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Comparison of thyroid transcription factor-1 expression by two monoclonal antibodies in schwannomas: the chosen clone matters

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To the editor:

We have read with great interest the recently published study by Wang et al [1] on aberrant expression of thyroid transcription factor-1 (TTF-1) in schwannomas. The authors described nuclear TTF-1 in 109 (67.7%) schwannomas, including 102 of 132 (77.9%) conventional, 1 of 20 (5%) cellular and 6 of 10 (60%) plexiform schwannomas. Nuclear staining was not identified in normal peripheral nerves and non-schwannoma peripheral nervous system lesions.

However, the authors used in this study the monoclonal anti−TTF-1 antibody clone SPT24 and did not explore the difference between the SPT24 clone (Leica/Novocastra) and the other main commercially available anti−TTF-1 antibody clone, 8G7G3/1 (Dako). There is strong evidence in the literature that an important factor influencing the prevalence of TTF-1 expression in tumors (other than those of pulmonary or thyroid origin) is the type of clone that is used [2,3]. This has also been demonstrated in publications documenting TTF-1 immunoreactivity in glial neoplasms [4,5], gynecologic carcinomas [6], breast carcinomas [3] and colorectal carcinomas [7,8].

Therefore, we analyzed TTF-1 expression in 60 additional schwannomas (including 44 conventional and 13 cellular subtypes) and compared the results obtained with the 8G7G3/1 and SPT24 TTF-1 clones (see Table 1 and Table 2). We also included in our study 3 cases of epithelioid schwannoma, a rare subtype of schwannoma, which was not tested in the current study by Wang et al [1]. We used the same combined scoring system to evaluate the intensity and distribution of nuclear TTF-1 staining as described by Wang et al. Notably, the SPT24 clone detected a much higher number of positive cases in both the conventional and cellular

subtypes. In conventional schwannomas, positivity with the SPT24 clone was detected in 37 of 44 (83%) cases as opposed to the 8G7G3/1 clone, which showed expression in 25 of 44 (56%) cases. With the SPT24 clone, strong and diffuse SPT24 staining for TTF-1 (score 8-9) was observed in 14 (44%) conventional schwannomas. On the contrary, none of the cases showed a diffuse and strong staining with the 8G7G3/1 clone, and in most of the 8G7G3/1-positive cases only focal and weak staining (score 2 to 5) was seen. Eight of 13 (61%) and 3 of 13 (23%) cellular schwannoma cases were only focally and weakly positive with the SPT24 and 8G7G3/1 clone, respectively. Compared to the results of Wang et al, we observed SPT24 anti−TTF-1 clone positivity in a higher percentage of cellular schwannoma cases. However, all positive cases of cellular schwannoma in our study showed only very focal and weak positivity (scores 2-3). Three epithelioid schwannomas, tested with both anti−TTF-1 antibody clones, were completely negative.

In summary, this comparative study of TTF-1 expression in schwannomas by two widely used anti−TTF-1 antibody clones, 8G7G3/1 and SPT24, showed TTF-1 expression with both clones, albeit expression with the 8G7G3/1 clone was seen in a much lower percentage of cases and was weaker in intensity and more focal in distribution compared to the SPT24 staining. With both antibody clones, TTF-1 expression was more prevalent in conventional schwannomas and was not seen in the rare epithelioid subtype. These findings further underscore the literature data that the sensitivity and specificity of TTF-1 staining is dependent on the antibody clone used [3,9].

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Table 1 TTF-1 expression in conventional schwannomas

TTF-1 expression	Wang et al [1]	Ghent study	
	SPT24-clone, n (%)	SPT24-clone, n (%)	8G7G3/1-clone, n (%)
Negative	29/131 (22%)	7/44 (17%)	19/44 (44%)
Weak	31/131 (24%)	12/44 (27%)	20/44 (45%)
Moderate	45/131 (34%)	11/44 (25%)	5/44 (11%)
Strong	26/131 (20%)	14/44 (31%)[a]	0/44 (0%)

[a]Eleven of the 14 strongly staining cases had score 8

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Table 2 TTF-1 expression in cellular schwannomas

TTF-1 expression	Wang et al [1]	Ghent study	
	SPT24-clone, n (%)	SPT24-clone, n (%)	8G7G3/1-clone, n (%)
Negative	19/20 (95%)	5/13 (39%)	10/13 (77%)
Weak	1/20 (5%)	8/13 (61%)[a]	3/13 (23%)
Moderate	0/20 (0%)	0/13 (0%)	0/13 (0%)
Strong	0/20 (0%)	0/13 (0%)	0/13 (0%)

[a]Five of the 8 weakly staining cases had a low score of 2 or 3