

NEWS

Cancer Cell Line Encyclopedia launched by Novartis and Broad Institute

A cancer cell line encyclopedia, which catalogs the genetic and molecular profiles of almost 1000 human cancer cell lines, has been developed as a result of a collaboration between Novartis and Broad Institute. The cataloged lines, used in R&D, are now publicly available and are intended for worldwide use to improve cancer clinical trial design.

The information included in the encyclopedia may help researchers identify those patients who could benefit from specific drugs; the researchers involved in the cataloging of these data suggest that cell-line collection such as this could enable a successful preclinical stratification schemata for anticancer agents. It is hoped that the emergence of personalized therapies could be assisted by the genetic prediction of drug response in a preclinical setting. “Without access to a systematically collected set of molecular data, researchers can’t match experiments from cell lines with patient tumors when new medicines become available,” said William Sellers, Global Head of Oncology, Novartis Institutes for BioMedical Research.

“Probing cell lines with medicines targeted at specific pathways, as done for the Cancer Cell Line Encyclopedia, provides a powerful tool for design of cancer treatment.”

President of the Novartis Institutes for BioMedical Research, Mark Fishman, expanded on this: “Cell lines reflect the genetic disturbances that drive cancers.

Probing cell lines with medicines targeted at specific pathways, as done for the Cancer Cell Line Encyclopedia, provides a powerful tool for design of cancer treatment.” He added: “We are placing this information in the public domain. We hope that many in industry and academia will use these data to discover new drug targets, to evaluate current therapies, and to facilitate treatment for their patients with cancer.”

The gene expressions, chromosomal copy number and massively parallel sequencing data from 947 human cancer cell lines are compiled in The Cancer Cell Line Encyclopedia. Researchers found evidence to suggest that, when coupled with the pharmacological profiles for 24 anticancer drugs across 479 of the cell lines, the encyclopedia allowed the identification of predictors of drug sensitivity that were genetic, lineage and gene-expression-based.

The results, published in *Nature*, also indicate that, in addition to known predictors, plasma cell lineage was associated with sensitivity to IGF1 receptor inhibitors. Specifically, *SLFN11* expression predicted sensitivity to topoisomerase inhibitors and *AHR* expression was correlated with MEK inhibitor efficacy in *NRAS*-mutant lines.

The profiling data from the cell lines are now freely available to the scientific community on the Broad Institute’s website.

– Written by Lucy Marum.

Sources: Press release: Novartis launches the Cancer Cell Line Encyclopedia (CCL) to catalogue world’s cancer cell lines. www.novartis.com/newsroom/media-releases/en/2012/1597980.shtml; Barretina J, Caponigro G, Stransky N *et al*. The Cancer Cell Line Encyclopedia enables predictive modeling of anticancer drug sensitivity. *Nature* 483(7391), 603–307 (2012).



Investment fund established to combat cancer drug ‘development gap’

In combination with the European Investment Fund, Cancer Research Technology – the commercial aspect of Cancer Research UK – has created a £50 million investment fund, with the aim of bridging the UK funding gap between early- and late-stage drug discoveries and development.

Recently, owing to the global financial crisis, significantly less financial support has been available for small biotechnology companies to invest in R&D. In a company press release, Cancer Research UK hailed it as a “bold step to fund the most innovative oncology research and to plug a large gap in the UK funding of drug discovery.”

The funding will initially amount to £25 million, rising to £50 million over the next 2 years if successful. A minimum of two-thirds of the investment fund has been allocated to fund cancer drug development of discoveries made by Cancer Research UK scientists. It is hoped the investment fund will facilitate

the development of drug discovery from initial concept through to Phase II clinical trials. The government strategy for UK life sciences has ambitious plans to enhance collaboration between research and businesses.

“This vital investment will nurture world-class innovation in drug development to bring potential new treatments to patients as quickly as possible” commented Harpal Kumar, Cancer Research UK’s Chief Executive Officer. “Our scientists and doctors have contributed to most of the world’s top cancer drugs, such as temozolomide – used worldwide to treat people with the most aggressive type of brain tumour – and through our research, we’ve contributed to the discovery or development of nearly 50 drugs now being tested in clinical trials. These drugs could also save many thousands of lives in the future.”

Kumar added “this new Cancer Research Technology Pioneer Fund will enable us to build on the progress already

made and provide a stepping stone to producing the cancer drugs of the future”.

Glyn Edwards, Chief Executive Officer of BioIndustry Association, a UK-based organization whose members are responsible for over 90% of the UK biotech entities in clinical trials, commented on the new investment fund, adding that it “will provide another financing option for companies and academics in the UK looking to translate their cancer-drug discoveries into clinical development.”

“The Fund arrives at a particularly good time for life sciences in the UK, following the launch last week by the Wellcome Trust of a £200 million venture fund and GlaxoSmithKline’s decision to invest £500 million in biopharmaceutical manufacturing in the UK” added Edwards.

– Written by Alexandra Hemsley.

Source: <http://info.cancerresearchuk.org/news/archive/pressrelease/2012-03--29-crt-eif-£50M-cancerfund>

New allergic disease regulator identified by researchers

Researchers from Cincinnati Children’s Hospital Medical Center (OH, USA), have identified a genetic signature for the regulation of IL-13, a key immune hormone.

The findings report that the microRNA miR-375 is regulated by IL-13, which, in turn, regulates how proallergic changes are induced by IL-13 in epithelial cells. This discovery illustrates a potential role for miR-375 in the treatment of allergic diseases, including asthma and eosinophilic esophagitis.

Marc E. Rothenberg, senior investigator in the study, explained: “The identification of a microRNA that regulates IL-13-induced changes and inflammatory pathways is a significant advancement for the understanding and future treatment of allergic disease.” He added that: “MiR-375 is proof-of-principle that

microRNAs are involved in fine tuning IL-13-mediated responses, which opens up a set of new possibilities for novel therapeutic targets for treatment of allergic disease.”

Changes in epithelial gene and protein expression, integral in the onset of allergic disease, are induced by IL-13. Investigators in the study used IL-13 to stimulate esophageal and bronchial human epithelial cells, then analyzed for differential microRNA expression.

The researchers noted that expression of miR-375 was downregulated after human esophageal squamous and bronchial epithelial cells were stimulated by IL-13. The IL-13-associated immunoinflammatory pathways were notably altered by the viral overexpression of miR-375 in epithelial cell cultures. Decreases in miR-375 were observed in

both the human cells and a transgenic mouse model. The researchers also assessed miR-375 in sufferers of eosinophilic esophagitis, an allergic disease characterized by IL-13 overproduction, and in healthy individuals.

The results suggest that decreased expression of miR-375 correlates with the degree of allergic inflammation and disease activity and that, in disease remission, miR-375 expression normalizes. The authors of the study suggest that these results highlight miR-375’s potential use as a disease-activity biomarker for certain allergic diseases.

– Written by Lucy Marum.

Source: Lu TX, Lim E-J, Wen T, Plassard AJ *et al.* MiR-375 is downregulated in epithelial cells after IL-13 stimulation and regulates an IL-13-induced epithelial transcriptome. *Mucosal Immunol.* doi:10.1038/mi.2012.16 (Epub ahead of print) (2012).

RAPID GENE Trial successfully utilizes point-of-care diagnostics for personalized antiplatelet medication

A new trial, conducted by researchers from the University of Ottawa Heart Institute (ON, Canada) has demonstrated a new point-of-care genetic test to successfully assess the appropriate drug therapy for patients after percutaneous coronary intervention (PCI). The cheek swab Spartan RX CYP2C19 bedside DNA test identifies patients who carry the *CYP2C19*2* allele, a result that is then used to determine the appropriate antiplatelet therapy for the patient.

The *CYP2C19*2* allele is associated with increased rates of major adverse events in patients who undergo PCI and are prescribed the standard Plavix® (clopidogrel) antiplatelet therapy. However,

assessment of appropriate pharmacogenetic strategies is currently limited by a lack of bedside genetic tests.

The researchers at the University of Ottawa Heart Institute enrolled 200 PCI patients in the trial and randomly assigned either rapid point-of-care genotyping or standard treatment. *CYP2C19*2* allele carriers were prescribed 10 mg Effient® (prasugrel) daily, the standard treatment group and noncarriers were given 75 mg Plavix daily. The point-of-care genetic test was reported to have a sensitivity of 100% and specificity of 99.3%. The results of the trial found none of the 23 carriers in the rapid genotyping group to have received inadequate protection,

measured by the elimination of high on-treatment platelet reactivity, compared to 30% of patients treated with standard therapy who did not receive adequate protection. Derek So (University of Ottawa Heart Institute) concludes, "For the first time in medicine, nurses were able to perform DNA testing at the patient's bedside. This is a significant step towards the vision of personalized medicine."

– Written by Jenaid Rees.

Source: Roberts JD, Wells GA, Le May MR *et al.* Point-of-care genetic testing for personalisation of antiplatelet treatment (RAPID GENE): a prospective, randomised, proof-of-concept trial. *The Lancet* doi:10.1016/S0140-6736(12)60161-5 (Epub ahead of print) (2012).

Alternative therapies can help alleviate symptoms of breast cancer treatment-induced menopause

Researchers from the Netherlands Cancer Institute (Amsterdam, The Netherlands) have found that menopausal symptoms induced by chemotherapy or hormonal therapy in younger women with breast cancer, can be considerably alleviated through the use of cognitive behavioral therapy (CBT) and physical exercise (PE). These findings were presented at the 8th European Breast Cancer Conference in March 2012.

Many cancer patients are faced with irreversible changes resulting from cancer treatment. One such change that some women face after breast cancer is treatment-induced menopause, involving such distressing symptoms as hot flushes, night sweats, vaginal dryness, weight gain, urinary incontinence and sexual dysfunction.

The researchers studied 411 breast cancer patients, averaging at 48 years of age, recruited from 14 hospitals in Amsterdam and Rotterdam (The Netherlands). The women were randomly assigned into four groups: CBT alone, PE alone, CBT and PE combined, and a control group. All patients receiving CBT and/or PE interventions showed an overall reduction in

the levels of menopausal symptoms compared with the control group. Even after 6 months, the women receiving CBT and/or PE reported these improvements.

"To our knowledge, this is the first study to investigate the efficacy of these two interventions specifically in women who have experienced acute, treatment-induced menopause," said Marc van Beurden (The Netherlands Cancer Institute). "This is a very important issue for the quality of life of younger breast cancer patients. Unlike healthy women starting the menopause, they are unable to take hormone replacement therapy to alleviate their symptoms. There are other drugs available, but they are only moderately effective and have troublesome side-effects."

The researchers noted that while the evidence that CBT and PE worked was

convincing, compliance to CBT during the study was poor and the frequency and intensity of the PE programme was also a challenge for many women. "We think that we have made an important step forward in improving the quality of life of these patients" continued van Beurden. "Based on input from patients, we are now developing an internet-based version of the CBT programme. We hope that this will further increase the accessibility and convenience of the interventions and lead to more women benefiting from their results."

– Written by Sam Rose.

Source: European Cancer Organisation/ European Breast Cancer Conference press release. www.ecco-org.eu/Global/News/EBCC8-PR/2012/03/22_03-Non-drug-treatments-help-alleviate-symptoms-of-treatment.aspx

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