東北大学脳科学 GCOE セミナー開催のお知らせ

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演題：ELAV-regulated RNA processing in synaptic plasticity

日時：6 月 21 日（火）13：00 から

会場：片平キャンパス・生命科学研究科本館　会議室（3 階）

要旨

The human brain is our most complex organ containing billions of cells often with unique identities and connections to other cells. Yet, we have only about 22'000 genes – about the same as fish and chicken. Alternative splicing is a key mechanism to generate molecular diversity and functional complexity in the brain. How regulation of alternative splicing contributes to the formation of synaptic connections and regulates synaptic plasticity, however, is largely elusive.

Neuron-specific ELAV (Embryonic Lethal Abnormal Visual System) from Drosophila melanogaster is the founding member of a family of proto-type RNA binding proteins including human Hu proteins (HuB-D and HuR). ELAV/Hu family proteins consist of three highly conserved RNA recognition motifs that bind AU-rich elements abundantly present in introns and untranslated regions of mRNAs. ELAV/Hu family proteins generally bind short motifs that are, however, highly redundant on a genomic scale. It is currently not understood how RNA binding proteins achieve gene specific regulation in a complex cellular environment.

We have identified Erect Wing (EWG), a transcriptional regulator homologous to human NRF-1 as a major target of ELAV in Drosophila. ELAV is necessary and sufficient for alternative splicing of ewg and expression of EWG protein, which dose-dependently regulates synaptic growth at third instar neuromuscular junctions (NMJ's).

Through a combination of phylogenomics, in vitro RNA binding studies and in vivo transgene analysis we have identified that multimerization of ELAV is key to gene-specific regulation of ewg pre-mRNA processing.

To obtain insights into ELAV regulated gene-networks operating in the regulation of synaptic growth we employed a functional genomics approach to analyze the role of EWG. Intriguingly, EWG regulates synaptic growth predominantly via genes involved in transcriptional and post-transcriptional regulation of gene expression suggesting an extensive regulatory network operating in this biological process. This gene network further integrates input from all major signaling pathways to regulate a limited number of effector genes.

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