For Immediate Release:

Scientists Identify Critical Genes for Down syndrome

Bethesda, Maryland – Down syndrome is a well-known cause of mental retardation and other medical problems, including early onset of Alzheimer disease. It has long been known that Down syndrome is associated with an individual having an additional copy of chromosome 21. Research findings reported in the July 18 advanced online publication of Nature Neuroscience have narrowed down the critical genetic elements responsible for some aspects of Down syndrome.

A team of scientists from the Uniformed Services University of the Health Sciences (USU) and Children’s National Medical Center (CNMC), led by Zygmunt Galdzicki, Ph.D., associate professor of Anatomy, Physiology and Genetics, USU, and Tarik F. Haydar, Ph.D., CNMC, now associate professor, Department of Anatomy and Neurobiology, Boston University School of Medicine, and corresponding author on the study), were able to identify Olig1 and Olig2 as two genes specific to the critical region of chromosome 21 associated with Down syndrome by using a specifically-engineered modification of the golden standard Down syndrome mouse model, Ts65Dn.

Previous studies including those by co-author Tyler Best, Ph.D., while a graduate student at USU, suggested that inhibitory activity is stronger in the Ts65Dn brain. This led researchers at USU and Children’s to hypothesize that genes controlling the inhibitory tone of the brain contribute to the cognitive changes associated with Down syndrome. By manipulating Olig1 and Olig2, genes present on the extra chromosome 21, the researchers were able to normalize key aspects of the inhibitory tone in brain regions involved in learning and memory. Thus, the balance of excitatory to inhibitory neurons is critically regulated by extra copies of these genes and they can drastically modify neurological development in Down syndrome.

“The results of this study demonstrate the critical effects of Olig1 and Olig2 on brain development and, in particular, on inhibitory networks in the brain,” said Dr. Galdzicki. “However, it is likely that additional genes are also involved in the effect. We hope the findings will lead to better strategies for early intervention, even during the pregnancy, to reduce neurological consequences of Down syndrome.

“This study again highlights that research on Down syndrome can provide us with new insight into the mechanisms that regulate brain growth and may help with better understanding other neurodevelopmental disorders such as autism,” he said. “These findings show the need to do more human studies and also suggest that Olig1 and Olig2 inhibitors may have a potential therapeutic role for Down syndrome individuals.”

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The Uniformed Services University of the Health Sciences, located in Bethesda, Maryland, on the grounds of the National Naval Medical Center, is a traditional U.S. academic health center with a unique emphasis on educating the next generation of health care providers and researchers in military medicine, tropical diseases, humanitarian assistance, as well as responses to disasters and other public health emergencies. USU’s nationally ranked military and civilian faculty conduct cutting edge research in the biomedical sciences and in areas specific to the DoD health care mission.