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Rat wild-type parathyroid hormone receptor (PTH-R) and mutant PTH-R^{P132L} show the different intracellular localization *in vitro*

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ABSTRACT

A replacement of proline with leucine at position 132 of the receptor for parathyroid hormone (PTH)/parathyroid hormone-related peptide (PTHrP), *i.e.*, PTH-R, has been discovered in human Blomstrand's lethal chondrodysplasia. As skeletal deformities in this type of chondrodysplasia appear to compromise the receptor binding to its ligands, we examined the possibility that rat PTH-R carrying P132L mutation (PTH-R^{P132L}) would result in abnormal intracellular localization. Osteoblastic MC3T3-E1 cells were transfected with expression vectors containing cDNAs encoding either wild-type PTH-R or mutant PTH-R^{P132L}. The cells expressing the wild-type PTH-R produced a receptor protein with a molecular mass of 66.3 kDa, which localized its immunoreactivity mainly on the cell surfaces. In contrast, the PTH-R^{P132L} was hardly detected on the cell surfaces, but accumulated within the rough-surfaced endoplasmic reticulum. Consistent with this localization, the cells expressing the mutant receptor failed to generate cyclic AMP in response to PTH. Furthermore, a remarkably weaker intensity of the 66.3 kDa band compared with the wild-type counterpart suggests that PTH-R^{P132L} is prone to degradation in the transfected cells. In summary, these findings indicate that defective transport of PTH-R^{P132L} to the cell surface would be a molecular basis for Blomstrand's

chondrodysplasia.

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