Zhiheng Xu, J Cell Sci Ther 2016, 7:1 (Suppl)
http://dx.doi.org/10.4172/2157-7013.C1.035

OMICS International
conferenceseries.com

6th World Congress on
Cell & Stem Cell Research
February 29-March 02, 2016 Philadelphia, USA

MEKK3 coordinates with FBW7 to regulate microcephaly associated protein WDR62 and neurogenesis

Zhiheng Xu
Chinese Academy of Sciences, China

Human autosomal recessive primary microcephaly (MCPH) is a neural developmental disorder hallmarked by significantly reduced brain size and variable intellectual disability. Mutation of WD40 repeat protein 62 (WDR62) is the second major cause of MCPH. We have reported recently that WDR62 regulates the maintenance of neural progenitor cells (NPCs) during cortical development through JNK1. However, the detailed biological function of WDR62 and the underlying mechanism by which WDR62 regulates JNK signaling are still not very clear. Here, we demonstrate that MEKK3 forms a complex with WDR62 to promote JNK signaling synergistically and regulate neurogenesis as well as brain size. MEKK3, WDR62 and JNK1 depletion or knockout phenocopy each other are in defects including premature NPC differentiation and reduced brain size. These defects can be rescued by the expression of transgenic JNK1, indicating that the complex controls neurogenesis through JNK signaling. We show further that WDR62 protein level is positively regulated by MEKK3 through JNK1-induced WDR62 phosphorylation. Meanwhile, WDR62 is also negatively regulated by specific phosphorylation of WDR62 at T1053, leading to the recruitment of the E3 ligase FBW7 and proteasomal degradation of WDR62. Our findings demonstrate that WDR62 controls the maintenance of NPCs via MEKK3 and JNK1 during cortical development and reveal the molecular mechanisms underlying MCPH pathogenesis.

Biography

Zhiheng Xu was awarded with MD in 1989 from the Second Military Medical University, Shanghai and a PhD in 1999 from Rutgers University, New Jersey. In 1999, he was a Postdoctoral and Research Associate at Columbia University, New York. He has received the Ruth L Kirschstein National Research Service Award in 2003 and the Distinguished Young Investigator Award, National Science Foundation (China) in 2007.

zhxu@genetics.ac.cn

Notes: