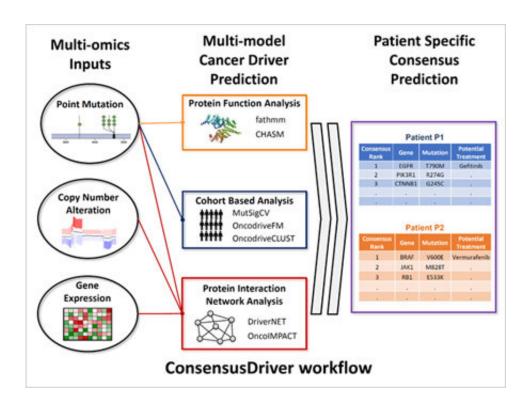


New algorithm predicts treatment targets for cancer using 'wisdom of the crowd'

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Workflow for the ConsensusDriver system in analysing patient tumours and identifying target treatments. Credit: A*STAR's Genome Institute of Singapore

Scientists in Singapore have made a unique discovery about how to treat cancers – when it comes to pinpointing cancer treatment targets, it is better to listen to many computer programmes rather than just one. Researchers have developed an advanced system that integrates this 'wisdom of the crowd' through a powerful consensus algorithm to isolate



the Achilles heel of each individual cancer tumour, helping scientists to better study different cancers and identify targeted treatments.

Cancer cells have thousands of genetic lesions but only a handful of these mutations give rise to a tumour. Identifying the 'driver' mutations that promote the uncontrolled growth of cancer cells in the body is a key challenge for the emerging field of precision oncology. This is the first time that scientists have identified a consensus algorithm that integrates various expert systems into a single accurate prediction for treatment targets in individual cancers.

To develop this system, researchers analysed data from more than 3,000 tumours, across 15 different cancer types including colon, breast, lung, stomach and liver cancer. They studied 18 different existing algorithms and found that each one of them on its own could not identify driver mutations in a significant proportion of patients. Furthermore, no single method was able to identify treatable drivers in more than 60 percent of patients. By noting that the methods had very different strengths and by combining them, the new system, known as ConsensusDriver, was able to identify treatment targets in nearly all patients studied, 80 percent of whom could be treated with existing drugs.

This work, recently published in Cancer Research, was jointly led by Dr. Denis Bertrand and Professor Niranjan Nagarajan from A*STAR's Genome Institute of Singapore (GIS), and included researchers from the National Cancer Centre Singapore (NCCS) and the National University of Singapore (NUS).

Cancer is among the leading causes of death worldwide and was responsible for 8.8 million deaths in 2015, and an estimated global economic impact of approximately US\$ 1.16 trillion in 20101. Over the years, breakthroughs in DNA sequencing technologies have allowed researchers to determine the complete genetic makeup of cancers. The



challenge now lies in crunching massive datasets to understand the unique genetic basis of an individual's disease. Researchers around the world and in Singapore are now racing to develop new computer algorithms, and participate in large collaborative projects such as The Cancer Genome Atlas.

Dr. Denis Bertrand, Staff Scientist at GIS and lead author of this work said, "Developing ConsensusDriver and working with The Cancer Genome Atlas has been an eye-opening experience. This is collaborative science on an international scale and we are making rapid advances in being able to give the right drug to the right patient at the right time."

Professor Nagarajan, Associate Director and Senior Group Leader at GIS, noted, "It is remarkable that computer algorithms have become a new weapon in the battle against cancer. Instead of clubbing <u>cancer cells</u> with drugs indiscriminately, we are now trying to computationally pinpoint genetic weaknesses to target them with drugs more precisely."

GIS Executive Director Professor Ng Huck Hui said, "The complexity of <u>cancer</u> genetics is one of the biggest challenges that we face in treating it. By precisely identifying actionable mutations, and tailoring treatments to individuals, we are moving a step closer to precision medicine. I am delighted to note the ongoing development of new algorithms and technologies by GIS scientists to achieve this vision."

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