

Abstract 15

dFMRP REGULATES MICROTUBULES AND GENETICALLY INTERACTS WITH THE MICROTUBULE SEVERING PROTEIN SPASTIN

Aiyu Yao, Shan Jin¹, Zhihua Liu, Xuehua Ma, Jing Tang, and Yong Q. Zhang

Key Laboratory of Molecular and Developmental Biology, Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing 100101, China
College of Life Sciences, Hubei University, Wuhan, Hubei 430062, China¹

Fragile X syndrome is the most common form of inherited mental retardation worldwide caused by the absence of fragile X mental retardation protein FMRP. FMRP represses the translation of microtubule associated protein 1B (MAP1B) and is required for the accelerated decline of MAP1B during active synaptogenesis in mouse neonatal brain development. dFMRP, the *Drosophila* homologue of FMRP, acts as a translational repressor of Futsch (the fly homolog of MAP1B) to regulate the growth and function of neuromuscular junction synapses. But the effect of FMRP on microtubules remains elusive. We report here that *dfmr1* mutants showed increased perinuclear microtubule density with defective microtubule network, while overexpression of *dfmr1* led to parallel bundles of microtubules instead of regular microtubule network in wild type. Similar microtubule defects were found in cell cultures from Fragile X patients. We also observed abnormal morphology of mitochondria and aberrant axonal transport of mitochondria in *dfmr1* mutant neurons. Genetic analyses revealed a synergistic interaction between *dfmr1* and *spastin*, which encodes the microtubule-severing protein Spastin, in regulating microtubule network formation, synapse development, and locomotion. Mutations in *spastin* result in a common neurodegenerative disease called hereditary spastic paraplegia. These results together indicate that dFMRP plays a critical role in controlling microtubule cytoskeleton, and that defective microtubules might account for, at least partially, the pathogenesis of Fragile X mental retardation.