HMT Newsletter

Friends and Colleagues,

This month we are excited to report the publication of our manuscript detailing our discovery of the first plasma biomarker for Major Depressive Disorder (MDD). This discovery has led to the development of a clinical assay currently in large scale validation in the US and Europe. Once readily available, this simple test will allow for more definitive diagnoses, personalized treatment plans, and the ability to track treatment response for MDD.

Biomarker discovery is like finding a needle in a haystack, but once found, can result in a significant improvement in the way we diagnose, treat, and monitor disease. The release of a plasma test kit for MDD is an example of personalized medicine from benchtop to bedside.

Sincerely,

Alexander Buko, PhD
Vice President
Human Metabolome Technologies America

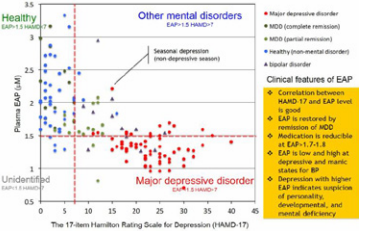
HMT Publication Spotlight

Plasma Metabolome Analysis of Patients with Major Depressive Disorder.

Kawamura N., et al. Psychiatry Clinical Neurosci. 2018 Jan 22

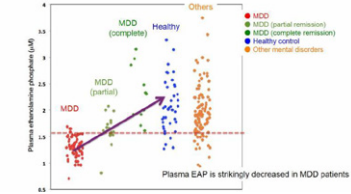
Measurement of plasma ethanolamine (EAP or PEA) correlates with the Hamilton Rating Scale for Depression improving sensitivity and selectivity for diagnosis

Treatment effectiveness of major depressive disorder (MDD) depends on early and accurate diagnostic efficacy. Unlike other medical conditions, there is, presently no practical and established diagnostic method for the objective assessment of MDD severity, subtypes, and treatment response monitoring. Routine medical and behavioral examinations based on interviews conducted by mental health specialists is the only available tool for diagnosing MDD.



However, the reliability of the Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV)-based structured clinical interview diagnosis (SCID) is still between 0.7 and 1.0. Moreover, the SCID is not amenable for clinical utility in the primary care setting, as it requires extensively trained doctors, takes a long time to administer, and is an interview-based psychometric examination. Thus, the need for the development of an objective tool for MDD is long overdue and warranted.

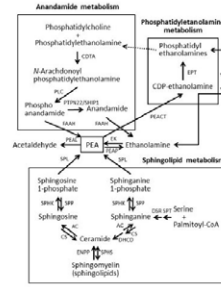
Plasma EAP is unique to MDD and therapeutic response



Not only is EAP significantly reduced in MDD patients compared to healthy controls, but is also independent of other generalized anxiety disorders which are often misdiagnosed. Furthermore, EAP levels will begin to return to normal once treatment is initiated and completed, hence a treatment response biomarker as well.

Biological Significance of EAP

As a phosphomonoester metabolite of phospholipids, EAP (PEA on diagram) is both a precursor and a by-product of phospholipid biosynthesis and breakdown respectively. As a precursor of phosphatidylethanolamine (PE), elevated EAP levels are known to reflect brain phospholipid turnover, an indicator of neural membrane synthesis and signal transduction. Interestingly, GABA binding and uptake are also modulated by an altered membrane level of PE. As a precursor for PE, EAP has been suggested to play a key role in myelination, since significantly high levels of EAP has been reported in purified myelin;and both EAP and taurine have been implicated in important cellular functions including osmoregulation, neuromodulation, and membrane stability. Since EAP lies at a vantage point where various phospholipid biosynthetic pathways converge, its cellular, tissue and organ levels depend a great deal on the relative contributions of the respective pathways; as EAP depends on its on-demand temporal physiological need either as a precursor or metabolite of phospholipids. Myelin EAP is essential for CTP: EAP cytidylyltransferase to catalyze the formation of CDP-ethanolamine for the subsequent completion of brain PE biosynthesis important for neural membrane integrity and signal transduction.



Conclusion

In summary, our discovery and release of a plasma test kit for the diagnosis and treatment response for MDD represents a step forward in personalized medicine and metabolite-based diagnostics.

- Reprints available upon request -

HMT Events

AACR 2018, Chicago, April 14th-18th

Visit our booth #3018 to speak with our metabolomics experts

Featured articles

Comparative analysis of cerebrospinal fluid metabolites in Alzheimer's disease and idiopathic normal pressure hydrocephalus in a Japanese cohort

Nagata Y., *et al., Biomarker Research*. 2018 **6**:5

Key Points:

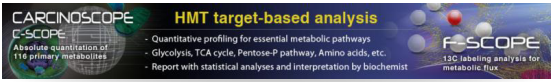
- AD symptoms resemble those of other neurodegenerative diseases, including idiopathic normal pressure hydrocephalus (iNPH), therefore it is difficult to distinguish AD from iNPH for a precise and early diagnosis
- Metabolomic profiling was performed on the CSF of patients with AD and iNPH with capillary electrophoresis-mass spectrometry.
- The authors found significantly increased levels of glycerate and N-acetylneuraminate and significantly decreased levels of serine and 2-hydroxybutyrate in the CSF of patients with AD compared to the CSF of patients with iNPH.
- Study identified four metabolites that could possibly discriminate between AD and iNPH, which previous research has shown are closely related to the risk factors, pathogenesis, and symptoms of AD.

Effects of cold exposure on metabolites in brown adipose tissue of rats

Hiroshima Y., *et al., Molecular Genetics and Metabolism Reports.* June 2018, **15**:36-42

Key Points:

- Brown adipose tissue (BAT) plays an important role in regulation of energy expenditure while adapting to a cold environment.
- BAT thermogenesis depends on uncoupling protein 1 (UCP1), which is expressed in the inner mitochondrial membranes of BAT.
- This study compared the relative levels of metabolites between the BAT of rats kept at room temperature (22°C) and of those exposed to a cold temperature (4°C) for 48 hr.
- The cold environment lead to lower levels of glycolysis and gluconeogenesis intermediates and higher levels of the tricarboxylic acid (TCA) cycle metabolites, fatty acids, and acyl-carnitine metabolites than control conditions in the BAT of rats.
- These results indicate that glycolysis and β-oxidation of fatty acids in BAT are positive biological pathways that contribute to the activation of thermogenesis by cold exposure.



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 Laura Shelton, PhD

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