



HMT Newsletter

Dear Friends,

As the first day of spring approaches, HMT America celebrates our 3rd year bringing our metabolomics capabilities to a global presence. It is only fitting that HMT Japan has just announced this month our new company, HMT Biomedical, dedicated to biomarker development. Whether we are working with clients across the US, presenting seminars in England and Scotland or expanding our support in Japan, I am proud of how HMT continues to build on our successes providing state-of-the-art quantitative metabolomics to a global community.

Sincerely,

Tsutomu Hoshiba
CEO
Human Metabolome Technologies America

HMT Updates

News release

HMT founds new company to accelerate biomarker business

On February 1st, HMT has founded a new company, HMT Biomedical, Inc., which will focus on the development and marketing of diagnostic biomarkers. The CEO, Mr. Toshiyasu Miyazaki said "We are happy to announce that HMT established new group company, HMT BioMedical Inc. for starting new activity to provide novel bio-markers, based on our metabolomics platform. We are planning to release our product for detecting the bio-marker which related with Major Depression Disorder, as research use only reagent in 2017, and will release our next product as in vitro diagnostic reagent in 2019."

Focused topics

HMT in-house seminar

"Quantitative Metabolic Profiling - On the Critical Path for Understanding Cancer Metabolism - "

We continue to travel presenting seminars focusing on the capabilities of CE-MS metabolomics and recent applications of cancer metabolism. HMT thanks all of those attending our seminars in the US and UK and for the valuable discussions that follow.

A deeper understanding of cancer metabolism requires quantitative analysis to establish specific metabolomic pathways, as well as, metabolic flux. More and more cancer researchers are turning to HMT for their quantitative profiling and flux analysis. Our latest presentations were in New York and the UK:

Weill Cornell Medical CLC Advanced Technology Seminar

February 11, Weill Cornell Medical College, Weill Greenberg Center, New York, NY, USA

University College London Cancer Center Technical Seminar

February 22, UCL Cancer Institute, Paul O'Gorman Building, London, UK

The Beatson Institute Technical Seminar

February 24, Beatson Institute for Cancer Research, Glasgow, UK

- Please let us know if you are interested in HMT in-house seminar at your site.

Role of metabolism in immunotherapy

In recent years, Immunotherapy has come to the forefront of cancer treatment options. With the discovery of cancer generated immune modulators, it became clear that if we could harness our own immune cells, cancer therapy could be revolutionized. This therapy relies on the stimulation of T-cells and the subsequent generation of CD4⁺ and CD8⁺ T lymphocytes that can effectively recognize tumor antigens. Currently, antibodies targeting T-cell checkpoints are in the clinic with dramatic results. The activation of T-cells however relies on a complex signaling framework resulting in the metabolic transformation of the T-cells. "Altering T cell metabolism can positively affect cell function and longevity, and perhaps placing more consideration on metabolic parameters when designing and implementing adoptive cellular immunotherapy would lead to better patient outcomes." (O, Sullivan and Pearce *et al.*) Typically, naïve or memory T-cells employ oxidative phosphorylation for the purpose of saving energy. However, the stimulation of T-cells into effector cells relies in part on the metabolic switch from oxidative phosphorylation to a primarily catabolic, glycolytic metabolic phenotype. "The engagement/disengagement of aerobic glycolysis represents a crucial mechanism controlling T cell effector status." (Melon *et al.*) The development of successful immune therapies will depend on this metabolic switch whose mechanism has yet to be fully elucidated. Metabolomics will be integral in the elucidation of this mechanism and in the further development of effective immunotherapies.

Continued Reading:

Targeting T cell metabolism for therapy.

David O'Sullivan and Erika L. P. *Trends in Immunology*, **36**: 2, 2015

T Cells and Cancer: How Metabolism Shapes Immunity.

Molon B., *et al. Front Immunol.* **7**: 20, 2016

Distinct Signaling of Coreceptors Regulates Specific Metabolism Pathways and Impacts Memory Development in CAR T Cells.

Kawalekar O.U., *et al. Immunity*, **44**, pp. 380 - 390, 2016.

Featured articles

A Trans-omics Mathematical Analysis Reveals Novel Functions of the Ornithine Metabolic Pathway in Cancer Stem Cells

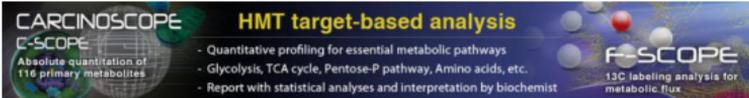
Jun Koseki *et al., Sci. Rep.*, **6**: 20726.

Bioinformatics and computational modelling are expected to offer innovative approaches in human medical science. In the present study, we performed computational analyses and made predictions using transcriptome and metabolome datasets obtained from fluorescence-based visualisations of chemotherapy-resistant cancer stem cells (CSCs) in the human oesophagus. This approach revealed an uncharacterized role for the ornithine metabolic pathway in the survival of chemotherapy-resistant CSCs.

Transketolase counteracts oxidative stress to drive cancer development

Iris Ming-Jing Xu *et al.*, *Proc Natl Acad Sci U S A.* **113**, E725-734.

Cancer cells experience an increase in oxidative stress. The pentose phosphate pathway (PPP) is a major biochemical pathway that generates antioxidant NADPH. Here, we show that transketolase (TKT), an enzyme in the PPP, is required for cancer growth because of its ability to affect the production of NADPH to counteract oxidative stress. We show that TKT expression is tightly regulated by the Nuclear Factor, Erythroid 2-Like 2 (NRF2)/Kelch-Like ECH-Associated Protein 1 (KEAP1)/BTB and CNC Homolog 1 (BACH1) oxidative stress sensor pathway in cancers. Disturbing the redox homeostasis of cancer cells by genetic knockdown or pharmacologic inhibition of TKT sensitizes cancer cells to existing targeted therapy (Sorafenib).



CARCINOSCOPE
C-SCOPE
Absolute quantitation of
116 primary metabolites

HMT target-based analysis

- Quantitative profiling for essential metabolic pathways
- Glycolysis, TCA cycle, Pentose-P pathway, Amino acids, etc.
- Report with statistical analyses and interpretation by biochemist

F-SCOPE
13C labeling analysis for
metabolic flux

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. Please find [more information](#) on our website.

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