Personalized medicine for cancer patients in a new technology era

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Published online today in *Nature*, a paper authored by over 200 members of the International Cancer Genome Consortium (ICGC) describes the beginnings of a Brave New World, a new era of personalised medicine for cancer patients.

Formed in 2008, the consortium brings together leading cancer researchers from around the world, working together to catalogue the genetic changes of the 50 most common cancers - 500 genomes from each cancer type - and make the results freely available on the internet.

"Given the tremendous potential for relatively low-cost genomic sequencing to reveal clinically useful information, we anticipate that in the not so distant future, partial or full cancer genomes will routinely be sequenced as part of the clinical evaluation of cancer patients," say the authors in the paper.

Their statement is fairly low-key, given the staggering scale of progress over the last couple of decades. The first human genome project, which sequenced half a dozen people, cost 1.5 billion dollars and took 15 years. The same amount of data can now be processed in a week at a fraction of the cost.

"This is already revolutionising the way we do cancer research," said Professor Andrew Biankin, member of the Nature paper's writing team, researcher at Sydney's Garvan Institute of Medical Research, surgeon at Sydney's Bankstown Hospital and co-leader of the Australian Pancreatic

Cancer Genome Initiative, the Australian project arm of the ICGC.

"The challenge in the past was to generate information. The challenge now is to manage the volume being generated daily - finding ways to interpret, test and apply it appropriately."

"The consortium is providing the global research community with the best possible research tool - how to select the next clinical trial. Whole genome sequencing allows us to pinpoint the exact molecular aberrations of each tumour. Understanding the aberrations allows you to target them with drugs."

"For example, you might find that the aberrations in a subtype of colon cancer are the same as the aberrations in a subtype of melanoma. In that case, the treatment that works in the colon cancer may be appropriate for the melanoma. So you'd go ahead and test it."

"The problem we have is the complexity of cancer. No two tumours are the same, even within the same type of cancer. They may look the same under the microscope, but their molecular aberrations vary greatly."

"When we treat a cancer, we give a person the drug that's most likely to work - within the limitations of our current understanding. The drug may not work for that individual, even though it works for the majority of patients with the same kind of cancer. If the treatment fails, we go onto the second-line treatment, which might also fail. By the time we get to the treatment that's actually going to work, it might be third or fourth down the line and the cancer may have advanced. In the case of pancreatic cancer, the patient has probably died."

"The consortium's internet-based databanks will help us treat specific cancers with specific treatments. Not only that, the information will help us understand why some treatments work and others do not, and then

design better drugs to target faulty elements or mechanisms."

"One of the first things we can do is pick the low hanging fruit - things not detected by the old technologies. For example, if an existing therapy targets molecular aberrations in one cancer type, yet its effects have not been explored in other cancer types, we now have a rapid way of identifying which of the unexplored cancers is a likely new target."

"B-RAFF inhibitors are a good example of a drug that shows promise for treating some kinds of melanoma. If you were to test the drug with 50 other cancers, it could take 50 years, using old methods and technologies."

"If you approach the problem with new technologies, you can quickly match the drug with molecular aberrations in specific cancers, and narrow the trial phase down to a few months."

Australia's and Canada's pancreatic project groups will be among the first to release initial data on the web, alongside the UK (breast cancer), China (gastric cancer) and Japan (liver cancer). The data release and web access is timed to coincide with the publication of the Nature paper.

There will be various tiers of access, with ethical guidelines and governance in place to regulate who can see what. The general public will be able to see general summaries, while members of the research community will be able to request detailed reports, depending on their needs.

Pancreatic cancer sequencing in Australia will be undertaken by Professor Sean Grimmond from the University of Queensland's Institute for Molecular Bioscience in Brisbane, co-leader of the Australian team with Professor Biankin.

"We've just done a handful of sequences - and already we know for sure that real cancer looks substantially different from the cell lines we've been using in the lab," said Biankin.

"We've hypothesised about that in the past, but having the evidence to prove the difference is exciting. Right from the outset we know everything there is to know about one person's tumour at the genomic, transcriptomic and epigenomic levels. We might not understand it, but we've got the data."

While not described in the paper, Biankin's group is using mice to host slices of human pancreatic tumour, effectively running pseudo clinical trials in the animals.

"It's great that we have the sequencing information as it allows us to run these parallel human-type trials in mice, testing a range of drugs against the specific molecular targets we know to exist in the tumour. It saves decades doing real clinical trials in people."

"While researchers have applied xenografts to mice in the past, they have not had the resources or information to run tests as speedily or systematically as this."

Australia is making a substantial contribution to the International Cancer Genome Consortium by tackling pancreatic cancer, one of the deadliest cancers and fourth most common cause of cancer death. The Australian team is being led by Professor Sean Grimmond from the University of Queensland's Institute for Molecular Bioscience in Brisbane and Professor Andrew Biankin from the Garvan Institute of Medical Research in Sydney. It also involves collaborative contributions from the Walter and Eliza Hall Institute of Medical Research in Melbourne, Johns Hopkins University in Maryland, the Ontario Institute for Cancer Research and the University of California, San Francisco.

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