

The origin of patients with inherited Medullary Thyroid Cancer (MTC) who are carriers of the rare exon 8 mutation (G533C) of the RET gene in Greece

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Introduction - Aim of the study

- Mutations in the ret gene (*RET*) are responsible for the transmission of inherited MTC.
- In recent years a high prevalence of the “rare” exon 8 mutation (G533C) has been found in patients with inherited MTC in Greece.
- The mutation has been detected in a family of Spanish origin, few French families and a case from Slovenia.
- The aim of this study was to record with more detail the place of origin of these families in the country as well as possible differences in the clinical phenotype between them.

Patients - Methods

- We analyzed the features of 44 patients with inherited MTC belonging to 22 families who were carriers of the ret G533C mutation.
- Data concerning their place of origin as well as that of their ancestors were collected.
- Patients were distributed in four age groups (G1-G4) according to age at diagnosis.

Results

The 4 age groups and the mean age at diagnosis are shown below (Table 1):

Groups	Age at diagnosis (yrs)	No of pts	Mean age (yrs)	Index cases
Group 1 (G1)	4-24	4	21.0±2.9	0
Group 2 (G2)	25-50	30	37.7±5.5	12
Group 3 (G3)	51-70	8	54.1±4.4	2
Group 4 (G4)	>70	2	72.5±0.7	1

- ✓ The patients belonged to 22 families.
- ✓ Fourteen patients were index cases diagnosed in our centre; the majority belonged to G2 (table 1).
- ✓ “Hot spots” for the origin of these families were recognized (Fig 1):
 - Nine families originated from central / western Greece in an area around lake Trichonis and Fokis (Fig 2).
 - Nine originated from Peloponnese (Lakonia (mount Paron region) and Arcadia, Fig 3).
 - Three from the Attika region (two from Pireaus, fig 1).
 - Four families from Asia Minor, all of them without any recognized familial relationship.
- ✓ No phenotype or outcome differences were found between the families from the various regions.

Conclusions

- The majority of the ret gene exon8 (G533C) carriers originate from Central/Western Greece and Peloponnese.
- Data from the international reports indicate that the exon 8 *RET* mutation is a “Mediterranean” mutation.
- Increased awareness for inherited disease is required for patients with apparently sporadic MTC originating from these areas, as the age at presentation is usually delayed (25-70 years).

Bibliography

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Fig 1. “Hot spots” for the origin of the families carrying the exon 8 *RET* mutation



Fig 2. Origin of families carrying the exon 8 *RET* mutation – lake Trichonis region



Fig 3. Origin of families carrying the exon 8 *RET* mutation - mount Paron region

