Friends and Colleagues,

HMT stands unique as a metabolomics resource with our capillary electrophoresis and quantitative approach to provide sensitive, comprehensive and quality metabolite profiling. In this May issue we are emphasizing our quantitative platforms. Tateishi et al. used our F-SCOPE platform to determine the C-13 flux of glycolytic intermediates in NAMPT pathway. They were able to identify inhibitors of the NAD+ pathway to attenuate glycolysis and induce cytotoxicity in glioblastomas. While Hirata et al. used F-SCOPE to measure isotopomers of C-13 glucose to establish FBP1 downregulation in HCC contributes to tumor progression and poor prognosis. Finally, Yoshimi et al. used our C-SCOPE platform to discover potential serum biomarkers for bipolar disorder progression.

I encourage you to use our quantitative options for your research needs and share our capabilities with others in your field.

Please note our current sales campaign and enjoy our interview with our co-founder, Professor Tomoyoshi Soga.

Sincerely,

Alexander Buko, PhD
Vice President
Human Metabolome Technologies America

HMT special interview

Professor Tomoyoshi Soga
Institute for Advanced Biosciences, Keio University

At the AACR Annual Meeting 2016 in New Orleans, we met with Dr. Tomoyoshi Soga, co-founder of Human Metabolome Technologies and professor at the Institute for Advanced Biosciences, Keio University. Professor Soga pioneered the development of capillary electrophoresis - mass spec (CE-MS) and actively leads metabolomics studies with this unique technology. We asked professor Soga about his research goals and the advantages of CE-MS technology.

Q. How did you get interested in CE-MS based metabolomics?

I started the development of CE while working for Agilent (formerly Hewlett-Packard). At first, I used stand-alone CE systems for the measurements of a variety of samples taking advantage of the unique separation ability of CE. However, I was limited to the identifications of analytes using
typical CE detectors. I then became inspired that the combination of the high resolution CE systems with mass spectrometry (MS) would enable me to measure and identify many more complex compounds. At this time my major targets for CE were not biological metabolites, but small anions and cations, because the concept of large scale metabolomics had not yet been established. However, I observed that many compounds involved in the primary metabolic pathways have hydrophilic and ionic properties, and their size and charge would be appropriate targets for CE-MS measurements. About this time I heard of an opportunity at Keio University for researchers to develop metabolomics platforms to support the growing needs from a multi-omics approach. It is at Keio University that I began to develop the CE-MS platform and CE-MS based metabolomics.

Q  What are the advantages of using CE-MS for metabolomics?

Because of the complexity of the metabolome, a separation of metabolite extracts is preferred to obtain the best analysis, hence liquid chromatography (LC) and gas chromatography (GC) have been used to separate complex metabolomes before MS analysis. While no separation method is universal, CE-MS has several advantages. CE has superior separation resolution capability for polar, ionic metabolites over reverse phase LC and GC techniques providing unique identifications and measurements of selected analytes. Using CE separation we can resolve and measure many key charged metabolite intermediates and isomers, especially those involved in the primary biological pathways using only a single method. In addition, CE is fast. Run times, efficient capillary washing and short re-equilibration times make for fast turnover from sample to sample. These efficiencies allow for fast analysis times and easier method optimization. With CE separations, we use simple electrolyte solutions. Combined with efficient mass transfer we minimize the ion suppression in MS that typically limits the detection and dynamic range in LC-MS metabolomics. Lastly, and importantly, CE-MS provides a better quantitative capability which adds critical value to metabolite profiling data. Lower ion suppression provides a better environment for accurate quantitation for biological samples (ref. 1). Superior resolution, separation of isomers, efficient mass transfer and lower ion suppression allow for high sensitivity, low variability and large dynamic range for quantitative analysis.

Q  What is the current focus in your group?

We are working on the characterization of metabolism in human tumor tissues. I believe that the value of our technology must be evaluated by not just its technical capabilities, but also by what problems it can address. Even with excellent technology, applications provide the true value. Cancer metabolism pathways are dominated by compounds favored for CE-MS analysis. For example, phosphorylated hexose intermediates, ATP, NADH and Acetyl-CoA are key glycolytic bioenergetic metabolites in cancer research easily measured by CE-MS. I believe we can provide valuable information and support in cancer metabolism using CE-MS. I am impressed with the advancements in cancer research in the United States and the key discoveries in cancer metabolism in recent years. However, a large part of those finding are based on in vitro studies using cultured cells, or xenograft models, which sometimes are insufficient to reflect the native and complex metabolic status in human conditions. My group has accumulated metabolic profiling data from many patient tumor biopsy samples. We hope to provide metabolic details about the biological changes in tumorigenesis. I am now preparing a review based on this approach to be published soon.

Q  Aside from cancer research, what other areas are driving metabolomics?

For many other diseases and conditions, the understanding of in vivo metabolism, i.e., the metabolic signaling between organs in the body, needs better understanding. For example, with exercise, metabolic changes in skeletal muscle are well known to affect the metabolism in other tissues including liver, heart, brain etc. We need to establish better models and approaches to understand metabolic changes in cells, tissues, organs and biofluids, including the gut microbiome for a complete picture of human metabolism.
What are your ideas about the future of HMT?

CE-MS based metabolomics is unique and has advantages which cannot be achieved by other conventional platforms such as LC-MS and GC-MS. Because of its uniqueness, it might take time to grow and prove its value. However, I expect HMT will achieve this goal by providing reliable, sensitive and quantitative data with full statistical and biological services supporting their client’s goals for mechanism of action, fundamental pathway analysis or biomarker discovery. On the other hand, the technological improvements by instrument manufacturers will challenge HMT’s uniqueness in this field so HMT must adapt to a changing and growing metabolomics field. I believe that HMT is not only providing critical and significant analysis services today, but also will create new possibilities based on this exciting technology.

References

Professor Tomoyoshi Soga
Institute for Advanced Biosciences, Keio University, Japan
Dr. Soga graduated with a B.S. from Keio University. He then spent 17 years as an application chemist for HPLC and CE at Agilent Technologies Inc. (formerly Hewlett-Packard Company) before earning his Ph.D. at Toyohashi University of Technology in 2000. He has been a pioneer for the development of CE-MS based metabolomics and in 2003 co-founded Human Metabolome Technologies Inc. (HMT). Currently, he is a professor at the Institute for Advanced Biosciences and adjunct professor at the School of Medicine, Keio University. (soga@sfc.keio.ac.jp)

HMT Updates

Campaign

Special Offer for metabolic profiling
Basic Scan or CARCINOSCOPE package: $4,000 / 6 samples

- Suitable for small polar molecules
- Variety of samples Cells, Tissues, Blood, Stool etc.
- Full statistical analysis and biological interpretation
- Offer expires on May 20, 2016

Featured articles

Myc-driven glycolysis is a therapeutic target in glioblastoma.

Deregulated Myc drives an oncogenic metabolic state, including pseudohypoxic glycolysis, adapted for the constitutive production of biomolecular precursors to feed rapid tumor cell growth. In glioblastoma (GBM), Myc facilitates renewal of the tumor initiating cell reservoir contributing to tumor maintenance. We investigated whether targeting the Myc-driven metabolic state could be a selectively toxic therapeutic strategy for GBM.

Link to Journal web site
Fructose-1,6-bisphosphatase (FBP1), the rate-limiting enzyme in gluconeogenesis, is reduced in expression in certain cancers where it has been hypothesized to act as a tumor suppressor, including in hepatocellular carcinoma (HCC). Here we report functional evidence supporting this hypothesis, providing a preclinical rationale to develop FBP1 as a therapeutic target for HCC treatment.

Link to Journal web site

Blood metabolomics analysis identifies abnormalities in the citric acid cycle, urea cycle, and amino acid metabolism in bipolar disorder.

Bipolar disorder (BD) is a severe and debilitating psychiatric disorder. However, the precise biological basis remains unknown, hampering the search for novel biomarkers. We performed a metabolomics analysis to discover novel peripheral biomarkers for BD. We quantified serum levels of 116 metabolites in mood-stabilized male BD patients (n = 54) and age-matched male healthy controls (n = 39). After multivariate logistic regression, serum levels of pyruvate, N-acetylglutamic acid, α-ketoglutarate, and arginine were...

Link to Journal web site

HMT is a leading company providing metabolomic profiling based on unique and high performance CE-MS technology. We complete over 400 projects a year and our technology has contributed to the advancement of research in a variety of scientific areas.

Edited by Takushi Oga, PhD