**INTRODUCTION**

MEN1 is characterised by parathyroid, pituitary and pancreatic tumours in association with neoplasia of intra-thoracic endocrine tissue, adrenal glands and cutaneous manifestations. Mutations of the tumour suppressor Menin are causative and affected patients possess heterozygous germline mutations in MEN1, with acquisition of a second hit in the wildtype allele initiating tumourigenesis. Phenotype-genotype correlations can provide insights into the molecular function of Menin and help guide management and surveillance. We therefore sought to analyse patients with MEN1 presenting to a tertiary centre.

**METHODS**

Case notes and electronic records were reviewed and those with a confirmed MEN1 phenotype were selected. Mutation loci and functional consequences were deduced using Ensembl and mutations were cross referenced with COSMIC and the Universal Mutation Database for MEN1. Chi-squared analysis was used to test for correlations between genotype and phenotype.

**RESULTS**

We identified 48 patients with MEN1. Of these 41 had confirmed mutations from either sequencing of exons 2-10 (62%) or targeted screening (38%). One patient underwent multiplex ligation dependent probe amplification but was found to be wild type. 23% of mutations were sporadic.

The functional consequences of the mutations were:
- Missense (17%)
- Nonsense (23%)
- Frameshift (33%)
- Intronic regions (13%)

All but one of these had been previously described to be pathogenetic.

One novel mutation was identified in exon 10, Q554X, which leads to a premature stop codon (Fig 3).

**DISCUSSION**

Our results reflect findings from previous studies suggesting that there are no obvious MEN1 phenotype-genotype correlations (Fig 2). Indeed, the disease is variable even between members of the same family bearing identical mutations.

A novel mutation, Q554X (Fig 3), was found in a patient with primary hyperparathyroidism and a gastrinoma. Deletion of 13 nucleotides in exon 10 is predicted to cause truncation at codon 554 resulting in loss of a nuclear localisation signal and the C terminus. This area is thought to be critical for DNA binding and the pathogenicity of this mutation emphasises the importance of this region in Menin function.

**REFERENCES**

Wautot, V. *et al.* "Germline Mutation Profile of MEN1 in Multiple Endocrine Neoplasia Type 1: Search for Correlation Between Phenotype and the Functional Domains of the MEN1 Protein" *Human Mutation* 20:35-47 (2002)