The Ret proto-oncogene is structurally related to the growing family of tyrosine kinase transmembrane receptors and is involved in GDNF signaling. By alternative splicing, two isoforms of the Ret proto-oncogene product are generated that differ from each other by having either 9 or 51 carboxy terminal amino acids. The Ret gene products include two glycosylated proteins of 150 kDa and 170 kDa and, in tunicamycin-treated cells, a non-glycosylated 120 kDa protein consistent with the predicted Ret molecular weight based on sequence analysis. Tumor-specific rearrangements of the Ret proto-oncogene have been identified in papillary thyroid carcinomas leading to the formation of different transforming fusion proteins sharing the tyrosine kinase domain of Ret. In contrast to the Ret proto-oncogene, the rearranged forms are constitutively phosphorylated on tyrosine and are translocated from the membrane to the cytoplasm. The putative binding site for either SH2 and PTB domains has been identified as Tyr 586 of Ret/Ptc2 (Tyr 1062 on proto-Ret). Tyr 1062 to the cytoplasm. The putative binding site for either SH2 and PTB domains has been identified as Tyr 586 of Ret/Ptc2 (Tyr 1062 on proto-Ret). Tyr 1062 shows features of a multifunctional docking site and Shc activation plays a key role in the transforming pathways triggered by Ret/Ptc oncoproteins.

REFERENCES


