

Iron-induced oxidative stress up-regulates calreticulin levels in intestinal epithelial (Caco-2) cells

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Calreticulin, a molecular chaperone involved in the folding of endoplasmic reticulum synthesized proteins, is also a shock protein induced by heat, food deprivation, and chemical stress. Mobilferrin, a cytosolic isoform of calreticulin, has been proposed to be an iron carrier for iron recently incoming into intestinal cells. To test the hypothesis that iron could affect calreticulin expression, we investigated the possible associations of calreticulin with iron metabolism. To that end, using Caco-2 cells as a model of intestinal epithelium, the mass and mRNA levels of calreticulin were evaluated as a function of the iron concentration in the culture media. Increasing the iron content in the culture from 1 to 20 μ M produced an increase in calreticulin mRNA and a two-fold increase in calreticulin. Increasing iron also induced oxidative damage to proteins, as assessed by the formation of 4-hydroxy-2-nonenal adducts. Co-culture of cells with the antioxidants quercetin, dimethyltiourea and