Correspondence

Diagnosis and Classification of Small Round-Cell Tumors of Childhood

To the Editor-in-Chief:

I read with interest the recent Commentary on the diagnosis and classification of small round-cell tumors of childhood that appeared in the July 1999 issue of the *Journal*.¹ However, two statements made in this Commentary warrant further analysis. First, the author states that "although several subtly different *EWS-FLI1* and *EWS* fusion transcripts have been identified to date, significant correlations between different chimeric *EWS* transcripts and clinical parameters have not been identified." This statement is not supported by a review of the literature. Since 1996, two independent groups have published data showing that *EWS-FLI1* fusion transcript structure is indeed prognostically significant in Ewing's sarcoma.^{2,3} Analogous observations have incidentally also been reported in alveolar rhabdomyosarcoma⁴ and synovial sarcoma.^{5,6}

The second statement that warrants further comment is that "the t(11;22) is not specific for the Ewing's family of tumors" because "recent studies have demonstrated that the t(11;22) translocation can be identified in some cases of neuroblastoma and rhabdomyosarcoma." This echoes a similar statement in the accompanying article.⁷ However, these two examples of the apparent nonspecificity of *EWS-FLI1* for Ewing's sarcoma require critical analysis. Regarding the report of *EWS-FLI1* in neuroblastoma,⁸ it should be noted that these results have not been independently reproduced and that they were demonstrated only by reverse transcriptase-polymerase chain reaction (RT-PCR), not by conventional cytogenetics, contrary to what is implied by the authors' sentence. The reported incidence of 17% is in fact difficult to reconcile with almost two decades of conventional cytogenetic analysis of neuroblastoma which has not detected the t(11;22) translocation in this tumor. Other groups have also failed to detect *EWS-FLI1* by RT-PCR in larger series of neuroblastomas.⁹ In reference to the report of *EWS-FLI1* in rhabdomyosarcoma,¹⁰ this also remains an isolated report of two cases of apparently typical primitive rhabdomyosarcoma, which were found to contain the translocation by RT-PCR (and in one case also by fluorescence *in situ* hybridization). However, other RT-PCR studies including a total of 92 rhabdomyosarcomas have failed to detect a single *EWS-FLI1*-positive case.^{9,11,12} These two rhabdomyosarcoma-like tumors containing *EWS-FLI1*¹⁰ may therefore be more closely related to the rare mixed phenotype tumors, which have been reported to contain *EWS-FLI1* by several groups.¹³⁻¹⁶

In summary, I would suggest that isolated reports such as these^{8,10} be presented critically and with appropriate

context provided. Studies that present unexpected findings inconsistent with the rest of the literature should always be carefully evaluated. The issues involved raise more than simply a question of specificity or nonspecificity of a given test. Rather, they impact fundamental concepts of the biology and nosology of these tumors. It is only through the critical analysis of our own data and those of other investigators that we can hope to make sense of these often puzzling tumors.

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