

Close Similarity between Receptor-Linked Tyrosine Phosphatase and Rat Brain Proteoglycan

Receptor-type protein-tyrosine phosphatase β (RPTP β or HPTP ζ ; Levy et al., 1993, Krueger and Saito, 1992) is expressed in specific regions of the developing and adult nervous system (Canoll et al., 1993). The extracellular domains of RPTP β and RPTP γ (Barnea et al., 1993) contain a domain with homology to the enzyme carbonic anhydrase (CAH). This region of RPTP β is very similar to a soluble rat brain chondroitin sulfate proteoglycan (3F8 PG). Comparison of the amino acid sequences of human RPTP β and rat 3F8 PG (Figure 1) shows that the CAH-like domains and the fibronectin type III repeats are 94% identical, whereas the cysteine-free domains of both proteins are 71% identical (Levy et al., 1993; Maurel et al., 1994).

Complementary DNA cloning and Northern analysis with different probes revealed the existence of three forms of RPTP β , probably generated by alternative splicing (Levy et al., 1993; Maurel et al., 1994). The 9.5 kb and 6.4 kb transcripts encode two transmembrane forms of RPTP β , whereas the 8.5 kb transcript encodes only a secreted form of the extracellular domain of RPTP β . Hence, the 3F8 PG represents the rat homolog of the entire extracellular domain of RPTP β (Maurel et al., 1994; Levy et al., 1993). Northern hybridization of RNA from mouse and rat brains provided a consistent picture of the existence of three forms of RPTP β : long and short membrane-associated forms and a variant that corresponds to the extracellular domain of RPTP β (Figure 2).

It had been demonstrated that the adhesion molecules N-CAM and Ng-CAM can bind to the 3F8 PG (Grumet et al., 1993). Moreover, immunohistochemical studies indicated that both RPTP β and the matrix protein tenascin are localized in overlapping regions of the central nervous system (Prieto et al., 1990; Canoll et al., 1993). The interaction between a receptor tyrosine phosphatase and proteins that

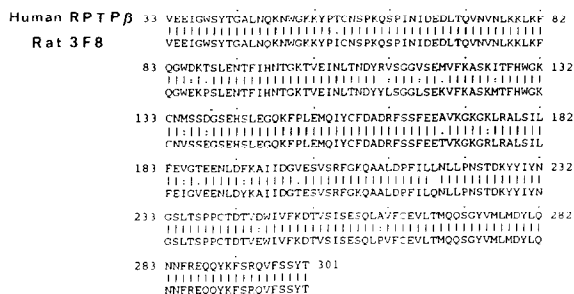


Figure 1. Comparison of the Sequences of Human RPTP β and Rat 3F8. The amino acid sequences of the CAH-like domains of human RPTP β (Levy et al., 1993) and rat 3F8 (Maurel et al., 1994) are aligned. Identical amino acids are indicated by a connecting line. The positions of the first and last amino acids in each line in the sequence of RPTP β are indicated.

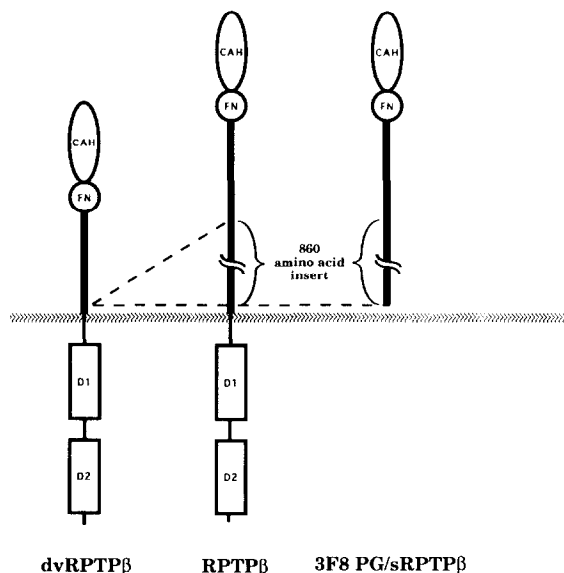


Figure 2. Schematic Presentation of the Three Forms of RPTP β . RPTP β , a deletion variant (dvRPTP β), and a secreted form (3F8 PG/sRPTP β) contain CAH-like domains (CAH), fibronectin type III repeats (FN), and spacers of variable length that are characterized by a very low content of cysteine residues (indicated by thick lines) in their extracellular portions. Two forms of RPTP β contain cytoplasmic tyrosine phosphatase domains (D1 and D2). The 860 amino acid insert in RPTP β and in 3F8 PG is denoted. The secreted form ends exactly where the sequences of the other two forms diverge.

mediate cell-cell interaction may have a role in development of the mammalian central nervous system.

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