We are proud to present this special one-day symposium, bringing together a number of distinguished thought leaders who will describe how they are implementing integrated systems approaches in their work. The planned presentations span a range of scientific disciplines and will be beneficial to anyone seeking to apply integrated systems approaches in their own research.

**Agenda**

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<th>Time</th>
<th>Session</th>
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<td>8:30 a.m.</td>
<td>Arrival, Continental Breakfast</td>
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| 9:00 a.m. – 9:15 a.m. | Welcome and Introductions  
Mary McBride, Agilent Technologies |
| 9:15 a.m. – 10:00 a.m. | The blood exposome and its role in disease etiology  
Steve Rappaport, UC Berkeley |
| 10:00 a.m. – 10:15 a.m. | Break |
| 10:15 a.m. – 11:00 a.m. | An 'Omic Checkup: Longitudinal Multi-omics for Personalized Medicine  
Brian Piening, Stanford U. |
| 11:00 a.m. – 11:45 a.m. | The Exposome: Identifying Drugs and Food Components in Human Cohort Samples Using Untargeted Metabolomics  
Oliver Fiehn, UC Davis |
| 11:45 a.m. – 12:45 pm | Lunch (provided) |
| 12:45 p.m. – 1:30 p.m. | A paleo-multiomics study of the stomach content of oldest human ice mummy the 5300y old Tyrolean Iceman or Otzi  
Rudolf Grimm, Agilent Technologies |
| 1:30 p.m. – 2:15 p.m. | Catalyzing Systems Medicine and Proactive P4 Medicine through a Longitudinal, Digital-Age Study of Well Individuals  
Rob Moritz, Institute for Systems Biology |
| 2:15 p.m. – 2:30 p.m. | Break |
| 2:30 p.m. – 3:15 p.m. | High Throughput Workflow for Metabolomic Profiling of Biological Samples  
Vaughn Miller, Agilent Technologies |
| 3:15 p.m. – 3:30 p.m. | Wrap up  
Mary McBride, Agilent Technologies |
| 3:30 p.m. – 4:30 p.m. | VIP Reception |

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THE BLOOD EXPOSOME AND ITS ROLE IN DISEASE ETIOLOGY

Stephen M. Rappaport, Ph.D., Professor of Environmental Health, University of California, Berkeley

While many researchers examine the genome to discover the causes of complex disorders, evidence points towards the exposome—the totality of exposures received by an individual—as being the primary cause of chronic diseases. Since exposures are inherently chemical in nature and arise from varied sources—foods, drugs, pollutants and human and microbiota metabolism—untargeted analysis of chemicals in human blood can be used to characterize exposomes. Causal exposures can be pinpointed by conducting exposome-wide association studies (EWAS) that compare blood concentrations of scores of chemicals between disease cases and controls.

AN ‘OMIC CHECKUP: LONGITUDINAL MULTI-OMICS FOR PERSONALIZED MEDICINE

Brian Piening, Ph.D., Postdoctoral Research Associate, Stanford University School of Medicine, Palo Alto, CA

With recent refinements and cost reductions in next generation sequencing (NGS), liquid-chromatography mass spectrometry and other high-throughput biomolecular technologies, our ability to implement ‘omics profiling for individualized healthcare is closer than ever. Here, I will describe a pipeline recently implemented at the Stanford Center for Genomics and Personalized Medicine that combines whole-genome sequencing with the regular monitoring of an immense spectrum of bioanalytes in blood and the microbiome. We have recently deployed this approach in a multi-year study of patients at risk for the development of type 2 diabetes mellitus (T2DM), monitoring these individuals over periods of health, disease and dietary perturbation. From these data we can reconstruct biological networks associated with health, illness and metabolic alteration that span genetic variation, gene and protein expression changes, the metabolite output of these cellular pathways as well as repopulation of the gut microbiome. In total, these large-scale longitudinal data offer a behind-the-scenes view of the complex biomolecular changes that underlie the transition between healthy and disease states.

THE EXPOSOME: IDENTIFYING DRUGS AND FOOD COMPONENTS IN HUMAN COHORT SAMPLES USING UNTARGETED METABOLOMICS

Prof. Oliver Fiehn, Ph.D., Director, West Coast Metabolomics Center, UC Davis Genome Center

The NIH West Coast Metabolomics Center at UC Davis employs accurate mass GC-QTOF MS and reverse phase as well as HILIC UPLC-QTOF MS platforms to screen for metabolic differences in blinded human cohort samples, for example in lung cancer or cardiovascular studies. Comprehensive analyses of these samples identifies over 150 primary metabolites and more than 300 individual complex lipids in lipidomic screens, in addition to specific metabolites such as S-adenosylmethionine, 1-methylcytosinamide, trimethylamine-N-oxide, carnitines, betaines or other polar cationic metabolites. While our focus is to reveal metabolic dysregulation that precedes or informs about human diseases, human cohort studies benefit from information that can further stratify or constrain groups of subjects and that could complement tools such as Food Frequency Questionnaires or co-medication information. Untargeted metabolomics with comprehensive mass spectral fragmentation analysis can yield such data. We give examples how the NIH West Coast Metabolomics Center found dozens of pharmaceutical agents in human lung tissue as well as in blood plasma of larger cohort studies. We highlight how the general metabolomics workflow helps detection and unambiguous identification of xenobiotics such as food components, pharmaceuticals as well as illicit drugs. We regard these results as significant validation towards the concept of comprehensive exposome analysis.

A PALEO-MULTIOMICS STUDY OF THE STOMACH CONTENT OF OLDEST HUMAN ICE MUMMY THE 5300Y OLD TYROLEAN ICEMAN OR OTZI

Rudolf Grimm, Agilent Technologies, Inc., Santa Clara, CA

Ötzi the Iceman is a well-preserved natural mummy of a man who lived about 5300 years ago. The mummy was found in September 1991 in the Ötztal Alps, hence Ötzi, near the Similaun mountain and Hauslabjoch on the border between Austria and Italy. He is the oldest known natural human ice mummy. We performed the first paleo-metomics study of this famous mummy including genomics, proteomics, glycomics, metabolomics, lipidomics and metallomics approaches. Complex multomics data will be presented from samples taking out of his stomach. Interesting insights will be given in his last meal(s) and health conditions before he got killed.

CATALYZING SYSTEMS MEDICINE AND PROACTIVE P4 MEDICINE THROUGH A LONGITUDINAL, DIGITAL-AGE STUDY OF WELL INDIVIDUALS

Robert Moritz, Ph.D., Institute for Systems Biology, Seattle, WA

Systems medicine is the application of systems-biology approaches to disease. At ISB, we are integrating biology, technology and computation approaches to create a predictive, personalized, preventive and participatory approach to medicine. This P4 Medicine will use this systems or holistic approach to analyze the enormous amounts of molecular, cellular, phenotypic and medical data that now can be generated for an individual. The goals are to prevent disease by identifying perturbations in biological networks, and countering those perturbations through therapeutic intervention. I will describe our plan to introduce P4 medicine into the current healthcare system with a P4 pilot program—a longitudinal, digital-age study on 100,000 well patients. We are already 10 months into a study of 107 well individual and the preliminary results from these studies are striking. To support this effort, we have developed new systems and repositories. I will discuss some of these tools that are capable of generating quantitatively accurate datasets. Examples of these include our developments in targeted proteomics utilizing SRM and applications to quantitative P4 Medicine.

HIGH THROUGHPUT WORKFLOW FOR METABOLOMIC PROFILING OF BIOLOGICAL SAMPLES

Vaughn Miller, Agilent Technologies, Inc.

Traditional LC/MS methodology is a powerful tool for performing metabolomic profiling of biological samples. However, the long chromatographic run times of 5-50 minutes often limit a user’s ability to optimize analytical methods or run large cohorts of samples in a timely and cost-effective manner. We have recently developed a high throughput workflow for metabolomics profiling utilizing the Agilent RapidFire SPE/MS system which is capable of performing MS-based analysis at speeds of <15 seconds per sample. Such speedy sample analysis facilities the efficient profiling of large data sets and has the ability to utilize multiple chromatographic chemistries or SPE methods. An overview of this new workflow which incorporates SPE/MS with data analysis software tools will be presented along with examples of the metabolomic profiling of human urine samples.

This information is subject to change without notice.