

THE ROLES OF *TP53* AND MITOCHONDRIAL MICROSATELLITE DNA ALTERATIONS IN THORACIC ESOPHAGEAL SQUAMOUS CELL CARCINOMAS

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Purpose.

We investigated the clinical associations among nuclear microsatellite DNA alteration (nMSA) near *TP53*, mitochondrial microsatellite DNA alteration (mtMSA) and p53 protein expression in thoracic esophageal squamous cell carcinoma (TESCC).

Methods.

Paired micro-dissected esophageal tissues from 66 TESCC patients were subjected to DNA extraction and analysis. D17S960 and poly-C tract (PCT) were chosen as microsatellite DNA markers to address loss of heterozygosity (LOH) / microsatellite instability (MSI) for *TP53* nMSA and mtDNA copy ratio / PCT sequencing variations for PCT mtMSA, respectively. The degree of p53 protein expression was analyzed by immunohistochemical staining (IHC).

Results.

From non-cancerous esophageal mucosa (n=66) to cancerous TESCC nests (n=66) and further metastatic lymph nodes (n=35), there was a trend of increased *TP53* LOH (19.7%, 34.8%, 37.1%; P=0.023), higher incidence of PCT homoplasmy (36.4%, 59.1%, 65.7%; P=0.002) and elevated mtDNA copy ratio (0.898, 1.139, 1.183; p=0.019) during TESCC evolution. From T1, T2, to T3 and then T4 cancerous nests during TESCC invasion, an increase of *TP53* LOH (12.5%, 16.7%, 34.8%, 52.2%; P=0.037) was observed, which correlated inversely with positive p53 protein expression (50.0%, 33.3%, 26.1%, 21.7%; P=0.058). Concomitant *TP53*nMSA and PCT mtMSA, including *TP53* LOH and increasing mtDNA copy ratio (P=0.073), and MSI and heteroplasmic PCT patterns / PCT mutations (P=0.078; P=0.074), were detected among the 66 cancerous TESCC nests.

Conclusion.

TESCC evolution with clonal expansion was validated from the view points of *TP53* nMSA and PCT mtMSA. Parallel occurrence of *TP53* nMSA and PCT mtMSA indicates a possible cause-effect relationship in TESCC evolution.

Key words:

Thoracic esophageal squamous cell carcinoma, Mitochondrial DNA, Poly-C tract, p53 gene, Microsatellite, Loss of heterozygosity