HMT Newsletter

Dear Friends,

As the long and record breaking Boston winter starts to show some signs of ending, I hope you too, wherever you live, are seeing some signs of spring. The good news here is that HMT's biomarker for depression has been approved by the U.S. Patent Office, and a new collaboration with Jiai Hospital in Japan has started. We at HMT hope this will help those suffering from this terrible illness. Additionally, HMT won the Nippon Bio Venture Award for 2015. We are pleased that our cutting-edge technology from Tsuruoka has been recognized for innovation in the biotech community.

Sincerely,

Tsutomu Hoshiba
President
Human Metabolome Technologies America

HMT Updates

EAP: Patent approval for MDD

HMT announced their patent about diagnostic biomarker of major depression has been approved in USA. United States Patent: 8951739

EAP New Clinical Collaboration

HMT and Toyoko Jiai Hospital signed a contract analysis agreement about diagnostics service for major depression disorder. As part of this collaboration HMT will provide a blood assay service testing for Ethanolaminephosphate (EAP) based on HMT's patent.

HMT wins Nippon Bio Venture Award

The 9th winner of the "Nippon Bio Venture Award", a prestigious award for bio venture companies has been given to a Keio University venture, Human Metabolome Technologies, for their metabolome analysis.

Biomarker

Reduced cerebrospinal fluid ethanolamine concentration in major depressive disorder.

Shintaro Ogawa *et al.*, *Scientific Reports*, 5, 7796, 2015

Amino acids play key roles in the function of the central nervous system. In the search for a biomarker for major depressive disorder (MDD), amino acids and related molecules in the cerebrospinal fluid (CSF) of 52 patients with MDD and 54 matched controls were measured.

Significant differences were found in four amino acid concentrations, but after Bonferroni correction, only ethanolamine (EA) levels remained significantly reduced in depressed patients. When patients with low EA and those with high EA levels were compared, the former had higher scores for overall depression severity and 'Somatic Anxiety' symptoms suggesting EA levels in CSF could be a state-dependent biomarker for a subtype of MDD.

From the metabolomics;The profiling of several primary amino acids and related molecules revealed that EA, which is involved in endocannabinoid metabolism, is a novel marker for the screening of MDD patients. The EA level in CSF was decreased in MDD patients and restored in treated patient groups. Moreover, the correlation between levels of EA and catabolites of neurotransmitters suggests that metabolomics is a powerful screening method for novel markers reflecting neurogenic metabolism in CSF.

Oncology

The drs tumor suppressor regulates glucose metabolism via lactate dehydrogenase-B.

Yukihiro Tambe *et al.*, *Molecular Carcinogenesis,* 10.1002/mc.22258, 2015

The regulation of glucose metabolism by drs, which contributes to suppression of malignant tumor formation was demonstrated by using comparisons of drs-KO and wild-type (WT) mouse embryonic fibroblasts (MEFs). In addition to the increase of extracellular lactate concentration and glucose consumption, intracellular metabolome changes suggested enhanced glycolysis in drs-KO cells. The expression of lactate dehydrogenase (LDH)-B was upregulated at the post-transcriptional level in drs-KO cells and increased LDH-B expression was suppressed by retroviral rescue of drs, indicating that LDH-B plays a critical role in glycolysis regulation mediated by drs. In WT cells transformed by activated K-ras, expression of endogenous drs mRNA was markedly suppressed and LDH-B expression was increased. In human cancer cell lines with low drs expression, LDH-B expression was increased. Furthermore, an LDH inhibitor suppressed anchorage-independent growth of human cancer cells and MEF cells transformed by activated K-ras. These results indicate that drs regulates glucose metabolism via LDH-B, and its down regulation may contribute to the Warburg effect, which is closely associated with the malignant progression of cancer cells.

From the metabolomics; the difference in intracellular metabolism was revealed between drs-KO and WT. From the monitoring of extracellular levels of glucose and its anaerobic metabolism product lactate, significant differences were detected after the late growth phase (Day 3). On the other hand, the intracellular metabolic profile revealed differences in glycolysis and the PPP during the early growth phase (Day 1). This suggests that changes in metabolism can occur earlier than the detection of changes in the extracellular metabolites.

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