

Stress of endoplasmic reticulum

The endoplasmic reticulum (ER) stress is a set of all possible influences that lead the endoplasmic reticulum out of homeostasis, which is mainly manifested by the accumulation of proteins that have not undergone the process of protein folding. In response, signaling pathways are triggered that are collectively referred to as the unfolded protein response (UPR). As a result, mRNA translation slows, misfolded proteins are degraded, chaperone gene expression increases, and the oxidative environment in the ER is maintained. In case of failure of regulatory mechanisms, apoptosis is triggered.

Common ER function

Under physiological conditions, the nascent polypeptide is labelled during mRNA translation and the entire ribosome-polypeptide-mRNA complex is sent to the appropriate site in the ER where the polypeptide is completed. N-glycosylation is performed and the oxidative environment of the ER ensures the formation of disulfide bridges



If misfolding occurs and the protein is misfolded, it threatens the entire endoplasmic reticulum by inducing the recruitment of other misfolded proteins. This is prevented by the binding of chaperones such as Grp78 (glucose regulated protein), and the protein is thus destined for endoplasmic reticulum associated degradation (ERAD).

Stress signalling pathways

- PERK kinase (eIF2 kinase)
- kinase family including Ire1 - triggers two forms of response:
 - Expression of chaperone genes, including Grp78, to ensure that proteins remain in an unfolded state and no misfolding occurs; expression occurs through translation of the mRNA of the transcription factor XBP1
 - binding and retention of Ca^{2+} in the ER
- transcription factor ATF6 (activating transcription factor) - influences XBP1 mRNA expression

Initiation of apoptosis

It is not yet properly explained, two routes are assumed, using:

- transcription factors, presumably Ire1 could upregulate the transcription factor GADD153/CHOP, which affects the balance between Bcl-2 and Bax;
- caspases, possibly casp-12.

Links

Related articles

- Chaperons

References

- JONÁK, Jiří. *Sbalování proteinů a jeho poruchy, onemocnění spojená s poruchami sbalování a agregací bílkovin* [přednáška k předmětu Patobiochemie 3, obor VL, 1. lékařská Univerzita Karlova]. Praha. 11.12.2015.

Used literature

- SZEGEZDI, Eva. *Molecular mechanism of ER stress* [online]. [cit. 2011-02-01]. <<http://www.nuigalway.ie/biochemistry/staff/samali/lab/EvaSzegezdi.html>>.
- Wikipedia contributors. *Unfolded protein response* [online]. [cit. 2011-02-01]. <https://en.wikipedia.org/w/index.php?title=Unfolded_protein_response&oldid=398120351>.

