

# Immunohistochemical Localization of RET Rearrangements in a Malaysian Papillary Thyroid Carcinoma Population

E Omar, MBBCH, N H Othman, MPath

Department of Pathology, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan

Sir,

Over the years there have been numerous publications on the prevalence of RET/PTC mutation in papillary thyroid carcinoma from different geographical locations around the world. Populations from the South East Asian and South Pacific areas have a high reported incidence of papillary carcinoma; for example the reported incidence of Filipino women is at 14.6 per 100,000<sup>2</sup>; while incidence in Melanesian women in 1985-1992 period were 35 per 100,000<sup>3</sup>. Yet, little is known regarding the prevalence of RET/PTC expression among this population. Chua et al<sup>1</sup> reported an incidence of RET/PTC expression of 70% among New Caledonian population. No reports of RET/PTC prevalence among South East Asian nations can be found in literature.

Our group had recently subjected 53 cases of papillary carcinoma, 50 cases of follicular adenoma and 66 cases of nodular hyperplasia (multinodular goiter) to immunohistochemistry for RET protein using a rabbit poly-clonal antibody for carboxyl terminal region of RET (Santa Cruz, Ca). This method was chosen for the study because reviews of previous studies have shown excellent concurrence between it and molecular methods of detection<sup>4,5,6</sup>, plus the obvious advantages of being able to simultaneously visualize RET expression

and histology of the tissue. In addition, a large number of cells can be screened and it is also less cumbersome.

We found a high prevalence of RET expression among our papillary carcinoma at 77% (38 of 53);  $p < 0.001$ . Interestingly, the follicular adenomas and nodular hyperplasia cases exhibited a low expression of RET of 18% (9 of 50 cases) and 22.7% (15 of 66) respectively. RET/PTC re-arrangement has been demonstrated in these lesions before<sup>7,8</sup>. It has been postulated that these positive follicular cell represented focal clonal expansion of neoplastic cells.

The North-Eastern population of Malaysia has a high incidence multinodular goiter<sup>9</sup>. Histological examination of multinodular goiter specimen at our centre, which caters for this region, found that 34% of it harboring carcinoma<sup>10</sup>; a high figure compared to international incidence of 4 to 17%<sup>11</sup>. With the high prevalence of RET expression among the papillary carcinoma cases, and concurrent RET expression in nodular hyperplasia lesions, we postulate that rearrangement of this gene is the initiating event for development of malignancy in these benign lesions and that nodular hyperplasia is a precursor lesion of thyroid carcinoma, at least in the local context.

This letter was accepted: 10 January 2003

Corresponding Author: Nor Hayati Othman, Pathology Department Hospital Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan

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