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Scientists Study New Medications for Depression

San Diego, Calif. (May 1, 2010) – Scientists at the Human BioMolecular Research Institute (HBRI) in San Diego, CA, in collaboration with West Virginia University Health Sciences Center in Morgantown, WV, Oregon Health and Science University and The Methamphetamine Abuse Research Center in Portland, OR, have been studying new approaches to serotonin and norepinephrine re-uptake inhibitors as novel medications development for depression and have published three papers on the subject*. Research showed that combining compounds that have similar functional activity into the same molecules may be effective in treating diseases such as depression.

Numerous clinical studies suggest that serotonin is involved in depression, and that elevating serotonin by serotonin re-uptake inhibition may be useful in treating depression. Certain antidepressants work by inhibiting the re-uptake of serotonin and norepinephrine in the brain. It was also known that inhibition of phosphodiesterase is also associated with antidepressant function. In separate studies, HBRI scientists took serotonin and norepinephrine re-uptake inhibitors, linked them to an inhibitor of phosphodiesterase using a five-carbon chain, and found that the dual inhibitors worked effectively to inhibit phosphodiesterase as well as serotonin and norepinephrine re-uptake, respectively.

To test these agents in small animals, scientists used mice to study the effects of inhibiting phosphodiesterase and serotonin or norepinephrine re-uptake on depressive behavior. The new multi-target compounds synthesized by linking a serotonin re-uptake inhibitor to a phosphodiesterase inhibitor showed promise. It may be that the combination of these two

inhibitors in the same molecule may expedite the antidepressant activity shown in the re-uptake inhibitor alone.

The dual function of serotonin re-uptake inhibition and phosphodiesterase inhibition linked together in the same molecule may be effective in treating depression in humans more rapidly and efficiently than current serotonin re-uptake agents alone.

About HBRI: The Human BioMolecular Research Institute is a non-profit research institute conducting basic research focused on unlocking biological and chemical principles related to diseases of the human brain, cardiovascular disease and cancer. The institute conducts fundamental studies of central nervous system disorders, heart disease and cancer including stem cell approaches and translates findings into new drug development to address human illness. In addition, the institute promotes scientific learning through community service and public access by disseminating information and sharing research with collaborators, colleagues and the public. For more information, visit www.HBRI.org.

***Cashman JR**, Ghirmai S (2009) Inhibition of serotonin and norepinephrine reuptake and inhibition of phosphodiesterase by multi-target inhibitors as potential agents for depression. *Bioorg Med Chem.* **17**:6890-7.

***Cashman JR**, Voelker T, Zhang H-T, O'Donnell JM (2009) Dual inhibitors of phosphodiesterase-4 and Serotonin re-uptake. *J. Med. Chem*. **52:** 1530-1539.

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