International team reveals 21 'signatures' in 30 common cancers

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An international team, including scientists from The University of Queensland and the Garvan Institute of Medical Research, has described the mutational processes that drive tumour development in 30 of the most common cancer types.

The discovery, published overnight in Nature, one of the world ' s leading scientific journals, could help to treat and prevent a wide range of cancers.

The team analysed 7042 tumours and identified 21 distinct mutational signatures and the cancer types in which they occur.

Professor Sean Grimmond, from UQ ' s Institute for Molecular Bioscience, said that different mutation-causing processes left different genetic ' signatures ' in cancer cells.

" All cancers are caused by genetic mutations, and in some cases we know the processes driving them, for example, tobacco smoking in lung cancer, however, our understanding of the causes of mutation in most cancers is remarkably limited, " Professor Grimmond said.

" This study allows us to pinpoint the root genetic cause of tumour development in common cancers and, in some cases, to identify the biological process that damages the DNA and gives rise to the cancer.

" For example, we found that a family of enzymes known as APOBECs, which can be activated in response to viruses, is linked to mutations in more than half of the 30 cancer types. "

All of the cancers contained two or more signatures, reflecting the variety of processes that contribute to cancer development.

Professor Andrew Biankin from the Garvan Institute and the University of Glasgow said the findings were exciting because it meant scientists could now start to explore the very mechanisms by which genes are damaged for many cancer types.

" It has potentially dramatic implications for early diagnosis, treatment, and particularly prevention in the future, " Professor Biankin said.

" If you can understand the chemical processes that are causing the genetic mutations in the first place, it provides a potential avenue for intervention.

" Childhood cancers showed the fewest mutations whereas cancers that were caused by exposure to known carcinogens such as tobacco and UV light had the highest prevalence of mutations.

" Whilst we have good data about the risk of tobacco and UV light, it took many years to discover

and here are undoubtedly other risk factors that may never be uncovered without examining the way genes are damaged.

“ It is likely we will be able to identify more mutational signatures as more cancers are sequenced and the analysis of these data is further refined. ”

The study was led by Ludmil Alexandrov and Professor Sir Mike Stratton from the Wellcome Trust Sanger Institute in London.

“ We have identified the majority of the mutational signatures that explain the genetic development and history of cancers in patients, ” said Ludmil Alexandrov, first author from the Wellcome Trust Sanger Institute.

“ We are now beginning to understand the complicated biological processes that occur over time and leave these residual mutational signatures on cancer genomes. ”

Australian authors included Professor Grimmond and Professor Biankin; Dr Nic Waddell and John Pearson from the Institute for Molecular Bioscience; Dr Marina Pajic from the Garvan Institute, The Australian Pancreatic Cancer Genome Initiative; and Professor Sunil Lakhani from UQ Centre for Clinical Research.

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About The Institute for Molecular Bioscience
The Institute for Molecular Bioscience (IMB) is a research institute of The University of Queensland that aims to improve quality of life by advancing personalised medicine, drug discovery and biotechnology.

Media: Bronwyn Adams, IMB Communications, 0418 575 247, 07 3346 2134 or b.adams@imb.uq.edu.au

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Alison Heather, Science Communications Manager, Garvan Institute, 0434 071 326, 02 9295 8128 or a.heather@garvan.org.au

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Media: Wellcome Trust Sanger Institute Media Manager Don Powell: +44 (0)1223 496 928, +44 (0)7753 7753 97, press.office@sanger.ac.uk

Brisbane St Lucia, QLD 4072
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