

# #302 - Breast Tumours with Intermediate Histological Grade can be Reclassified into Prognostically Distinct Groups by Gene Expression Profiling

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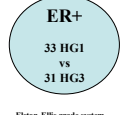
## Background

- Histological grade has long been recognized to provide significant prognostic information
- Whilst grade 1 and 3 tumors are clearly associated with different prognoses, those classified as grade 2 (~40%) represent a difficulty in clinical decision making
- Inter-observer variability results in poor reproducibility across institutions

## Material and Methods

~ 1000 tumor samples

Training set: N = 64



Ehtes-Ellis grade system

Affymetrix U133A  
22,283 probe sets

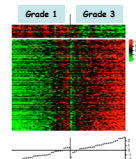
### Validation sets

Original Datasets  
Luminal Population  
AJ125 N=125  
TRANSBIG N=385

External published datasets: N = 500

Sorlie et al. PNAS, 2001 (STNO)  
Sotiriou et al. PNAS, 2003 (NCT)  
Van de Vijver et al. NEJM, 2002  
NK12(U) = untreated  
NK12(T) = treated

### Defining Genomic Grade in the training set



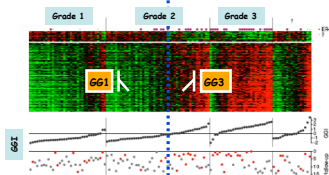
128 probe sets of "Grade Signature" (97 genes) FDC>0

$$GGI = scale \left[ \sum_{j \in U_3} x_j - \sum_{j \in U_1} x_j - cutoff \right]$$

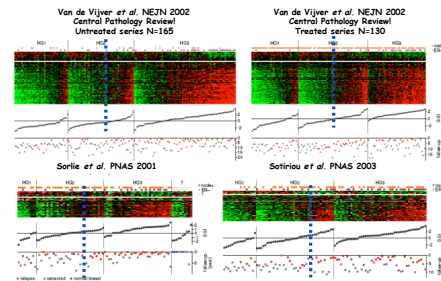
Define GGI score (Gene-expression Grade Index):

- Concordance with histological grade
- Prognostic value of GGI

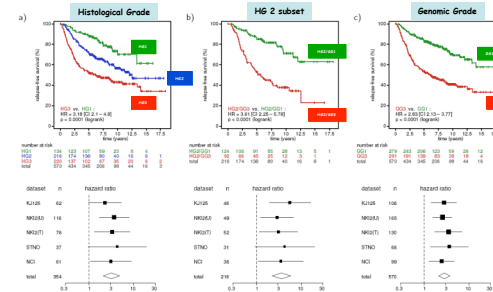
### Histological Grade 2 (HG2) Tumors are a Mixture of Genomic Grade 1 and 3 Tumors



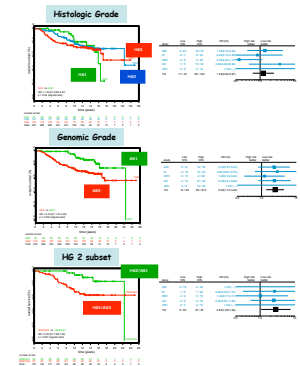
### Consistent Distribution of GG in Different Populations and Microarrays Platforms



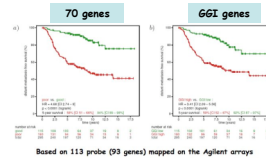
### Clinical Outcome



### TRANSBIG validation series (Use of Mammaprint®)



### Comparison between the gene-expression grade index (GGI) and the 70-gene signature



### Conclusions

- HG2 tumors are a mixture of HG1 and HG3 cases based on the genomic grade
- Gene-expression based grading can significantly improve current grading system for the prognosis assessment of breast cancer
- Genomic grade was highly reproducible across multiple independent datasets and across different microarray platforms