



# HMT Newsletter

Dear Researchers,

The calendar tells me that it's April, but since we just endured our 10th weekend in a row with a snow storm, I'm not so sure. Yet opening day of the baseball season is nearly here and I am already planning some sunny summer afternoons with a cold beer and the Red Sox. There's nothing better - unless of course they end up in last place again this year! I hope that wherever you are, spring is in the air.

The role of metabolism in cellular differentiation has generated a lot of attention recently. Because the metabolic changes associated with cellular differentiation show strong parallels to similar changes in cancer cells, metabolomics can be a powerful platform to integrate knowledge discovered in these two areas. We will be present at AACR 2015 in Philadelphia. Please stop by our booth 1657 to discuss your metabolomics needs or questions. We are looking forward to talking with you and supporting your research goals.

Sincerely,  
Tsutomu Hoshiba  
President  
Human Metabolome Technologies America

## HMT Updates

### Conference Information

#### American Association for Cancer Research (AACR) Annual Meeting 2015

April 18-25, Pennsylvania Convention Center, Philadelphia, PA  
Booth No. 1657

HMT will join AACR in support of research in cancer metabolism. We will also introduce our new quantitative service packages for isotope labeling analysis with several applications. Please drop by our booth to see what is new and share your research with us so we can create the right metabolic profile to meet your needs.

## Cellular differentiation

Oxidative respiration is involved in osteoclast differentiation to supply epigenetic substrate.

### **DNA methyltransferase 3a regulates osteoclast differentiation by coupling to an S-adenosylmethionine-producing metabolic pathway.**

Keizo Nishikawa *et al.*, *Nature Medicine*, **21**, 281-287, 2015

DNA methyltransferase 3a (Dnmt3a) is identified as a transcription factor regulating osteoclastogenesis via epigenetic repression of anti-osteoclastogenic genes. The expression of Dnmt3a is increased under the stimulation by an essential cytokine receptor activator of nuclear factor- $\kappa$ B ligand (RANKL) and accompanied with activation of oxidative metabolism for the supplement of methyl donor, S-adenosylmethionine (SAM). This study highlights the importance of monitoring energetic metabolism in the epigenetic process of cellular differentiation.  
<http://www.nature.com/nm/journal/v21/n3/abs/nm.3774.html?lang=en>

### Lysine demethylase LSD1 coordinates glycolytic and mitochondrial metabolism in hepatocellular carcinoma cells.

Akihisa Sakamoto *et al.*, *Cancer Research*, 2015 (Online First: February 3)

Lysine specific demethylase-1 (LSD1) has an essential role in human hepatocellular carcinoma (HCC) cells not only as an epigenetic factor, but also as a metabolic regulator involved in the shift from mitochondrial to glycolytic metabolism. Inhibition of LSD1 reduced glucose uptake and glycolytic activity via the inactivation of hypoxia-inducible factor HIF-1 $\alpha$  thus modulating expression of GLUT1 and glycolytic enzymes. By contrast, LSD1 inhibition activated expression of a set of genes for mitochondrial metabolism with concomitant increase of methylated histone H3 at lysine 4 in the promoter region. This study demonstrates the important role of epigenetic factors in metabolic adaptation of cancer cells.

<http://cancerres.aacrjournals.org/content/early/2015/02/03/0008-5472.CAN-14-1560.abstract?sid=3b1d845f-d706-415a-b014-77f158961f65>

### Recent Publications

L-cysteine reversibly inhibits glucose-induced biphasic insulin secretion and ATP production by inactivating PKM2. [*Proc. Natl. Acad. Sci. U S A*, **112**, E1067-1076, 2015]

<http://www.pnas.org/content/112/10/E1067.long>

Lysine-specific demethylase 2 suppresses lipid influx and metabolism in hepatic cells.

[*Molecular and Cellular Biology*, **35**, pp. 1068-1080, 2015]

<http://mcb.asm.org/content/35/7/1068>

Pyruvate kinase M2, but not M1, allele maintains immature metabolic states of murine embryonic stem cells. [*Regenerative Therapy*, **1**, pp. 63-71, 2015]

<http://www.sciencedirect.com/science/article/pii/S2352320415000103>

Regulation of Primary Metabolic Pathways in Oyster Mushroom Mycelia Induced by Blue Light Stimulation: Accumulation of Shikimic Acid. [*Scientific Reports*, **5**:8630, 2015]

<http://www.nature.com/srep/2015/150227/srep08630/full/srep08630.html>

Manual therapy ameliorates delayed-onset muscle soreness and alters muscle metabolites in rats. [*Physiological Reports*, **3**, e12279, 2015]

<http://physreports.physiology.org/content/3/2/e12279.most-read>

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: <http://humanmetabolome.com/en/applications.html>



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