

# **Epigenetic mechanisms underlying brain function**

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Long non-coding RNAs (lncRNAs) have been increasingly appreciated as an integral component in gene regulatory networks. Genome-wide features of their origin and expression patterns ascribed a prominent role for lncRNAs to the regulation of protein-coding genes, and also suggest a potential link to many human diseases. Recent studies have begun to unravel the intricate regulatory mechanism of lncRNAs occurring at multiple levels. We have previously discovered that a novel class of lncRNAs, termed as enhancer RNA (eRNA), is dynamically expressed from functionally active neuronal enhancers. Unlike other lncRNAs, the induction of eRNA is rapid and transient, and tightly regulated by external stimuli such as neuronal activity. Epigenomic analyses in many different cell types unequivocally suggest that eRNA is a hallmark of functionally active enhancers. This feature of eRNAs has enabled us to investigate the molecular function of eRNAs in gene expression and brain function, and dynamic coordination mechanism of enhancer clusters that ensures robust induction of target genes in response to various stimuli. We are also investigating the biogenesis mechanism of eRNAs. Our studies collectively suggest that transcription at enhancers and eRNAs might represent a new layer of complexity in the molecular architecture of many human diseases.