International Journal of
Molecular Sciences

IMPACT FACTOR 6.208

Indexed in: PubMed

Special Issue Reprint

Mechanisms of ER Protein Import

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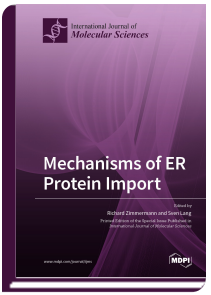
mdpi.com/books/pdfview/book/5416

ISBN 978-3-0365-4094-8 (hardback)
ISBN 978-3-0365-4093-1 (PDF)



Protein import into the endoplasmic reticulum (ER) is the first step in the biogenesis of approximately 10,000 different soluble and membrane proteins of human cells, which amounts to about 30% of the proteome. Most of these proteins fulfill their functions either in the membrane or lumen of the ER plus the nuclear envelope, in one of the organelles of the pathways for endo- and exocytosis (ERGIC, Golgi apparatus, endosome, lysosome, and trafficking vesicles), or at the cell surface as plasma membrane or secreted proteins. An increasing number of membrane proteins destined to lipid droplets, peroxisomes or mitochondria are first targeted to and inserted into the ER membrane prior to their integration into budding lipid droplets or peroxisomes or prior to their delivery to mitochondria via the ER-SURF pathway. ER protein import involves two stages, ER targeting, which guarantees membrane specificity, and the insertion of nascent membrane proteins into or translocation of soluble precursor polypeptides across the ER membrane. In most cases, both processes depend on amino-terminal signal peptides or transmembrane helices, which serve as signal peptide equivalents. However, the targeting reaction can also involve the ER targeting of specific mRNAs or ribosome–nascent chain complexes. Both processes may occur co- or post-translationally and are facilitated by various sophisticated machineries, which reside in the cytosol and the ER membrane, respectively. Except for resident ER and mitochondrial membrane proteins, the mature proteins are delivered to their functional locations by vesicular transport.

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