Cyclin E is a more powerful predictor of breast cancer outcome than proliferation

To the editor—We thank Borg *et al*. for their *News and Views* article[1] highlighting our publication in the 14 November 2002 *New England Journal of Medicine*, in which we correlated the expression of low-molecular-weight isoforms of cyclin E to poor survival in breast cancer[2]. We would like to draw attention, however, to an error in their review, in which they mistakenly stated that we did not include cell proliferation indices such as Ki-67 in conjunction with our cyclin E analysis. The prognostic value of Ki-67 and ploidy as measures of proliferation and S-phase fraction were clearly shown in Table 1 of our paper. When evaluated by Ki-67 staining, 15% of patients with a negative proliferation index had died of breast cancer within five years, compared with 37% with a high proliferation index. In addition, 19% of patients with diploid tumors died of disease by five years, compared with 33% with aneuploid tumors. In contrast, only 5% of patients with low cyclin E levels died of breast cancer within five years, whereas 78% of patients with high cyclin E levels died of their disease. Although Ki-67 and ploidy were significant in the univariate analysis, they lost significance in the multivariate model. Cyclin E remained the single most significant predictor of survival, at least ten times more powerful than either proliferation or ploidy. The reviewers also questioned the exclusion of tumor grade from our analysis. Data regarding the prognostic value of tumor grade in patients with smaller, node-negative tumors, a substantial proportion of our study cohort, are not consistent[3–5]. In fact, variability in the literature regarding tumor grade and prognosis led the Breast Task Force to exclude this variable from the recent American Joint Committee on Cancer (AJCC) breast cancer staging update[6]. Because of these issues of reliability and clinical use, we decided not to compare tumor grade with cyclin E. We hope this clarifies the issues raised by Borg *et al*. regarding our data analysis.

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3. Kollias, J. *et al.* The prognosis of small primary breast cancers. *Eur. J. Cancer.* **35**, 908–912 (1999).
4. Rosner, D. & Lane, W.W. Should all patients with node-negative breast cancer receive adjuvant therapy? Identifying additional subsets of low-risk patients who are highly curable by surgery alone. *Cancer* **68**, 1482–1494 (1991).
5. Reed, W. *et al.* The prognostic value of p53 and c-erbB-2 immunostaining is overrated for patients with lymph node negative breast carcinoma: a multivariate analysis of prognostic factors in 613 patients with a follow-up of 14-30 years. *Cancer* **88**, 804–813 (2000).
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How to submit microarray data

Nature Medicine will implement a new policy regarding microarray experiments on 1 December 2002. As discussed in a recent editorial in *Nature* (**419**, 323; 2002), *Nature Medicine* will now require authors to submit microarray data in accordance with the Minimal Information About a Microarray Experiment guidelines issued by the Microarray Gene Expression Data society. The guidelines include a checklist of relevant information that should be included with every new microarray submission, and can be found online at http://www.mged.org/Workgroups/MIAME/miame_checklist.html. The supplementary information must be supplied with the manuscript on five compact discs, at the time of submission, in a format compatible with commonly available software packages. We will also require that data central to the paper's conclusions be deposited in a public database for microarray data and accession numbers provided, where available, at or before acceptance for publication. By adopting this policy, we hope that the explicit description of experimental design and methods will facilitate the review and replication of microarray results.