A study first showed that inhibition of activating transcription factor 6 (ATF6) by apelin-13 could reduce endoplasmic reticulum (ER)-stress-mediated apoptosis and blood brain barrier (BBB) disruption after SAH.

Xu et al., chose apelin13, ATF6 and CCAAT/enhancer-binding protein (C/EBP) homologous protein (CHOP) siRNAs to verify the hypothesis. Brain water content, neurological behavior and Evans Blue(EB) were assessed at 24h after SAH. Western blot analysis and reverse transcription-polymerase chain reaction (RT-PCR) were applied to evaluate the expression of targets in both protein and mRNA levels. Neuronal apoptosis was assessed with Terminal deoxynucleotidyl transferase (TdT)-mediated dUTP nick end labeling (TUNEL) and caspase-3 staining. The results showed that the levels of ATF6, and its downstream protein, CHOP were upregulated and reached the peak at 24h after SAH. ATF6 was highly expressed in neurons. The administration of apelin-13 could significantly reduce the mRNA and protein levels of ATF6, and its downstream targets, CHOP and caspase-3, but increase the Bcl-2/Bax ratio, Claudin-5, Occludin and ZO-1. What's more, the administration of apelin-13 could reduce brain edema, ameliorate BBB disruption and improve neurological functions. However, the CHOP siRNA could significantly reverse the pro-apoptotic effect induced by the increased ATF6 level after SAH. Apelin-13 could exert its neuroprotective effects via suppression of ATF6/CHOP arm of ER-stress-response pathway in the early brain injury after SAH [1].

1)
Xu W, Gao L, Li T, Zheng J, Shao A, Zhang J. Apelin-13 Alleviates Early Brain Injury after Subarachnoid Hemorrhage via Suppression of Endoplasmic Reticulum Stress-Mediated Apoptosis and Blood-Brain Barrier Disruption: Possible involvement of ATF6/CHOP Pathway. Neuroscience. 2018 Jul 20. pii: S0306-4522(18)30498-6. doi: 10.1016/j.neuroscience.2018.07.023. [Epub ahead of print] PubMed PMID: 30036660.