Patients with MEN2B also have mucosal neuromas, intestinal ganglioneuromas and a marfanoid habitus with skeletal deformations and joint laxity but without the vascular and ophthalmologic abnormalities. They often do not have a family history of the disease and harbour a de novo mutation.

**FMTC Syndrome**

Familial MTC (FMTC) is the mildest variant of MEN2. It has been diagnosed more frequently in recent years (35-40% of all cases).\(^5\) In patients with FMTC, there is a strong predisposition to develop MTC with a very low incidence of the other clinical manifestations of MEN2A. The diagnosis of FMTC can only be considered when four or more family members across a wide range of ages have isolated MTC. The clinical course of MTC in FMTC in general is more benign than for individuals with MEN2A and MEN2B and typically has a late onset or no clinically manifest disease. The prognosis for FMTC is relatively good; however, aggressive MTC tumours and even death due to MTC have been reported in cases harbouring codon 804 mutations. A family history is often inadequate in establishing diagnosis of familial disease, a more thorough evaluation by genetic and biochemical screening often revealing a family history of MTC in patients originally thought to have the sporadic form of the disease.

**RET Proto-Oncogene: Structure, Function and Mutations**

The RET gene has 21 exons and encodes a tyrosine kinase receptor that appears to transduce growth and differentiation signals in several developing tissues including those derived from the neural crest. The protein consists of an extracellular part with a ligand-binding domain, a cadherin (Ca\(^{2+}\)-dependent cell adhesion)-like domain and a cysteine-rich domain close to the cell membrane. It has a single transmembrane domain and an intracellular part with two tyrosine kinase subdomains, TK1 and TK2. The RET protein is activated upon ligand-induced dimerization.\(^6\) RET is expressed in neuroendocrine cells such as C-cells, the precursors of MTC, and in pheochromocytomas. Hereditary MTC is caused by autosomal dominant gain-of-function mutations in the RET proto-oncogene.