

**P018** BBF2H7, a novel transmembrane bZIP transcription factor, is a new type of ER stress transducer

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Endoplasmic reticulum (ER) stress transducers IRE1, PERK and ATF6 are well known to transduce signals from the ER to the cytoplasm and nucleus when unfolded proteins accumulate in the ER. Recently, we identified OASIS as a novel ER stress transducer expressed in astrocytes.

We report here that BBF2H7, originally identified as a novel human protein whose C-terminal part was fused to the FUS genes in low grade fibromyxoid sarcoma, is structurally homologous to OASIS. BBF2H7, an ER-resident transmembrane protein with the bZIP domain in the cytoplasmic portion, is cleaved at the membrane in response to ER stress. The cleaved fragments of the BBF2H7 translocate into the nucleus and can bind directly to CRE site to activate transcription of target genes. Interestingly, although BBF2H7 protein is not expressed in normal conditions, it is markedly induced at the translational level during ER stress, suggesting that BBF2H7 might contribute to only the late phase of UPR signaling. In a mouse model of focal brain ischemia, BBF2H7 protein is prominently induced in neurons in the peri-infarction region. Taken together, our results suggest that BBF2H7 is a novel ER stress transducer and could play important roles in preventing accumulation of unfolded proteins in damaged neurons.