Malaysian J Pathol 2017; 39(1) : 95 – 96

LETTER TO EDITOR

Prevalence of *BRAF*^{V600E} mutation in Asian patients with thyroid cancer

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Dear Editor,

I read with interest the recent article of Navarro-Locsin *et al* from the Philippines on the local rate of *BRAF*^{V600E} mutation in thyroid cancer.[1] *BRAF*^{V600E} is a key genetic event in the initiation and progression of papillary thyroid carcinoma (PTC).[2] It is a well-established diagnostic marker useful in the preoperative evaluation of indeterminate thyroid nodules. In addition, *BRAF* mutation attracts substantial interest as a therapeutic target and prognostic tool. It is believed that knowing the local *BRAF* mutation rate is of importance not only to the particular patient but also to health care providers. *BRAF* testing alone (opposite to multi-target gene panels) is deemed to be more cost-effective in regions with high prevalence of *BRAF* mutation.

A rate of *BRAF*^{V600E} in PTC was extensively reported from Western countries (USA and Europe), with the consistent prevalence of 40-45% across different regions.[2] Summary on *BRAF* mutation rate in Asian countries is shown in Fig. 1. Available data from South and Southeast Asia are very

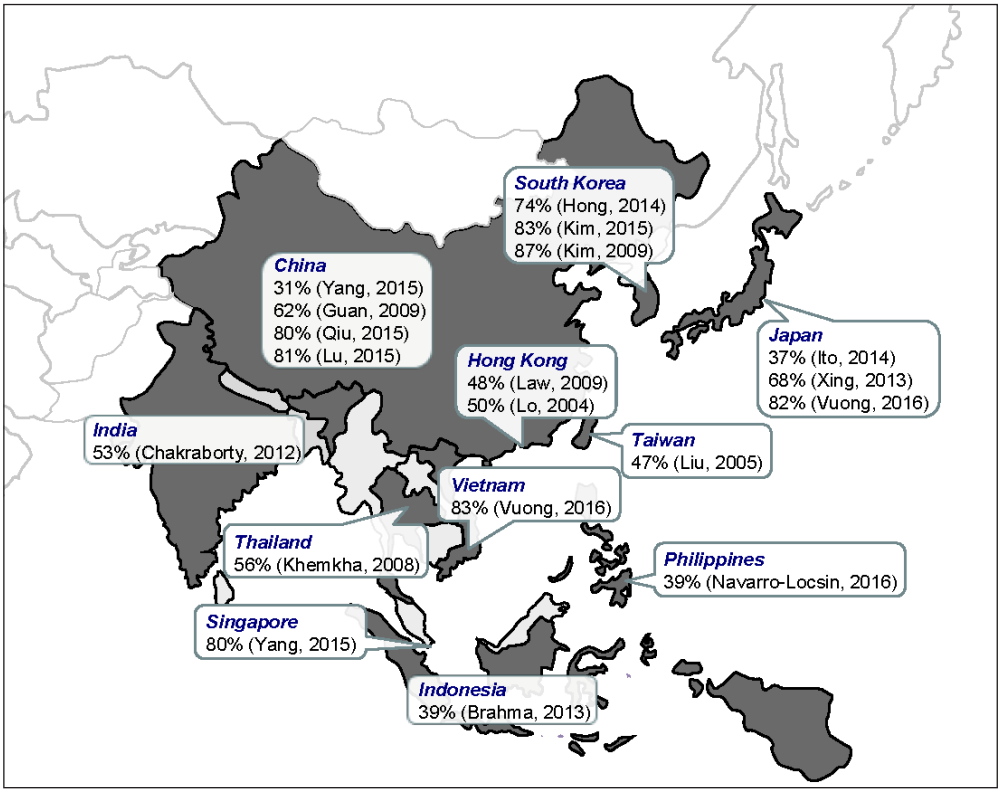

FIG. 1: Prevalence of *BRAF*^{V600E} mutation in Asian patients with papillary thyroid carcinoma
Full references are available from the author on request

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scarce, usually limited to 1-2 reports from a country, always based on small sample size. The rates from India, Thailand, Indonesia, Hong Kong, and Taiwan appear to be approximately similar (40-50%). In contrast, more abundant Chinese studies showed wide variation (30-80%). A *BRAF*^{V600E} rate in far neighbors, Australia and the Middle East, was reported as similar to the USA and Europe (45%). Japan and South Korea with 60-90% prevalence of *BRAF* mutation stands out from the above countries.[3] Whether such a striking difference is attributed by geography (iodine intake, pollutants), ethnicity (Asians vs. Caucasians, with their genetics and habits), or other factors (prevalence of Hashimoto's thyroiditis, histological variant, etc.) is not fully understood. The overall Asian rates of *BRAF* mutation in thyroid cancer are significantly higher than those from Western countries.[3]

In their study, Navarro-Locsin *et al* found 38.5% of *BRAF*^{V600E} in the Filipino cohort of patients with thyroid cancer. Considering that all the tumours were classic PTC, such rate is unexpectedly low. This poses an interesting question about other genetic events, which could drive thyroid cancer development in the studied cohort. PTC classic variant is typically initiated by *BRA*F mutation (up to 75%), while mutually exclusive gene fusions (mainly *RET/PTC*) are found less frequently.[4] This study is also discordant with an earlier report, which found *BRAF* mutation in 83.8% of classic PTC in Filipino population in Hawaii.[5] The controversy may be explained by technical issues, low sample number, selection bias, or specific characteristics of the studied population. However, apart from this minor concern, the main issue learned from the Filipino study is that despite significant research interest and practical promises *BRAF* mutation remains largely underexplored in Southeast Asian patients with thyroid cancer. More efforts are needed to set up large multi-institutional studies with the aim to establish the national prevalence of *BRAF* mutation in thyroid cancer across ASEAN countries.

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