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Frequent V600E and other non-hotspot BRAF mutations in adult differentiated thyroid cancer

Murugan Avaniyapuram Kannan, Qasem E, Al-Hindi H, Shi Y and Alzahrani A S

King Faisal Specialist Hospital and Research Center, KSA

BRAF is the most frequently mutated gene in differentiated thyroid cancer (DTC). Previous studies on DTC have well documented high rates of the BRAFV600E mutation in patients of mixed ages. However, the prevalence of hotspot and non-hotspot BRAF mutations and its significance in pure adult DTCs is not yet well determined. In this study we determine the frequency of classical BRAF mutation and other rare BRAF mutations in pure adult DTCs. A total of 221 tumor samples consisting of 17 multi nodular goiters (MNG) and 204 adult DTC samples (Age >18 years) were analyzed for mutations in exon 15 of the BRAF gene by PCR amplification of tumor genomic DNAs and direct sequencing of amplicons using Sanger sequencing. Obtained results were correlated to clinical characteristic features of DTCs. Overall; BRAF mutations were identified in 48.5% (99/204) of adult DTCs. Three rare non-hotspot mutations (T599I, T599dup and K601E) were detected in 4 tumor samples (2%). One (K601E) of these non-hotspot mutations occurred in conventional papillary thyroid cancer and other three (T599I, T599dup and K601E) were found in follicular variant PTC. We found significant association between BRAFV600E mutation and age ($P<0.0001$), extrathyroidal invasion ($P=0.017$), lymph node metastasis ($P=0.038$) and TNM stage III/IV ($P=0.001$). Our study is the first to report BRAF mutations in a pure adult sample of DTCs of Saudi Arabian ethnicity. Our results show a high rate and a strong prognostic role of the classical BRAFV600E mutation and also suggest a common occurrence of non-hot spot mutations in adult DTC.

Biography

Murugan Avaniyapuram Kannan has completed his PhD from the Department of Molecular Oncology, Tokyo Medical and Dental University, Tokyo, Japan and Postdoctoral studies from Hoshi University, Tokyo, Japan and The Johns Hopkins University School of Medicine, Baltimore, USA. Currently, he is a Scientist in the Department of Molecular Oncology, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia. He has published more than 30 papers in reputed journals and holding a patent for identification of novel ALK mutations in anaplastic thyroid cancer. His research focuses on molecular biology of head and neck squamous cell carcinoma and thyroid cancer identifying molecular therapeutic targets and biomarkers. He has been serving as a Reviewer in *Thyroid*, *PLOS One*, *Cancer Research*, *Tumor Biology*, *Endocrine Related Cancer* and *Oral Oncology*.

akmurugan@gmail.com

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