



# HMT Newsletter

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Dear Researchers,

Welcome to the October 2015 issue of the HMT newsletter. I hope this finds you all in good health and ready for autumn.

We are pleased to announce our newest development in the diagnosis of major depressive disorder (MDD) using our patented metabolite biomarker blood assay with a licensing contract with a global partner, Sysmex. Under this contract Sysmex will develop an assay kit for Phosphoethanolamine (PEA), our biomarker for MDD. This assay can be a corner stone demonstrating metabolomics as a promising health care discovery and clinical field supporting medical diagnostics of disease including psychiatric disorders.

Other research areas of health care that HMT has been exploring includes the understanding of the microbiota and its relationship to disease. In this October issue, we introduce articles showing our approach and results into microbiome research.

Sincerely,

Tsutomu (Tom) Hoshiba  
CEO  
Human Metabolome Technologies America

## HMT Updates

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### Personalized Healthcare

Human Metabolome Technologies, Inc., announced on September, 29th, 2015 a Licensing agreement with Sysmex Corporation (Hyogo, Japan) for the Non-exclusive license of HMT's enzymatic assay for Phosphoethanolamine (PEA), a diagnostic marker of major depressive disorder (MDD).

### Conference Information

**AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics**  
November 5 - 9, Boston, Massachusetts, USA

Please drop by our booth (115) to see what is new and share your research goals with us.

## Featured Articles

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The microbiota is one of the largest sources of metabolites in our body, but its engagement in our body homeostasis is still veiled. The communication between this large bacterial community and host is mediated by substances in the intestine, which include proteins and metabolites. The profiling of these compounds tells us something about signaling molecules, including those that may provide health benefits and those that may challenge our health. Because intestinal metabolites include a variety of water soluble compounds, capillary electrophoresis mass spectrometry (CE-MS) provides quantitative profiling for many metabolic intermediates or products from the microbiota.

## Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome.

Shin Yoshimoto *et al.*, *Nature*, **499**, 97-101, 2013.

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The authors discovered that obesity increases the risk of hepatocellular carcinoma (HCC) in a mouse model depending on the existence of specific microbiota. Based on the hypothesis that specific microbiome products are mediators of tumor induction, they performed a blood metabolome analysis and screening with deoxycholic acid (DCA) as a biomarker of oncogenesis. Interestingly, the regulation of DCA levels influenced the occurrence of HCC, suggesting that DCA is a major signal for obesity and microflora dependent HCC.

## Upregulation of colonic luminal polyamines produced by intestinal microbiota delays senescence in mice.

Ryoko Kibe *et al.*, *Scientific Reports*, **4**: 4548, 2014.

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The production of polyamines by the microflora is thought to influence host quality of life. The authors screened human fecal samples for metabolites that show a strong correlation with polyamine level and discovered that Arginine (Arg) is major precursor of polyamine production in the intestines. Arg intake enhanced polyamine production in the model microbiota system and increased their levels in a mouse body. Furthermore, oral administration of Arg in combination with the probiotic bifidobacteria influenced lifespan and memory function in the mouse model.

## Alteration of the Intestinal Environment by Lubiprostone Is Associated with Amelioration of Adenine-Induced CKD.

Sadayoshi Ito *et al.*, *Journal of the American Society of Nephrology*, **26**, 1787-1794, 2015.

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The authors characterize the changes in the microbiota after the treatment of lubiprostone using a chronic kidney disease (CKD) model. Oral administration altered the microbiome in mice with renal failure, and altered the levels of uremic toxins in the blood. Because these microbiota derived metabolites, such as indoxyl sulfate, hippurate, and recently discovered uremic toxin trans-aconitate, decreased after the treatment, lubiprostone was considered to ameliorate the progression of CKD by improving the microbiota and intestinal environment.

## Our Recent Applications

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### **Mode of Bioenergetic Metabolism during B Cell Differentiation in the Intestine Determines the Distinct Requirement for Vitamin B1.**

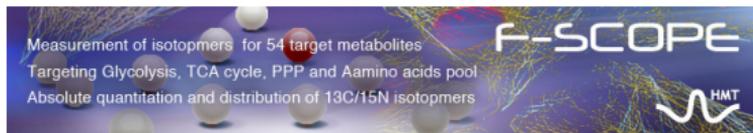
Jun Kunisawa *et al.*, *Cell Reports*, 2015

Bioenergetic metabolism varies during cell differentiation, but details of B cell metabolism remain unclear. Here, we show the metabolic changes during B cell differentiation in the intestine, where B cells differentiate into IgA+ plasma cells (PCs). Naive B cells in the Peyer's patches (PPs) and IgA+ PCs in the intestinal lamina propria (iLP) both used the tricarboxylic acid (TCA) cycle, but only IgA+ PCs underwent glycolysis.

### **Role of CCN2 in Amino Acid Metabolism of Chondrocytes.**

Yurika Murase *et al.*, *Journal of Cellular Biochemistry*, 2015

CCN2/connective tissue growth factor (CTGF) is a multi-functional molecule that promotes harmonized development and regeneration of cartilage through its matricellular interactions with a variety of extracellular biomolecules. Thus, deficiencies in CCN2 supply profoundly affects a variety of cellular activities including basic metabolism. A previous study showed that the expression of a number of ribosomal protein genes was markedly enhanced in Ccn2-null chondrocytes. Therefore, in this study, we analyzed the impact of CCN2 on amino acid and protein metabolism in chondrocytes. Comparative metabolome analysis of the amino acids in Ccn2-null and wild-type mouse chondrocytes revealed stable decreases in the cellular levels of all of the essential amino acids.



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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