

Largest study of genomes and cancer treatments releases first results

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The largest study to correlate genetics with response to cancer drugs releases its first results today. The researchers behind the study, based at Massachusetts General Hospital Cancer Center and the Wellcome Trust Sanger Institute, describe in this initial dataset the responses of 350 cancer samples to 18 anticancer therapeutics.

These first results, made freely available on the Genomics of Drug Sensitivity website (http://www.sanger.ac.uk/genetics/CGP/translation/), will help cancer researchers around the world to seek better understanding of cancer genetics and could help to improve treatment regimens.

"Today is our first glimpse of this complex interface, where genomes meet cancer medicine," says Dr Andy Futreal, co-leader of the <u>Cancer Genome Project</u> at the Wellcome Trust Sanger Institute. "We will, over the course of this work, add to this picture, identifying genetic changes that can inform clinical decisions, with the hope of improving treatment.

"By producing a carefully curated set of data to serve the cancer research community, we hope to produce a database for improving patient response during <u>cancer treatment</u>."

How a patient responds to anticancer treatment is known to be determined in large part by the combination of mutations in her or his cancer cells. The better this relationship is understood, the better treatment can be targeted to the particular tumour.



The aim of the five-year, international drug-sensitivity study is to find the best combinations of treatments for a wide range of cancer types: roughly 1000 cancer cell lines will be exposed to 400 anticancer treatments, alone or in combination, to determine the most effective drug or combination of drugs in the lab.

The therapies include known anticancer drugs as well as others in preclinical development.

To make the study as comprehensive as possible, the researchers have selected 1000 genetically characterised cell lines that include common cancers such as breast, colorectal and lung. Each cell line has been genetically fingerprinted and this data will also be publicly available on the website. Importantly, the researchers will take promising leads from the cancer samples in the lab to be verified in clinical specimens: the findings will be used to design clinical studies in which treatment will be selected based on a patient's cancer mutation spectrum.

The new data released today draw on large-scale analyses of cancer genomes to identify genomic markers of sensitivity to anticancer drugs.

The first data release confirms several genes that predict therapeutic response in different cancer types. These include sensitivity of melanoma, a deadly form of skin cancer, with activating mutations in the gene BRAF to molecular therapeutics targeting this protein, a therapeutic strategy that is currently being exploited in the clinical setting. These first results provide a striking example of the power of this approach to identify genetic factors that determine drug response.

"It is very encouraging that we are able to clearly identify drug-gene interactions that are known to have clinical impact at an early stage in the study," says Dr Ultan McDermott, Faculty Investigator at the Wellcome Trust Sanger Institute. "It suggests that we will discover many



novel interactions even before we have the full complement of cancer cell lines and drugs screened.

"We have already studied more gene mutation-drug interactions than any previous work but, more importantly, we are putting in place a mechanism to ensure rapid dissemination of our results to enable worldwide collaborative research. By ensuring that all the drug sensitivity data and correlative analysis is freely available in an easy-to-use website, we hope to enable and support the important work of the wider community of cancer researchers."

Further results from this study should, over its five-year term, identify interactions between mutations and drug sensitivities most likely to translate into benefit for patients: at the moment we do not have sufficient understanding of the complexity of cancer drug response to optimise treatment based on a person's genome.

"We need better information linking tumour genotypes to drug sensitivities across the broad spectrum of cancer heterogeneity, and then we need to be in position to apply that research foundation to improve patient care," says Professor Daniel Haber, Director of the Cancer Centre at Massachusetts General Hospital and Harvard Medical School. "The effectiveness of novel targeted cancer agents could be substantially improved by directing treatment towards those patients that genetic study suggests are most likely to benefit, thus 'personalising' cancer treatment."

The comprehensive results include correlating drug sensitivity with measurements of mutations in key cancer genes, structural changes in the <u>cancer cells</u> (copy number information) and differences in gene activity, making this the largest project of its type and a unique resource for cancer researchers around the world.



"This is one of the Sanger Institute's first large-scale explorations into the therapeutics of human disease," says Professor Mike Stratton, coleader of the Cancer Genome Project and Director of the Wellcome Trust Sanger Institute. "I am delighted to see the early results from our partnership with the team at Massachusetts General Hospital. Collaboration is essential in cancer research: this important project is part of wider efforts to bring international expertise to bear on cancer."

Provided by Wellcome Trust Sanger Institute

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