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未折疊蛋白反應

Antibodies for Unfolded Protein Response

弘晉有限公司

未折疊蛋白反應 (Unfolded Protein Response, UPR)

是一種當真核細胞發生內質網壓力(Endoplasmic Reticulum Stress)時活化的訊息傳遞機制，內質網壓力是由於未折疊蛋白在內質網中的累積造成，例如大量蛋白質需求、病毒感染、突變蛋白表現、缺氧、能量剝奪(Energy Deprivation)或暴露於過多的氧化壓力等條件可引發UPR或內質網壓力。

UPR具有三個主要功能：

(i)阻斷蛋白質轉譯以恢復體內平衡

(ii)正向調控蛋白質折疊相關分子伴護蛋白(Molecular Chaperones)

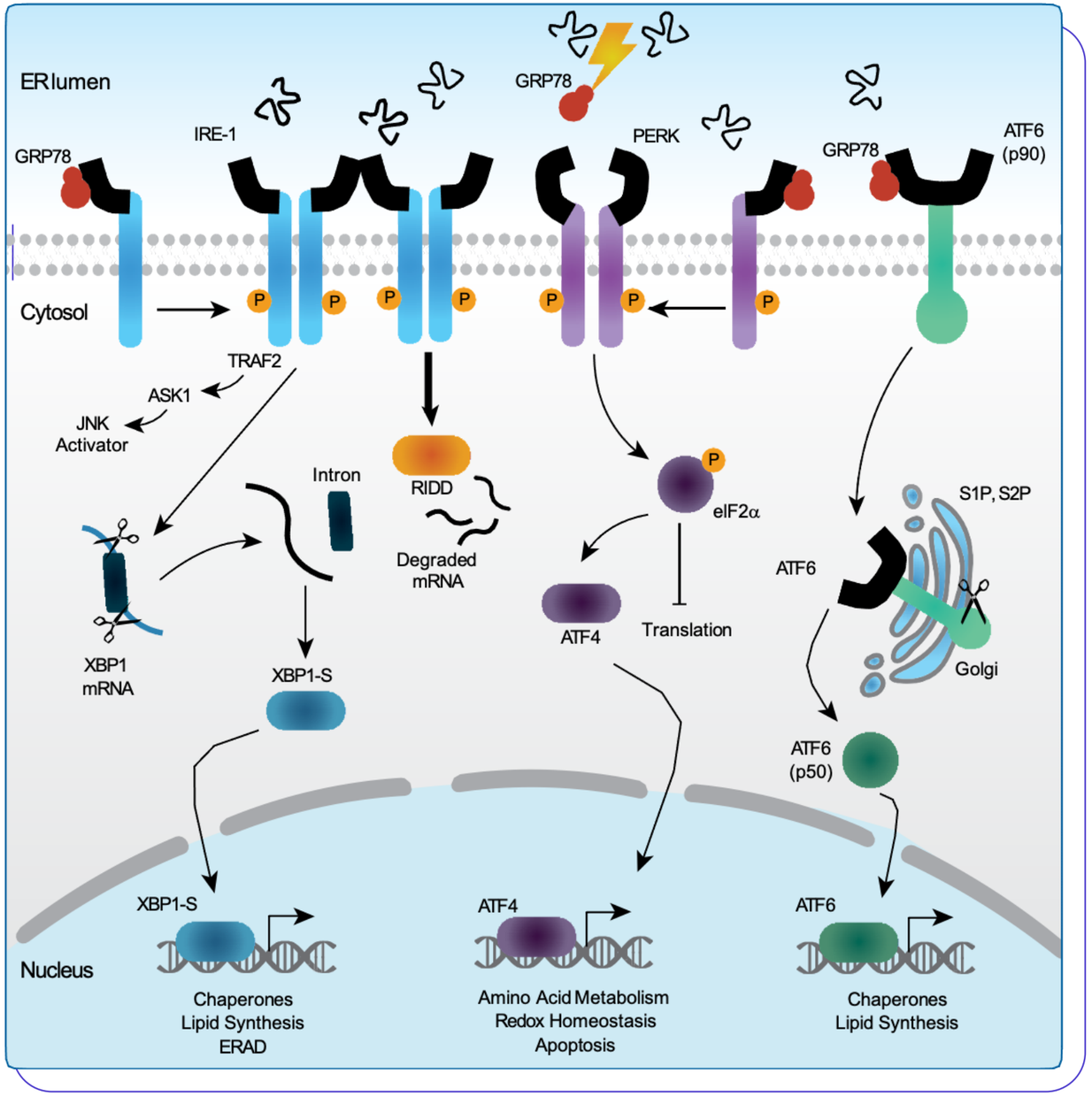
(iii)上調負責辨認內質網中錯誤/未折疊蛋白的訊息傳遞以進行泛素所引導的蛋白質降解

當內質網壓力未得到緩解時，UPR可誘導細胞凋亡並導致細胞死亡。已知UPR持續過度活化與許多人類疾病有關，包括癌症、高血糖症、自體免疫性疾病、肝病、視網膜病變、急性肺損傷和神經退化。因此，了解UPR訊號的完整機制對於評估其在正常和/或疾病條件下的生物學效應，以及發展針對UPR相關疾病的預防和治療措施至關重要。

Regulation of UPR Signaling

UPR訊號透過位於內質網的三種主要效應蛋白進行調節：inositol-requiring enzyme 1(IRE1)、activating transcription factor 6(ATF6)和protein kinase RNA-like ER kinase(PERK)。這些蛋白質透過與glucose response protein 78(GRP78/BiP)結合而保持在未活化/膜結合狀態。在與未折疊蛋白相互作用後，GRP78從UPR效應蛋白中釋放出來，從而導致這些效應蛋白的活化。UPR通常藉由內質網壓力訊號的三個傳遞路徑精心安排的相互作用活化(詳見下方路徑圖)。

UPR induction in mammalian cells



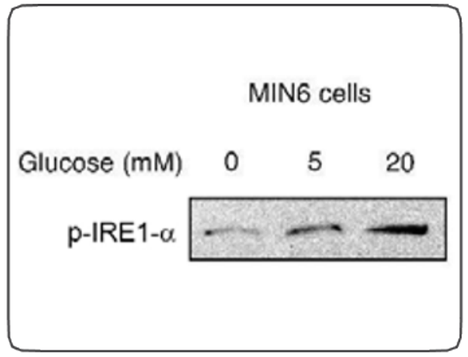
Inositol-Requiring Enzyme 1 Alpha (IRE1 Alpha)

IRE1 alpha，預測分子量約爲109.7kDa，是一種內質網常駐蛋白，在所有組織類型中普遍都會表現。它是一種在內質網中的單次I型跨膜蛋白，會與其他幾種蛋白質相互作用，包括GRP78、DAB2IP、TRAF2和TAOK3。

在UPR活化後，IRE1 α經歷二聚化(dimerization)/自磷酸化修飾後活化(例如phospho-Ser724 IRE1α)IRE1α的活化形式隨後誘導轉錄因子XBP1的mRNA剪接。從XBP1中去除內含子會導致XBP1的活化態(XBP1-S，XBP1 splicing form)的表現，進而正向調控ER伴護蛋白，以及ER相關蛋白降解(ER-associated protein degradation，ERAD)路徑和脂質代謝的基因。

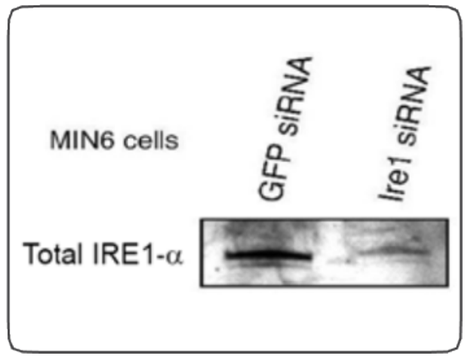
透過非XBP1依賴性路徑，IRE1與腫瘤壞死因子(TNF)受體相關因子2(Tumour necrosis factor receptor-associated factor 2，TRAF2)結合並誘導JUN氨基末端酶(JUN amino-terminal kinase，JNK)活化。已知這種相互作用可調節自噬作用和細胞凋亡。IRE1的內切核糖核酸酶活性還誘導調節型IRE1依賴衰解(Regulated IRE1-Dependent mRNA Decay，RIDD)，這與脂質合成代謝和細胞凋亡有關。

IRE1 α還參與細胞週期停滯、胰島素代謝、血管生成和巨自噬作用(Macroautophagy)調節的過程。



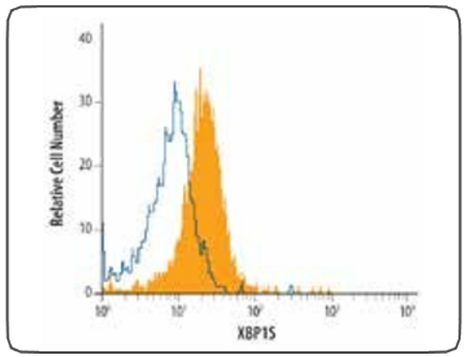
pSer724 IRE1 alpha Antibody [NB100-2323*]

Western blot (WB) detection of pSer724 IRE1 alpha Min6 cells treated with increasing concentrations of glucose for 3 hours prior to lysate preparation.



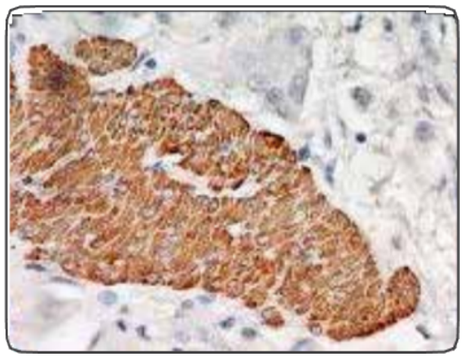
IRE1 alpha Antibody (Total) [NB100-2324]

WB detection of total IRE1 alpha protein in lysates from Min6 cells which were transfected with GFP-siRNA or Ire1-siRNA.



XBP1 Antibody (S Isoform) [MAB4257]

FLOW analysis of PFA fixed and saponin permeabilized RPMI 8226 human multiple myeloma cells using XBP1S antibody (filled histogram) or isotype control (MAB002, open histogram) with APC-conjugated secondary antibody (F0101B).



TRAF2 Antibody (33A1293) [NB100-56715]

IHC-P analysis of a formalin-fixed tissue section of human transitional cell carcinoma of the urinary bladder. Signal was developed using HRP-DAB method and the nuclei were counterstained using hematoxylin.

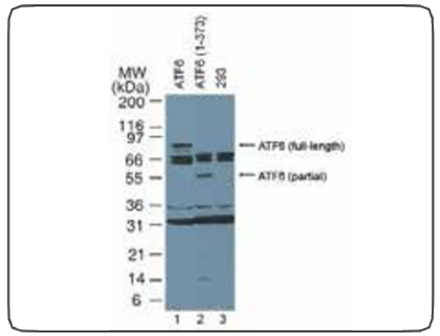
*Most cited phospho-IRE1 alpha antibody among offerings from all antibody companies.

Activating Transcription Factor 6 (ATF6)

ATF6是一種跨膜醣蛋白和轉錄活化蛋白，可在發生內質網壓力時活化啟動UPR。ATF6的預測分子量爲74.5kDa。然而，在西方墨點法中可以檢測到大約90kDa的ATF6，因爲該蛋白質經常發生醣基化，形成ATF6的p90版本。

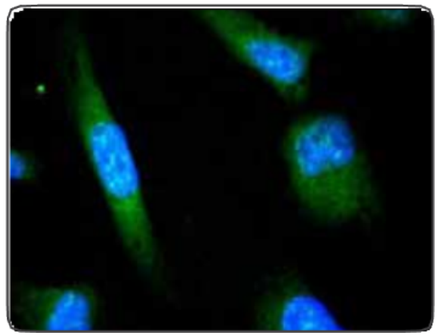
在感受到內質網壓力後，p90被轉運到高基氏體，在那裡透過S1P蛋白酶(site 1 protease)和S2P蛋白酶(site 2 protease)進行加工，釋放N端加工的cAMP依賴性ATF-6 α形式(cytosolic/cleaved-ATF6, p50)。切割的p50形式的ATF6轉移到細胞核，在細胞核中它與ERSE(ER stress response element)上的DNA結合，以調節ER相關蛋白降解(ERAD)和UPR基因。

除了透過ERSE和ERAD調控內質網壓力反應外，p50還調控XBP1蛋白的轉錄，以及誘導細胞凋亡、調控RNA聚合酶II啟動子的轉錄、眼睛組織發育和視覺感知(visual perception)。



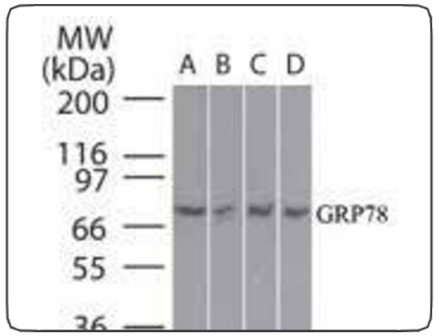
ATF6 Antibody (70B1413.1)[NBP1-40256]

WB analysis of HEK293 cells transfected with full-length ATF6, or with partial ATF6 protein (AA 1-373), and the non-transfected control cells.



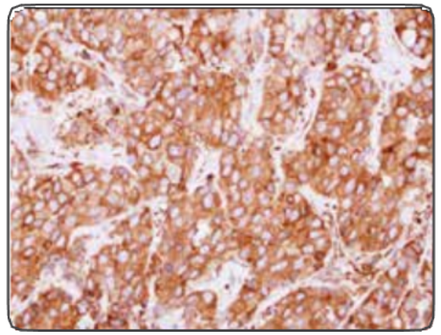
ATF6 Antibody [NBP1-75478]

ICC/IF analysis of HeLa cells using ATF6 antibody with detection employing FITC conjugated secondary (green).
Nuclei were counterstained with DAPI (blue).



GRP78/HSPA5 Antibody [NB100-56411]

WB analysis of lysates from HeLa cells (A), human liver (B), mouse liver (C), and rat liver (D) tissues using GPR78 antibody with detection employing HRP labelled secondary and PicoTect ECL substrate.



ERp72 Antibody [NBP2-16371]

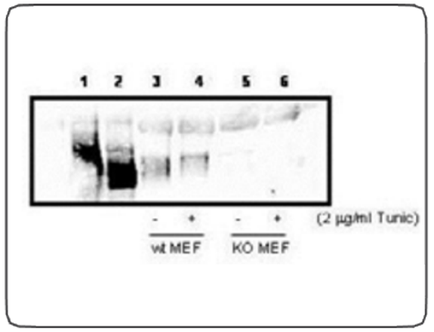
IHC analysis of a formalin fixed and paraffin-embedded tissue section of breast cancer using ERp72 antibody with HRP-DAB detection. Nuclei were counterstained using hematoxylin.

Protein kinase RNA-like ER Kinase (PERK)

PERK，預測分子量爲125.2kDa，是一種跨膜蛋白酶，屬於PEK蛋白家族，以其參與胰島素的作用而聞名。在內質網壓力反應和UPR活化時，PERK起到抑制新蛋白質轉譯的作用。

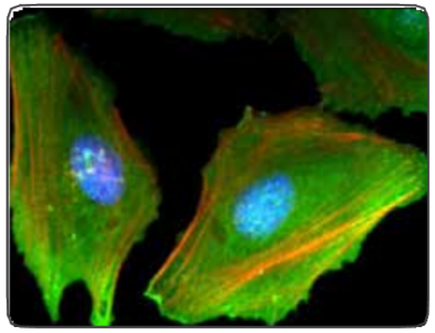
具體來說，內質網壓力導致PERK在內質網腔內的結構域(N端)寡聚化(oligomerization)，這促進了PERK在細胞質結構域(C端)在Thr-982處的反式自磷酸化(trans-autophosphorylation)。因此，通常將Thr-982位點的磷酸化形式的PERK評估爲內質網壓力的程度。

活化的PERK使eIF2 α(eukaryotic translation initiation factor 2 alpha)磷酸化，從而抑制蛋白質的轉譯以維持體內平衡。然而Phospho-eIF2　alpha並不會影響ATF4的轉譯。在累積後，ATF4移動至細胞核，在那裡它誘導ER伴護蛋白、自噬/凋亡基因(尤其是CHOP)、氧化反應基因的表現，並活化氨基酸代謝訊息傳遞路徑。PERK在UPR期間促進細胞週期退出(cell cycle exit)，並參與粒線體形態和功能的調節。



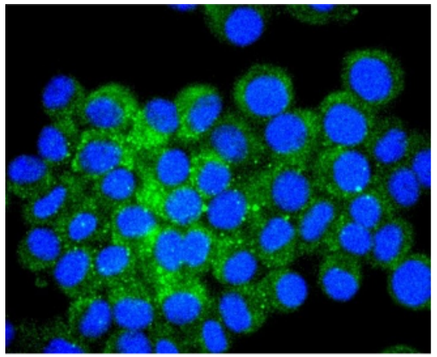
PERK Antibody [NBP1-78017]

WB analysis of lysates from PERK over-expressing 293T cells (lanes 1 & 2), Wild type MEFs (Lanes 3 & 4), and PERK knock-out MEFs (lanes 5 & 6). The MEFs were treated with vehicle (-) or Tunicamycin (+) for induction of ER stress.



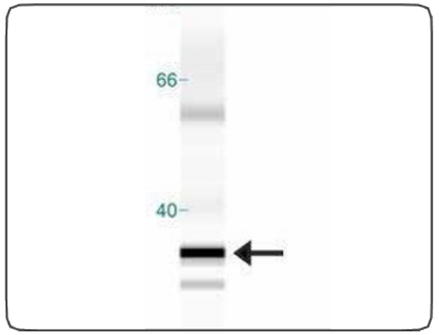
eIF2A Antibody (3A7B11) [NBP2-26296]

ICC/IF analysis of HeLa cells using eIF2A antibody with Dylight 488 (green) conjugated secondary antibody. Nuclei were counterstained with DAPI (blue). Alpha-tubulin was labelled using anti-tubulin with Dylight 550 (red) conjugated secondary antibody.



ATF4 Antibody (SD20-92) [NBP2-67766]

Immunocytochemistry/Immunofluorescence: ATF4 Antibody (SD20-92) [NBP2-67766] - Staining ATF4 in N2A cells (green). The nuclear counter stain is DAPI (blue). Cells were fixed in paraformaldehyde, permeabilised with 0.25% Triton X-100/PBS.



GADD153/CHOP Antibody (9C8) [NB600-1335]

Simple Western lane view shows a specific band for CHOP/GADD153 in 1.0 mg/ml of HeLa lysate. This experiment was performed under reducing conditions using the 12-230 kDa separation system.

Catalog	Product	Applications	Components
NBP2-52746	ER Stress / UPR Antibody Pack	WB, IHC, IHC-P	NBP1-06277SS: GRP78/HSPA5 Antibody - BSA Free NBP1-77681SS: XBP1 Antibody - BSA Free NBP2-13172-0.025ml: GADD153/CHOP Antibody - BSA Free NB100-2323SS: IRE1 alpha [p Ser724] Antibody - BSA Free NBP1-40256SS: ATF6 Antibody (70B1413.1) - BSA Free NB100-2324SS: IRE1 alpha Antibody