HEIDELBERG, 6 August 2012 – Intellectual disability due to **Fragile X** and **Down syndromes** involves similar molecular pathways report researchers in *The EMBO Journal*. The two disorders share disturbances in the molecular events that regulate the way nerve cells develop dendritic spines, the small extensions found on the surface of nerve cells that are crucial for communication in the brain.

“We have shown for the first time that some of the proteins altered in Fragile X and Down syndromes are common molecular triggers of intellectual disability in both disorders,” said Kyung-Tai Min, one of the lead authors of the study and a professor at Indiana University and the Ulsan National Institute of Science and Technology in Korea. “Specifically, two proteins interact with each other in a way that limits the formation of spines or protrusions on the surface of dendrites.” He added: “These outgrowths of the cell are essential for the formation of new contacts with other nerve cells and for the successful transmission of nerve signals. When the spines are impaired, information transfer is impeded and mental retardation takes hold.”

Intellectual disability is a developmental brain disorder that leads to impaired cognitive performance and mental retardation. Two of the most prevalent genetic causes of intellectual disability in humans are Fragile X and Down syndromes. Fragile X syndrome arises from a single gene mutation that prevents the synthesis of a protein required for neural development (Fragile X mental retardation protein). The presence of all or a part of a third copy of chromosome 21 in cells causes Down syndrome. Although both syndromes arise due to these fundamental genetic differences, the researchers identified a shared molecular pathway in mice that leads to intellectual disability for both disorders.

The mice that were used in the experiments are model systems for the study of Fragile X syndrome and Down syndrome. Down syndrome mice have difficulties with memory and brain function, and the formation of the heart is often compromised, symptoms that are also observed in humans with Down syndrome. Both model systems are very useful to scientists looking to dissect the molecular events that occur as the disorders take hold.

The scientists revealed that the Down syndrome critical region 1 protein (DSCR1) interacts with Fragile X mental retardation protein (FMRP) to regulate dendritic spine formation and local protein synthesis. By using specific antibodies that bind to the proteins as well as fluorescent labeling techniques they showed that DSCR1 specifically interacts with the phosphorylated form of FMRP. The overlapping molecular pathways of intellectual disability in both genetic disorders suggest that a common therapeutic approach might be feasible for both syndromes.

Min remarked: “We believe these experiments provide an important step forward in understanding the multiple roles of DSCR1 in neurons and in identifying a molecular interaction that is closely linked to intellectual disability for both syndromes.”

DSCR1 interacts with FMRP and is required for spine morphogenesis and local protein synthesis

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Read the paper: doi:10.1038/emboj.2012.190