversion, we observed that the amount of 8-oxo-dG was reduced by Tat. When OGG1 was knocked-down by small interfering RNA (siRNA), Tat increased the amount of 8-oxo-dG, thus confirming the role of OGG1 in preventing the formation of 8-oxo-dG. These findings collectively indicate a possibility that Tat may play a role in the maintenance of genetic integrity of the proviral and host cellular genomes by upregulating OGG1 as a feed-forward mechanism.