The Functions of an ER Stress Sensor OASIS in vitro and in vivo.

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The endoplasmic reticulum (ER) is susceptible to various stresses that provoke the accumulation of unfolded proteins in the ER. Excessive or long-termed stresses in the ER result in apoptotic cell death involving activation of caspase-12 and –3, and Ask-1-JNK pathway. Eukaryotic cells can adapt for survival to deal with an accumulation of unfolded proteins in the ER by increasing transcription of genes encoding ER-resident chaperones such as GRP78/BiP to facilitate protein folding. The induction system is termed the unfolded protein response (UPR). It has been reported that IRE1 and PERK, transmembrane kinases, and ATF6, a transmembrane transcription factor, are mediators of the UPR through sensing accumulation of unfolded proteins. Cell fates after ER stress are regulated by the balance of both apoptotis and the UPR signaling. Recently, we identified a novel ER stress sensor, OASIS, which is specifically expressed in astrocytes and osteoblasts. This protein is a transmembrane protein containing bZIP domain. The functional analyses of OASIS showed that 1) it was cleaved within the ER membrane in response to the ER stress. 2) overexpression of OASIS induced the transcription of GRP78/BiP mRNA through the activation of cyclic AMP responsive element (CRE) and ER stress responsive element (ERSE), 3) its stable cell lines were resistant to ER stress compared with the control cells. These results indicate that the ER-resident transcription factor OASIS may be a candidate for leading astrocytes and osteoblasts to protect against ER stress. In this symposium, I will also talk about the phenotype of OASIS deficient mice that shows abnormal formation of bone tissues.