Letter to the Editor


Letter

Since the identification of a second estrogen receptor (ER), ERβ, in the mid-1990s (1), much effort has been directed into trying to define its biological role, particularly in breast cancer. Unlike its sibling, ERα, which predicts a favorable disease outcome and response to antiestrogen therapy, the function of ERβ remains obscure.

In an interesting recent article, Fuqua et al. (2) have gone some way to address this by reporting immunohistochemical detection of ERβ in one of the largest studies conducted to date, comprising 242 breast tumors. At least superficially their results are in excellent concordance with the largest immunohistochemical study to date of ERβ expression in breast cancer, in which 319 breast tumors were evaluated (Ref. 3; Table 1). Both studies used the same primary antibody, 14C8, which has proved consistently reliable in our hands (3–5), and the Allred scoring system (6) was used to determine receptor positivity. However, a fundamental difference between these studies was the cutoff used to categorize tumors as ERβ positive. Fuqua et al. (2) used a value of 2, which is consistent with the accepted criterion for ERα, whereas we used a value of 4. As Fuqua et al. correctly pointed out, there is at present no recognized consensus for scoring ERβ; therefore, assigning a cutoff value remains arbitrary. In the study by Fuqua et al. there was a relatively even distribution of scores throughout the cohort, whereas in our study >50% of cases achieved the maximum score of 8/8. The relatively high number of lobular carcinomas in our study (111) may have posed a selection bias because, with few exceptions, they strongly expressed ERβ. It would be interesting to know the distribution of tumor types in the cohort studied by Fuqua et al. Other confounding variables may include the time elapsed between when the sections were cut and when immunohistochemistry was performed (we have observed that ERβ antigen degrades very rapidly in cut sections1) or even as a result of ethic differences between the two study cohorts, as reported for mRNA in African-American women compared with Caucasians (7).

Until immunohistochemical expression can be correlated with endocrine response in a clinical context, the appropriate threshold for scoring a tumor “positive” for ERβ will remain ambiguous. ERβ may well turn out to be an important contender in dictating hormone responsiveness, but until there is a recognized consensus on the best way to interpret its presence in the clinical setting, its contribution will remain obscure. Future studies are needed that would allow interlab-

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Table 1 Comparison of estrogen receptor β expression in breast cancer in two recent immunohistochemical studies

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>a</th>
<th>b</th>
<th>a+b*</th>
<th>b*</th>
<th>a</th>
<th>b</th>
<th>a+b</th>
<th>a+</th>
<th>a+b</th>
<th>a</th>
<th>b</th>
<th>a+b</th>
<th>ERβ-positive correlations</th>
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<tbody>
<tr>
<td>Fuqua et al.</td>
<td>234</td>
<td>75</td>
<td>76</td>
<td>62</td>
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<td>15</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td>Aneuploidy</td>
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<td>Skliris et al.</td>
<td>319</td>
<td>74</td>
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<td>18</td>
<td>8</td>
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<td></td>
<td></td>
<td></td>
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<td>ERα, PR</td>
</tr>
</tbody>
</table>

Notes: 1. ER, estrogen receptor; PR, progesterone receptor.
2. ERα-positive tumors were defined as tumors expressing >50% of nuclei.

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References


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1. Our unpublished observations.

Valerie Speirs


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