特別講演会のお知らせ

演題：Mitigation of non-canonical BMP signaling ameliorates the synaptic abnormality in Fragile X syndrome

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日時：平成27年2月2日（月）16：00～18：00

場所：北海道大学薬学部1階　第２講義室

主催：北海道大学大学院薬学研究院　日本薬学会北海道支部
共催：日本生化学会北海道支部　　北海道分子生物学研究会

概要

Loss-of-expression or -function of fragile X mental retardation 1 (FMR1) protein (FMRP) causes fragile X syndrome (FXS), a commonly inherited form of cognitive and behavioral abnormality and increases the risk of autism spectrum disorders (ASDs). Molecular pathogenesis of FXS and ASDs as a result of aberrant FMPR, however, is not well understood. Here we report that abnormality in Bone Morphogenetic Protein (BMP) signaling pathway plays an essential role in the pathogenesis of FXS. We found that BMP Receptor, Type 2 (BMPR2) protein expression is regulated at the translation step via the mRNA sequence encoding the carboxyl-terminal domain (CTDseq) by FMRP. At the neuromuscular junction (NMJ) in FMR1 null Drosophila mutants, synaptic abnormalities are progressively rescued by the deletion of one and two alleles of wishful thinking (wit), the Drosophila homolog of the BMPR2. Mutation or absence of FMRP in mouse results in increased expression of BMPR2 and aberrant activation of its downstream signaling pathways and promote actin remodeling mediated by non-canonical BMP signaling via CTD of BMPR2. Mitigating CTD-dependent signal is sufficient to ameliorate neuronal abnormality. Thus, our study raises the possibility that non-canonical BMPR2-CTD-dependent signaling pathway as novel therapeutic targets for the cognitive and behavioral abnormalities in FXS and ASDs.

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