Manganese regulation research highlighted as a NIEHS Paper of the Month

The University of Texas at Austin College of Pharmacy professor Dr. Somshuvra Mukhopadhyay’s NIH funded research shows important development in the treatment of Parkinson’s disease

AUSTIN, Texas — The University of Texas at Austin College of Pharmacy continues its research excellence through the accomplishments of its talented and dedicated faculty. Somshuvra Mukhopadhyay, M.B.B.S., Ph.D., assistant professor in the Division of Pharmacology and Toxicology, recently led research focused on how brain manganese is regulated by activity of the gene SLC30A10 in the digestive system. The research was supported by grant funding from the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health (NIH) to Dr. Mukhopadhyay. The NIEHS recently highlighted the research as one of March 2019’s Papers of the Month, a notable accomplishment as just one of numerous NIH-funded research papers released.

The research, titled “SLC30A10 transporter in the digestive system regulates brain manganese under basal conditions while brain SLC30A10 protects against neurotoxicity,” was performed by Dr. Mukhopadhyay’s group at UT Austin with important contributions from the lab of Donald Smith, Ph.D., professor of Microbiology and Environmental Toxicology at the University of California, Santa Cruz. The researchers showed that brain manganese is regulated by activity of the gene SLC30A10 in the digestive system. This finding provides a novel mechanism for how manganese levels are normally regulated and suggests that changes to SLC30A10 activity in the digestive system may affect neurological outcomes from manganese exposure.

"The importance of the digestive system in regulating manganese levels in the brain suggests that drugs, which increase manganese excretion may be useful for the treatment for parkinsonism caused by manganese poisoning,” says Dr. Mukhopadhyay. “This is now a major focus of work in our laboratory."

Previous studies have shown that loss of function of the gene SLC30A10 in the whole body can cause manganese neurotoxicity, but how manganese is regulated is unclear. The researchers compared brain manganese levels in mice lacking SLC30A10 in the whole body to mice lacking SLC30A10 in the liver, brain, and gastrointestinal tract. The researchers observed the
unexpected result that, under normal body conditions, activity of SLC30A10 in the gastrointestinal tract and liver, and not the brain or just the liver, regulated brain manganese. They also found that expression of SLC30A10 in the brain became important when tissue manganese levels increased. With increased manganese exposure, activity of SLC30A10 in the brain reduced manganese levels and protected against neurotoxicity.

“In showing the overall importance of the digestive tract in regulating body and brain manganese,” says Dr. Smith from UC Santa Cruz, “the study findings underscore the importance of understanding how development of manganese absorption/excretion processes in the digestive tract affect susceptibility to manganese exposure and neurotoxicity across the lifespan.” The results described previously unknown complexities in the control of manganese in the brain under normal and elevated exposure conditions.

According to the authors, this may have important implications for treatment of those exposed to toxic amounts of the metal, because the work raised the possibility that drugs that enhance levels or activity of SLC30A10 in the digestive system might increase manganese excretion before it reaches the brain. This may be integral in the ongoing study and treatment of parkinsonism.

The Mukhopadhyay Lab in The University of Texas at Austin College of Pharmacy focuses on understanding cell biology of human disease. Its two major research projects involve parkinsonism and metal homeostasis, and intracellular trafficking of Shiga and related bacterial toxins. This research paper focuses primarily on the first research project. Metals, such as iron, manganese, and copper, are essential for life, but become toxic at elevated levels and cause severe neurological diseases, such as parkinsonism.

Dr. Somshuvra Mukhopadhyay received a Bachelor of Medicine, Bachelor of Surgery at Topiwala National Medical College in Mumbai, India in 2004, and received a Doctor of Philosophy in Cell Biology at New York Medical College in 2008. He was a post-doctoral fellow with Dr. Adam Linstedt at Carnegie Mellon University from 2008 to 2013. Dr. Mukhopadhyay came to The University of Texas at Austin in January of 2013 and works with the College of Pharmacy’s Division of Pharmacology and Toxicology, as well as the College of Natural Sciences’ Institute for Cellular and Molecular Biology, and the Institute for Neurosciences, a multidisciplinary graduate program.

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