Integrative high-throughput sequencing in personalized oncology

Scientists from the University of Michigan Comprehensive Cancer Center and Michigan Center for Translational Pathology (MCTP) (Ann Arbor, MI, USA) have recently presented the results of a pilot study which aimed to explore the practical challenges of genome sequencing in clinical oncology.

The project, called MI-ONCOSEQ, involved patients with advanced or refractory cancer and aimed to match them with existing clinical trials, based on the biomarkers identified. For each patient, the whole-genome sequencing of the tumor, the targeted whole-exome sequencing of tumor and normal DNA, and the transcriptome sequencing (RNA-Seq) of the tumor were performed to identify potentially informative mutations. With this approach, several classes of carcinogenic mutations including structural rearrangements, copy number alterations, point mutations, and gene expression alterations were detected. These data were subsequently carefully analyzed and interpreted by the Sequencing Tumor Board, University of Michigan, Ann Arbor, MI, USA. Entire analysis, from tumor biopsy to final decision, took approximately 28 days for each patient.

As reported in November 2011 issue of the *Science Translational Medicine*, the study initially began by testing the sequencing strategy on human prostate cancer mice xenografts. Later, two patients were enrolled in a clinical pilot study: one with colorectal cancer and one with melanoma. Potential clinical trials were identified for both of these patients. At the American Society of Clinical Oncology (ASCO) Annual Meeting, which took place in June 2012 in Chicago, USA, already 50 patients were reported to have been enrolled in this pilot study. In 60% of these patients, actionable mutations have been detected and 3 of these patients were included in clinical trials based on the results obtained in MI-ONCOSEQ. The authors of this study claim that the use of high-throughput sequencing for identifying biomarker-driven treatment options not only opens the door for personalized oncology, but it also presents a number of logistical challenges, such as how to make the results available cost-effectively and in a clinically relevant timeframe.

Source

Roychowdhury S., Iyer M.K., Robinson D.R., Lonigro R.J., Wu Y.M., Cao X., Kalyana-Sundaram S., Sam L., Balbin O.A., Quist M.J., Barrette T., Everett J., Siddiqui J., Kunju L.P., Navone N., Araujo J.C., Troncoso P., Logothetis C.J., Innis J.W., Smith D.C., Lao C.D., Kim S.Y., Roberts J.S., Gruber S.B., Pienta K.J., Talpaz M., Chinnaiyan A.M. (2011) *Personalized oncology through integrative high-throughput sequencing: a pilot study*. Sci. Transl. Med. 3(111): 111ra121.

University of Michigan Health System (UMHS) Press Release, 30 November 2011. (http://www.uofmhealth.org/news/cancer-sequencing-1130).

10th Carbohydrate Bioengineering Meeting

The Institute of Microbiology of the Academy of Sciences of the Czech Republic will organize the *10th Carbohydrate Bioengineering Meeting (CBM10)* that will be held in Prague (the Czech Republic), on April 21-24, 2013. The main topics of the conference include: the mechanisms and structure-function relationships of carbohydrate modifying enzymes; glycomics and systems' glycobiology; synthesis, the structure and function of carbohydrates and glycoconjugates; carbohydrate and enzyme engineering; carbohydrates in health and medicine, new materials and nanomaterials from carbohydrates as renewable resources. Among the invited speakers, there will be distinguished specialists from European and American institutes.

Poster abstracts can be submitted until 31st of January 2013. The list of invited speakers and information on the registration and venue are available at the event's website: http://www.cbm10.org.

12th International Symposium on the Genetics of Industrial Microorganisms

The *12th International Symposium on the Genetics of Industrial Microorganisms (GIM-2013)* will take place in Cancun QR, Mexico, during June 23-28, 2013. The conference aims to create a forum for discussion on current topics related to the genetic manipulation of industrial microorganisms used for biotechnological processes. Plenary lectures and symposia will be focused on genetic

VIEWS and NEWS section is prepared by Joanna Przybył

exploitation of industrial microorganisms for food and metabolite processing, alcoholic and non-alcoholic fermentations, biofuel production and bioremediation. Attendees of *GIM-2013* will have the opportunity to present results of their research during a poster session. The symposium will also provide an excellent opportunity for the academic and industrial leaders in genetic manipulation of industrial microorganisms to meet and exchange ideas, as well as gain an insight into the future perspectives in this field.

For more information visit, the symposium website: http://www.smbb.com.mx/GIM2013-Cancun.

Novel consolidated bioprocess for biofuel production in *E. coli*

In December 2011, the *Proceedings of the National Academy of Sciences* (PNAS) published the results of an interesting work describing a novel approach to biofuel production. A multi-institutional team of researchers led by Prof. Jay D. Keasling from the Joint BioEnergy Institute (Emeryville, USA) aimed to engineer *Escherichia coli* to both: digest plant biomass and produce hydrocarbons that have the properties of petrochemical fuels. They modified *E. coli* in a way as to have them grow using both the cellulose and hemicellulose fractions of several types of plant biomass pretreated with ionic liquids. Engineered bacteria strains express cellulase, xylanase, beta-glucosidase and xylobiosidase enzymes under the control of native *E. coli* promoters selected to optimize growth on model cellulosic and hemicellulosic substrates. These strains were further genetically modified to express components of biofuel synthesis pathways, in order to produce fuel substitutes or precursors for gasoline, diesel and jet fuel. Engineered *E. coli* were capable of generating all three types of biofuels directly from ionic liquid-treated *Panicum virgatum*, commonly known as switchgrass, without externally supplied hydrolase enzymes. This work demonstrates a consolidated bioprocess which could substantially lower the cost of biofuel production because the currently used methods require expensive enzyme cocktails to digest cellulose and hemicellulose into sugars. It has been estimated that the production and purification of those enzymes cost about 25 cents per liter of the final biofuel. Prof. Keasling's team claims that the use of genetically modified *E. coli* may provide an economical route to production of advanced biofuels.

Source

Bokinsky G., Peralta-Yahya P.P., George A., Holmes B.M., Steen E.J., Dietrich J., Soon Lee T., Tullman-Ercek D., Voigt C.A., Simmons B.A., Keasling J.D. (2011) *Synthesis of three advanced biofuels from ionic liquid-pretreated switchgrass using engineered Escherichia coli*. Proc. Natl. Acad. Sci. USA 108(50): 19949-19954.

ScienceNOW, *Fuel From Waste?* Robert F. Service, 5 December 2011. (http://news.sciencemag.org/sciencenow/2011/12/fuel-from-waste.html).

Protein Engineering: New Approaches and Applications

The University of Chester (Chester, United Kingdom) will host the *Protein Engineering: New Approaches and Applications* conference on 10-12 April, 2013. The event is organized jointly by two British organizations: the Biochemical Society and the Protein Society.

Protein engineering is currently undergoing a renaissance with the advent of new technological approaches to address some of the major emerging areas in THE life sciences. Protein engineering also provides valuable and fundamental understanding regarding the construction and function of natural proteins, which, in turn, will inevitably improve the ability to generate the next generation of novel proteins, including advanced biopharmaceuticals.

This meeting will assemble a diverse group of leading protein engineers and will highlight the recent advances in the current understanding of how proteins can be manipulated towards an intended function applicable in synthetic biology, bioprocessing and nanotechnology. Topics included in the program will cover computational protein engineering, directed evolution, constructing functional biocatalysts, synthetic biology and engineering protein-protein interfaces.

The abstract submission deadline is 6 February, 2013. All attendees, particularly researchers in the early stages of their career, are invited to submit a poster abstract for consideration as an oral communication. Information concerning invited speakers, required abstract format, registration fees and preliminary program is available at: http://www.biochemistry.org/tabid/379/MeetingNo/SA143/view/Conference/default.aspx.

Tomato genome published

The Tomato Genome Consortium published a high-quality genome sequence of domesticated tomato – *Solanum lycopersicum*. Specifically, DNA of inbred tomato *Heinz 1706* was sequenced and assembled using a method combining Sanger and *next-generation* technologies. The results of this work revealed that tomato possesses almost 35 000 of protein-coding genes located on 12 chromosomes. Genes responsible for virtually all essential features such as nutritional content, taste, color and natural pest resistance have been localized and characterized.

The Tomato Genome Consortium is a multi-national collaboration initiative involving scientists from the United States, Argentina, Belgium, China, France, Germany, India, Israel, Italy, Japan, the Netherlands, South Korea, Spain and the United Kingdom. In the U.S., the project was led by James Giovannoni from the Boyce Thompson Institute for Plant Research located at the Cornell University (Ithaca, NY) and the U.S. Department of Agriculture, Agricultural Research Service (Ithaca, NY). The researcher claims that with this accomplishment it will be easier and less costly to decode the sequences of other tomato varieties. Decoding tomato genome for the first time cost millions of dollars but for subsequent types of tomato it may cost no more than $10 000, as may be estimated based on these initial data. The knowledge of tomato genome sequence may potentially have important implications in the improvement of food nutritional quality and security. Complete results of this project are available at the http://solgenomics.net website.

Source

The Boyce Thompson Institute for Plant Research and Cornell University Press Office Release, 30 May 2012. (http://bti.cornell.edu/index.php?page=NewsDetails&id=135)

The Tomato Genome Consortium (2012) *The tomato genome sequence provides insights into fleshy fruit evolution*. Nature 485: 635-641.

Use of Google algorithm to identify pancreatic cancer biomarkers

PLOS Computational Biology has recently published an interesting paper describing the application of Google algorithm in the search for pancreatic cancer biomarkers. German and Austrian researchers created a NetRank algorithm which couples gene expression measurements with a network of known relationships between the genes' products. NetRank was based on the PageRank algorithm, which is used by Google search engine to identify websites that are the most relevant to the indicated search term.

The authors of this work explain that *recently, powerful methods have become available to systematically read genomic information of patient samples. The major remaining challenge is how to spot, among the thousands of changes, those few that are relevant for tumor aggressiveness and thereby affecting patient survival*. The scientists claim that they made use of the fact that genes and proteins in a cell never act alone, but form a network of interactions. This is, in a certain way, similar to the finding of relevant information in large networks of web documents and hyperlinks, which has been mastered by Google with their PageRank algorithm. On the same basis, the authors report that the NetRank algorithm can identify genes that are better indicators for survival than the genes found by traditional algorithms such as Pearson correlation of gene expression data with patients' survival.

This approach was applied to gene expression profiles obtained from 30 pancreatic cancer patients and it revealed seven candidate marker genes prognostic for the outcome. The prognostic value of these seven candidate markers was further validated using immunohistochemistry on an independent set of 412 pancreatic cancer samples. Signatures derived from these candidate genes were independently predictive of outcome and superior to established clinical prognostic factors such as tumor grade, size, and nodal status.

The authors summarize that *as the amount of genomic data of individual tumors grows rapidly, our algorithm meets the need for powerful computational approaches that are key to exploit these data for personalized cancer therapies in clinical practice*.

Source

Winter C., Kristiansen G., Kersting S., Roy J., Aust D., Knösel T., Rümmele P., Jahnke B., Hentrich V., Rückert F., Niedergethmann M., Weichert W., Bahra M., Schlitt H.J., Settmacher U., Friess H., Büchler M., Saeger H.D., Schroeder M., Pilarsky C., Grützmann R (2012) *Google goes cancer: improving outcome prediction for cancer patients by network-based ranking of marker genes*. PLoS Comput. Biol. 8(5): e1002511.