

# Elucidation of correlation between adult diseases and carcinogenesis by nucleic-acid adducts analysis

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In recent years, many epidemiological investigators reported the correlation between adult diseases and carcinogenesis, but there are few crucial chemically evidence of correlation.

DNA adducts are known as initiators of gene mutation and subsequent carcinogenesis. DNA adducts are formed by a number of exogenous and endogenous factors. On the other hand, reactive species such as reactive oxygen species (ROS) are produced in patients afflicted with lifestyle-related disease involving diabetes mellitus (DM). Lipid hydroperoxide (LPO) derived from unsaturated fatty acid such as arachidonic acids by ROS or cyclooxygenase-2 reacts with DNA bases (dG, dA, and dC). Subsequently, DNA adducts such as heptanone etheno (Hε)- and etheno (ε)- DNA adducts are formed in vivo. In this study, we determined the levels of several DNA adducts in tissues of diabetic mice as compared with normal mice with LC/MS/MS method. First, we synthesized standard and DNA adducts (Hε-dG, dA, dC, and ε-dA) and internal standard compounds labeled with stable isotopes, and set up the analytical LC/MS/MS conditions to detect these compounds with high sensitivity. Next we detected several DNA adducts in liver of type 2 DM mice (KK-A<sup>y</sup>) higher than those of normal mice (C57BL). This is the first study that DNA adducts derived from LPO increase in living organisms with DM.

In conclusion, we developed analytical methods for detecting DNA adducts derived from LPO in biological samples with LC/MS/MS. Additionally, we demonstrated that all DNA adduct levels are increased in diabetic conditions. Therefore, it is suggested that those DNA adducts might be markers that demonstrate the correlation between DM and carcinogenesis, and we need to investigate further.