The heterodimeric peptide transporter TAP belongs to the ABC transporter family. Sequence comparisons with the P-glycoprotein and cystic fibrosis transmembrane conductance regulator and the functional properties of selective amino acids in these ABC transporters postulated that the glutamic acid at position 263 and the phenylalanine at position 265 of the TAP1 subunit could affect peptide transporter function. To define the role of both amino acids, TAP1 mutants containing a deletion or a substitution to alanine at position 263 or 265 were generated and stably expressed in murine and human TAP1(-/-) cells. The different TAP1 mutants were characterized in terms of expression and function of TAP, MHC class I surface expression, immune recognition, and species-specific differences. The phenotype of murine and human cells expressing human TAP1 mutants with a deletion or substitution of Glu(263) was comparable to that of TAP1(-/-) cells. In contrast, murine and human TAP1 mutant cells containing a deletion or mutation of Phe(265) of the TAP1 subunit exhibit wild-type TAP function. This was associated with high levels of MHC class I surface expression and recognition by specific CTL, which was comparable to that of wild-type TAP1-transfected control cells. Thus, biochemical and functional evidence is presented that the Glu(263) of the TAP1 protein, but not the Phe(265), is...
critical for proper TAP function.