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Thymic epithelial tumours present the number of known and novel gene variants in molecular analysis using targeted next-generation sequencing

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Background/Objectives: The biology of thymic epithelial tumours (TETs), including thymomas (TMs) and thymic carcinomas (TCs), and particularly the extent of molecular dysregulation, is poorly understood. We evaluated somatic and germline variants in genes commonly mutated in solid tumours using next-generation sequencing (NGS).

Methods: In total, 53 (19 TMs and 34 TCs) archival tissue samples were analysed for nonsynonymous variants (SNVs, Indels) in 15 genes by targeted NGS (reference genome: hg19/GRCh37).

Results: Ten variants in *TP53* (G154V, R158P, L194H, R267fs, R273C, R306*, Q317*), *ERBB2* (V773M), *KIT* (L576P), and *KRAS* (Q61L) considered somatic and pathogenic/likely pathogenic were detected in 10 of 34 (29.4%) TCs. No somatic pathogenic/likely pathogenic SNVs were found in TMs. New and rare variants of uncertain clinical significance were found in *ERBB2* (S703R), *KIT* (I690V), and *FOXL2* (P157S) in 3 of 19 (16%) TMs. The most frequent germline SNVs were *TP53* P72R (94% TETs), *ERBB2* I655V (40% TETs), and *KIT* M541L (9% TETs). No significant difference in median disease-free survival (DFS) was found between TC patients with and without pathogenic variants (p = 0.190); however, a trend toward a longer DFS was observed in the latter (16.0 vs. 30.0 months, respectively).

Conclusion: NGS analysis of TETs revealed several somatic variants in genes related to the p53, AKT, MAPK, and K-Ras signalling pathways. TCs showed greater genetic dysregulation than TMs. *KIT* alterations in TCs have potential as therapeutic targets. The germline and rare variants reported in this study increase the number of known genetic alterations in TETs.