International Agency for Research on Cancer

World Health Organization

PRESS RELEASE
N° 252

24 July 2017

Bringing genome-wide sequencing of tumours into epidemiology

IARC and partners pioneer a new multidisciplinary approach to identify DNA mutation spectra for a wide range of carcinogens

Lyon, France, 24 July 2017 – A new study[1] published today in *Genome Research* models a first-of-its-kind approach to exploring the causes of cancer by combining cell and animal experimental studies with genome-wide sequencing of human tumours. Specific patterns of DNA mutations identified in human tumours were reproduced via in vivo and in vitro experimental studies, providing key insights into the mutagenic agents that underlie the development of cancer.

"This novel integrative approach provides important mechanistic evidence that an environmental agent can produce characteristic DNA changes, which are involved in the subsequent development of cancer," explains Dr Jiri Zavadil, who is the Head of the Molecular Mechanisms and Biomarkers Group at the International Agency for Research on Cancer (IARC) and is one of the coordinators of the research.

The study by the Duke-NUS Medical School, the National Cancer Centre Singapore (NCCS), and IARC presents the first whole-genome data on the mutation spectra of aflatoxin B_1 exposure, generated from more than 40 000 mutations in four experimental systems comprising rodent liver tumours and human cells.

Exposure to a particular carcinogen can leave a mutational signature, a distinctive fingerprint of mutations on the genome. The study confirmed the presence of a specific aflatoxin signature in liver cancer cases around the world.

"These results will help us understand which parts of the world are still burdened by liver cancer caused by aflatoxin exposure, so that measures can be taken to reduce exposure," stresses Dr Steve Rozen from the Duke-NUS Medical School in Singapore, who is a senior author of the article.

"We are now investigating how these DNA changes, in combination with hepatitis B virus infection, lead to the development of liver cancers," says Professor Kanaga Sabapathy, who is the Head of the Division of Cellular and Molecular Research at NCCS and is also a senior author of the article. "We hope that research will help us to further understand the mechanisms at play in order to prevent the development of these cancers."

Aflatoxin exposure is a major public health risk in parts of Africa and Asia, partly because of its synergy with chronic hepatitis B virus infection, which dramatically increases the risk of liver cancer.

---

[1] Huang MN, Yu W, Teoh WW, Ardin M, Jusakul A, Ng A, et al. Genome-scale mutational signatures of aflatoxin in cells, mice and human tumours. *Genome Res*. Published online 24 July 2017. http://www.genome.org/cgi/doi/10.1101/gr.220038.116

Bringing genome-wide sequencing of tumours into epidemiology

IARC and partners pioneer a new multidisciplinary approach to identify DNA mutation spectra for a wide range of carcinogens

The reported mutational signature provides evidence of varying levels of exposure to aflatoxin B_1 in liver cancer cases from Asian countries – 16% of cases from Hong Kong Special Administrative Region compared with 1% of cases from Japan – but the signature is also found in a small proportion of cases from North America and Europe, indicating that exposure to aflatoxin in high-income countries may also play a role in some liver cancers diagnosed in these regions.

“One of the great values of the approach is that it establishes a framework linking human, animal, and cell model data that can be applied to any suspected carcinogen that is mutagenic,” says IARC Director Dr Christopher Wild. “This new method could play a key role in the future identification of cancer-causing agents, an important first step to prevention.”

For more information, please contact

Véronique Terrasse, Communications Group, at +33 (0)4 72 73 83 66 or terrassev@iarc.fr
or com@iarc.fr

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 and 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 would like to be removed from our press release e-mailing list, please write to com@iarc.fr.