Unmasking the deadly secrets of pancreatic cancer

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(Medical Xpress)—A large-scale study that defines the complexity of underlying mutations responsible for pancreatic cancers in more than 100 patients was published in *Nature*.

The analysis represents the first report from Australia's contribution to the International Cancer Genome Consortium (ICGC), which brings together the world's leading scientists to identify the genetic drivers behind 50 different cancer types.

Pancreatic cancer has the highest mortality rate of all the major cancers and is one of the few for which survival has not improved substantially over the past 40 years. It is the fourth-leading cause of cancer death.

Professor Sean Grimmond, from the Institute for Molecular Bioscience (IMB) at The University of Queensland, and Professor Andrew Biankin, from The Kinghorn Cancer Centre at Sydney's Garvan Institute of Medical Research/ St. Vincent's Hospital led an international team of more than 100 researchers that sequenced the genomes of 100 pancreatic tumours and compared them to normal tissue to determine the genetic changes that lead to this cancer.

"We found over 2,000 mutated genes in total, ranging from the KRAS gene, which was mutated in about 90 per cent of samples, to hundreds of gene mutations that were only present in 1 or 2 per cent of tumours," Professor Grimmond said.

"So while tumours may look very similar under the microscope, genetic analysis reveals as many variations in each tumour as there are patients.

"This demonstrates that so-called 'pancreatic cancer' is not one disease, but many, and suggests that people who seemingly have the same cancer might need to be treated quite differently."

Professor Biankin said such individual genetic diagnoses and treatments represent the future of healthcare.

"In this study, we found a set of genes, the axon guidance pathway, that is frequently damaged in pancreatic cancer patients and is associated with a potentially poorer outcome for those patients. It is a new marker of pancreatic cancer that can be used to direct prognoses and treatments.

"'Personalised medicine', where the molecular profile of a patient is matched to the best treatment, is the way the world is moving for many diseases, not just cancer."

"The challenge now will be in moving from population healthcare and a 'one drug fits all' model to personalised healthcare. First we must take the time to develop the necessary genetic knowledge and implement health systems to translate that knowledge effectively."

Professors Biankin and Grimmond acknowledged the vital assistance of the Australian Pancreatic Cancer Genome Initiative, a network of more than 20 hospitals and research institutions Australia-wide, with over 200 members – surgeons, pathologists, nurses and researchers - that all contributed to the project (www.pancreaticcancer.net.au).

They also collaborated with colleagues from the Baylor College of Medicine and The Methodist Hospital Research Institute in Texas, the Ontario Institute for Cancer Research, Johns Hopkins University in

Maryland, the University of California San Francisco, the University of Verona, the Cambridge Research Institute and the Sanger Centre in the UK.

The ICGC project is being funded through $27.5 million from the National Health and Medical Research Council of Australia (NH&MRC), its largest-ever single grant.

NHMRC Chief Executive Officer, Professor Warwick Anderson said that "NHMRC is proud to have been the major funding contributor to this research, and I am delighted that breakthroughs have been made in understanding the genetic basis of this disease.

"This positive outcome is evidence of NHMRC supporting the very best research and researchers, and the importance of our involvement in strong national and international collaborations.

"The ultimate goal of our funding is healthier citizens, both in Australia and overseas, and this research will certainly lead to a better understanding of this issue."

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