

## BRAF and Thyroid Cancer

The article by Quong et al, in this issue, has reported that B-type Raf kinase (BRAF) mutation correlated with pathological aggressiveness. It is well known that BRAF mutation is one of the major causes of the aberrant activation of mitogen-activated protein kinases (MAPK) pathway in many human cancers, such as papillary thyroid carcinoma (PTC), melanoma, colorectal, brain, ovary.<sup>1</sup> It is found in up to 60% cases of conventional PTC where the most common mutation is V600E leading to uncontrolled cell growth, angiogenesis, invasion and metastatic processes.<sup>2</sup> Various studies have shown significant association between BRAF and advanced tumor stages, lymph node metastasis, extrathyroidal extension with odds ratio of 2.14, 1.83, 2.50 respectively.<sup>1</sup> The presence of BRAF mutations is associated with PTC recurrence, loss of radioactive iodine avidity requiring aggressive management by surgery, radiotherapy and also increased mortality.<sup>1,3</sup> Recent studies have shown close association between BRAF and silencing of many significant tumor suppressor genes of PTC, such as death-associated protein kinase (DAPK), tissue inhibitor of matrix metalloproteinase-3 and iodide metabolizing genes of thyroperoxidase and sodium/iodide symporter.<sup>1</sup> Thus, there is fundamental association between BRAF mutation and increased aggression, progression of PTC.<sup>4</sup> Preoperatively, BRAF mutation can be easily detected by FNAC of the nodules using colorimetric mutation detection assay, fluorescence melting curve analysis and help in better planning of both surgical and medical treatments.<sup>3</sup> Extensive research is being done to develop novel BRAF inhibitors and their combinations with other immunotherapeutic and conventional chemotherapy agents which can suppress the MAPK pathway.<sup>5</sup> The results of these clinical trials are being eagerly awaited as these may lead to fundamental changes in management of PTC.<sup>1</sup>

## REFERENCES

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