

Experimental and pan-cancer genome analyses reveal widespread contribution of acrylamide exposure to carcinogenesis in humans

Lyon, France, 7 March 2019 – A new study¹ published today in the journal *Genome Research* reports a tumour-specific mutation spectrum introduced into the genome by glycidamide, which is a metabolite of acrylamide. People can commonly be exposed to acrylamide through dietary sources² as well as tobacco smoke.

Acrylamide is carcinogenic to rodents, and a number of epidemiological studies of cancer in humans have found weak positive associations between dietary exposure to acrylamide and some cancer types. However, robust mechanistic evidence of the mutagenic effects of acrylamide had been lacking.

This collaborative study, led by the Molecular Mechanisms and Biomarkers Group at the International Agency for Research on Cancer (IARC), has now established the presence of a distinctive fingerprint of glycidamide-induced changes in the genome.

This so-called mutational signature is found in an unexpectedly wide range of human cancer types. The study combined cell-based experimental studies with genome-wide sequencing and innovative computational interrogation of human pan-cancer databases. This approach enabled the IARC team and their collaborators at the United States Food and Drug Administration and at the Duke-NUS Medical School and the National Cancer Centre Singapore to make this discovery.

“This integrative approach provides important mechanistic evidence that a commonplace dietary and lifestyle agent can produce highly characteristic DNA damage, thereby potentially contributing to the development of cancer,” explains IARC scientist Dr Jiri Zavadil, who is the principal coordinator of the research and the senior author of the article.

Some mutational signatures may elude identification when studies use only computational analyses of pan-cancer genomics data – currently the standard in the field. Thanks to the experimental modelling of the signature of glycidamide, the researchers could reveal its broad presence in a variety of cancer types linked either to tobacco smoking (involving the lung, head and neck, and liver, where it co-occurs with the signature of benzo[a]pyrene, a major tobacco-related carcinogen) or to other sources, such as common dietary or occupational exposures (affecting the liver, kidney, bile duct, cervix, colon, and uterus).

¹ Zhivagui M, Ng AWT, Ardin M, Churchwell MI, Pandey M, Renard C, et al. (2019). Experimental and pan-cancer genome analyses reveal widespread contribution of acrylamide exposure to carcinogenesis in humans. *Genome Res.* Published online 7 March 2019.

² Acrylamide can be formed in carbohydrate-rich foods when they are cooked at high temperatures for extended periods.

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“The potential role of acrylamide in cancer has been under scrutiny for some time, although actual exposure to acrylamide has been challenging to measure in epidemiological studies,” says Dr Marc Gunter, Head of the IARC Section of Nutrition and Metabolism. “This new study provides intriguing evidence that acrylamide can cause specific mutations in humans that may lead to cancer development. Additional mechanistic and population-level research is now needed to address more deeply the role of acrylamide in cancer development.”

“Such future investigations may ultimately provide a robust rationale for reducing the exposure to acrylamide in the general population,” concludes Dr Zavadil.

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The International Agency for Research on Cancer (IARC) is part of the World Health Organization. Its mission is to coordinate and conduct research on the causes of human cancer, the mechanisms of carcinogenesis, and to develop scientific strategies for cancer control. The Agency is involved in both epidemiological and laboratory research and disseminates scientific information through publications, meetings, courses, and fellowships. If you wish your name to be removed from our press release e-mailing list, please write to com@iarc.fr.