CC/2019/07

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Recent Paper: Experimental and pan-cancer genome analyses reveal widespread contribution of 2 acrylamide exposure to carcinogenesis in human

1. This paper by Zhivagui and co-authors was recently published in Genome Research and is attached at Annex A.

2. Humans are frequently exposed to acrylamide which is found in a wide range of sources including heated starchy foods and tobacco smoke. Acrylamide causes cancer in rodents but epidemiological studies conducted to date are limited and inconclusive on the association of human cancers with acrylamide exposure. The mechanism of acrylamide carcinogenicity is postulated to be through its mutagenic metabolite glycidamide.

3. The authors report identification of a novel and unique mutational signature imprinted by acrylamide through the effects of its reactive metabolite glycidamide identified from cell cultures. The glycidamide mutational signature was found in one-third of approximately 1,600 human tumour genomes from 19 tumour types in 14 organs. The glycidamide signature was observed in cancers of the lung (88% of tumours), liver (73%), kidney (>70%), bile duct (57%), cervix (50%) and to a lesser extent in additional cancer types.

4. There were no data on the source of the acrylamide exposure nor correlation with the locations of these cancers. However, this study identifies signatures in a significant number of lung cancer tumours and smoking is a source of acrylamide exposure but the involvement of other known carcinogens in smoke cannot be excluded.

5. While the study finds signatures matching those identified, it does not appear to provide evidence that these signatures in cancers are caused by glycidamide exposure.

6. The use and interpretation of mutational spectra in risk assessment is being monitored by independent experts on the Committee on Mutagenicity (COM) but as yet there is no consensus on their strengths and limitations.

7. Members are asked to comment on the following questions:

   i. Do members consider that the study provides robust evidence suggest that acrylamide is implicated in a significant number of human cancers.

   ii. Do members consider this study provides evidence to strengthen conclusions that the mechanism of acrylamide carcinogenicity in rodents is through glycidamide mutagenicity and applicable to humans.

   Members may wish to consider the following questions

   iii. Do members consider the mutation spectra reported should be considered unique to glycidimide.

   iv. Do members consider the methodology used to identify the spectra appropriate and reliable

   v. Do members consider that further verification and validation of the spectra are required and if so can they indicate what would be required.

Secretariat
March 2019

References

Zhivagui M, Ng AWT, Ardin M, Churchwell MI, Pandey M, Renard C, Villar S, Cahais V, Robitaille A, Bouaoun L, Heguy A, Guyton KZ, Stampfer MR, McKay J, Hollstein M, Olivier M, Rozen SG, Beland FA, Korenjak M, Zavadil J (2019) Experimental and pan-cancer genome analyses reveal widespread contribution of acrylamide exposure to carcinogenesis in humans. Genome Research 29, 1-11.

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Further supplementary materials are available here:
https://genome.cshlp.org/content/early/2019/03/05/gr.242453.118/suppl/DC1

This paper is attached; it is not being made publicly available for copyright reasons

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