determined previously[5] (**Fig. 1**). This analysis showed a striking overlap in classification: the 26-gene SDPP signature produced a poor outcome cluster with 76% basal tumors (supervised classification, **Table 1a**; 91% in unsupervised classification, data not shown).

This suggests strong dependence between the poor-outcome SDPP subtype and the Sorlie basal subtype and points to the possibility that the stroma microenvironment may be involved in development of the basal type of breast cancer. Clearly, a number of reasons for the discovered overlap are conceivable, including morphological differences; in a gene ontology analysis, Finak *et al.*[1] found that genes related to proliferation were overrepresented in the poor outcome stroma.

To validate the association, we investigated the overlap in two additional breast cancer datasets: the Netherland Cancer Institute (NKI) data[6] and the Finak *et al.*[1] stroma data in which the SDPP subtypes were discovered. These analyses seem to confirm a relationship: Fisher's tests for independence between the poor-outcome stroma subtype and basal subtype were significant in both groups (**Table 1b**,**c**). The association was also confirmed by clustering with 163 class-distinctive genes (**Table 1** and **Supplementary Figs. 1** and **2** online). Of note, similar patterns of overlap in the Finak *et al.*[1] stroma data and the two whole-tumor data sets suggest that the basal subtype—as characterized by Sorlie *et al.*[2]—is probably defined partly by stromal gene expression.

Our findings may seem to conflict with that of Finak *et al.*[1], who report that the SDPP predicts outcome independently. We would, however, like to emphasize that the discovered association in no way precludes the possibility that the SDPP has independent prognostic capacity. The relevance is biological rather than clinical: investigation of this unrecognized link between the SDPP-derived poor-outcome group and the earlier described basal type of breast cancer may provide further insight regarding the stroma-epithelium interaction in breast cancer.

Kristian Wennmalm, Arne Östman & Jonas Bergh

Department of Oncology and Pathology, Karolinska Institutet, Stockholm S-171 76, Sweden.

1. Finak, G. *et al. Nat. Med.* **14**, 518–527 (2008).
2. Sorlie, T. *et al. Proc. Natl. Acad. Sci. USA* **98**, 10869–10874 (2001).
3. Karnoub, A.E. *et al. Nature* **449**, 557–563 (2007).
4. Finak, G. *et al. Breast Cancer Res.* **8**, R58 (2006).
5. Calza, S. *et al. Breast Cancer Res.* **8**, R34 (2006).
6. van de Vijver, M.J. *et al. N. Engl. J. Med.* **347**, 1999–2009 (2002).
7. Miller, L.D. *et al. Proc. Natl. Acad. Sci. USA* **102**, 13550–13555 (2005).

Finak *et al.* reply:

In our previous report in *Nature Medicine*[1], hierarchical clustering of breast tumor stromal-specific gene expression data revealed a group of subjects enriched for poor clinical outcome. From 163 genes differentially expressed between this cluster and the remaining samples, we derived a predictor consisting of 26 (SDPP) and showed that it predicted poor clinical outcome in multiple breast tumor data sets. The SDPP was explicitly constructed to bias against outcome-linked genes that strongly associated with histopathological subtypes (defined by immunohistochemistry) rather than as a measure of which stroma cluster a tumor belongs to. We clarify the points raised by Wennmalm *et al.*[2] In contrast to our approach, Wennmalm *et al.*[2] use the 26 SDPP genes to train a classifier to predict membership in our poor-outcome stroma cluster rather than to predict clinical outcome, a fundamentally different goal than that of our report[1] and one for which the SDPP genes are unlikely to be an optimal choice. Consistent with our stated results (Table 2 in ref. 1), Wennmalm *et al.*[2] observe that their poor-outcome cluster is enriched for basal tumors. However, their use of the Sorlie *et al.*[3] centroids to assign tumor subtypes in our stroma gene expression data is, in our opinion, incorrect, as many of the genes in these centroids are epithelial specific. Consequently, Wennmalm *et al.*[2] assigned subtypes that are in disagreement with the immunohistopathology data, as their results predict five HER2-positive and eight basal tumors, whereas we reported ten HER2-positive and six triple-negative (basal) tumors. Because the stroma generally does not possess the estrogen receptor or HER2 signatures, it is likely to be confounded with the triple-negative (basal) subtype owing to the lack of ER or HER2 expression, thus increasing the apparent percentage of these tumors. We reported a similar observation for normal breast tissue[4].

Greg Finak[1], Nicholas Bertos[2], Michael Hallett[3] & Morag Park[2,3]

[1]Computational Biology Unit, Institut des Recherches Cliniques de Montreal, 110 Pine Avenue West, Montreal, Quebec H2W 1R7, Canada. [2]Breast Cancer Functional Genomics Group, 1160 Pine Avenue West, Montreal, Quebec H3A 1A3, Canada. [3]Department of Biochemistry, 3655 Promenade Sir William Osler, McGill University, Montreal, Québec H3G 1Y6, Canada.
e-mail: morag.park@mcgill.ca

1. Finak, G. *et al. Nat. Med.* **14**, 518–527 (2008).
2. Wennmalm, K., Ostman, A. & Bergh, J. *Nat. Med.* **15**, 237–238 (2009).
3. Sorlie, T. *et al. Proc. Natl. Acad. Sci. USA* **98**, 10869–10874 (2001).
4. Finak, G. *et al. Breast Cancer Res.* **8**, R58 (2006).

The preimplantation embryo and Jewish law

To the Editor:

We read with interest the report of Jon Evans in the News section of *Nature Medicine*[1] summarizing the recent conference sponsored by the Progress Educational Trust entitled "Is the Embryo Sacrosanct? Multi-Faith Perspectives." To our chagrin, the report provided a most misleading one-sentence summary of the normative Jewish Law (Halachic) perspective on this complicated major biomedical ethical issue.

The article states that under Jewish Law "an embryo is regarded as containing life in potential and should therefore be treated with the utmost care and attention." In reality, this truism in no way reflects the detailed, practical, real-world implementation of the Halacha (Jewish religious law), a perspective that most definitely differs from the one that was promulgated in the recent Vatican proclamation entitled *Dignitas Personae* (*The Dignity of a Person*) or that was advocated by Lee Rayfield, the Anglican Bishop of Swindon.

Jewish law distinguishes six stages of human development, the first three of which are pertinent to the issue of stem cell research and our discussion: (i) the preimplantation embryo (from fertilization to implantation); (ii) the embryo (from implantation to identifiable organogenesis—that is, until 40 days after conception); (iii) the fetus (from organogenesis until potential viability—40 days after conception until 20 or more weeks); (iv) the viable fetus (from 20 or more weeks until onset of labor); (v) the 'dislodged' fetus (from the beginning of the second stage of labor until birth); and (vi) the neonate.