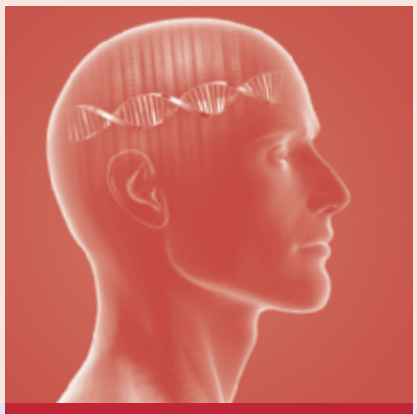

OMICS & SYSTEMS BIOLOGY

BRIEFS

Sigma, Cofactor Genomics to develop rat genome database

ST. LOUIS—Sigma Life Science' SAGE Labs initiative has partnered with Cofactor Genomics in an effort to sequence genomes for six of the most widely used strains of rat. As part of the agreement, Cofactor Genomics plans to generate and analyze sequence data using next-generation sequencing systems, while SAGE Labs plans to provide the samples and to host a new, free public database at sageresearchmodels.com later this year.

"With the costs of whole genome sequencing rapidly coming down, it is now far more feasible to understand the genomes of the most widely used model organisms such as the rat," says Dr. Edward Weinstein, director of SAGE Labs at Sigma Life Science. "Sigma Life Science and its SAGE Labs initiative plan to lead the way in revealing these new genomes and making the information publicly available."

Debiopharm, Marina Biotech team up on bladder cancer

LAUSANNE, Switzerland—The Debiopharm Group, a global independent biopharmaceutical development group of companies with a main focus in oncology and serious medical conditions, and Marina Biotech Inc., an RNAi-based drug discovery and development company, have entered into an exclusive agreement to advance to market an RNAi-based therapy for the treatment of non-muscle invasive bladder cancer. Debiopharm, which will have full responsibility for the development and commercialization of any products arising from the partnership, will pay Marina Biotech up to $25 million based on predefined research and development milestones as well as royalties on the sales of products resulting from the partnership. In addition, all Marina Biotech research and development costs for the bladder cancer program will be funded by Debiopharm. Further terms of the agreement were not disclosed.

ISB, P&G form skin disease, systems biology partnership

SEATTLE—The Institute for Systems Biology (ISB) and Procter & Gamble have formed a collaborative partnership that will focus on research to characterize the systems biology of various skin conditions, including skin aging. The partnership marries ISB's expertise in regulatory network inference and modeling with P&G's expertise in skin biology and dermatology to characterize and develop models of the global molecular changes that occur in skin under different conditions. The partnership will also include work on the systems biology of respiratory rhinovirus infection. The collaboration is focused on fundamental research to explore basic biologic mechanisms, with the intention of uncovering important molecular processes involved in skin aging and rhinovirus infections.

Genomics for the win against cancer?

TGen and Genomic Health discover genes affecting cancer drug oxaliplatin, publishing paper calling for more research into mechanisms influencing the drug's activity

BY JEFFREY BOULEY

PHOENIX, Ariz.—Suggesting that genomic research could help physicians better target the use of oxaliplatin in treating colorectal cancer patients, the Translational Genomics Research Institute (TGen) and Redwood City, Calif.-based Genomic Health Inc. recently published a paper titled "Functional Genomics Reveals Diverse Cellular Processes that Modulate Tumor Cell Response to Oxaliplatin" for *Molecular Cancer Research*, one of six peer-reviewed scientific journals published by the Philadelphia-based American Association for Cancer Research. The paper currently appears in the online version of the journal and is pending print publication.

Oxaliplatin is widely used in colon cancer and is used early in the disease process, after surgery in those cancers that are likely to recur. It is also used in advanced disease to slow progression of the cancer when it has become metastatic.

The problem is that a significant percentage of patients suffer serious side effects from the drug, including prolonged damage to the nervous system, "creating an urgent need to identify genes that are responsible for drug sensitivity or resistance, which results in directing therapy to those most likely to benefit," according to the TGen-Genomic Health study.

Neurotoxicity associated with oxaliplatin is most commonly manifested as pain or a loss of sensation in the hands and feet, which can markedly downgrade a patient's quality of life and ability to work. These symptoms are

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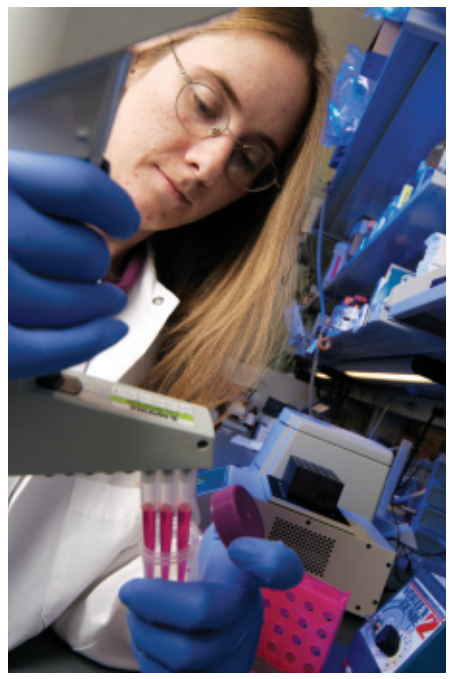

TGen's researchers already had the assay in place to do the siRNA screening that Genomic Health needed, helping not only Genomic Health itself, but leading to the publication of data that might help physicians focus in on better use of oxaliplatin or help researchers discover better drugs to replace it one day.

Setting the standard

European project sets goal of standardizing human genome sequencing

BY DAVID HUTTON

BARCELONA, Spain—A consortium of European DNA sequencing centers have established the new Genetic European Variation in Disease (GEUVADIS) initiative, bringing together leading medical genome sequencing laboratories to define technological and ethical standards and to promote multidisciplinary training for the global scientific and medical community.

The initiative is coordinated by Dr. Xavier Estivill of the Centre for Genomic Regulation in Barcelona, Spain, and supported by the European Commission. It includes 17 international partners throughout Europe and the United States.

The genesis of GEUVADIS dates back several years, according to Estivill. The concept was presented by Estivill at the Eurobioforum 2008, which is supported by the European Science Foundation.

"The project started after several discussions among scientists working in the field of medical genomics, raising the need of a European participation in medical genomics sequencing," he says. "After that meeting and some discussion with the European Commission and some additional scientists, it was clear that a project could be presented for funding by the EC that

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Dr. Xavier Estivill of the Centre for Genomic Regulation in Barcelona, Spain, says the new Genetic European Variation in Disease (GEUVADIS) initiative has three goals: "First, it's about creating a common framework of European investigators that perform large-scale sequencing projects in genomics medicine to set up larger projects for specific disorders of interest for the European population. Secondly, we want to set up standards in medical genomics sequencing across sequencing sites and technologies, allowing efficient quality control of technologies and data produced. Finally, we will produce common guidelines on how to share this data while respecting the participants' privacy, and how to translate these results into prevention, diagnosis and curing of a wide variety of diseases, ranging from leukemia to mental retardation."

Putting SMA on the map

Rules-Based Medicine's MAP platform helps Spinal Muscular Atrophy Foundation reach biomarkers milestone

BY LORI LESKO

NEW YORK—Navigating with a special "map," the Spinal Muscular Atrophy (SMA) Foundation has reached the first milestone in a program aimed at developing plasma protein biomarkers to treat SMA patients. The direction to this goal was provided by the Rules-Based Medicine's (RBM) Multi-Analyte Profiling (MAP) technology platform.

RBM's biomarker testing service provides clinical researchers, physicians and healthcare providers with reproducible, quantitative, multiplexed data for hundreds of proteins to advance drug development and patient care. According to the company, its MAP technology offers preclinical and clinical researchers broad, cost-effective protein analyses in multiple species from a small sample volume. MAP technology also supports RBM's mission to develop diagnostics that aid in

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SMA

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the detection of complex diseases and conditions in areas of unmet medical need such as neuropsychiatry, nephrology, immunology and cardiology.

Founded in 2003, the SMA Foundation is a nonprofit organization dedicated to accelerating progress toward a treatment and cure for SMA through targeted funding of clinical research and novel drug development efforts. Since its inception, the foundation has awarded more than $60 million in sponsored research agreements.

RBM's role in this collaborative effort has been to discover and confirm plasma protein biomarker candidates previously identified from the multi-center Biomarkers for SMA (BforSMA) clinical study executed in 2008 and 2009 by the SMA Foundation, says Christopher Martin, RBM spokesman.

"The Foundation and RBM entered into an agreement in the summer of 2010 to develop a panel of plasma protein biomarkers—important tools in drug development as they can provide information on whether a drug is working and a patient is doing better with a simple blood sample," Martin says.

Biomarkers are particularly useful "when the disease state is associated with slow disease progression, and the target tissues that are primarily affected are not directly accessible (in the central nervous system), as in the case of SMA," he says. "In this stage of the collaboration, the SMA Foundation provided BforSMA plasma samples to RBM for processing on the DiscoveryMAP platform—plus an additional set of 70 biomarker assays. Candidate biomarkers were found that significantly differentiated between disease and control groups and correlated with SMA disease severity."

The SMA Foundation and RBM "are continuing to analyze these results and plan to create a specific panel of biomarker assays for use in clinical trials exploring new treatments for SMA, and ultimately become useful for helping to track disease progression in patients," he says. "The next milestone will be the commercial release of this SMA panel."

Karen Chen, chief scientific officer of the SMA Foundation, explained that biomarkers are critical to accelerating therapeutic development for any disease.

"(Biomarkers) are even more important for rare diseases like SMA, where patient populations are small and mostly consist of children," Chen says. "We are excited to work with RBM ... and evaluate responses to treatments more efficiently, and minimize the burden of clinical trials for patients and families."

Rules-Based Medicine's role in this collaborative effort has been to discover and confirm plasma protein biomarker candidates previously identified from the multi-center Biomarkers for SMA (BforSMA) clinical study executed in 2008 and 2009 by the SMA Foundation.

Identifying specific biomarkers is expected to not only help assess drug efficacy, but shorten the duration of clinical trials for SMA therapies, she says.

Dr. Darryl De Vivo, pediatric neurologist and director of the SMA Clinical Research Center at Columbia University Medical Center, describes the disease as "very grave, very rare."

"SMA is the second most common autosomal recessive condition (behind cystic fibrosis) affecting humans. Parents are carriers," De Vivo says. "It is life-altering in all cases and life-threatening in the most severe cases. Children affected with SMA are weak, may have trouble breathing and are at risk for scoliosis."

The SMA Foundation estimates that approximately one in 6,000 to 10,000 babies worldwide are born annually with SMA, a motor neuron disease and the leading genetic cause of death among infants and toddlers. Characterized by selective loss of nerve cells in the spinal cord, the disease leads to increasing muscle weakness and atrophy, leading to the progressive inability to walk, stand, sit up and breathe, depending on the severity of the disease.

"We are delighted to support the efforts of the SMA Foundation to develop better treatments for this terrible disease," said Craig Benson, CEO of RBM. "The confirmation and validation of biomarker patterns on our platform and the availability of testing services through our CLIA-certified lab will accelerate the development of new treatments for SMA." **ddn**

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could help to coordinate European efforts in medical genomic sequencing."

Emmanouil Dermitzakis, Louis-Jeantet professor in the Department of Genetic Medicine and Development at the University of Geneva Medical School in Switzerland, says the project "started from an idea of a few people looking for funding to do genome sequencing in disease samples and came to fruition by the joint efforts of multiple European PIs."

"The focus of GEUVADIS is to establish standardization and implementation of methodologies for the use of next-generation sequencing methods in research and clinic," Dermitzakis says.

The project has received funding of $2.7 million under the EU's Seventh Framework Programme for a project period of 36 months, which began in October.

"The aim of this project is threefold," Estivill tells *ddn*. "First, it's about creating a common framework of European investigators that perform large-scale sequencing projects in genomics medicine to set up larger projects for specific disorders of interest for the European population. Secondly, we want to set up standards in medical genomics sequencing across sequencing sites and technologies, allowing efficient quality control of technologies and data produced. Finally, we will produce common guidelines on how to share this data while respecting the participants' privacy, and how to translate these results into prevention, diagnosis and curing of a wide variety of diseases, ranging from leukemia to mental retardation."

Estivill notes that the "CRG coordinates the project and participates in quality control, handling, analysis and interpretation of sequence data and other functional datasets and biological and medical interpretation of sequence data." CRG has medical genomic sequencing as one of its main priorities, he says.

"We hope to achieve leadership in some key projects of medical genomic sequencing that we are involved in," Estivill adds. "These are in the area of neuropsychiatric and neurodegenerative diseases."

The GEUVADIS Project will include top sequencing centers in Europe and the United States, including: France's National Genotyping Center and National Institute for Health and Medical Research; Germany's Max-Planck Institute of Human Genetics, Helmholtz Zentrum München-German Research Center for Environmental Health, Christian-Albrechts University and Applied Biosystems Deutschland GmbH; the Netherlands' Radboud University Nijmegen Medical Centre and Leiden University Medical Center; Spain's Centre for Genomic Regulation, National Centre for Genomic Analysis and University of Santiago de Compostela; Sweden's Uppsala University; Switzerland's University of Geneva; the

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United Kingdom's Wellcome Trust Sanger Institute, European Bioinformatics Institute and Illumina Cambridge Ltd.; and the United States' Johns Hopkins University School of Medicine.

GEUVADIS participants were selected based upon their expertise in the field of medical sequencing in all aspects, including technical, computational and ethical.

In terms of technical expertise, 12 of the 17 partners possess the latest sequencing machines (Illumina HighSeq200 and SoLiD) and have long-term expertise in the field. Illumina and Life Technologies are also part of the consortium, which opens a window for fruitful discussion and collaboration between users and designers of these machines.

Computational consideration includes the presence of the EMBL/EBI in the consortium, bringing in highly valuable expertise in issues related to data storing, access and exchange.

Covering the ethical aspect is Anne Cambon-Thomsen, who is responsible for ELSI issues in the project, and leads a multidisciplinary team on "Genomics and Public Health," involving human and social sciences as well as life sciences. She also leads a "Genetics and Society" platform at the Toulouse-Midi-Pyrénées Genopole.

A growing number of research projects have flourished in response to the increasingly rapid evolution of these technologies, which has led to an unprecedented surge in new biological data. There are now several large-scale sequencing projects, like the 1000 Genomes project and the International Cancer Genomics Consortium, that are analyzing thousands of samples from different populations and disease status. GEUVADIS investigators are partners of these large-scales projects. The production of this large amount of data poses major challenges that the GEUVADIS consortium is going to tackle in Europe.

Estivill says it is crucial that scientists participate early in the analysis of the ethical and societal dimensions of their work.

"As genome sequencing technologies become cheaper and more available, they are increasingly used in wider and wider contexts," he says. "They raise contradictory, and sometimes passionate expectations and apprehensions in the society. Within and aside of the medical setting, they have to be implemented in a responsible way, to ensure that patients (or clients of direct-to-consumer genetic testing companies) correctly understand the meaning, and the limits of the information obtained."

"To fill the gap between the technological fascination and speed, and the responsible implementation of genome sequencing, it is crucial that scientists participate early in the analysis of the ethical and societal dimensions of their work," adds Cambon-Thomsen. "This dimension is a lively axis of the work in GEUVADIS."

Estivill notes that a number of pitfalls are to be avoided: Researchers who advocate the long-term usefulness of these technologies have their responsibility in ensuring that no discrimination is exercised on human beings because phenotype predictions from sequence variation, he says.

> "[It] is crucial that scientists participate early in the analysis of the ethical and societal dimensions of their work."
>
> —ANNE CAMBON-THOMSEN, LEADER OF MULTIDISCIPLINARY TEAM ON "GENOMICS AND PUBLIC HEALTH"

The effort is focusing on privacy issues as well as freedom of choice and mutual respect, and one challenge will be to determine whether these issues can be satisfactorily addressed by the consortium.

"First of all, rules of access to data and of protection of intellectual property are well-established within the consortium," Estivill explains. "Particular care is provided when dealing with patients' data that we will collect, discuss and might exchange within the consortium. Secondly, researchers in the project who are not familiar with these ELSI issues will be directly involved in debates on the ethical and societal implications of their work." **ddn**

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