A new method for detecting urinary biomarkers of DNA damage induced by acrylamide exposure via tobacco smoke and diet

A collaborative research study between professors at National Taiwan University and researchers across universities in Taiwan[i] provides the first quantitative analysis of a new risk-associated biomarker for acrylamide exposure from tobacco smoke and diet.

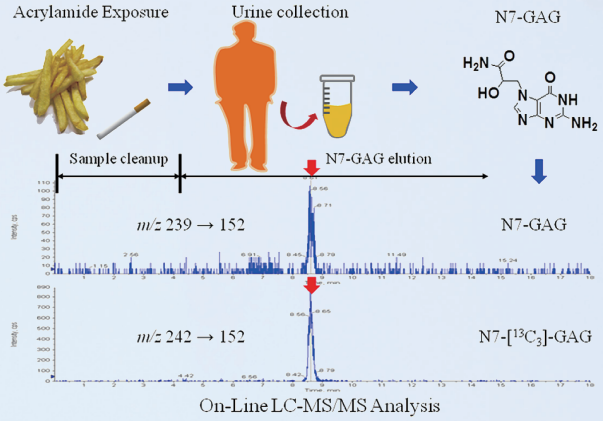
Background information

Acrylamide (AA) is an industrial chemical widely used in the production of polymers and copolymers for many applications. In addition to occupational exposure, the general public might also be exposed to AA from the consumption of foods processed at high temperatures and from cigarette smoking. Exposure to AA has been found to be associated with neurotoxicity and reproductive toxicity. On the basis of evidence established by animal studies and inconclusive epidemiology studies, the International Agency for Research on Cancer has classified AA as a probable human carcinogen (Group 2A). The current understanding of the mechanism by which AA causes cancer suggests that absorbed AA can be metabolically converted to glycidamide (GA), which reacts with DNA bases and forms DNA adducts, thus leading to potential DNA damage and cancer. Among the nine identified AA-induced DNA adducts in mice, N7-(2-carbamoyl-2-hydroxyethyl)-guanine (N7-GAG) is the most abundant adduct. Although N7-GAG has not been analyzed in DNA from human tissue, this segment might be depurinated to form purine sites in the DNA backbone and subsequently excreted in the urine. Because urine samples are easy to assess through non-invasive methods, the urinary DNA adducts might serve as exposure indicators and potential cancer risk-associated biomarkers in molecular epidemiology studies.

About the research

NTU professors and researchers from other universities conducted a study entitled "Potential Association of Urinary N7-(2-carbamoyl-2-hydroxyethyl)-guanine with the Dietary Acrylamide Intake of Smokers and Nonsmokers", which was recently published in Chemical Research in Toxicology. To confirm the genotoxicity of AA and its active species in humans, Professor Kuen-Yuh Wu and colleagues have developed a method to analyze urinary N7-GAG to assess AA exposure from tobacco smoke and dietary intake. Urinary samples were collected from smokers and non-smokers with no history of occupational exposure to AA. Isotope-dilution liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) was used to analyze the samples. Other metabolites, such as urinary AAMA and cotinine, were also measured by using LC-MS/MS, and statistical comparisons with the levels of urinary N7-GAG were performed to provide a better understanding of the association between this metabolite and dietary exposure to AA.

Wu and his team have found that urinary N7-GAG is associated with solely AAMA, thus implying that AAMA might also serve as a surrogate biomarker for DNA damage induced by AA exposure. The urinary N7-GAG of non-smokers and smokers is significantly associated with a low level of dietary AA intake. Their results confirm that the urinary N7-GAG of smokers and non-smokers is caused by exposure to AA, either through food consumption or tobacco smoke exposure. Wu and his team have also found that N7-GAG formation in non-smokers without an occupational exposure history most probably reflects the consumption of foods processed at high temperatures. The mechanisms underlying the carcinogenicity of AA remain unclear; however, these results, which demonstrate an association between the urinary excretion of N7-GAG and recent exposure to AA, indicate a new mechanism by which AA causes cancer (i.e.,



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potential genotoxicity via DNA alkylation). The newly developed analysis of urinary N7-GAG is a non-invasive method to measure DNA alkylation by GA, and N7-GAG may be a valuable biomarker for confirming the active metabolite of AA responsible for DNA alkylation, which results in mutagenicity in humans. In addition, N7-GAG might also serve as a chemical-specific and potential risk-associated biomarker in molecular epidemiology studies.

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