# Gene-expression profiles to predict distant metastasis of lymph-node-negative primary breast cancer

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#### Summary

Background Genome-wide measures of gene expression can identify patterns of gene activity that subclassify tumours and might provide a better means than is currently available for individual risk assessment in patients with lymph-node-negative breast cancer.

Methods We analysed, with Affymetrix Human U133a GeneChips, the expression of 22 000 transcripts from total RNA of frozen tumour samples from 286 lymph-node-negative patients who had not received adjuvant systemic treatment.

Findings In a training set of 115 tumours, we identified a 76-gene signature consisting of 60 genes for patients positive for oestrogen receptors (ER) and 16 genes for ER-negative patients. This signature showed 93% sensitivity and 48% specificity in a subsequent independent testing set of 171 lymph-node-negative patients. The gene profile was highly informative in identifying patients who developed distant metastases within 5 years (hazard ratio  $5 \cdot 67$  [95% CI  $2 \cdot 59-12 \cdot 4$ ]), even when corrected for traditional prognostic factors in multivariate analysis ( $5 \cdot 55$  [ $2 \cdot 46-12 \cdot 5$ ]). The 76-gene profile also represented a strong prognostic factor for the development of metastasis in the subgroups of 84 premenopausal patients ( $9 \cdot 60$  [ $2 \cdot 28-40 \cdot 5$ ]), 87 postmenopausal patients ( $4 \cdot 04$  [ $1 \cdot 57-10 \cdot 4$ ]), and 79 patients with tumours of 10–20 mm ( $14 \cdot 1$  [ $3 \cdot 34-59 \cdot 2$ ]), a group of patients for whom prediction of prognosis is especially difficult.

Interpretation The identified signature provides a powerful tool for identification of patients at high risk of distant recurrence. The ability to identify patients who have a favourable prognosis could, after independent confirmation, allow clinicians to avoid adjuvant systemic therapy or to choose less aggressive therapeutic options.

#### Introduction

About 60-70% of patients with lymph-node-negative breast cancer are cured by local or regional treatment alone.<sup>1,2</sup> The most widely used treatment guidelines are the St Gallen<sup>3</sup> and the US National Institutes of Health<sup>4</sup> consensus criteria. These guidelines recommend adjuvant systemic therapy for 85-90% of lymph-nodenegative patients. There is a need for specific definition of an individual patient's risk of disease recurrence to ensure that she receives appropriate therapy. Currently, few diagnostic tools are available to identify at-risk patients. To date, gene-expression patterns have been used to classify breast tumours into clinically relevant subtypes.<sup>5-21</sup> We report a comprehensive genome-wide assessment of gene expression to identify broadly applicable prognostic markers.5,6 In this study, we aimed to develop a gene-expression-based algorithm and to use it to provide quantitative predictions on disease outcome for patients with lymph-node-negative breast cancer.

## **Methods**

## Patients' samples

We selected from our tumour bank at the Erasmus Medical Center (Rotterdam, Netherlands) frozen tumour samples from patients with lymph-nodenegative breast cancer who were treated during 1980-95, but who did not receive systemic neoadjuvant or adjuvant therapy. Tumour samples were submitted to our reference laboratory from 25 regional hospitals for measurements of steroid-hormone receptors. Guidelines for primary treatment were similar for all hospitals. Selection of tumours aimed to avoid bias. On the assumption of a relapse rate of 25-30% in 5 years, and a substantial loss of tumours for quality-control reasons, 436 samples of invasive tumours were processed. Patients with poor, intermediate, and good clinical outcome were included. Samples were rejected on the basis of insufficient tumour content (53), poor RNA quality (77), or poor chip quality (20); thus, 286 samples were eligible for further analysis. The study was approved by institutional medical ethics committee (number 02.953). The median age of the patients at surgery was 52 years (range 26-83). 219 had undergone breast-conserving surgery and 67 modified radical mastectomy. Radiotherapy was given to 248 patients (87%) according to our institutional protocol. The proportions of patients who underwent breast-conserving therapy and radiotherapy are normal for lymph-node-negative disease. Patients were included irrespective of radiotherapy status because this study did not aim to investigate the effects of a specific type of surgery or adjuvant radiotherapy. Furthermore, other studies have shown that

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#### Figure 1: Profile for selection of samples for analysis and unsupervised clustering analysis of gene-expression data for 286 patients with lymphnode-negative breast cancer

ER status was used to identify subgroups. Each subgroup was then analysed separately for selection of markers. The patients in a subgroup were assigned to a training set or a testing set. The markers selected from each subgroup were combined to form a single signature to predict tumour recurrence for all patients in the testing set as a whole. The left panel of the clustering analysis is a view of the 17 819 informative genes. Red indicates high relative expression, green relative low expression. Each column is a sample and each row is a gene. The right panel shows enlarged views of two dominant gene clusters that had drastic differential expression between the two subgroups of patients. The upper gene cluster has a group of 282 downregulated genes in the ER-positive subgroup, and the lower gene cluster is represented by a group of 339 upregulated genes in the ER-positive subgroup. The label bar at the foot of each dendrogram indicates the patient's ER status measured by routine asays.

radiotherapy has no clear effect on distant disease recurrence.<sup>22</sup> Lymph-node negativity was based on pathological examination by regional pathologists.<sup>23</sup> All 286 tumour samples were confirmed to have sufficient (>70%) tumour and uniform involvement of tumour in 5 µm frozen sections stained with haematoxylin and eosin. Amounts of oestrogen receptors (ER) and progesterone receptors (PR) were measured by ligandbinding assay, EIA,<sup>24</sup> or immunohistochemistry (nine tumours). The cut-off value for classification of patients as positive or negative for ER and PR was 10 fmol per mg protein or 10% positive tumour cells. Postoperative follow-up involved examinations every 3 months for 2 years, every 6 months for years 3–5, and every 12 months from year 5. The date of diagnosis of metastasis was defined as that at confirmation of metastasis after symptoms reported by the patient, detection of clinical signs, or at regular follow-up.

#### Gene-expression analysis

Total RNA was isolated from 20–40 cryostat sections of 30 µm thickness (50–100 mg) with RNAzol B (Campro Scientific, Veenendaal, Netherlands). Biotinylated targets were prepared by published methods (Affymetrix, Santa Clara, CA, USA)<sup>25</sup> and hybridised to the Affymetrix oligonucleotide microarray U133a GeneChip. Arrays were scanned by standard Affymetrix protocols. Each probe set was treated as a separate gene. Expression values were calculated by use of Affymetrix GeneChip analysis software MAS 5.0. Chips with average intensity of less than 40 or background signal of more than 100 were rejected. For chip normalisation, probe sets were scaled to a target intensity of 600, and scale mask files were not selected.

## Statistical methods

17 819 genes were "present" in two or more samples and were eligible for hierarchical clustering. Before clustering, the expression level of each gene was divided by its median expression level in the patients. This standardisation step limited the effect of the magnitude of expression of genes, and grouped together genes with similar patterns of expression in the clustering analysis. To identify subgroups of patients, we carried out average linkage hierarchical clustering on both the genes and the samples using GeneSpring 6.0. To identify genes that discriminated patients who developed distant metastases from those remaining metastasis-free for 5 years, we used two supervised class prediction approaches. In the first approach, 286 patients were randomly assigned to training and testing sets of 80 and 206 patients, respectively. Kaplan-Meier survival curves<sup>26</sup> for the two sets were examined to ensure that there was no significant difference and that no bias was introduced

#### Panel: Calculation of relapse scores

Relapse score = 
$$A \cdot I + \sum_{i=1}^{60} I \cdot w_{i} \cdot H \cdot (1-I) + \sum_{j=1}^{16} (1-I) \cdot w_{j} \cdot W_{j}$$

I=1 if ER is more than 10 fmol per mg protein; I=0 if ER is 10 fmol per mg protein or less; w<sub>i</sub> is the standardised Cox's regression coefficient for an ER-positive marker; x<sub>i</sub> is the expression value of the ER-positive marker on a log<sub>2</sub> scale; w<sub>j</sub> is the standardised Cox's regression coefficient for an ER-negative marker; x is the expression value of the ER-negative marker on a log<sub>2</sub> scale; A and B are constants.

by the random selection of the training and testing sets. In the second approach, patients were allocated to one of two subgroups stratified by ER status (figure 1). Each subgroup was analysed separately for selection of markers. Patients in the ER-positive subgroup were randomly allocated into training and testing sets of 80 and 129 patients, respectively. The ER-negative subgroup was randomly divided into training and testing sets of 35 and 42 patients, respectively. Markers selected from each subgroup training set were combined to form a single signature to predict tumour metastasis for both ER-positive and ER-negative patients in a subsequent independent validation.

The sample size of the training set was determined by a resampling method to ensure its statistical confidence level. Briefly, the number of patients in the training set started at 15 patients and was increased in steps of five. For a given sample size, ten training sets with randomly selected patients were made. A gene signature was constructed from each of the training sets and tested in a designated testing set of patients by analysis of the receiver operating characteristic (ROC) curve with distant metastasis within 5 years as the defining point. The mean and the coefficient of variation of the area under the curve (AUC) for a given sample size were calculated. A minimum number of patients required for the training set was chosen at the point at which the average AUC reached a plateau and the coefficient of variation of the ten AUC was less than 5%.

Genes were selected as follows. First, univariate Cox's proportional-hazards regression was used to identify genes for which expression (on a log, scale) was correlated with the length of distant-metastasis-free survival. To reduce the effect of multiple testing and to test the robustness of the selected genes, the Cox's model was constructed with bootstrapping of the patients in the training set.27 Briefly, 400 bootstrap samples of the training set were constructed, each with 80 patients randomly chosen with replacement. A Cox's model was run on each of the bootstrap samples. A bootstrap score was created for each gene by removing the top and bottom 5% p values and averaging the inverses of the remaining bootstrap p values. This score was used to rank the genes. To construct a multiple gene signature, combinations of gene markers were tested by adding one gene at a time according to the rank order. ROC analysis with distant metastasis within 5 years as the defining point was done to calculate the AUC for each signature with increasing number of genes until a maximum AUC value was reached.

The relapse score was used to calculate each patient's risk of distant metastasis (panel). The score was defined as the linear combination of weighted expression signals with the standardised Cox's regression coefficient as the weight.

The threshold was determined from the ROC curve of the training set to ensure 100% sensitivity and the highest specificity. Values of constants A of 313.5 and B of 280 were chosen to centre the threshold of relapse score to zero for both ER-positive and ER-negative patients. Patients with positive or negative relapse scores were classified as those with poor or good prognosis, respectively. The gene signature and the cut-off were validated in the testing set. Kaplan-Meier survival plots and log-rank tests were used to assess the differences in time to distant metastasis of the predicted high-risk and low-risk groups. Odds ratios were calculated as the ratio of the odds of distant metastasis between the patients predicted to experience relapse and those predicted to remain relapse free.

Univariate and multivariate analyses with Cox's proportional-hazards regression were done on the individual clinical variables with and without the gene signature. The hazard ratio and its 95% CI were derived from these results. Statistical analyses used S-Plus software (version 6.1).

# Pathway analysis

A functional class was assigned to each prognostic signature gene. Pathway analysis was done with Ingenuity software (version 1.0). Affymetrix probes were used as input to search for biological networks built by the software. Biological networks identified by

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Poor         148 (52%)         37 (46%)         24 (69%)         87 (51%)           Moderate         42 (15%)         12 (15%)         3 (9%)         27 (16%)           Good         7 (2%)         2 (3%)         2 (6%)         3 (2%)           Unknown         89 (31%)         29 (36%)         6 (17%)         54 (32%)           ER status*         -         -         -         -           Positive         209 (73%)         80 (100%)         0         129 (75%)           Negative         77 (27%)         0         35 (100%)         42 (25%)           PR status*         -         -         -         -           Positive         165 (58%)         59 (74%)         5 (14%)         101 (59%)           Negative         111 (39%)         19 (24%)         29 (83%)         63 (37%)           Unknown         10 (3%)         2 (2%)         1 (3%)         7 (4%)           Metastases withits years         -         -         -         -           Yes         93 (33%)         24 (30%)         13 (37%)         56 (33%)           No         183 (64%)         51 (64%)         17 (49%)         115 (67%)           Censored         10 (3%)	Grade				
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Good         7 (2%)         2 (3%)         2 (6%)         3 (2%)           Unknown         89 (31%)         29 (36%)         6 (17%)         54 (32%)           ER staus*               Positive         209 (73%)         80 (100%)         0         129 (75%)           Negative         77 (27%)         0         35 (100%)         42 (25%)           PR status*           74 (27%)         101 (59%)           Positive         165 (58%)         59 (74%)         5 (14%)         101 (59%)           Negative         111 (39%)         19 (24%)         29 (83%)         63 (37%)           Unknown         10 (3%)         2 (2%)         1 (3%)         7 (4%)           Metastases within 5 verv           7 (49%)           Yes         93 (33%)         24 (30%)         13 (37%)         56 (33%)           No         183 (64%)         51 (64%)         17 (49%)         115 (67%)           Censored         10 (3%)         56 (63)         50 (44%)         0	Moderate	42 (15%)	12 (15%)	3 (9%)	27 (16%)
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Positive         209 (73%)         80 (100%)         0         129 (75%)           Negative         77 (27%)         0         35 (100%)         42 (25%)           PR status*               Positive         165 (58%)         59 (74%)         5 (14%)         101 (59%)           Negative         111 (39%)         19 (24%)         29 (83%)         63 (37%)           Unknown         10 (3%)         2 (30%)         13 (37%)         56 (33%)           Metastases within 5 years         year         year         year         year           Yes         93 (33%)         24 (30%)         13 (37%)         56 (33%)           No         183 (64%)         51 (64%)         17 (49%)         115 (67%)           Censored         10 (3%)         5 (6%)         5 (14%)         0	ER status*				
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PR status*           Positive         165 (58%)         59 (74%)         5 (14%)         101 (59%)           Negative         111 (39%)         19 (24%)         29 (83%)         63 (37%)           Unknown         10 (3%)         2 (2%)         1 (3%)         7 (4%)           Metastases within 5 years         5         56 (33%)         56 (33%)           No         183 (64%)         51 (64%)         17 (49%)         115 (67%)           Censored         10 (3%)         5 (6%)         5 (14%)         0	Negative	77 (27%)	0	35 (100%)	42 (25%)
Positive         165 (58%)         59 (74%)         5 (14%)         101 (59%)           Negative         111 (39%)         19 (24%)         29 (83%)         63 (37%)           Unknown         10 (3%)         2 (2%)         1 (3%)         7 (4%)           Metastases within 5 years         7         7 (4%)         5 (33%)           Yes         93 (33%)         24 (30%)         13 (37%)         56 (33%)           No         183 (64%)         51 (64%)         17 (49%)         115 (67%)           Censored         10 (3%)         5 (6%)         5 (14%)         0	PR status*				
Negative         111 (39%)         19 (24%)         29 (83%)         63 (37%)           Unknown         10 (3%)         2 (2%)         1 (3%)         7 (4%)           Metastases within 5 years         Ves         93 (33%)         24 (30%)         13 (37%)         56 (33%)           No         183 (64%)         51 (64%)         17 (49%)         115 (67%)           Censored         10 (3%)         5 (6%)         5 (14%)         0	Positive	165 (58%)	59 (74%)	5 (14%)	101 (59%)
Unknown         10 (3%)         2 (2%)         1 (3%)         7 (4%)           Metastases within 5 years          5         5         5         5         5         6         3         5         6         3         5         6         3         5         6         3         5         6         3         5         6         3         115         6         7         4         5         6         3         115         6         7         4         9         135         6         3         115         6         7         115         6         7         115         6         7         115         6         7         115         6         7         115         6         7         115         6         7         115         6         7         115	Negative	111 (39%)	19 (24%)	29 (83%)	63 (37%)
Metastases within 5 years         5000000000000000000000000000000000000	Unknown	10 (3%)	2 (2%)	1 (3%)	7 (4%)
Yes         93 (33%)         24 (30%)         13 (37%)         56 (33%)           No         183 (64%)         51 (64%)         17 (49%)         115 (67%)           Censored         10 (3%)         5 (6%)         5 (14%)         0	Metastases within 5 yea	ars			
No         183 (64%)         51 (64%)         17 (49%)         115 (67%)           Censored         10 (3%)         5 (6%)         5 (14%)         0	Yes	93 (33%)	24 (30%)	13 (37%)	56 (33%)
Censored 10 (3%) 5 (6%) 5 (14%) 0	No	183 (64%)	51 (64%)	17 (49%)	115 (67%)
	Censored	10 (3%)	5 (6%)	5 (14%)	0

Data are number of patients unless otherwise stated. \*Positive=>10 fmol per mg protein or >10% positive tumour cells.

Table 1: Clinical and pathological characteristics of patients and their tumours



Figure 2: Establishment of the 76-gene profile and Kaplan-Meier analysis for distant-metastasis-free and overall survival

the program were assessed in the context of general functional classes by GO ontology classification. Pathways with two or more genes in the prognostic signature were selected and investigated.

#### Role of the funding sources

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# Results

The median follow-up for the 198 patients who survived was 101 months (range 20–171). Of the

286 patients included, 93 (33%) showed evidence of distant metastasis within 5 years and were counted as failures in analysis of distant-metastasis-free survival. Five (2%) patients died without evidence of disease and were censored at last follow-up. 83 (29%) died after previous relapse. Therefore, 88 patients (31%) were failures in the analysis of overall survival.

Clinical and pathological features of 286 patients are summarised in table 1. There were no differences among the groups in age or menopausal status. The ER-negative training group had a slightly higher proportion of larger tumours and, as expected, more poor-grade tumours than the ER-positive training group. The validation group of 171 patients (129 ERpositive, 42 ER-negative) did not differ from the total group of 286 patients in any of the characteristics of patients or tumours.

Two approaches were used to identify markers predictive of disease relapse. First, we randomly divided all the 286 patients (ER-positive and ERnegative combined) into a training set and a testing set. 35 genes were selected from 80 patients in the training

Articles



Figure 3: Analysis of distant-metastasis-free and overall survival in subgroups of patients with lymph-node-negative breast cancer

set and a Cox's model to predict the occurrence of distant metastasis was built. Moderate prognostic value was observed (data not shown). Unsupervised clustering analysis showed two distinct subgroups highly correlated with the tumour ER status ( $\chi^2$  test, p<0.0001; figure 1), which supported our second approach in which patients were first grouped on the basis of ER status. Each subgroup was analysed for selection of markers. 76 genes were selected from patients in the training sets (60 for the ER-positive group, 16 for the ER-negative group; figure 2). With the selected genes and ER status taken together, a Cox's

model to predict recurrence of cancer was built for all lymph-node-negative patients. Validation of the 76-gene predictor in the testing set of 171 patients produced an ROC with an AUC of 0.694, sensitivity of 93% (52/56), and specificity of 48% (55/115; figure 2). Patients with a relapse score above the threshold of the prognostic signature have an odds ratio of 11.9 (95% CI 4.04–35.1; p<0.0001) to develop distant metastasis within 5 years. As the control, randomly selected 76-gene sets were generated. These produced ROC with an average AUC value of 0.515, sensitivity of 91%, and specificity of 12% in the testing group.

	Univariate analysis		Multivariate analysi	s*
	Hazard ratio (95% CI)	р	Hazard ratio (95% CI	) p
Age 41–55 years vs ≪40 years	1.16 (0.51-2.65)	0.7180	1.14 (0.45-2.91)	0.7809
Age 56-70 years vs ≪40 years	1.32 (0.56-3.10)	0.5280	0.87 (0.26-2.93)	0.8232
Age ≥70 years vs ≤40 years	0.95 (0.32-2.82)	0.9225	0.61 (0.15-2.60)	0.5072
Postmenopausal vs premenopausal	1.24 (0.76-2.03)	0.3909	1.53 (0.68-3.44)	0.3056
Stages II and III vs stage I	1.08 (0.66-1.77)	0.7619	2.57 (0.23-29.4)	0.4468
Differentiation†	0.38 (0.16-0.90)	0.0281	0.60 (0.24-1.46)	0.2590
Tumour >20 vs ≤20 mm	1.06 (0.65-1.74)	0.8158	0.34 (0.03-3.90)	0.3849
ER positive vs negative	1.09 (0.61-1.98)	0.7649	1.05 (0.54-2.04)	0.8935
PR positive vs negative	0.83 (0.51-1.38)	0.4777	0.85 (0.47-1.53)	0.5882
76-gene signature	5.67 (2.59-12.4)	<0.0001	5.55 (2.46-12.5)	<0.0001

\*The multivariate model included 162 patients, owing to missing values in nine. †Grade: moderate/good vs poor; unknown grade was included as a separate group.

Table 2: Univariate and multivariate analyses for distant-metastasis-free survival in the testing set of 171 patients

Patients stratified by such a gene set would have an odds ratio of 1.3 (0.50-3.90; p=0.8) for development of metastases, indicating a random classification. In addition, the Kaplan-Meier analyses for distantmetastasis-free and overall survival as a function of the 76-gene signature showed highly significant differences in time to metastasis between the groups predicted to have good and poor prognosis (figure 2). At 60 months and 80 months, the respective absolute differences in distant-metastasis-free survival between the groups with predicited good and poor prognosis were 40% (93% vs 53%) and 39% (88% vs 49%), and those in overall survival were 27% (97% vs 70%) and 32% (95% vs 63%) respectively.

The 76-gene profile also represented a strong prognostic factor for the development of distant metastasis in the subgroups of 84 premenopausal patients (hazard ratio 9.60), 87 postmenopausal patients (4.04), and 79 patients with tumour sizes of 10-20 mm (14.1; figure 3).

Univariate and multivariate Cox's regression analyses are summarised in table 2. Other than the 76-gene signature, only grade was significant in univariate analyses and moderate/good differentiation was associated with favourable distant-metastasis-free survival. Multivariate regression estimation of hazard ratio for the occurrence of tumour metastasis within 5 years was 5.55 (p<0.0001), indicating that the 76-gene set represents an independent prognostic signature strongly associated with a higher risk of tumour metastasis. Univariate and multivariate analyses were also done separately for ER-positive and ER-negative patients; the 76-gene signature was also an independent prognostic variable in the subgroups stratified by ER status (data not shown).

The function of the 76 genes (table 3) in the prognostic signature was analysed to relate the genes to biological pathways. Although 18 of the 76 genes have unknown function, several pathways or biochemical

activities were identified that were well represented, such as cell death, cell cycle and proliferation, DNA replication and repair, and immune response (table 4). Genes implicated in disease progression were found, including calpain2, origin recognition protein, dualspecificity phosphatases, Rho-GDP dissociation inhibitor, tumour necrosis factor (TNF) superfamily protein, complement component 3, microtubuleassociated protein, protein phosphatase 1, and apoptosis regulator BCL-G. Furthermore, previously characterised prognostic genes such as cyclin E2<sup>28</sup> and CD44<sup>29</sup> were in the gene signature.

The dataset has been submitted to the NCBI/ Genbank GEO database (series entry GSE2034).

# Discussion

We provide results of an analysis of primary tumours from 286 patients with lymph-node-negative breast cancer of all age-groups and tumour sizes. The patients had not received adjuvant systemic therapy, so the multigene assessment of prognosis was not subject to potentially confounding contributions by predictive factors related to systemic treatment.

The study revealed a 76-gene signature that accurately predicts distant tumour recurrence. This signature could be applied to all lymph-node-negative patients independently of age, tumour size and grade, and ER status. In Cox's multivariate analysis for distantmetastasis-free survival, the 76-gene signature was the only significant variable, superseding clinical variables, including grade. After 5 years, absolute differences in distant-metastasis-free and overall survival between the patients with the good and poor 76-gene signatures were 40% and 27%, respectively. Of the patients with goodprognosis signatures, 7% developed distant metastases and 3% died within 5 years. If further validated, this signature will yield a positive predictive value of 37% and a negative predictive value of 95%, on the assumption of a 25% rate of disease recurrence in lymph-node-negative patients. In particular, this signature could be valuable for defining the risk of recurrence for the increasing proportion of T1 tumours (<2 cm). Comparison with the St Gallen and National Institutes of Health guidelines was instructive. Although ensuring that the same number of high-risk patients would receive the necessary treatment, our 76-gene signature would recommend systemic adjuvant chemotherapy to only 52% of low-risk patients, compared with 90% and 89% by the St Gallen and National Institutes of Health guidelines (table 5). Our gene signature, if further confirmed, could result in a reduction of the number of low-risk lymph-node-negative patients who would be recommended to have unnecessary adjuvant systemic therapy (table 5).

The 76 genes in our prognostic signature belong to many functional classes, which suggests that different paths could lead to disease progression. The signature

VietNot 2001         VietNot 2001         Open 1000         Open 2001	Gene	Standard Cox coefficient	Cox p value	Gene description
Pingle of Pingle         Pingle of Pingle Pingl	For ER-positive	group		
12771         -1.85         -0.000         (M. 01/56.1.10E+-4.000 sight) merchan protein (D21 (02.718))           202618.4         -3.41         -0.000         (M. 01/56.1.10E+4.000 sight) merchan bits (0.016.0.01.8).           202618.4         -3.93         -0.000         (M. 01/56.1.10E+4.000 sight) merchan bits (0.016.0.01.8).           202618.4         -3.93         -0.000         (M. 01/56.1.10E+4.000 sight) merchan bits (0.016.0.01.8).           202618.4         -3.93         -0.000         (M. 01/56.1.10E+4.000 sight) merchan bits (0.016.0.01.8).           202618.4         -3.93         -0.000         (M. 01/56.1.10E+4.000 sight) merchan bits (0.016.0.01.8).           202618.4         -3.93         -0.000         (M. 01/56.1.10E+4.000 sight) merchan bits (0.016.0.01.8).           202618.4         -3.93         -0.000         (Conserma include g.A.1.0.2.1.10E+4.0.000 sight) merchan bits (0.016.0.000 sight) merchan bits (0.016.0.000 sight) merchan bits (0.016.0.000 sight) merchan bits (0.017.0.000 sight) mercha	219340_s_at	-3.83	0.00005	qb:AF123759.1 /DEF=Homo sapiens putative transmembrane protein (CLN8) mRNA, complete cds
2024.8.         -95.         -0000         -0000.0.         -00	217771_at	-3.865	0.00001	gb:NM_016548.1 /DEF=Homo sapiens golgi membrane protein GP73 (LOC51280)
2025.2.         -0.21         0.0010         gMM. 0015C.1.(DC1-those spaces index data 31 (increduces - windows flock) 01.35           20015.2.         3.26         0.0003         gdddddddd gddd/255 (increduces index monethin and increduces index flock) 01.05           20015.2.         3.36         0.0003         gddddddd gdd/255 (increduces index monethin and increduces index flock) 01.01           20015.2.         3.37         0.003         gddddddd gdd/255 (increduces index monethin and increduces index flock) 01.01           20015.2.         3.37         0.003         gddddddddddddddddddddddddddddddddddd	202418_at	3.63	0.00002	gb:NM_020470.1 /DEF=Homo sapiens putative transmembrane protein; homologue of yeast Golgi membrane protein Yif1p
2019/L.S.L.3.960.00000.0000000.00000000.00000000000000000000000000000000000	206295_at	-3·471	0.00016	gb:NM_001562.1 /DEF=Homo sapiens interleukin 18 (interferon- $\gamma$ -inducing factor) (IL18)
19405.2	201091_s_at	3.506	0.00008	Consensus includes gb:BE748755 /heterochromatin-like protein 1
2025.4.1         392         0.0006         gbMM_002/10.10FF:interage protein phosphare.6. cably: Submit, YoSGm (PF1C0)           2026.5.2.1         393         0.0003         gbM_114021.10FT:interage protein filterage protein filter	204015_s_at	-3.476	0.00001	gb:BC002671.1 /DEF=Homo sapiens, dual specificity phosphatase 4
2095.2	200726_at	3.392	0.00006	gb:NM_002710.1 /DEF=Homo sapiens protein phosphatase 1, catalytic subunit, $\gamma$ isoform (PPP1CC)
123542_LA:         3-301         0.003         Generation Andrea Applicable 2015           123752_LA:         3-374         0.0032         Generation Andrea Applicable 2015           123752_LA:         3-374         0.0032         gbMM_000541_0F1-1kmm supports complement 201701           123752_LA:         3-374         0.0033         gbMM_0107211_0F1-1kmm supports complement 201701           123752_LA:         3-374         0.0004         gbMM_00554_0171-1kmm supports complement 201701           12375_LA:         3-375         0.0004         gbMM_00554_0171-1kmm supports complement 201701           12374_LA:         3-375         0.0006         gbMM_00554_0171-1kmm support complement 201701000           12374_LA:         3-386         0.0007         gbMM_00554_0171-1kmm support complement 20170200           12005_LA:         3-386         0.0007         gbMM_00534_0171-1kmm support complement 20170200           12005_LA:         3-396         0.0007         gbMM_00534_0171-1kmmm support complement 20170200	200965_s_at	-3.353	0.0008	gb:NM_006720.1 /DEF=Homo sapiens actin binding LIM protein 1 (ABLIM), transcript variant ABLIM-s
21382.2	210314_x_at	-3.301	0.00038	gb:AF114013.1 /DEF=Homo sapiens TNF-related death ligand-1γ
127767_21         -3174         0.0022         0.NMM_0000641,0F3-Henro segines component 1(3):           32688_2.4.         338         0.0022         0.NMM_01779.10.0F3-Henro segines hypothesial production and inform 8(1106 <sup>5</sup> )           32697_2.4.         338         0.0020         0.NMM_01779.10.0F3-Henro segines hypothesial production and inform 8(1106 <sup>5</sup> )           32767_2.4.         395         0.0024         0.NMM_005951.10F3-Henro segines conformerome associated propendix (ICAP-C)           21768_2.4.         395         0.00024         0.NMM_005951.10F3-Henro segines conformerome associated propendix (ICAP-C)           21768_2.4.         395         0.00004         0.NMJ_01591.0F3-Henro segines conformerome associated propendix (ICAP-C)           21768_2.4.         395         0.00004         0.NMJ_01591.0F3-Henro segines conformeroseme associated propendix (ICAP-C)           21768_2.4.         395         0.00004         0.NMJ_01591.0F3-Henro segines conformeroseme associated propendix (ICAP-C)           21768_2.4.         395         0.00002         0.00002         0.00002         0.00002           21764_2.4.         395         0.00002         0.00002         0.00002         0.00002         0.00002         0.00002         0.00002         0.00002         0.00002         0.00002         0.00002         0.00002         0.00002         0.000002         0	221882_s_at	3.101	0.00033	Consensus includes gb:Al636233 five-span transmembrane protein M83
21358	217767_at	-3.174	0.00128	gb:NM_000064.1 /DEF=Homo sapiens complement component 3 (C3)
24073.2, xl         336         0.0000         0.NMU.03729.10F-Hence ageines choronomes to lapen reading frames (CLIORF)           21852.2, xl         -305         0.0033         0.04033	219588_s_at	3.083	0.0002	gb:NM_017760.1 /DEF=Homo sapiens hypothetical protein FLJ20311
21355 2.,1       -364       00000       Concretor indexis advice graph (AL2 310)         2135 2.,1       -365       000001       graph (AL2 312)         2135 31       -363       000001       graph (AL2 312)         2135 31       -363       000001       graph (AL2 312)         2135 31       -363       00001       graph (AL2 312)         2137 31       -363       00002       graph (AL2 312)         2137 31       -363       00002       graph (AL2 312)         2137 31       -364       00002       graph (AL2 312)         2137 31       -364       00002       graph (AL3 312)         2137 31       -363       00002       graph (AL3 312)         2137 31       -363       00002       graph (AL3 312)         2137 31       -364       00002       graph (AL3 312)         2137 31       -377       00032       graph (AL3 312) <td< td=""><td>204073_s_at</td><td>3.336</td><td>0.00005</td><td>gb:NM_013279.1 /DEF=Homo sapiens chromosome 11open reading frame 9 (C110RF9)</td></td<>	204073_s_at	3.336	0.00005	gb:NM_013279.1 /DEF=Homo sapiens chromosome 11open reading frame 9 (C110RF9)
21382	212567_s_at	-3.054	0.00063	Consensus includes gb:AL523310 putative translation initiation factor
2019134 Jal       3995       0.0004       gb/MA (0.0542). [U/H=m0003 signed formozine seques column (0.0005) (0.054.0)         12028 Jal       -308       0.00005       gb/M 12507.1 [U/H=m0003 signed formozine conglets solumn (0.0005)         12028 Jal       -308       0.00005       gb/M 12507.1 [U/H=m0003 signed formozine conglets solumn (0.0005)         12028 Jal       -398       0.0000       gb/M 12507.1 [U/H=m0003 signed formozine conglets solumn (0.0005)         12028 Jal       -398       0.0000       gb/M 12507.1 [U/H=m0003 signed formozine conglets solumn (0.0007)         12024 Jal       -398       0.0000       gb/M 12527.1 [U/H=m0003 signed formozine conglets solumn (0.00074)         12024 Jal       -398       0.00005       gb/M 12524.2 [U/H AA/226 gpres product (0.00074)         12024 Jal       -398       0.00005       gb/M AU 00534.2 [U/H=m0003 signed formozine form	211382_s_at	-3.025	0.00332	gb:AF220152.2 /DEF=Homo sapiens IACC2 mRNA
21341, 1       -51/3       0.0003       gbr/m, 0.3292.01, 1027-1000.0000       00063       gbr/m, 0.3292.01, 1027-1000.0000         21367, 2, 3       31/5       0.00015       gbr/m, 0.1197-1, 1007-1000.0000 proses (PRO2000)       10063.01         21367, 2, 3       31/5       0.00015       gbr/m, 0.01577-1, 1007-1000.0000 proses (PRO2000)       1007-1000.00000       1007-1000.00000         2137, 2, 4       -9300       0.00015       gbr/m, 0.01577-1000.0000       1007-1000.00000       1007-1000.00000         2137, 2, 4       -9300       0.0002       gbr/m, 0.01572.01.00000       1007-1000.00000       1007-1000.00000         2137, 2, 4       -931       0.0002       gbr/m, 0.0514.1 / 1027-1000 sagines to the tot opportunity (br/mining hunching and hund hund brood group system)       1007-1000.00000         10234, 2, 4       -931       0.0002       gbr/m, 0.00514.1 / 1027-1000 sagines to the tot opportunity (br/mining hunching and hund hund brood group system)       1007-1000.00000         10234, 2, 4       -935       0.00005       gbr/m, 0.00513.1 / 1027-1000.00000       1000000000000000000000000000000000000	201663_s_at	3.095	0.00044	gb:NM_005495.1 /DEF=Homo sapiens chromosome-associated polypeptide C (CAP-C)
12005.2.1         2.982         0.0000         (ph.F.1.25)//.107-refers sepres flow press south 1.000.3           12005.6.1         3.955         0.0000         (ph.F.1.25)/.107-refers sepres flow flow south 1.000.3           12007.6.1         3.955         0.0000         (ph.F.1.25)/.107-refers sepres flow flow south 1.000.3           12007.6.1         3.957         1.0000.1         (ph.K.1.077-0.0000.1         (ph.K.1.077-0.0000.1           12007.6.1         3.957         1.0000.1         (ph.K.1.077-0.0000.1         (ph.K.1.077-0.0000.1           12007.6.1         3.957         1.0000.3         (ph.K.1.077-0.0000.1         (ph.K.1.077-0.0000.1           12007.6.1         3.958         0.0000.3         (ph.K.1.077-0.0000.1         (ph.K.1.077-0.0000.1           12007.6.1         3.958         0.0000.5         (ph.K.1.077-0.0000.1         (ph.K.1.077-0.0000.1         (ph.K.1.077-0.0000.1           12007.6.1         3.954         0.00000.5         (ph.K.1.077-0.0000.1         (ph.K	221344_at	-3.1/5	0.00031	gb:Nw_013950.1/DEF=Homo sdpiens oriactory receptor, family 12, Subramity D, member 2 (OK12D2)
10116_2.ml         3 08         00000         4ph.135877.1 MV.2 (increase instruments of them sources in Apr.18 He 1.Pe.gs.A0019987.1 gb.NM.005496.1 gb.A1136877.1           10116_4.ml         - 711         00002         4ph.ML.0179.1 (InFerne sogens ICMA/07 (BokMO7K8)           10116_4.ml         - 711         00002         4ph.ML.0179.1 (InFerne sogens ICMA/07 (BokMO7K8)           10116_4.ml         - 718         00002         4ph.ML.00534.1 (InFerne sogens ICMA/07 (BokMO7K8)           10124_4.ml         - 786         000029         4ph.ML.00534.1 (InFerne sogens ICMA/07 (BokMO7K8)           10124_4.ml         - 786         000029         4ph.ML.00534.1 (InFerne sogens ICMA/07 (BokMO7K8)           10134_4.ml         - 796         000059         4ph.ML.00534.1 (InFerne sogens ICMA/07 (BokMO7K8)           10135_2.ml         - 968         000009         4ph.ML.00534.1 (InFerne sogens ICMA/07 (BokMO7K8)           10135_2.ml         - 796         000059         4ph.ML.00534.1 (InFerne sogens ICMA/07 (BokMO7K8)           10135_2.ml         - 777         00038         4ph.ML.00534.1 (InFerne sogens ICAA/07 (InFerne sogens ICAA/07 (InFerne sogens ICAA/07 (InFerne sogens ICAA/07 (INFER)           11375_2.ml         - 777         00039         4ph.ML.02639.1 (InFerne sogens ICAA/07 (INFER)         4ph.ML.02639.1 (InFerne sogens ICAA/07 (INFER)           11376_2.ml         - 777         00039	210028_S_at	-3.002	0.00016	gb-NM_0141001/DEE-Jama cainars PDO2000 protein (VPDO200)
12:10:12.12         12:10:12         10:10:12	210/02_5_at	3.085	0.00010	go. μ. 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
10.111         -2.71         0.003         ephth.00593.1.057-4.0003.pp.04.0004         (0.097.0)           10.101.4.x.#         -2.93         0.003         gehth.00593.1.057-4.0003.pp.04.0010.ph.04.001.0004.001.0004.001.0004.001.00100.0010.0010.0010.0010.0010.0010	219724 s at	-2.992	0.0004	ab:NM 014796.1 /DFF=Homo sapiens KIAA0748 gene product (KIAA0748)
12101 L_X at       -2448       0.0003       Concreases includes gloAM3323 (7044 artiges (horma pdi racis houd group system)         120240 at       -2895       0.0002       gb-NM 0.05131 (10F1-Horm sagines point (Norsphila)-Kie kance (HM)         120470 at       -2894       0.0005       gb-NM 0.05141 (10F1-Horm sagines to float for kance (HM)         120458 bs. at       2915       0.0005       gb-NM 0.05141 (10F1-Horm sagines that for kance float for kance (HM)         120458 bs. at       2944       0.0006       gb-NM 0.04141 (10F1-Horm sagines float for kance float for kance (HM)         120458 bs. at       2948       0.0006       gb-NM 0.04141 (10F1-Horm sagines float for kance (HM)         12178 bs. at       2844       0.0005       gb-NM 0.05191 (10F1-Horm sagines float for protein MCC11335 (MC11335)         12178 bs. at       2854       0.0003       gb-NM 0.02420 (10F1-Horm sagines float for protein MCC1335 (MC11335)         12178 bs. at       2777       0.0016       gb-NM 0.02420 (10F1-Horm sagines thorber in H22446 (H22446) (H27446 (H22446) (H27446) (H2744	204014 at	-2.791	0.0007	db:NM 001394.2/DEF=Homo saviens dual specificity phosphatase 4 (DUSPA)
02240.m         231         0007         gb-NM_00593.01_07E -Home sepiers pole (Drosphila) like kinace (PK)           02570.01         2395         000055         gb-NM_00512.01E -Home sepiers nonconcer ankarer of SNE like (Drosphila kinase suppressor of ns) (NK1)           02578.5.st         2395         000055         gb-NM_00512.01E -Home sepiers nonconcer ankarer of SNE like (Drosphila kinase suppressor of ns) (NK1)           02578.5.st         2395         000055         gb-NM_00512.01E -Home sepiers nonconcer ankarer of SNE like (Drosphila) kinase suppressor of ns) (NK1)           02579.1.st         2395         000055         gb-NM_00512.01E -Home sepiers nonconcer ankare of SNE like (Drosphila) kinase suppressor of ns) (NK1)           02578.5.st         2424         000055         gb-NM_00512.01E -Home sepiers (Circl 1305           021795.5.st         2477         000054         gb-NM_0722.01E -Home sepiers (Circl 1305           021795.5.st         2477         000054         gb-NM_0722.01E -Home sepiers noncircl 1305 db -Home sepiers (Circl 1305 db -Home sepiers (Circl 1305 db - Home sepiers) (Circl 1305 db - Home sepi	212014 x at	-2.948	0.00039	Consensus includes qb:A1493245 /CD44 antiqen (homing function and Indian blood aroup system)
DipApat         - 2895         0.0005         gb.NMU_0551 12 (DFE-Home segines : Marce or GFSE-Heic Docspoth Hist Hasse suppressor of nas) (CNK1)           DipApat_S_st         2915         0.0005         gb.NMU_05152 (DFE-Home segines : Marce market methodes HIAHH)           DipApat_S_st         2915         0.0005         gb.NMU_05152 (DFE-Home segines : Marce market methodes and the segines : Marce market methodes : Market market methodes : Market : Market methodes : Market method	202240 at	2.931	0.0002	db:NM_005030.1 /DEF=Homo sapiens polo (Drosophila)-like kinase (PLK)
09888.0, s.t.         2944         0.005         gbHM.003432.0 EFE-Hone seginare Ha histone family, member H(H4P)         The transmission of transmissi transmission of transmission of transmission of transm	204740_at	-2.896	0.00052	gb:NM_006314.1 /DEF=Homo sapiens connector enhancer of KSR-like (Drosophila kinase suppressor of ras) (CNK1)
19476.5.xt         2915         0005         dph.NL.004111.3 /DFi-Hom sequers face dono.closes (1910)           20391.xt         2-868         00060         dph.NL.00470.1 /DEI-Hom sequers face foct-function (1910) (FKPP1)           21176.x.st         2-874         00060         dph.NL.005470.1 /DEI-Hom sequers face foct-function (1010) (FKP1)           21202.s.st         2-875         00016         dph.NL.005470.1 /DEI-Hom sequers face foct-function (1010) (FKP1)           21203.s.st         2-884         00003         dph.NL.005470.1 /DEI-Hom sequers face foct-function (1010) (FKP1)           21203.s.st         2-884         00003         dph.NL.005420.1 /DEI-Hom sequers face foct-function (1010) (FKP1)           20488.s.s.st         2-875         00031         dph.NL.007122.1 /DEF-Hom sequers face face face face face face face face	208180_s_at	2.924	0.0005	gb:NM_003543.2 /DEF=Homo sapiens H4 histone family, member H (H4FH)
19339.4.       -2968       00009       gbtM0.00447.0.1/DEF-Homo sapines FK506-binding protein 2 (150KP2)         121176.2., at       -277       0039       gbtM0.01597.1/DEF-Homo sapines CG-4 protein (LOCS1033)         121208.2. at       -2455       00005       gbtM0.01597.1/DEF-Homo sapines Aco McC11335 (McC11335)         12178.2., at       -2842       00005       gbtM0.0260.55.1 IDEF-Homo sapines Aco McC1138 (McC1335)         121883.3., at       -2842       00005       gbtM0.02420.1 IDEF-Homo sapines Aco McC1138 (McC1335)         121783.4.       -2745       00005       Consensus includes gbtA072039 Invariased (Incopnibl-IHer /R-gbt/B7864.1 gbtA752379.1 gbtMM_004210.1         12168.3.4.       -2745       00005       gbtM0.0210.1 IDEF-Homo sapines Approteinal agree         12168.4.       -2779       00012       Gonessus includes gbtM0.02002 IDEF-Homa sapines proteosme (Incosome, macropain) 265 UbMC0.0013 IDEF-Homo sapines Super Start (Incosome, macropain) 265 UbMC0.0014.1 (TATE), 276 (MCC)         121847.8., at       2.83       00003       gbtM0.00231 IDEF-Homo sapines proteosme (Incosome, macropain) 265 UbMC0.0014.1 (TATE), 276 (MCC)         121848.5., at, z       -274       00013       Gonessus includes gbtA175221 (DEF-Homo sapine StM1422220 (DE72434E2220)         121843.5., at       -274       00013       Gonessus includes gbtA175221 (DEF-Homo sapine StM14221 (DEF-Homo sapine StM14221 (DEF-Homo sapine StM1422220)	204768_s_at	2.915	0.00055	gb:NM_004111.3 /DEF=Homo sapiens flap structure-specific endonuclease 1 (FEN1)
211762_st       2.824       0.006       gbBc005978.1/DEF-4mon sequines (Augoophenin a.)         212012_st       -2.777       0.0036       gbNM.030819.1/DEF-4mon sequines (Col-1 protein (NGC13335)         212102_st_at       -2.854       0.0005       gbNM.030819.1/DEF-4mon sequines hypothetical protein MGC13335 (MGC1335)         211778_x.at       -2.854       0.0005       gbNM.024209.1/DEF-4mon sequines hypothetical protein FU23464 (FU23468)         21888_st_at       -2.857       0.0016       gbNM.020221/DEF-4mon sequines hypothetical protein FU23468 (FU23468)         2188_st_at       -2.875       0.0012       Consensus includes gbL070202/DEF-4mon sequines hypothetical protein hybothetical protein hybothetic	203391_at	-2.968	0.00099	gb:NM_004470.1 /DEF=Homo sapiens FK506-binding protein 2 (13kD) (FKBP2)
1318/14.       -277       0.039       gbNM.03091.1907.10EF-4mon sapiers. Clo-41 protein (10C51033)         121202.8.z.s.t.       -265       0.0016       gbNM.03081.190F-4mon sapiers. More MGC11333 (MGC11335)         121179.x.st.       -2842       0.0003       gbNM.03081.190F-4mon sapiers. More MGC11335 (MGC11335)         120883.t.s.t.       -2852       0.0003       Consensus includes gbA/D72023 [neuralised [Puzy468] (Puzy469)         120188.t.s.t.       -2754       0.0004       gbNM.030251.10FF-4mon sapiers inchomatin-specific transcription elongation factor, 140 kBa submit (FACTP140)         120188.t.s.t.       -2754       0.0004       gbNM.030251.10FF-4mon sapiers inchomatin-specific transcription elongation factor, 140 kBa submit (FACTP140)         120188.t.s.t.       -2745       0.0004       gbNM.030251.10FF-4mon sapiers protessome [nscoma]in 265 submit, ATPase.2 (PSMC2)         121847.s.t.       278       0.0003       gbNM.030251.10FF-4mon sapiers protessome [nscoma]in 265 submit, ATPase.2 (PSMC2)         121847.s.t.       -274       0.0003       gbNM.030251.10FF-4mon sapiers solutes carrier family 35 (MF-3Ma sapiers)         129353.s.t.       -274       0.0016       consensus includes gbA/B79554/4 (Putativ zin finger protein NYERH-34 antigen         129353.s.t.       -2716       0.0016       consensus includes gbA/B59554/4 (Putativ zin finger protein NYERH-34 antigen         12953.s.t.       -2	211762_s_at	2.824	0.00086	gb:BC005978.1 /DEF=Homo sapiens, karyopherin $lpha$ 2 (RAG cohort 1, importin $lpha$ 1)
212102 s.nt       -2655       0.0016       gb/MU.030819.1/DEF-10mo sapiers hypothetical protein M231833 (MGC11335)         21177 s.z.t.       -2854       0.00051       gb/MU.02469.1/DEF-14mon sapiers hypothetical protein H234868 (H123468)         210888 s.g.t.       -2855       0.00051       gb/MU.02469.1/DEF-14mon sapiers hypothetical protein H23468 (H123468)         21038 s.g.t.       -2779       0.0014       gb/MU.00129.1/DEF-14mon sapiers chromatin-specific transcription elongation factor, 140 kDa subunit (FACTP140)         21138 s.g.t.       -2779       0.0014       gb/MU.00129.1/DEF-14mon sapiers h70 befactoscome (proscome macrophil) 265 subunit, ATPsep, (PSMC2)         21184 s.g.t.       -2745       0.00069       gb/MU.00129.1/DEF-14mon sapiers proteome (proscome macrophil) 265 subunit, ATPsep, (PSMC2)         21184 s.g.t.       -2745       0.00019       Gomensus includes gb/M27002/DEF-14mon sapiers protein N274p342220 (DEF-24442220)         211491 s.g.t.       -2743       0.00164       Gomensus includes gb/M27002/DEF-14mon sapiers protein N274p342220 (DEF-24442220)         211491 s.g.t.       -2743       0.00164       Consensus includes gb/M270547 (JMA10405 protein         20305 s.g.t.       -2743       0.00164       Consensus includes gb/M270547 (JMA104072)         211491 s.g.t.       -2765       0.00176       Gomensus includes gb/M270547 (JMA104072)         212181 s.g.t.t.       -2715	218914_at	-2.777	0.00398	gb:NM_015997.1/DEF=Homo sapiens CGI-41 protein (LOC51093)
111792, x.t.         -2854         0.00051         gbtR0.000515,51,DEF-Home sapiers hypothetical protein F1J23468 (F1J23468)           124883, x.t.         -2853         0.00031         Consensus includes gbtAA772033 (neuralised (Drosophila)-like (F1,Eq.bUR7664,1 gbtAF2023729,1 gbtAML_004210.1           12781, x.t.         -2777         0.00014         gbtAML_0245221, DEF-Home sapiers chromatin-genes chromatin-gene chromatin-genes chromatin-genes chromatin-genes chromatin-gene	221028_s_at	-2.635	0.0016	gb:NM_030819.1/DEF=Homo sapiens hypothetical protein MGC11335 (MGC11335)
121883.s.t.       242       04005       gbMM.024021.01       gbMM.024021.01         04888.s.t.       2435       040035       consensus includes gbA770203 [neuralised] (Drosphila) ilke [R1-gbU8264.1 gbA7029729.1 gbMM.004210.1         121781.s.t.       2.777       04016       gbMM.007192.1 /DEF-IHomo sapiers chromatin-specific transcription elongation factor, 140 kDa subunit (FACTP140)         12188.s.t.       2.775       040025       consensus includes gbU70702.0 /DEF-IHomo sapiers protestace (prosome, manopain) 265 subunit, ATPase, 2 (PSMC2)         1218478.s.t.       2.883       040031       gbMM.01712.1 /DEF-IHomo sapiers SpMDteECD (DKF2p4342220)         1214919.s.t.       -2.744       040038       gbMM.00412.1 /DEF-IHomo sapiers SpMDteECD (DKF2p4342220)         1214919.s.t.       -2.743       040038       consensus includes SpU87904 (RAA1085 protein         120366.s.g.t.       -2.744       040038       gbMM.00416.1 /DEF-IHomo sapiers solute carler family 35 (CMR-salia acid transporter), member 1 (SLC35A1)         120364.s.t.       -2.651       040037       gbMM.004102.1 /DEF-IHomo sapiers solute carler family 35 (CMR-salia acid         121701.s.t.       -2.651       040037       gbMM.040702.1 /DEF-IHomo sapiers solute carler family 35 (CMR-salia acid         121501.s.t.       -2.715       04035       gbMM.040765.1 /DEF-IHomo sapiers solute carler family 35 (CMR-salia acid         1215101.s.t.	211779_x_at	-2.854	0.00053	gb:BC006155.1/DEF=Homo sapiens, clone MGC:13188
204869_2,11         -2635         00033         Consensus includes gh/AV/203 (neutralized (utrospinial-inter, 140, 064, 1g) AV/23/23, 1g, 0004, 054, 1g)           20138_st         -2777         000164         gh/ML_001221 (DEF+finitized) (GD) § (ARHGDIB)           20138_st         -2745         000024         gh/ML_001221 (DEF+finitized) (GD) § (ARHGDIB)           20168_st         -2743         000033         (DEF+finitized) (GD) § (ARHGDIB)           20168_st         -2743         00013         Consensus includes gh/ML012512 (DEF+finitized) (GD) § (ARHGDIB)           20183_st         -2743         00013         Gomensus includes gh/ML012512 (DEF+finitized) (GD) § (ARHGDIB)           20193_st_at         -2743         00013         Gomensus includes gh/ML01251 (DEF+finitized) (GD) § (ARHGDIB)           20193_st_at         -2743         000038         gib/ML01251 (DEF+finitized) (GD) § (ARHGDIB)           20193_st_at         -2743         000038         gib/ML00451 (DEF+finitized) (GD) § (ARHGDIB)           20193_st_at         -2751         00015         Consensus includes gh/A1724 (JAIL1) (DEF+finitized) (GD) § (ARHGDIB)           20193_st_at         -2715         00037         Gomensus includes gh/A1724 (JAIL1) (DEF+finitized) (GD) § (ARHGDIB)           21102_st_at         -2667         000029         gb/ML00595 (JDEF+finitized) (ARHGDIB)         Gomensus includes gh/A1724 (JAIL1)	218883_s_at	2.842	0.00051	gb:NM_024029.1 /UEF=Homo sapiens hypothetical protein FLJ23468 (FLJ23468)
12/102_nt       2/77       000149       givmc_00_192_1/U_1 = nonus applies thomatan-specific standards including applied examples of endigation match, 144 kds solutin (1, Kdr 144 kd)         101368_st       2.775       000026       girkm_001175.1 /DEF-Home sepires Rbs GDP dissociation inhibitor (GDI) β (ARHGDIB)         10188_st       2.78       000036       girkm_001751.1 /DEF-Home sepires Rbs GDP dissociation inhibitor (GDI) β (ARHGDIB)         1244918_st       2.883       000131       girkmo sepires rbs proteine sepires rbs mass more inport sociation inhibitor (GDI) β (ARHGDIB)         1244918_st       2.883       000130       Consensus includes girk3094 (KAA1085 protein         029835_st       -2.743       000038       girkmo sepires, Similar to CD44 antigen (homing function and Indian blood group system)         121747_st       -2.761       00014       Consensus includes girks 10/052-10/05	204000_S_at	-2.035	0.00164	Consensus includes gb:AA//2093 (neuralised (brosophila)-like /rt=gb:0a/od4:1 gb:Art/29/29.1 gb:NNM_004210.1
121300.1         2.735         0.0022         gb:NM_00280.1175,1/0EF-Homo sapiers sphore for plassociation inhibitor (GDI) § (ARHGDI8)           1218478_s.tt         2.739         0.00049         gb:NM_00280.31.0EF-Homo sapiers sphore for plassociation inhibitor (GDI) § (ARHGDI8)           1218478_s.tt         2.739         0.00049         gb:NM_001175,1/0EF-Homo sapiers sphore for plassociation inhibitor (GDI) § (ARHGDI8)           1218478_s.tt         2.734         0.0018         gb:NE00472.1./DEF-Homo sapiers sphore inhibitor (GDI) § (ARHGDI8)           129935_x.xt         -2.743         0.0008         gb:NE00472.1./DEF-Homo sapiers spinis 100424 antigen (homing function and Indian blood group system)           12747L_at         -2.761         0.0014         Consensus includes gb:AI1765.2.1./DEF-Homo sapiers spinis 105 (CDR 2)           1291616_s.at         -2.781         0.0037         Consensus includes gb:BF055474 / putative zinc finger protein NV-REN-34 antigen           1291510_at         -2.687         0.00376         Consensus includes gb:BF055474 / putative zinc finger protein NV-REN-34 antigen           121816_s.at         -2.715         0.00376         Consensus includes gb:BF055474 / putative zinc finger protein NV-REN-34 antigen           121820_at         -2.867         0.0038         Consensus includes gb:BF055474 / putative zinc finger protein NV-REN-34 antigen           121810_at         -2.616         0.00026         gb:NM	21/015_at	-2.759	0.00104	gb.1w_00/32/1761 - Informations supress chromatin-specific transcription elongation factor, 140 Kba subonit (FACT 140) Consensus includes oh-1107802/IDEE-Human Tis11d nene
201068_3_xt       2.79       0.00049       gb:NN_002803.1 /DEF-Homo sapiens proteasome (prosome, macropain) 265 subunit, ATPase, 2 (PSMC2)         218478_s_at       2883       0.00031       gb:NN_017512.1 /DEF-Homo sapiens typothetical protein         209835_x_at       -2.794       0.0013       gb:RO_04372.1 /DEF-Homo sapiens typothetical protein         209835_x_at       -2.743       0.00038       gb:RO_04372.1 /DEF-Homo sapiens, Similar to CD44 antigen (homing function and Indian blood group system)         217471_at       -2.761       0.0016       Consensus includes gb:ALT17652.1 /DEF-Homo sapiens mRNA         209305_s_at       -2.831       0.00535       gb:NN_006416.1 /DEF-Homo sapiens yoth recein (NA-REN-34 antigen         21816_s_at       -2.715       0.0037       gb:NN_006596.1 /DEF-Homo sapiens yoth recein (NA-REN-34 antigen         21816_s_at       -2.716       0.0038       consensus includes gb:AV693985 (Hz variant gere 2         21853_s_at       -2.631       0.0025       gb:NN_017951.1 /DEF-Homo sapiens mBinanon associated protein         21853_s_at       -2.641       0.0032       gb:NN_017951.1 /DEF-Homo sapiens yotherase (DAR directed), k0 (POL0)         21710_at       -2.847       0.0038       consensus includes gb:AV693985 (Hz variant gere 2       2.851         21853_s_at       -2.641       0.0037       consensus includes gb:AV63737 /Hs:234898 (ESTs, Weaky s	201288 at	-2.745	0.00086	consensor microsoft of the second s
218478_5_at       283       0.00031       gbNM_017612.1 /DEF-Homo sapiens hypothetical protein DK72p434E2220 (DK72p434E2220)         214919_5_at       -2734       0.00039       gbsDM_004372.1 /DEF-Homo sapiens similar to CD44 antigen (homing function and Indian blood group system)         217471_at       -2761       0.00164       Consensus includes gbs.N117652.1 /DEF-Homo sapiens solute carrier familiar to CD44 antigen (homing function and Indian blood group system)         203306_5_at       -2831       0.00535       gbNM_004702.1 /DEF-Homo sapiens solute carrier familiar to CD44 antigen (homing function and Indian blood group system)         213510_at       -2659       0.00076       Consensus includes gbs.B5055474 / putative zinc finge protein NY-REN-34 antigen         213510_at       -2687       0.00438       Consensus includes gbs.B5055474 / putative zinc finge protein NY-REN-34 antigen         215510_at       -2687       0.00438       Consensus includes gbs.M509398 / fut variant gene 2         215510_at       -2687       0.00222       gbNM_0178593 / DEF-Homo sapiens molynemase (DNA directed), 0(POL0)         215510_at       -2764       0.00367       Consensus includes gb.M509398 / fut variant gene 2         215510_at       -2641       0.00537       Consensus includes gb.M059637 / Hz 234898 ESTS, Weakly similar to 2109260A B cell growth factor Homo sapiens similar to 2109260A ant 210950A ant 210950A ant 210950A ant 220500 (DNB 40000595 / DEF-Homo sapiens mbRN for LST-102 (DEF1A2) <td>201068_s_at</td> <td>2.79</td> <td>0.00049</td> <td>db:NM_002803.1 /DEF=Homo sapiens proteasome (prosome, macropain) 26S subunit, ATPase, 2 (PSMC2)</td>	201068_s_at	2.79	0.00049	db:NM_002803.1 /DEF=Homo sapiens proteasome (prosome, macropain) 26S subunit, ATPase, 2 (PSMC2)
214919.5.st       -2794       0.00139       Consensus includes gb:R39094 /KIA11085 protein         209355_xat       -2743       0.00088       gb:BC004372.1/DEF=Homo sapiers, Similar to CD44 antigen (homing function and Indian blood group system)         217471_at       -2761       0.00153       gb:NM_006416.1/DEF=Homo sapiers, Similar to CD44 antigen (homing function and Indian blood group system)         20304_at       -2659       0.00073       gb:NM_006416.1/DEF=Homo sapiers system (CNE2)         21816_s_at       -27.15       0.00376       Consensus includes gb:R505474 / putative zinc finger protein NY-REN-34 antigen         219510_at       2836       0.00029       gb:NM_006956.1/DEF=Homo sapiers optime rase (NoA directed), 0 (POLO)         217102_at       -2687       0.00438       Consensus includes gb:R505474 / putative zinc finger protein NY-REN-34 antigen         215510_at       -2716       0.00039       Consensus includes gb:R5055474 / putative zinc finger protein NY-REN-34 antigen         215510_at       -2716       0.00039       Consensus includes gb:R5055174 / putative zinc finger protein Signific NDP         215513_x_x_x_x_t       -2641       0.00537       Consensus includes gb:R5055174 / PUTative zinc finger protein FIJ20517 (FIJ20517)         215633_x_x_x_t       -2646       0.0037       Consensus includes gb:R505317 / hr:324898 ETS1, Wash similar to 2109260A B cell growth factor Homo sapiers Similar betepatoma-derived g	218478_s_at	2.883	0.00031	db:NM_017612.1 /DEF=Homo sapiens hypothetical protein DKFZp434E2220 (DKFZp434E2220)
19085.x.tt         -2743         0.00088         gb:BC004372.1/DEF-Homo sapiens, Similar to CN4 antigen (homing function and Indian blood group system)           217471_at         -2761         0.00164         Consensus includes gb:AL117652.1/DEF-Homo sapiens solute carrie family 35 (CMF-sialic acid transporter), member 1 (SLC35A1)           203306_s_at         -2831         0.0073         gb:NM_006416.1/DEF-Homo sapiens solute carrie family 35 (CME2)           212816_s_at         -2715         0.0036         consensus includes gb:BF055474 / putative zinc finger protein NV-REN-3 antigen           219510_at         -2836         0.0003         gb:NM_006596.1/DEF-Homo sapiens polymerase (DNA directed), 0(POL0)           21710_at         -2687         0.00438         Consensus includes gb:AF04410.1/DEF-Homo sapiens malignancy-associated protein           218513_at         -2716         0.00039         consensus includes gb:AV639385/ts variant gene 2           218533_s.at         -2703         0.00232         gb:NM_0075951/DEF-Homo sapiers NB/No for L51-NP protein           219532_s.at         -2686         0.00479         consensus includes gb:AV13720 / Momo sapiers NB/NA for L51-NP protein           219533_s.at         -2646         0.00479         consensus includes gb:AV13720 / Momo sapiers NB/NA for L51-NP protein           219543_s_s.at         -2646         0.00459         consensus includes gb:AV13720 / Momo sapiens nativa metalion elong	214919_s_at	-2.794	0.00139	Consensus includes gb:R39094 /KIAA1085 protein
121741_at       -2761       0.00164       Consensus includes gb:Al117652.1.0EEF-Homo sapiens mRNA         203306_s_at       -2831       0.0053       gb:NM_006416.1.0EF-Homo sapiens solute carrier family 35 (CMP-sialic aid transporter), member 1 (SLC35A1)         20534_at       -2715       0.0037       gb:NM_004702.1.0EF-Homo sapiens solute carrier family 35 (CMP-sialic aid transporter), member 1 (SLC35A1)         21816_s_at       -2715       0.00376       Consensus includes gb:FPS55474 / putative zinc finger protein NY-REN-34 antigen         219510_at       -2887       0.00438       Consensus includes gb:FPS55474 / putative zinc finger protein NY-REN-34 antigen         219510_at       -2687       0.00438       Consensus includes gb:FP-Homo sapiens polymerase (DNA directed), 0 (POLQ)         219510_at       -2761       0.00039       Consensus includes gb:AV0439385 /ets variant gene 2         215513_s_at       -2704       0.00037       Consensus includes gb:AV053937 /Hs 234898 ESTs, Weakly similar to 2109260A B cell growth factor Homo sapiens solicades 2102827 (FL20517)         219523_s_at       -2684       0.0037       Consensus includes gb:U90303.1/DEF-Homo sapiens sincadel-D (BICD) mRNA, alternatively spliced, partial cds         21953_s_at       -2768       0.00325       consensus includes gb:U90303.1/DEF-Homo sapiens NENA for US120001 RNA, alternativel ypliced, partial cds         214805_at       -2687       0.0035       consensusi	209835_x_at	-2.743	0.00088	gb:BC004372.1 /DEF=Homo sapiens, Similar to CD44 antigen (homing function and Indian blood group system)
203305_s.at       -2631       0.00533       gb:NM_006416.1 /DEF=Homo sapiens solute carrier family 35 (CMP-sialic acid transporter), member 1 (SLC35A1)         205034_at       2659       0.00073       gb:NM_006596.1 /DEF=Homo sapiens solute 21 (CCNE2)         213816_s.gt       -2715       0.0038       Consensus includes gb:BP055474 / putative zinc finger protein NY-REN-34 antigen         219510_at       -2687       0.00438       Consensus includes gb:AP0641410.1 /DEF=Homo sapiens malignancy-associated protein         206683_at       -2661       0.0022       gb:NM_005596.1 /DEF=Homo sapiens malignancy-associated protein         218510_at       -2687       0.00438       Consensus includes gb:AV693985 /ets variant gene 2         218510_at       -2716       0.00037       go:nesnus includes gb:AV19207 //Homo sapiens insphore hoteial protein Fly20517 (Fly20517)         219533_s.gt       2-686       0.00037       Consensus includes gb:AV193209 //Homo sapiens since NA for IST-1N protein         219486_at       -2654       0.0036       Consensus includes gb:AV193209 //Homo sapiens bicaudal-D (BICD) mRNA, alternatively spliced, partial cds         219496_at       -2654       0.0035       gb:MM_01958.1 /DEF=Homo sapiens insclauda in elongation factor 1 a 2 (EEF1A2)         219456_at       -2758       0.00222       Consensus includes gb:AV133202.1 /DEF=Homo sapiens mRNA; cDNA DKF2p434C1722         219460_at <t< td=""><td>217471_at</td><td>-2.761</td><td>0.00164</td><td>Consensus includes gb:AL117652.1 /DEF=Homo sapiens mRNA</td></t<>	217471_at	-2.761	0.00164	Consensus includes gb:AL117652.1 /DEF=Homo sapiens mRNA
205934, at         2-659         0-00073         gb:NM_004702.1 /DEF=Homo sapiens (ChE2)           221816_5_st         -2-715         0-00376         Consensus includes gb:BF055474 / putative zinc finger protein NY-REN-34 antigen           219510_at         2-836         0-00029         gb:NM_006596.1 /DEF=Homo sapiens polymerase (DNA directed), 0 (POLQ)           21710_at         -2-631         0-0026         gb:NM_017859.1 /DEF=Homo sapiens polymerase (DNA directed), 0 (POLQ)           21510_at         -2-716         0-00038         Consensus includes gb:AV693985 /ets variant gene 2           218533_sta         2-703         0-00232         gb:NM_017859.1 /DEF=Homo sapiens myotherial proteins FL20517 (FL20517)           215633_x,at         -2-641         0-00537         Consensus includes gb:AV0731720 /Homo sapiens maligname, associated protein           214806_at         -2-654         0-00363         Consensus includes gb:AU73720 /Hes34898 ESTs, Weakly similar to 2109260A Beel growth factor Homo sapiens           214806_at         -2-654         0-00363         Consensus includes gb:AU3102.1 /DEF=Homo sapiens supians factor Homo sapiens of transition elongation factor 1 a 2 (EEF1A2)           212916_at         -2-654         0-00363         Consensus includes gb:AU33102.1 /DEF=Homo sapiens malign protein           214806_at         -2-758         0-00222         consensus includes gb:AU33102.1 /DEF=Homo sapiens mRNA; cDNA DKF2p434C1722 </td <td>203306_s_at</td> <td>-2.831</td> <td>0.00535</td> <td>gb:NM_006416.1/DEF=Homo sapiens solute carrier family 35 (CMP-sialic acid transporter), member 1 (SLC35A1)</td>	203306_s_at	-2.831	0.00535	gb:NM_006416.1/DEF=Homo sapiens solute carrier family 35 (CMP-sialic acid transporter), member 1 (SLC35A1)
221816_s.at       -2715       0.00376       Consensus includes gb:P055474 / putative zinc hinger protein NV-REN-34 antigen         219510_at       2836       0.00029       gb:NM_006596.1 / DEF-Homo sapiens polymerase (DNA directed), 0 (POLQ)         219510_at       -2687       0.00438       Consensus includes gb:AF041410.1 / DEF-Homo sapiens malignancy-associated protein         218531_s.at       -2611       0.00226       gb:NM_20559.1 / DEF-Homo sapiens supotwerase (DNA directed), 0 (POLQ)         218533_s.at       -2703       0.00232       gb:NM_017859.1 / DEF-Homo sapiens supothetical protein FU_20517 (FU_20517)         218533_s.at       -2686       0.00439       Consensus includes gb:AV03988 ETS, Weakly similar to 2109260A B cell growth factor Homo sapiens         214806_at       -2654       0.0036       Consensus includes gb:AV0373720 / Homo sapiens shicaudal-D (BICD) mRNA, alternatively spliced, partial cds         204540_at       2659       0.00059       gb:NM_001958.1 / DEF-Homo sapiens sicaudal-D (BICD) mRNA, alternatively spliced, partial cds         204540_at       -2654       0.0036       Consensus includes gb:BF055311 / hypothetical protein         204541_at       -2758       0.00222       Consensus includes gb:BF055311 / hypothetical protein         20454_at       -2764       0.00518       gb:NM_101859157         205050_xat       -2664       0.0053       gb:NM_10216F-H	205034_at	2.659	0.00073	gb:NM_004702.1 /DEF=Homo sapiens cyclin E2 (CCNE2)
2159.0.at       2-635       0-00029       go:MM_000595.0.1/DET+Homo sapiens paigners Alignancy-associated protein         217102.at       2-631       0-00438       Consensus includes gb:AV693985 / tots variant gene 2         218533.s_at       2-716       0-00032       gb:MM_017895 / 1/DET=Human Ca2-activated neutral protease large subunit (CANP)         215531.s_at       2-703       0-00222       gb:MM_017895 / 1/DET=Human Ga2-activated neutral protease large subunit (CANP)         21533.s_at       2-704       0-00537       Consensus includes gb:AV1713720 /Homo sapiens mNRA for LST-1N protein         219282.at       2-666       0-00479       Consensus includes gb:AV0713720 /Homo sapiens bicaudal-D (BICD) mRNA, alternatively spliced, partial cds         214866.at       2-654       0-00033       Consensus includes gb:AV13720 /Homo sapiens nRNA for LST-1N protein         21916.at       2-758       0-00022       Consensus includes gb:AV137102 /Homo sapiens mRNA; cDNA DKFZp434C1722         204540.at       2-694       0-00518       gb:AH1_2012.1/DET=Homo sapiens nRNA; cDNA DKFZp434C1722         209502.x.at       2-702       0-00048       Consensus includes gb:AV13102.1 /DET=Homo sapiens nRNA; cDNA DKFZp434C1722         209542.at       2-711       0-00156       gb:MN_004659.1 /DET=Homo sapiens nRNA; cDNA DKFZp434C1722         209524.at       2-771       0-00156       gb:MN_004659.1 /DET=Ho	221816_s_at	-2.715	0.00376	Consensus includes gb:B+055474 / putative zinc hinger protein NY-REN-34 antigen
21/102_at       -2.647       0.0035       Consension includes gib CAPC04741.0.1 / DEF=Homo Supplems Intending Subcent I (CANP)         208683_at       -2.651       0.00226       gb:M23254.1 / DEF=Homo Sapiens Insport the IJ20517 (FLJ20517)         215510_at       -2.716       0.0039       Consensus includes gb:AV693985 / ets variant gene 2         218533_s_at       -2.703       0.0022       gb:M23254.1 / DEF=Homo Sapiens Insport the IJ20517 (FLJ20517)         215633_xat       -2.641       0.00537       Consensus includes gb:AV73720 / Homo sapiens sincludes ID2050A for LST-1N protein         21928_at       -2.686       0.00479       Consensus includes gb:U90030.1/DEF=Homo sapiens bicaudal-D (BICD) mRNA, alternatively spliced, partial cds         204540_at       -2.695       0.00095       gb:MV_01958.1 / DEF=Homo sapiens evalyotic translation elongation factor 1 α 2 (EEF1A2)         2161693_xat       -2.758       0.00222       Consensus includes gb:BF055311 / hypothetical protein         216293_xat       -2.702       0.00084       Consensus includes gb:BF055311 / hypothetical protein         20550_xat       -2.694       0.00518       gb:AF114012.1 / DEF=Homo sapiens mRNA; CDNA DKFZp434C1722         209500_xat       -2.604       0.00526       gb:BK_006325.1 / DEF=Homo sapiens, GPA and S-phase expressed 1         Terremetrix         To 0.00056       gb:M	219510_at	2.830	0.00029	gb:INM_UOUS_SUL_I/IEF=HOMO sapiens polymerase (UNA directed), a (POLQ)
215510_at         -2.716         0.00220         gb:nN_01785p.1/DEF=Homo sapiens hypothetical protein FLJ20517 (FLJ20517)           21550_31_xat         -2.703         0.00232         gb:nN_01785p.1/DEF=Homo sapiens hypothetical protein FLJ20517 (FLJ20517)           215633_x_at         -2.641         0.00537         Consensus includes gb:AV713720 (Homo sapiens mRNA for LST-1N protein           212928_at         -2.686         0.00479         Consensus includes gb:AD57637 /HS.234898 ESTs, Weakly similar to 2109260A B cell growth factor Homo sapiens           214806_at         -2.654         0.0033         Consensus includes gb:L90030.1/DEF=Homo sapiens bicaudal-D (BICD) mRNA, alternatively spliced, partial cds           204540_at         2.695         0.00022         Consensus includes gb:L90030.1/DEF=Homo sapiens bicaudal-D (BICD) mRNA, alternatively spliced, partial cds           204540_at         2.695         0.00084         Consensus includes gb:R131302.1 /DEF=Homo sapiens bicaudal-D (BICD) mRNA, alternatively spliced, partial cds           20950_xat         -2.710         0.00084         Consensus includes gb:R110412.1 /DEF=Homo sapiens mRNA; ONA DKF2p434C1722           20950_xat         -2.711         0.00049         Homo sapiens cDNA FIL10418 fis, done NT2RP1000130, moderately similar to hepatoma-derived growth factor           20118_s_at         -2.771         0.0015         gb:NM_0022841.1 /DEF=Homo sapiens mRNA; for α-1 type II collagen.           218430_s_s	21/102_at	-2.631	0.00226	chisensus includes guizal 041410.1 / DEL = 10110 suprens many nancy-associated protein nh:M2225/11/DEE-Human Ca2-activated neutral protease large subjunit (CANP)
218533_s_at       2703       0.0023       gb:NM_017859.1/DEF Homo sapiens hypothetical protein FLJ20517 (FLJ20517)         215633_s_at       -2641       0.00537       Consensus includes gb:AV713720 /Homo sapiens mRNA for LST-1N protein         21928_at       -2686       0.00479       Consensus includes gb:AV057637 /Hs.234898 ESTs, Weakly similar to 2109260A B cell growth factor <i>Homo sapiens</i> 214806_at       -2654       0.00363       Consensus includes gb:J0057637 /Hs.234898 ESTs, Weakly similar to 2109260A B cell growth factor <i>Homo sapiens</i> 204540_at       2695       0.000363       Consensus includes gb:J005311 /DEF=Homo sapiens bicaudal-D (BICD) mRNA, alternatively spliced, partial cds         204540_at       2695       0.00022       Consensus includes gb:BF053311 / hpothetical protein         216693_x_at       2.702       0.00084       Consensus includes gb:AL133102.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         20950_x_at       2.694       0.00518       gb:AF114012.1 /DEF=Homo sapiens matrix metalloproteinase 23A (MMP23A)         209524_at       2.711       0.00049       Homo sapiens cDNA FLJ10418 fis, clone NT2RP1000130, moderately similar to hepatoma-derived growth factor         207118_s_at       -2644       0.0025       gb:BC006325.1 /DEF=Homo sapiens hypothetical protein FLJ12994 (FLJ12994)         211040_x_at       2.604       0.0025       gb:BC006325.1 /DEF=Homo sapiens shypothetical protein FLJ12994	215510 at	-2.716	0.00089	Consensus includes ab:AV693985 /ets variant age 2
215633 x.at       -2-641       0-00537       Consensus includes gb:AV713720 / Homo sapiens mRNA for IST-1N protein         221928_at       -2-686       0-00479       Consensus includes gb:AV713720 / Homo sapiens mRNA for IST-1N protein         214806_at       -2-654       0-00363       Consensus includes gb:AV713720 / Homo sapiens bicaudal-D (BICD) mRNA, alternatively spliced, partial cds         204540_at       2-695       0-00095       gb:NM_001958.1 /DEF=Homo sapiens evkaryotic translation elongation factor 1 α 2 (EEF1A2)         2116_at       -2-758       0-0022       Consensus includes gb:AL13102.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         209500_x_at       -2-694       0-00518       gb:AF114012.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         209500_x_at       -2-771       0-00054       gb:NM_004659.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         209511_s_s_at       -2-771       0-00156       gb:NM_004659.1 /DEF=Homo sapiens, c2 and S-phase expressed 1         ToreEnergative group         T18430.5_at       -3-771       0-00156       gb:NM_0022841.1 /DEF=Homo sapiens forter FU12994 (FU12994)       211040_x_at       2-604       0-0025       gb:NM_0022841.1 /DEF=Homo sapiens forter in FU12994 (FU12994)       217404_s_at       3-224       0-00036       Consensus includes gb:X16468.1 /DEF=Homo sapiens for ant trype II collagen.       205848_at       -3-225       0-00011 <td>218533 s at</td> <td>2.703</td> <td>0.00232</td> <td>db:NM 017859.1/DEF=Homo saviens hypothetical protein FLI20517 (FLI20517)</td>	218533 s at	2.703	0.00232	db:NM 017859.1/DEF=Homo saviens hypothetical protein FLI20517 (FLI20517)
2112LThe formation of the forma	215633 x at	-2.641	0.00537	Consensus includes qb:AV713720 /Homo sapiens mRNA for LST-1N protein
214806_at       -2.654       0.00363       Consensus includes gb:U90030.1/DEF=Homo sapiens bicaudal-D (BICD) mRNA, alternatively spliced, partial cds         204540_at       2.695       0.00095       gb:NM_001958.1/DEF=Homo sapiens eukaryotic translation elongation factor 1 α 2 (EEF1A2)         221916_at       -2.758       0.00222       Consensus includes gb:BF055311 / hypothetical protein         216693_x_at       2.702       0.00084       Consensus includes gb:AL133102.1 / DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         209500_x_at       -2.694       0.00518       gb:AF114012.1 / DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         20950_x_at       -2.771       0.00049       Homo sapiens cDNA FLJ10418 fis, clone NT2RP1000130, moderately similar to hepatoma-derived growth factor         207118_s_at       -2.771       0.00156       gb:NM_004595.1 / DEF=Homo sapiens matrix metalloproteinase 23A (MMP23A)         211040_x_at       2.604       0.0028       gb:BC006325.1 / DEF=Homo sapiens, G-2 and S-phase expressed 1         E         218430_s_at       -3.495       0.00011       gb:NM_0022841.1 / DEF=Homo sapiens growth areat-specific 2 (GAS2)         217404_s_at       3.224       0.00036       Consensus includes gb:X16468.1 / DEF=Homo sapiens Sint C (GAS2)         214915_at       -3.325       0.00011       gb:NM_005256.1 / DEF=Homo sapiens growth areat-specific 2 (GAS2)	221928_at	-2.686	0.00479	Consensus includes qb:AI057637 /Hs.234898 ESTs, Weakly similar to 2109260A B cell growth factor Homo sapiens
204540_at       2.695       0.00095       gb:NM_001958.1 /DEF=Homo sapiens eukaryotic translation elongation factor 1 or 2 (EEF1A2)         221916_at       -2.758       0.00222       Consensus includes gb:BF055311 / hypothetical protein         216693_x_at       2.702       0.00084       Consensus includes gb:AL133102.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         20950_x_at       -2.694       0.00518       gb:AF114012.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         20950_x_at       -2.694       0.00518       gb:AF114012.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         20952_4_at       2.711       0.00049       Hom sapiens cDNA FLJ10418 fis, done NT2RP1000130, moderately sinilar to hepatoma-derived growth factor         20114_x_at       2.604       0.0025       gb:CM06325.1 /DEF=Homo sapiens matrix metalloproteinase 23A (MMP23A)         211040_x_at       2.604       0.0026       gb:SM_0022841.1/DEF=Homo sapiens, G-2 and S-phase expressed1         21244_s_at       3.244       0.00036       Consensus includes gb:X16468.1 /DEF=Homo sapiens for an try pel I collagen.         21494_s_at       3.224       0.00036       Consensus includes gb:X16468.1 /DEF=Homo sapiens protein FLJ12994 (FLJ12994)         214915_at       -3.455       0.00071       gb:NM_00525.6.1 /DEF=Homo sapiens growth arrest-specific 2 (GAS2)         214915_at       -3.455       0.00075       Konsensus incl	214806_at	-2.654	0.00363	Consensus includes gb:U90030.1 / DEF=Homo sapiens bicaudal-D (BICD) mRNA, alternatively spliced, partial cds
221916_at       -2.758       0.00222       Consensus includes gb:BF055311 / hypothetical protein         216693_x_at       2.702       0.00084       Consensus includes gb:AL133102.1 /DEF=Homo sapiens mRNA; cDNA DKF2p434C1722         20950_x_at       -2.694       0.00518       gb:AF114012.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         20950_x_at       -2.694       0.00518       gb:AF114012.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722         20952_at       2.711       0.00049       Homo sapiens cDNA FLJ01418 fis, clone NT2RP1000130, moderately similar to hepatoma-derived growth factor         207118_s_at       -2.771       0.00156       gb:BC006325.1 /DEF=Homo sapiens matrix metalloproteinase 23A (MMP23A)         211040_x_at       2.604       0.0025       gb:BC006325.1 /DEF=Homo sapiens, G-2 and S-phase expresed 1         21144_s_at       -3.495       0.00011       gb:NM_0022841.1 /DEF=Homo sapiens for 2 and S-phase expresed 1         217404_s_at       -3.495       0.00011       gb:NM_0022841.1 /DEF=Homo sapiens growth arest-specific 2 (GAS2)         21494_s_at       -3.225       0.00041       gb:NM_00525.61 /DEF=Homo sapiens growth arest-specific 2 (GAS2)         21491_s_at       -3.415       0.00057       Homo sapiens CDNA FLI1780 fis, clone HEMBA1005931, weakly similar to zin finger protein 83         216010_x_at       -3.055       0.000575       Consensus includes gb:D8324	204540_at	2.695	0.00095	gb:NM_001958.1 /DEF=Homo sapiens eukaryotic translation elongation factor 1 α 2 (EEF1A2)
216693_xat         2.702         0.00084         Consensus includes gb:AL133102.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722           20950_xat         -2.694         0.00518         gb:AF114012.1 /DEF=Homo sapiens TNF-related death ligand-1β mRNA           20950_xat         -2.711         0.00049         Homo sapiens CNA REP10418 fs, clone NT2RP1000130, moderately similar to hepatoma-derived growth factor           207118_sat         -2.771         0.00156         gb:NM_004659.1 /DEF=Homo sapiens matrix metalloproteinase 23A (MMP23A)           211040_xat         2.604         0.0025         gb:BC006325.1 /DEF=Homo sapiens, G-2 and S-phase expressed 1           21144_sat         2.604         0.0001         gb:NM_0022841.1 /DEF=Homo sapiens, G-2 and S-phase expressed 1           218430_sat         -3.495         0.00011         gb:NM_0022841.1 /DEF=Homo sapiens go: and S-phase expression           217404_sat         3.224         0.00036         Consensus includes gb:X16468.1 /DEF=Homo sapiens fG-2 (GAS2)           214915_at         -3.425         0.00041         gb:NM_002556.1 /DEF=Homo sapiens growth arrest-specific 2 (GAS2)           214915_at         -3.435         0.00057         Homo sapiens CDN A FUIT180 fis, clone HEMBA1005931, weakly similar to zin finger protein 83           216010_xat         -3.037         0.00057         Konsensus includes gb:D89324 /DEF=Homo sapiens DNA for alpha(1,31,4) fucosyltransferase      <	221916_at	-2.758	0.00222	Consensus includes gb:BF055311 / hypothetical protein
209500_xat         -2.694         0-00518         gb:AF114012.1 / DEF=Homo sapiens TNF-related death ligand-1β mRNA           209524_at         2.711         0-00049         Homo sapiens CDNA FLJ10418 fis, clone NT2RP1000130, moderately similar to hepatoma-derived growth factor           20718_sat         -2.771         0-00156         gb:NM_004659.1 / DEF=Homo sapiens matrix metalloproteinase 23A (MMP23A)           211040_xat         2.604         0-0025         gb:BC006325.1 / DEF=Homo sapiens, G-2 and S-phase expressed 1           For En-engative         For En-engative         For Elemengative         For Elemengative           217404_sat         3.224         0-00036         Consensus includes gb:X16468.1 / DEF=Homo sapiens growth arrest-specific 2 (GAS2)           214915_at         -3.425         0-00041         gb:NM_005256.1 / DEF=Homo sapiens growth arrest-specific 2 (GAS2)           214915_at         -3.435         0-00057         Homo sapiens CDNA FLJ11780 fis, clone HEMBA1005931, weakly similar to zin finger protein 83           216010_xat         -3.037         0-00057         Consensus includes gb:DB324 / DEF=Homo sapiens DNA for alpha (1,31,4) fucosyltransferase           204631_at         -3.036         0-00075         Sonsensus includes gb:DB324 / DEF=Homo sapiens DNA for alpha (1,31,4) fucosyltransferase           204631_at         -3.037         0-0005         Sonsensus includes gb:DB324 / DEF=Homo sapiens DNA for alpha (1	216693_x_at	2.702	0.00084	Consensus includes gb:AL133102.1 /DEF=Homo sapiens mRNA; cDNA DKFZp434C1722
209524_at         2·711         0-00049         Homo sapiens CDNA FLJ10418 fis, clone NT2RP1000130, moderately similar to hepatoma-derived growth factor           207118_s_at         -2·771         0-00156         gb:NM_004659.1 /DEF=Homo sapiens matrix metalloproteinase 23A (MMP23A)           211040_x_at         2-604         0-00285         gb:BC006325.1 /DEF=Homo sapiens, G-2 and S-phase expressed 1           For ER-negative growt           218430_s_at         -3·495         0-0001         gb:NM_022841.1 /DEF=Homo sapiens hypothetical protein FLJ12994 (FLJ12994)           217404_s_at         3·224         0-00036         Consensus includes gb:X16468.1 /DEF=Human mRNA for α-1 type II collagen.           205848_at         -3·225         0-00041         gb:NM_005256.1 /DEF=Homo sapiens growth arrest-specific 2 (GAS2)           214915_at         -3·145         0-00057         Homo sapiens cDNA FLJ11780 fis, clone HEMBA1005931, weakly similar to zinc finger protein 83           216010_x_at         -3·037         0-00071         gb:NM_017534.1 /DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)           202687_s_at         -3·066         0-00072         gb:U57059.1 /DEF=Homo sapiens MPO-2 ligand mRNA         Continued	209500_x_at	-2.694	0.00518	gb:AF114012.1 /DEF=Homo sapiens TNF-related death ligand-1 $eta$ mRNA
207118_s_at       -2-771       0-00156       gb:NM_004659.1/DEF=Homo sapiens matrix metalloproteinase 23A (MMP23A)         211040_x_at       2-604       0-00285       gb:BC006325.1/DEF=Homo sapiens, G-2 and S-phase expressed 1         For ER-negative group         218430_s_at       -3-495       0-00011       gb:NM_002841.1/DEF=Homo sapiens hypothetical protein FUJ12994 (FUJ12994)         217404_s_at       3-224       0-00036       Consensus includes gb:X16468.1/DEF=Human mRNA for α-1 type II collagen.         205848_at       -3-225       0-00011       gb:NM_005256.1/DEF=Homo sapiens growth arrest-specific 2 (GAS2)         214915_at       -3-145       0-00057       Homo sapiens cDNA FLJ11780 fs, clone HEMBA1005931, weakly similar to zinc finger protein 83         216010_x_at       -3-055       0-00075       Consensus includes gb:DB3924 /DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)         20687_s_at       -3.066       0-00072       gb:U57059.1/DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)	209524_at	2.711	0.00049	Homo sapiens cDNA FLJ10418 fis, clone NT2RP1000130, moderately similar to hepatoma-derived growth factor
211040_x_at       2-604       0-00285       gb:BC.006325.1 / DEF=Homo sapiens, G-2 and S-phase expressed 1         For ER-negative group         218430_s_at       -3-495       0-00011       gb:NM_022841.1 / DEF=Homo sapiens hypothetical protein FLJ12994 (FLJ12994)         217404_s_at       3-224       0-00036       Consensus includes gb:X16468.1 / DEF=Human mRNA for α-1 type II collagen.         205848_at       -3-225       0-00041       gb:NM_005256.1 / DEF=Homo sapiens growth arrest-specific 2 (GAS2)         214915_at       -3-145       0-00057       Homo sapiens cDNA FLJ11780 fis, clone HEMBA1005931, weakly similar to zinc finger protein 83         216010_x_at       -3-055       0-00075       Consensus includes gb:D83324 / DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)         20687_s_at       -3.066       0-00072       gb:U57059.1 / DEF=Homo sapiens Apo-2 ligand mRNA       Continued	207118_s_at	-2.771	0.00156	gb:NM_004659.1 /DEF=Homo sapiens matrix metalloproteinase 23A (MMP23A)
218430_s_at       -3:495       0.00011       gb:NM_022841.1/DEF=Homo sapiens hypothetical protein FLJ12994 (FLJ12994)         217404_s_at       3:224       0.00036       Consensus includes gb:X16468.1/DEF=Human mRNA for α-1 type II collagen.         205848_at       -3:225       0.00041       gb:NM_005256.1/DEF=Homo sapiens growth arrest-specific 2 (GAS2)         214915_at       -3:145       0.00057       Homo sapiens cDNA FLJ11780 fis, clone HEMBA1005931, weakly similar to zinc finger protein 83         216010_x_at       -3:055       0.00075       Consensus includes gb:D89324 /DEF=Homo sapiens DNA for alpha (1,31,4) fucosyltransferase         204631_at       -3:037       0.00091       gb:NM_017534.1/DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)         202687_s_at       -3:066       0.00072       gb:U57059.1/DEF=Homo sapiens Apo-2 ligand mRNA       Continued	211040_x_at	2.604	0.00285	gb:BCUUb325.1/DEF=Homo sapiens, G-2 and S-phase expressed 1
217404_s_at         3-22         0-00036         Consensus includes gb:X16468.1 /DEF=Human mRNA for a-1 type II collagen.           205848_at         -3-225         0-00041         gb:NM_005256.1 /DEF=Human mRNA for a-1 type II collagen.           214915_at         -3-145         0-00057         Homo sapiens cDNA FLJ11780 fis, clone HEMBA1005931, weakly similar to zinc finger protein 83           216010_xat         -3-055         0-00075         Consensus includes gb:D89324 /DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)           202687_s_at         -3.066         0-00072         gb:U57059.1 /DEF=Homo sapiens Apo-2 ligand mRNA         Continued	218/20 c at	= group	0.00011	ah-NM_022841.1 /DEE-Hama saniens hypothetical protein El 12004 /El 12004)
205848_at     -3·25     0·00041     gb:NM_005256.1/DEF=Homo sapiens growth arrest-specific 2 (GAS2)       214915_at     -3·145     0·00057     Homo sapiens cDNA FLJ11780 fis, clone HEMBA1005931, weakly similar to zinc finger protein 83       216010_x.at     -3·055     0·00075     Consensus includes gb:D89324 /DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)       20687_s.at     -3·066     0·00072     gb:U57059.1/DEF=Homo sapiens Apo-2 ligand mRNA     Continued	210430_5_at	3.774	0.00036	Consensus includes ab:X164681/DFF=Human mRNA for a-1 type II collagen
214915_at         -3:145         0-00057         Homo sapiens cDNA FLJ11780 fis, clone HEMBA1005931, weakly similar to zinc finger protein 83           216010_x.at         -3:055         0-00075         Consensus includes gb:D89324 /DEF=Homo sapiens DNA for alpha (1,31,4) fucosyltransferase           204631_at         -3:037         0-00091         gb:NM_017534.1 /DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)           202687_s_at         -3:066         0-00072         gb:U57059.1 /DEF=Homo sapiens Apo-2 ligand mRNA         Continued	205848 at	-3.225	0.00041	ab:NM 005256.1/DEF=Homo sapiens growth arrest-specific 2 (GAS2)
216010_x_at         -3.055         0.00075         Consensus includes gb:D89324 /DEF=Homo sapiens DNA for alpha (1,31,4) fucosyltransferase           204631_at         -3.037         0.00091         gb:NM_017534.1 /DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)           202687_s_at         -3.066         0.00072         gb:U57059.1 /DEF=Homo sapiens Apo-2 ligand mRNA         Continued	214915 at	-3.145	0.00057	Homo sapiens cDNA FLJ11780 fis, clone HEMBA1005931, weakly similar to zinc finger protein 83
204631_at         -3.037         0.00091         gb:NM_017534.1/DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)           202687_s_at         -3.066         0.00072         gb:U57059.1/DEF=Homo sapiens Apo-2 ligand mRNA         Continued	216010_x_at	-3.055	0.00075	Consensus includes gb:D89324 /DEF=Homo sapiens DNA for alpha (1,31,4) fucosyltransferase
202687_s_at -3.066 0.00072 gb:U57059.1/DEF=Homo sapiens Apo-2 ligand mRNA Continued	204631_at	-3.037	0.00091	gb:NM_017534.1 /DEF=Homo sapiens myosin, heavy polypeptide 2, skeletal muscle, adult (MYH2)
	202687_s_at	-3.066	0.00072	gb:U57059.1 /DEF=Homo sapiens Apo-2 ligand mRNA Continued

Continued Gene	Standard Cox coefficient C	Cox p value	Gene description
221634_at	3.06 0	0.00077	qb:BC000596.1 /DEF=Homo sapiens, Similar to ribosomal protein L23a, clone MGC:2597
220886_at	-2.985 0	0.00081	gb:NM_018558.1 /DEF=Homo sapiens GABA receptor, θ (GABRQ)
202239_at	-2.983 0	0.00104	db:NM_006437.2 /DEF=Homo sapiens ADP-ribosyltransferase (NAD+; poly (ADP-ribose) polymerase)-like 1 (ADPRTL1)
204218_at	-3.022 0	0.00095	gb:NM_014042.1 /DEF=Homo sapiens DKFZP564M082 protein (DKFZP564M082)
221241_s_at	-3.054 0	0.00082	gb:NM_030766.1 /DEF=Homo sapiens apoptosis regulator BCL-G (BCLG)
209862_s_at	-3.006 0	0.00098	gb:BC001233.1 /DEF=Homo sapiens, Similar to KIAA0092 gene product, clone MGC:4896
217019_at	-2.917 0	0.00134	Contains a novel gene and the 5 part of a gene for a novel protein similar to X-linked ribosomal protein 4 (RPS4X)
210593_at	-2.924 0	0.00149	gb:M55580.1 /DEF=Human spermidinespermine N1-acetyltransferase
216103_at	-2.882 0	0.0017	Consensus includes gb:AB014607.1 /DEF=Homo sapiens mRNA for KIAA0707 protein

Table 3: 76 genes from the prognostic signature

included well-characterised genes and 18 unknown genes. This finding could explain the superior performance of this signature compared with other prognostic factors. Although genes involved in cell death, cell proliferation, and transcriptional regulation were found in both groups of patients stratified by ER status, the 60 genes selected for the ER-positive group and the 16 selected for the ER-negative group had no overlap. This result supports the idea that the extent of heterogeneity and the underlying mechanisms for disease progression could differ for the two ER-based subgroups of breast-cancer patients.

Comparison of our results with those of Van de Vijver and colleagues<sup>12</sup> is difficult because of differences in patients, techniques, and materials used. Their study included node-negative and node-positive patients, who had or had not received adjuvant systemic therapy, and only women younger than 53 years. Furthermore, the microarray platforms used in the studies differ— Affymetrix and Agilent. Of the 70 genes in the study by van't Veer and co-workers,<sup>11</sup> 48 are present on the Affymetrix U133a array, whereas only 38 of our 76 genes are present on the Agilent array. There is a three-gene

Functional class	76-gene signature
Cell death	TNFSF10, TNFSF13, MAP4, CD44, IL18, GAS2, NEFL, EEF1A2, BCLG, C3
Cell cycle	CCNE2, CD44, MAP4, SMC4L1, TNFSF10, AP2A2, FEN1, KPNA2, ORC3L, PLK1
Proliferation	CD44, IL18, TNFSF10, TNFSF13, PPP1CC, CAPN2, PLK1, SAT
DNA replication, recombination, and repair	TNFSF10, SMC4L1, FEN1, ORC3L, KPNA2, SUPT16H, POLQ, ADPRTL1
Immune response	TNFSF10, CD44, IL18, TNFSF13, ARHGDIB, C3
Growth	PPP1CC, CD44, IL18, TNFSF10, SAT, HDGFRP3
Cellular assembly and organisation	MAP4, NEFL, TNFSF10, PLK1, AP2A2, SMC4L1
Transcription	KPNA2, DUSP4, SUPT16H, DKFZP434E2220, PHF11, ETV2
Cell-to-cell signalling and interaction	CD44, IL18, TNFSF10, TNFSF13, C3
Survival	TNFSF10, TNFSF13, CD44, NEFL
Development	IL18, TNFSF10, COL2A1
Cell morphology	CAPN2, CD44, TACC2
Protein synthesis	IL18, TNFSF10, EEF1A2
ATP binding	PRO2000, URKL1, ACACB
DNA binding	HIST1H4H, DKFZP434E2220, PHF11
Colony formation	CD44, TNFSF10
Adhesion	CD44, TMEM8
Neurogenesis	CLN8, NEURL
Golgi apparatus	GOLPH2, BICD1
Kinase activity	CNK1, URKL1
Transferase activity	FUT3, ADPRTL1

Table 4: Pathway analysis of the 76 genes from the prognostic signature

Method	Patients guided to receive adjuvant chemotherapy in the testing set		
	Metastatic disease at 5 years	Free of metastatic disease at 5 years	
St Gallen	52/55 (95%)	104/115 (90%)	
National Institutes of Health	52/55 (95%)	101/114 (89%)	
76-gene signature	52/56 (93%)	60/115 (52%)	
St Gallen consensus criteria: tumo (any one of these criteria). Natior	our ≥2 cm, ER negative nal Institutes of Health:	e, grade 2–3, patient <35 years tumour >1 cm.	

Table 5: Comparison of the 76-gene signature and the current conventional consensus on treatment of breast cancer

overlap between the two signatures (cyclin E2, origin recognition complex, and TNF superfamily protein). Despite the apparent difference, both signatures included genes that identified several common pathways that might be involved in tumour recurrence. This finding supports the idea that although there might be redundancy in gene members, effective signatures could be required to include representation of specific pathways.

The strengths of our study compared with the study of Van de Vijver and colleagues<sup>12</sup> are the larger number of untreated lymph-node-negative patients (286 vs 141), and the independence of our 76-gene signature with respect to age, menopausal status, and tumour size. The validation set of patients is completely without overlap with the training set, in contrast to 90% of other reports.<sup>30</sup> In conclusion, since only 30-40% of untreated lymphnode-negative patients develop tumour recurrence, our prognostic signature could provide a powerful tool to identify those patients at low risk preventing overtreatment in substantial numbers of patients. If confirmed in subsequent studies, the recommendation of adjuvant systemic therapy in patients with lymphnode-negative primary breast cancer could be guided by this prognostic signature. The predictive value of our gene signature with respect to the efficacy of different modes of systemic therapy could be tested in the adjuvant setting or in patients with metastatic disease.

#### Contributors

Y Wang, J G M Klijn, E M J J Berns, D Atkins, and J A Foekens designed the study, interpreted the data, and wrote the report. Y Zhang, J Yu, and T Jatkoe analysed the data and developed the prognostic signature. M Timmermans and D Talantov were responsible for laboratory experiments and pathological assessment of the tissue samples. F Yang and A M Sieuwerts did laboratory experiments on the isolation of RNA and quality assessment. M P Look and M E Meijer-van Gelder collected and handled the patients' data and contributed to the survival analyses.

#### Conflict of interest statement

YW, YZ, FY, DT, JY, TJ, and DA are employed by Veridex LLC, a Johnson & Johnson Company, which is in the business of commercialising diagnostic products. The other authors declare no conflicts of interest.

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