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The human asialoglycoprotein receptor H1 is anchored in the membrane by a single stretch of 20 hydrophobic amino acids; the hydrophilic amino terminus faces the cytoplasm, and the carboxyl terminus is exoplasmic. We show here that glycosylation and insertion of the asialoglycoprotein receptor into the endoplasmic reticulum membrane is cotranslational and SRP-dependent and occurs without proteolytic cleavage. The membrane-anchor domain is necessary for membrane insertion, since a receptor with the segment deleted is neither inserted nor glycosylated. The segment is also sufficient for membrane insertion, since it will initiate translocation of a carboxy-terminal domain of rat alpha-tubulin across the membrane. We propose that a helical hairpin mechanism of membrane insertion is used both by cleaved amino-terminal and uncleaved internal signal sequences.

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