

第89回 埼玉大学脳科学セミナー

主催: 埼玉大学脳末梢科学研究センター

RNAの化学修飾@神経シナプス

Synaptic epitranscriptomics and dynamic RNA imaging

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日時: 2018年3月20日 (火) 16:20~

場所: 理学部 講義実験棟 2番教室

A localized transcriptome at the synapse facilitates synapse-, stimulus-, and transcript-specific synthesis of the local proteome in response to neuronal activity. While enzyme-mediated mRNA modifications have been shown to regulate cellular mRNA turnover and translation, the role of these modifications in regulating synaptic RNA has not been studied. We established low-input m6A-seq of synaptosomal RNA to determine the chemically modified local transcriptome in healthy adult mouse forebrain and identified 4,469 selectively enriched m6A sites in 2,921 genes, which we refer to as the synaptic m6A epitranscriptome (SME). SME is functionally enriched in synthesis and modulation of tripartite synapses, and in pathways implicated in neurodevelopmental and neuropsychiatric diseases. Interrupting m6A-mediated regulation via knockdown of readers in hippocampal neurons alters expression of SME member *Apc*, and causes synaptic malfunctions manifesting immature spine morphology and dampened excitatory synaptic transmission concomitant with decreased PSD-95 clustering and GluA1 surface expression. Our findings indicate that chemical modifications of synaptic mRNAs critically contribute to synaptic function.

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