Histone deacetylase 9 (HDAC9) has been reported to be elevated in ischemic brain injury, but its mechanism in stroke is still enigmatic. Shen et al. aimed to unveil the manner of regulation of HDAC9 expression and the effect of HDAC9 activation on neuronal function in cerebral ischemia. MicroRNAs (miRNAs) targeting HDAC9 were predicted utilizing bioinformatics analysis. We then constructed the oxygen glucose deprivation (OGD) cell model and the middle cerebral artery occlusion (MCAO) rat model, and elucidated the expression of CCCTC binding factor (CTCF)/miR-383-5p/HDAC9. Targeting between miR-383-5p and HDAC9 was verified by dual-luciferase reporter assay and RNAi. After conducting an overexpression/knockdown assay, we assessed neuronal impairment and brain injury. We found that CTCF inhibited miR-383-5p expression via its enrichment in the promoter region of miR-383-5p, whereas the miR-383-5p targeted and inhibited HDAC9 expression. In the OGD model and the MCAO model, we confirmed that elevation of HDAC9 regulated by the CTCF/miR-383-5p/HDAC9 pathway mediated apoptosis induced by endoplasmic reticulum stress, while reduction of HDAC9 alleviated apoptosis and the symptoms of cerebral infarction in MCAO rats. Thus, the CTCF/miR-383-5p/HDAC9 pathway may present a target for drug development against ischemic brain injury [1].

1)
Shen J, Han Q, Li W, Chen X, Lu J, Zheng J, Xue S. miR-383-5p Regulated by the Transcription Factor CTCF Affects Neuronal Impairment in Cerebral Ischemia by Mediating Deacetylase HDAC9 Activity. Mol Neurobiol. 2022 Aug 4. doi: 10.1007/s12035-022-02840-4. Epub ahead of print. PMID: 35927544.