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Contrasting functions of calreticulin and calnexin in glycoprotein folding and ER quality control.

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Abstract

Calreticulin and calnexin are homologous lectins that serve as molecular chaperones for glycoproteins in the endoplasmic reticulum of eukaryotic cells. Here we show that calreticulin depletion specifically accelerates the maturation of cellular and viral glycoproteins with a modest decrease in folding efficiency. Calnexin depletion prevents proper maturation of some proteins such as influenza hemagglutinin but does not interfere appreciably with the maturation of several others. A dramatic loss of stringency in the ER quality control with transport at the cell surface of misfolded glycoprotein conformers is only observed when substrate access to both calreticulin and calnexin is prevented. Although not fully interchangeable during assistance of glycoprotein folding, calreticulin and calnexin may work, independently, as efficient and crucial factors for retention in the ER of nonnative polypeptides.

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