S1-casein is required for the efficient transport of ß- and AlphaS1-caseins from the ER to the Golgi apparatus of mammary epithelial cells

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αS1-casein is required for the efficient transport of ß- and κ-caseins from the ER to the Golgi apparatus of mammary epithelial cells

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In lactating mammary epithelial cells (MEC), interaction of the caseins (Cns) with each other is believed to occur after their transport out of the RER, via calcium mediated-aggregation subsequent to their phosphorylation in the Golgi apparatus. We show here that, in MEC from αS1-Cn-deficient goat, the rate of transport of the other Cns out of the RER is highly reduced whereas the secretion of whey proteins is not significantly affected. This leads to the accumulation of immature Cns in the RER which dramatically dilates to accommodate these proteins. However, Cn submicelles and micelles were still observed in the late secretory pathway, TGN, secretory vesicles and lumen of the acini. In contrast, no accumulation was detected in MEC which do not express ß-Cn. In MEC secreting intermediate amount of αS1-Cn, Cn accumulation was weaker and the transport of αS1-Cn to the Golgi occurred with similar kinetic to that measured in control cells. Accumulation of Cns in the RER was therefore dependent upon the relative proportion of αS1-Cn, the rate of transport of the later being independent of its level of expression. Similarly, in PRL-treated MEC HC11 which did not expressed αS-Cns, accumulation of ß-Cn in distended RER cisternae was observed. In conjunction to Cn accumulation in the RER, the amount of ER-resident proteins (GRP94, GRP78/BiP, PDI) increased. However, permeabilization of ER vesicles allowed the recovery of accumulated Cns in a soluble form. We conclude that optimal export of the Cns out of the RER is dependent upon αS1-Cn. Our data suggest that αS1-Cn interacts with the other Cns in the RER and that the formation of this complex is required for their efficient export to the Golgi apparatus. (This work was partly supported by INRA (A. I. P. "Glande Mammaire") and by the EU-TMR Research Network ERB-FMRX-CT96-0023.)