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Short Report

From systems biology and functional genomics to personalized health

5th Biologie Prospective Santorini Conference, Island of Santorini, Greece, September 30–October 2, 2010

The 5th Santorini Conference, organized by *Biologie Prospective* (Prof. Gérard Siest) and the university Cardiovascular Genetics team, EA 4373 (Dr. Sophie Visvikis-Siest), brought together 170 participants from the academic and industrial world of 30 different countries.

For the first time it was organized jointly with the AACC (American Association of Clinical Chemistry) and the CSLM (Chinese Society of Laboratory Medicine).

Three major topics were developed over three days: Systems Biology, Nutrigenomics, and Pharmacogenomics, illuminated particularly by genome-wide association studies.

The conference started with a satellite meeting specifically on genome-wide association studies (GWAS). The successive speakers – John P.A. Ioannidis (Stanford University, USA), Philippe Froguel (UMR 8199, CNRS and Institut Pasteur, Lille, France; Genomic Medicine, Imperial College London, UK), Sophie Visvikis-Siest (EA 4373 Cardiovascular Genetics, Henri Poincaré University, Nancy, France), and Eleftheria Zeggini (Wellcome Trust Sanger Institute, Cambridge, UK) – showed how this approach is developing with the aim of identifying novel variants of chronic diseases. Applications in type 2 diabetes, cardiovascular diseases, and pancreatic or neuropsychiatric conditions have all revealed potential new markers with openings towards gene-gene and gene-environment interactions. Limitations were also openly discussed, in particular differences between populations, as well as the importance of demonstrating the effects of structural variants.

Allen Roses (Deane Drug Discovery Institute, Durham, NC, USA) also presented a new aspect for predicting Alzheimer's disease by sequencing a specific region involving the Apo E and TOMM 40 (a mitochondrial transporter) genes. The risk can be estimated better from studying their linkage.

In addition to all these papers, there were presentations by manufacturers (Genomatix, Illumina, Bruker, and Affymetrix) who, through the quality of their devices, have greatly contributed to the development of this discipline.

The conference then went further into the subject with a very stimulating presentation by Andreas Papassotiropoulos (University of Basel, Switzerland) on the links between genetics and memory in man. Using genetic markers, such relationships can be demonstrated for emotional memory and certain medicinal compounds can be tested. Often, however, cellular models simpler than the human must be used to be able to progress more rapidly.

Knowledge of epigenetics can also be integrated into a systems biology strategy, and although these data allow the evolution of man to be understood, they can also be useful for better defining the metabolic pathways that are involved in multifactorial diseases. The proteins found in these pathways are no longer simple markers but are directly involved through being multiprotein complexes, the allosteric and cooperative properties of which must be integrated.

In this systems biology approach, the effect of the environment, in particular of biological rhythms, is useful information for adapting treatments and doses, for example, of anticancer drugs. Here again, cellular modeling provides a great deal of information.

Inflammation is often at the heart of any chronic condition. After a short session on infectious diseases such as AIDS and tuberculosis, with propositions for new markers, the following papers highlighted the major similarities between rheumatoid and atherosclerotic conditions, often through the involvement of NF-κB transcription factors. Lipid activators or mediators are also implicated in the regulation and control of these inflammatory processes. Micro-RNAs and heat shock proteins have been suggested as potential biomarkers, but discoveries in this area could be derived from new screening strategies using novel methods based on antibodies produced against the atherosclerotic plaque proteins subsequently identified in the plasma by mass spectrometry.

The second day was dominated by nutrigenomics which aims at a better understanding of the individual responses that we each have on ingesting proteins, carbohydrates, and lipids. Owing to very sophisticated mass spectrometry methods and other physicochemical techniques, trials on healthy volunteers subjected to different diets have shown variations in the metabolites in the plasma, particularly the amino acids. Owing to these results the capacity for adaptation over time can be tested, and its variation in each individual.

More specific papers showed the effects of variations in unsaturated fatty acids or zinc on the response to glucose or cytokines measured in the plasma of obese children or diabetic or insulin-resistant patients. Circulating blood cells can sometimes form interesting substitutes for following variations in tissue which are difficult to access.

Finally, the last day was entirely dedicated to pharmacogenetics and pharmacogenomics. After an introduction recalling the history and development of this discipline by Urs A. Meyer (Biozentrum, Basel University, Switzerland), examples were

discussed of the usefulness and difficulties of using genetics to predict reactions to treatment with antivirals, statins, anticoagulants or aggregation inhibiting agents. Variable effects in populations such as Chinese and Thai have been found for certain antidepressant drugs.

In a morning devoted to fundamental progress, the influence of transcription factors and regulator regions on small RNAs established a new basis for our understanding of drug interactions. As well as oxidative enzymes and P450 cytochromes, the function of transporters is now seen as being more and more important: they are also involved in interactions between drugs and natural substances. Finally, the variation in all of these enzymes should not be forgotten in the diseases of organs containing them, particularly the liver.

Pharmacogenetics is not limited to drug metabolism but also concerns the pharmacological targets, particularly G proteins which are an integral part of many surface receptors and neurotransmitters. They influence the response to antidepressant treatment, vasoconstrictor and lipolytic effects via many specific mechanisms.

Finally, in a more practical session and round table led by Bryan Dechairo (Medco Health Solutions Inc, Bethesda, MD, USA) and Alain Huriez (Europe Personalized Medicine Diagnostics – EPEMED – and TcLand Expression, Nantes, France), the very slow introduction of genetic and genomic markers in personalized therapy was discussed following specific presentations on the pharmacogenomics of cardiovascular, immunosuppressant, antidepressant, and anticancer drugs.

A more detailed account of the conference and the round table will also be published in *Personalized Medicine* and *Pharmacogenomics*.