
# A Physicist's Approach to Breast Cancer

Gyan Bhanot

Rutgers/CINJ

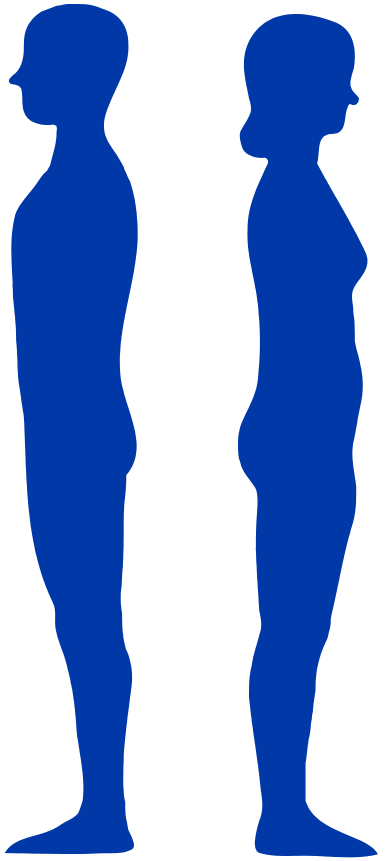
# The three laws

- Work with Clinicians – they know more than you
- Cancer = Death. Focus on improving outcome
- Be humble. Your ego has no place in this

# KNOW THE ENEMY

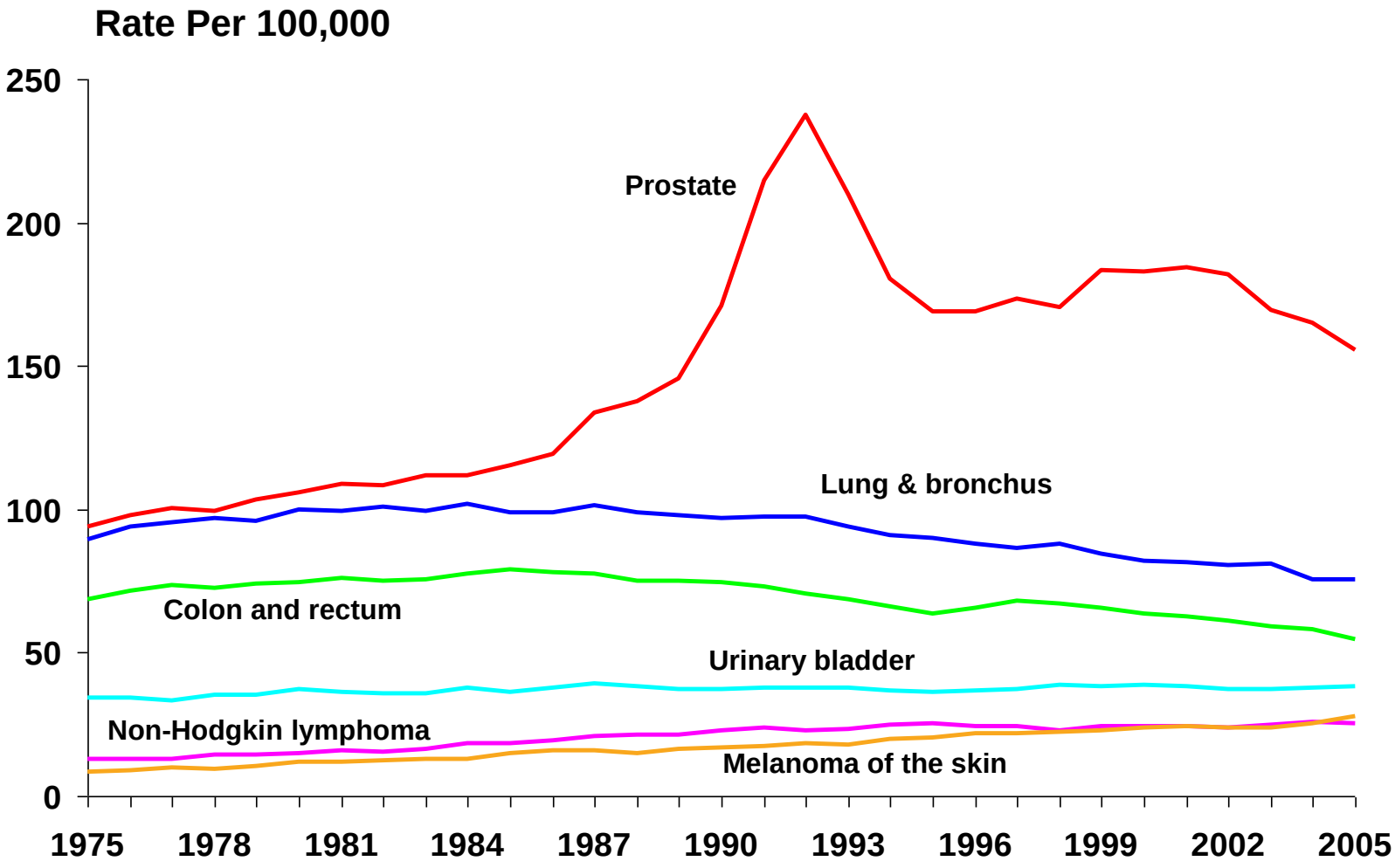
## 2009 Estimated US Cancer Cases*

| Men 766,130 | | Women 713,220 | |
|---|---|---|---|
| **Prostate** | **25%** | **27%** | **Breast** |
| Lung & bronchus | 15% | 14% | Lung & bronchus |
| Colon & rectum | 10% | 10% | Colon & rectum |
| Urinary bladder | 7% | 6% | Uterine corpus |
| Melanoma of skin | 5% | 4% | Non-Hodgkin lymphoma |
| Non-Hodgkin lymphoma | 5% | 4% | Melanoma of skin |
| Kidney & renal pelvis | 5% | 4% | Thyroid |
| Leukemia | 3% | 3% | Kidney & renal pelvis |
| Oral cavity | 3% | 3% | Ovary |
| Pancreas | 3% | 3% | Pancreas |
| All Other Sites | 19% | 22% | All Other Sites |



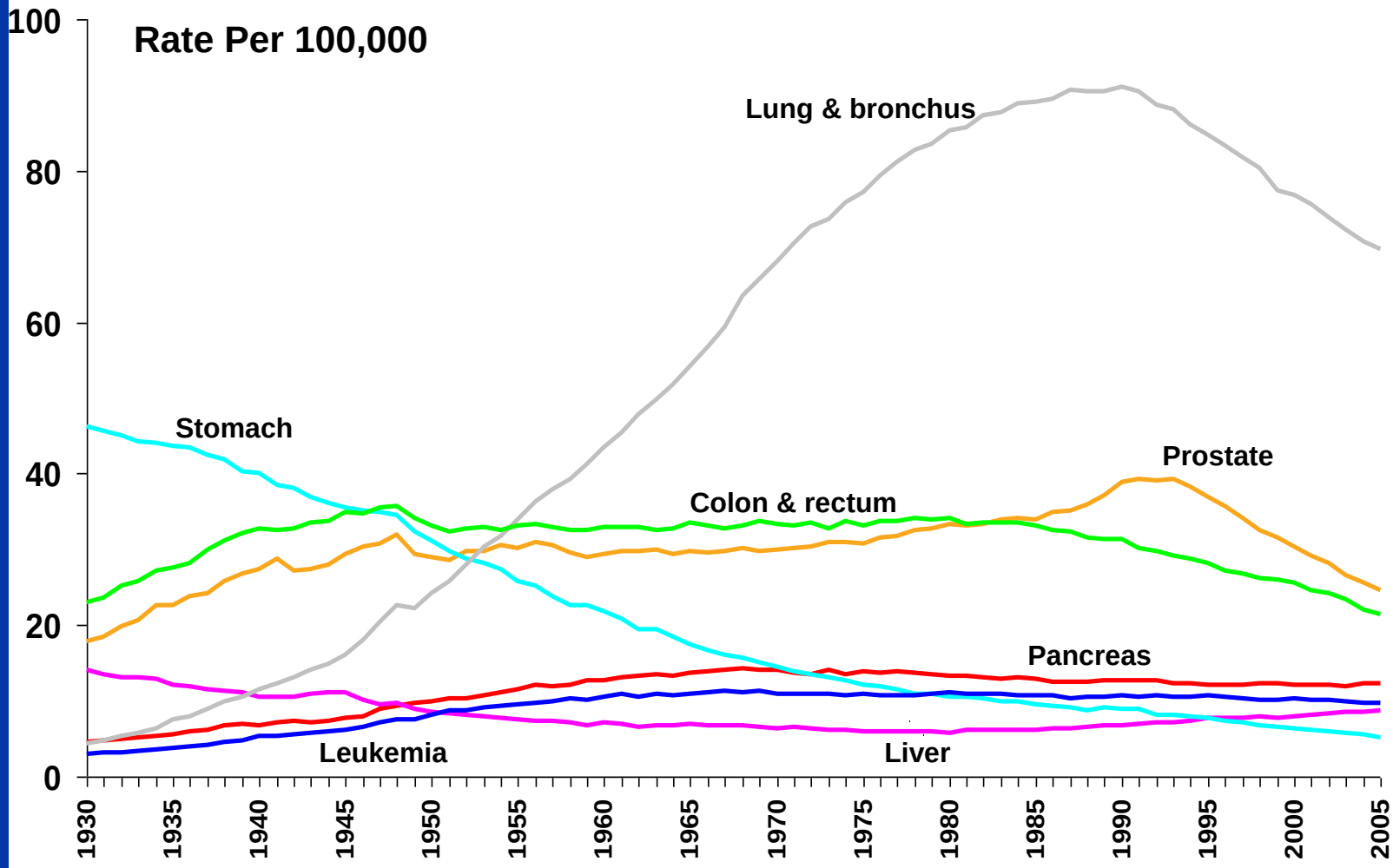
*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.
Source American Cancer Society, 2009.

# Cancer Incidence Rates* Among Men, US, 1975-2005



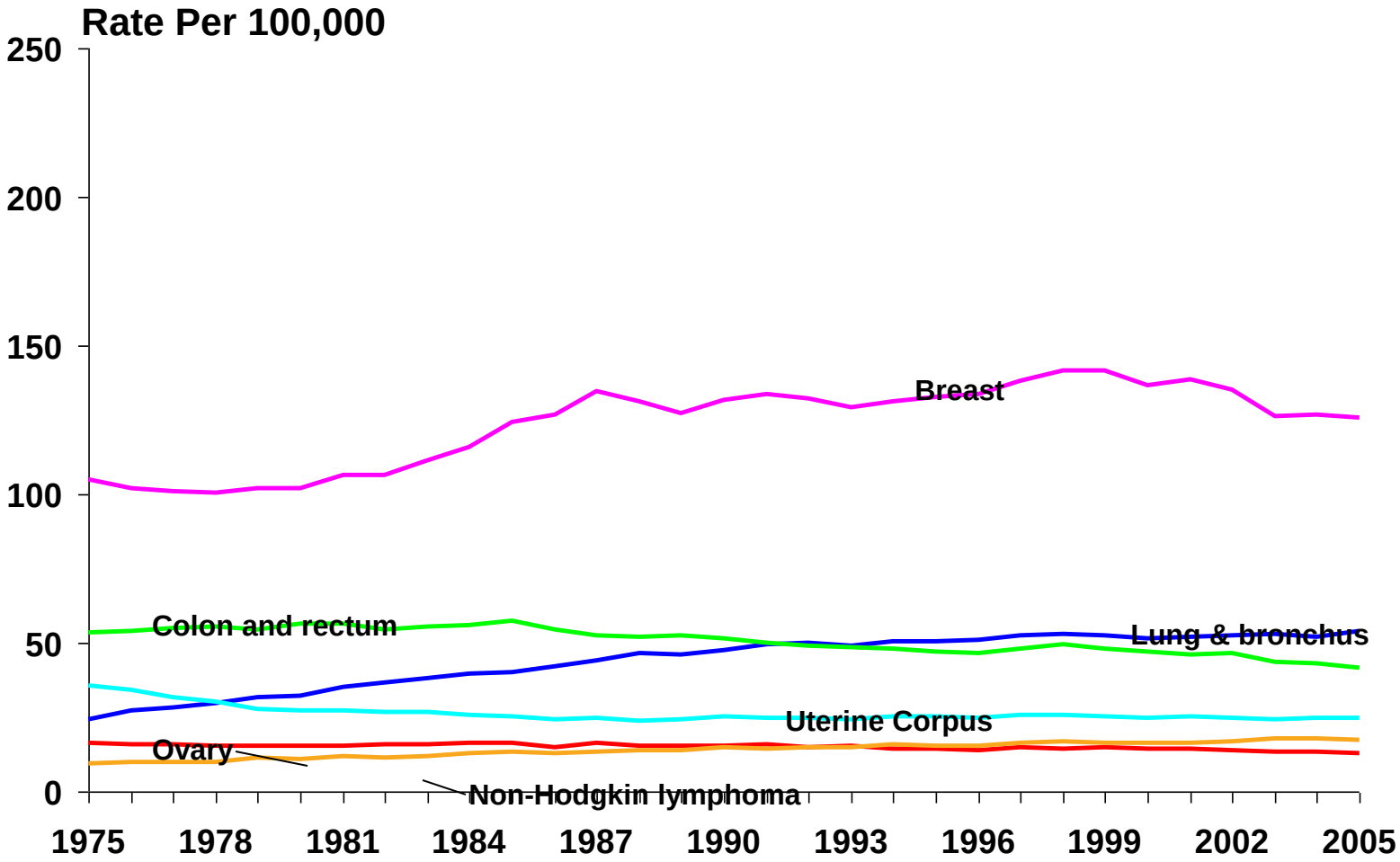

*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.
Source Surveillance, Epidemiology, and End Results Program, Delay-adjusted Incidence database
SEER Incidence Delay-adjusted Rates, 9 Registries, 1975-2005, National Cancer Institute, 2008.

# Cancer Death Rates* Among Men, US,1930-2005



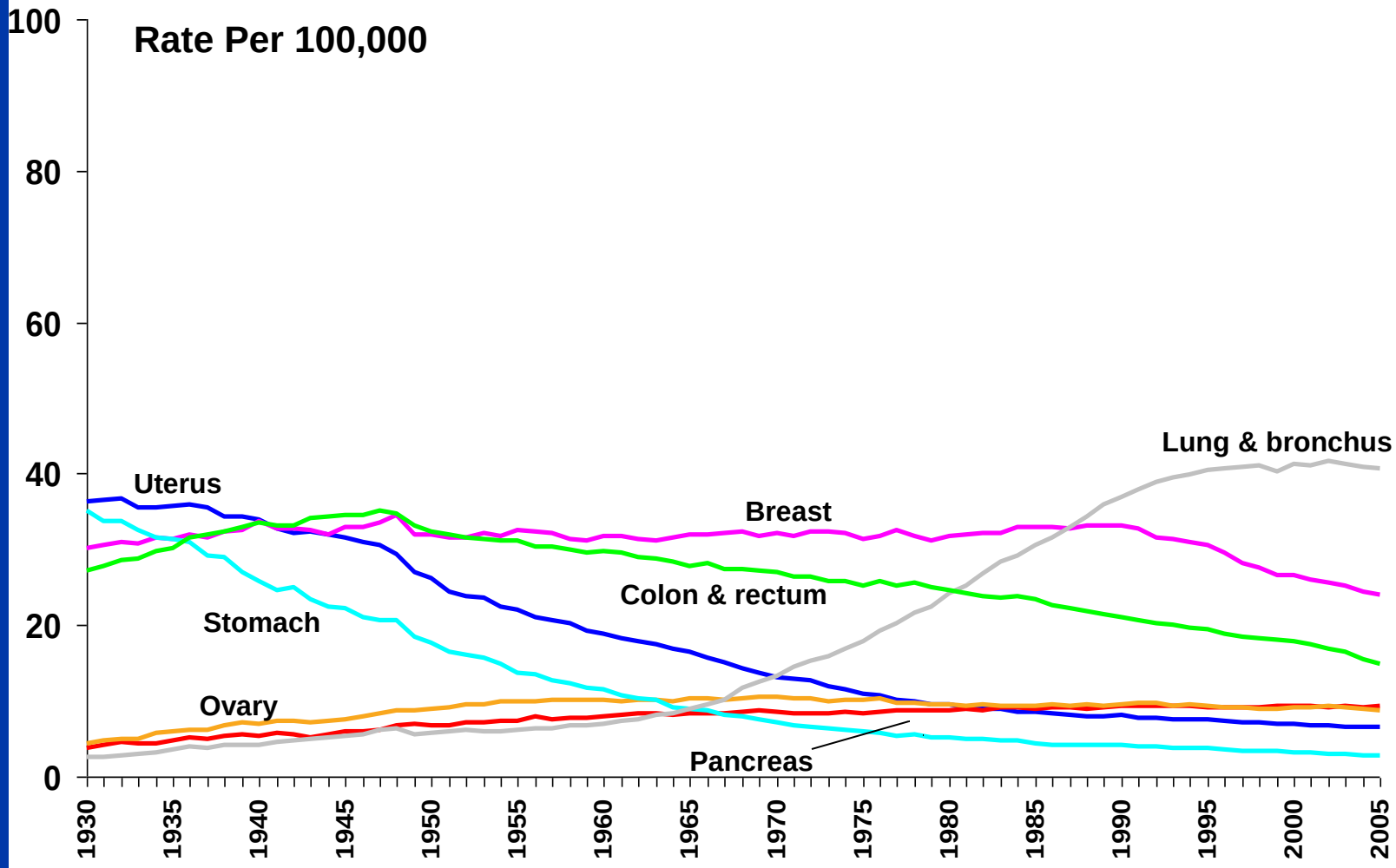

*Age-adjusted to the 2000 US standard population.
Source: US Mortality Data 1960-2005, US Mortality Volumes 1930-1959,
National Center for Health Statistics, Centers for Disease Control and Prevention, 2008.

# Cancer Incidence Rates* Among Women, US, 1975-2005

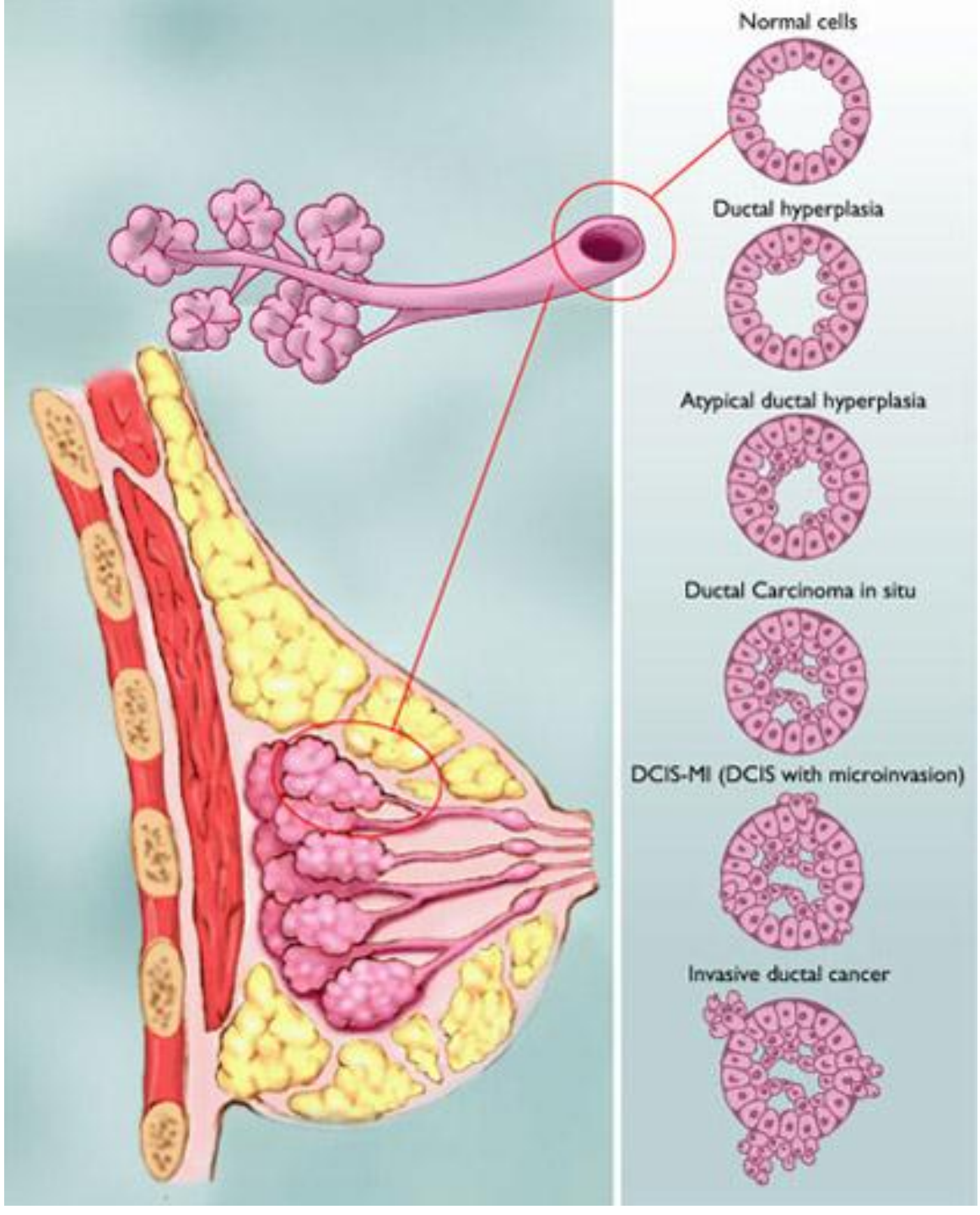



***Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.**
**Source Surveillance, Epidemiology, and End Results Program, Delay-adjusted Incidence database SEER Incidence Delay-adjusted Rates, 9 Registries, 1975-2005, National Cancer Institute, 2008.**

# Cancer Death Rates* Among Women, US,1930-2005




*Age-adjusted to the 2000 US standard population.
Source: US Mortality Data 1960-2005, US Mortality Volumes 1930-1959,
National Center for Health Statistics, Centers for Disease Control and Prevention, 2008.




Normal

ADH

ADH

DCIS

DCIS-MI

IDC

# Risk Factors

1. Age
2. Family History
3. Susceptibility genes (BRCA1 and BRCA2)
4. **Endocrinological Factors**
5. Dietary factors (?)
6. Benign Breast Disease

# Endocrinologic Factors

Increased Risk:

Early menarche

Nulliparity

Late first pregnancy

Hormone Replacement Therapy

Decreased Risk:

late menarche

Early and repeated pregnancy

Early menopause

Prolonged lactation

# Heterogeneous disease

Estrogen Receptor:

1. 60-70% expresses ER
2. ER+ BrCa often responds to anti-estrogen therapy
3. ER- BrCa more aggressive, no hormonal Rx, more common in younger women
4. Tamoxifen treatment decreases risk of new ER+ BrCa but does not affect incidence of ER- BrCa.

HER2/neu:

1. 20-30% have amplification of HER2
2. More aggressive, higher grade
3. Some respond to Rx with trastuzumab/Herceptin

Gene Expression Array Analysis:

Can it be used to impact clincal care?

Define biologically relevant subtypes?

Predict natural history?

Predict response to Rx ?

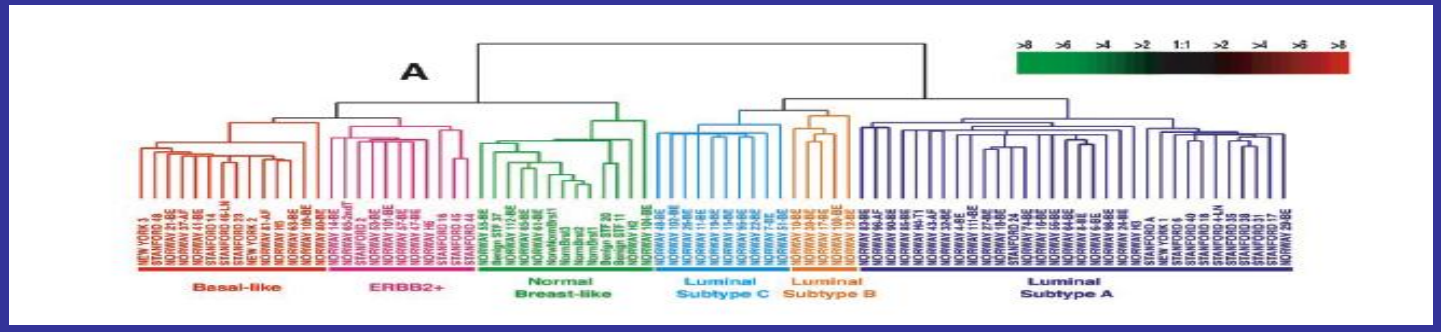
Pros: generates much data on many genes

Cons: generates much data on many genes.

number of variables >> number of samples

→ OVERFITTING

# BrCa subtypes have distinct molecular signatures



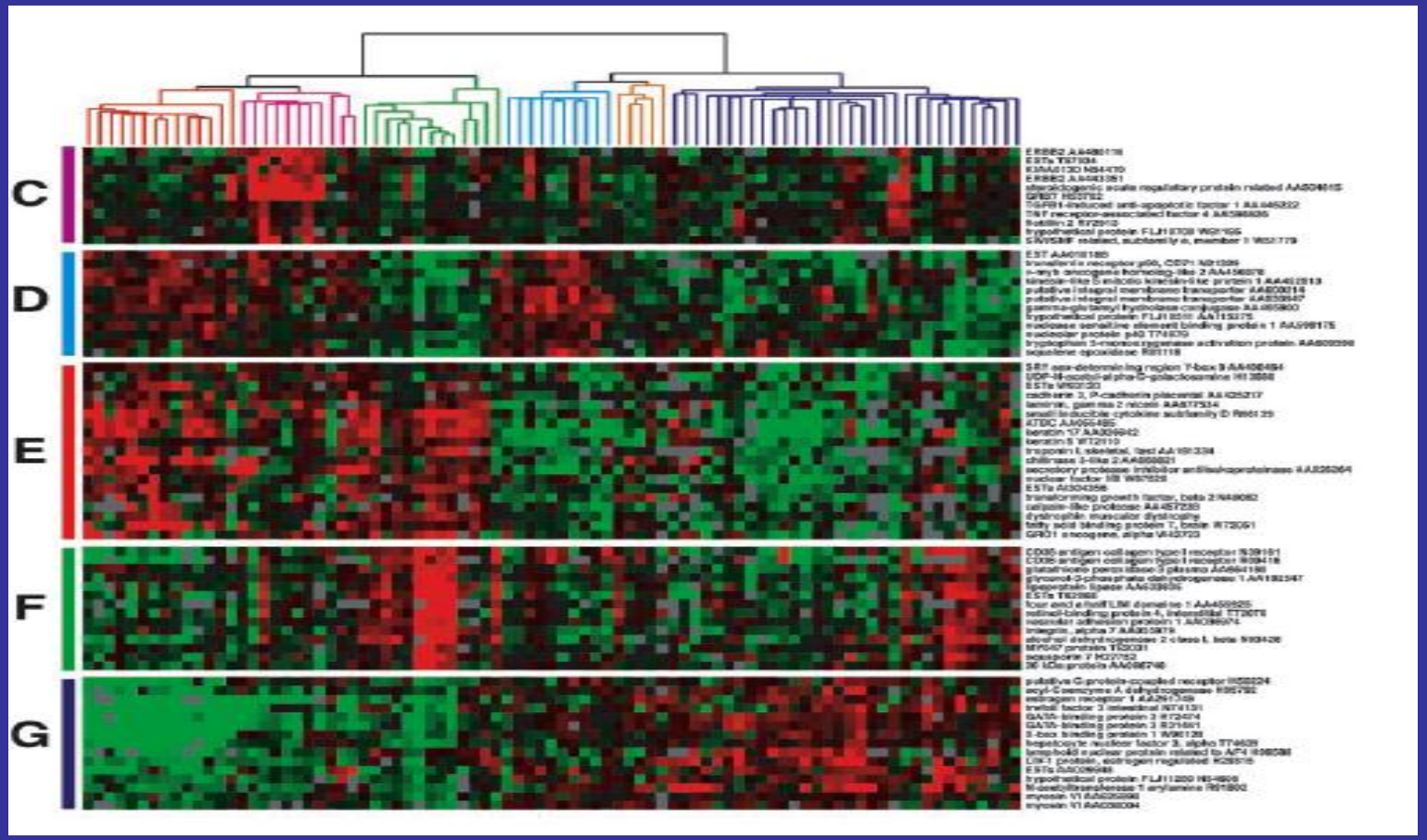

HER2

????

Basal

Normal

Luminal



# Currently Available Predictive Panels

- Paik et al *: NEJM* 351 (27), 2817 (2004)
  21 genes predicting outcome in node negative, ER+ patients
  **Oncotype DX™ (In clinical use in US)**

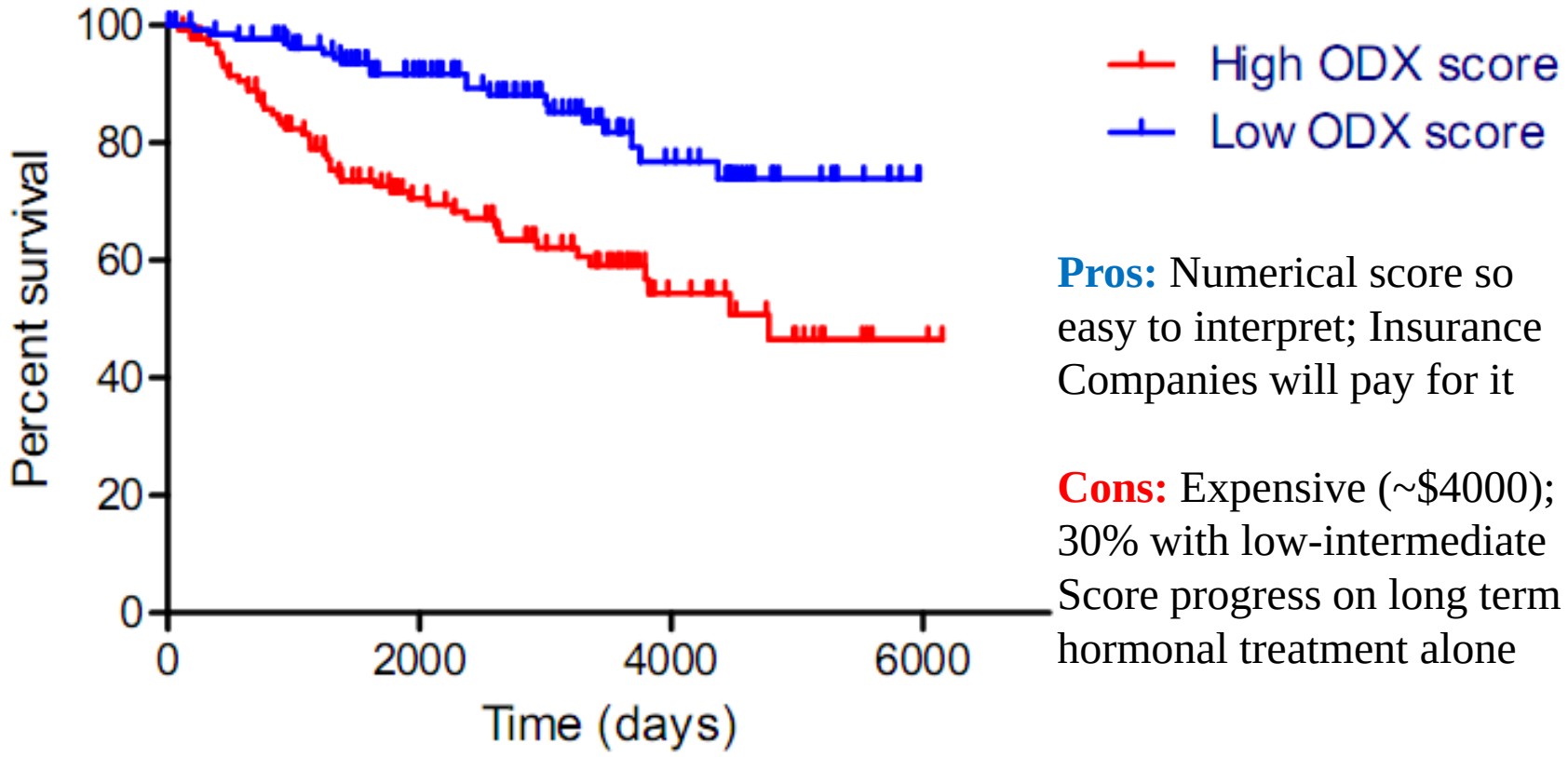
- van't Veer et al: *Nature medicine* 9 (8), 999 (2003) 70 genes correlated with clinical outcome in large mixed cohort
  **Mammaprint® (USFDA Approved, Clinical use in Europe – but on decline)**

- Wang et al : *Lancet* 365 (9460), 671 (2005)
  76 genes correlated with recurrence
  **Rotterdam signature**

# Oncotype Dx® (Genomic Health)

**RT-PCR based assay, measures mRNA levels of 21 genes: HER2, GRB7, GSTM1, CD68, BAG1, invasion markers (MMP11,CTSL2), proliferation markers (Ki67,STK15,Survivin,CCNB1,MYBL2), ER and reference markers.**

**ODX score is a linear combination of normalized gene expression levels.**




**Pros:** Numerical score so easy to interpret; Insurance Companies will pay for it

**Cons:** Expensive (~$4000); 30% with low-intermediate Score progress on long term hormonal treatment alone

# Some Simple Bioinformatics Tools to identify patterns in high throughput data:

Clustering

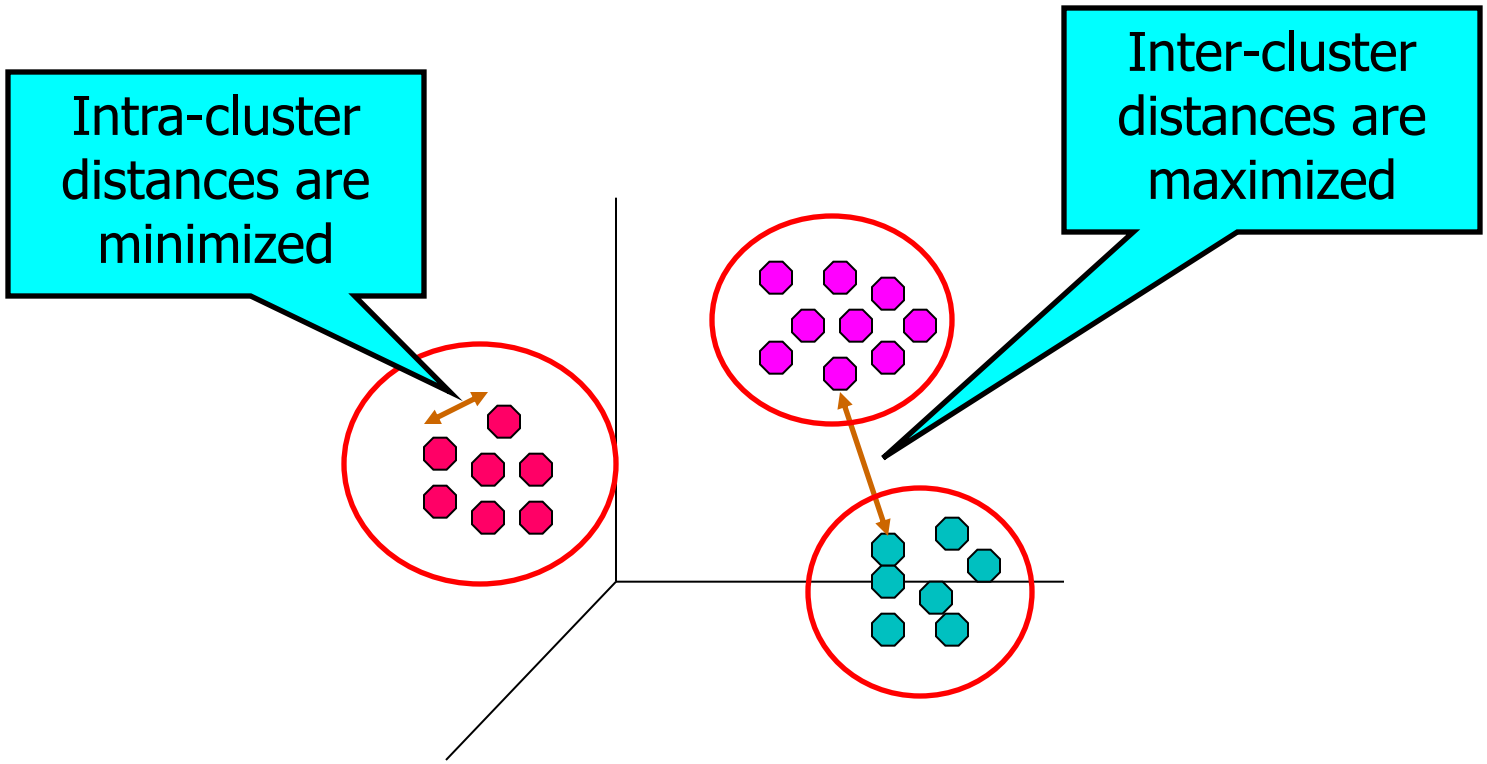
Principal Component Analysis (PCA)

Logical Analysis of Data (LAD)

Network Analysis

# What is Cluster Analysis?

- Finding groups of objects such that the objects in a group will be similar (or related) to one another and different from (or unrelated to) the objects in other groups



# Unsupervised Consensus Ensemble Clustering

- Unsupervised Clustering
  - Group expression data into clusters
  - Maximize intra-cluster similarity
  - Minimize inter-cluster similarity
- Ensemble:
  - Apply many Clustering Techniques
  - Apply many Data Perturbations (bootstrap)
  - Combine Results into Agreement Matrix

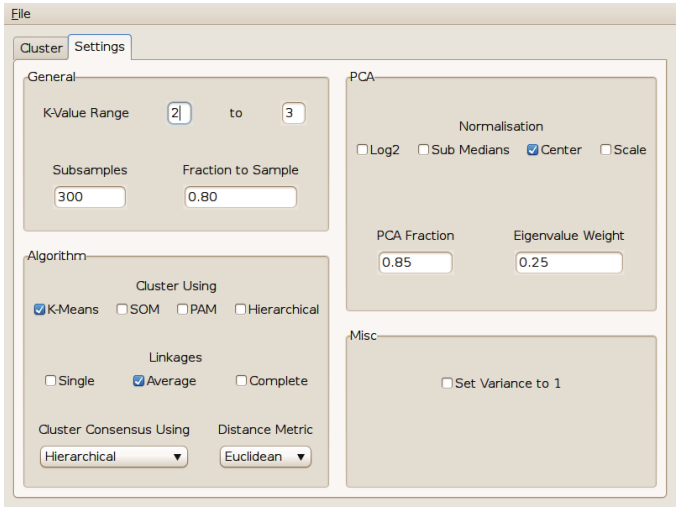
# Clustering Methods Used

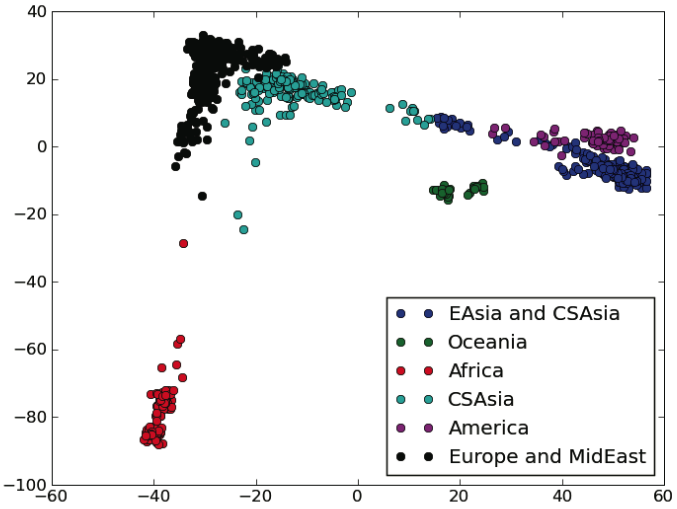
- Partition Relocation Methods
  - PAM, CLARA, k-Means, Graph-Partitioning
- Agglomerative Methods
  - Average Linkage, Complete Linkage, Mcquitty, Ward, Centroid metrics, bagglo
- Probabilistic Methods
  - Expectation Maximization (EM), Entropy Based Clustering (ENCLUST), SOM,

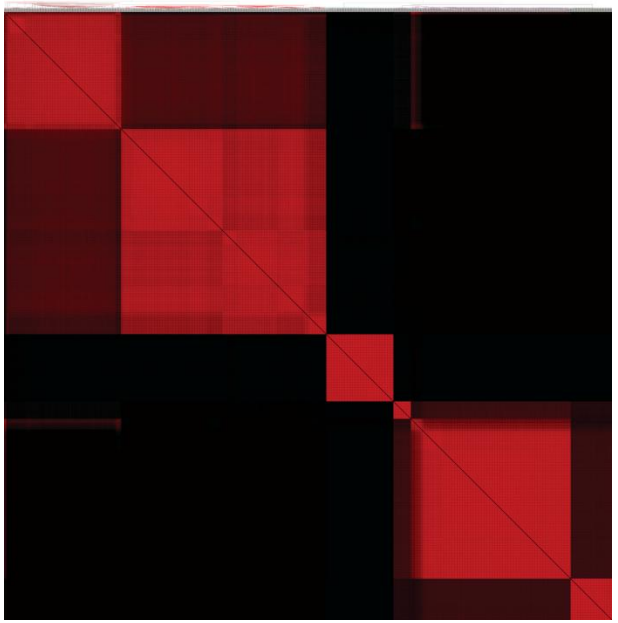
# Agreement Matrix

- Combine bootstrap results per method into $N_{sample}$ x $N_{sample}$ matrix M(i,j).
- M(i,j) = probability that i, j are in same cluster.
- Sort rows to get block diagonal form
- Combine matrices across clustering methods
- Re-sort to get final Agreement Matrix

# ConsensusCluster: A tool for unsupervised cluster discovery in numerical data



***Seiler M, Huang CC, Szalma S, Bhanot G. ConsensusCluster: a software tool for unsupervised cluster discovery in numerical data. OMICS 2010, 14(1):109.***

# Study 1: Immune Infiltrate and HER2+ disease: Data from Wang et al, Lancet, 2005

**Tumor Bank at the Erasmus Medical Center (Rotterdam, Netherlands)**

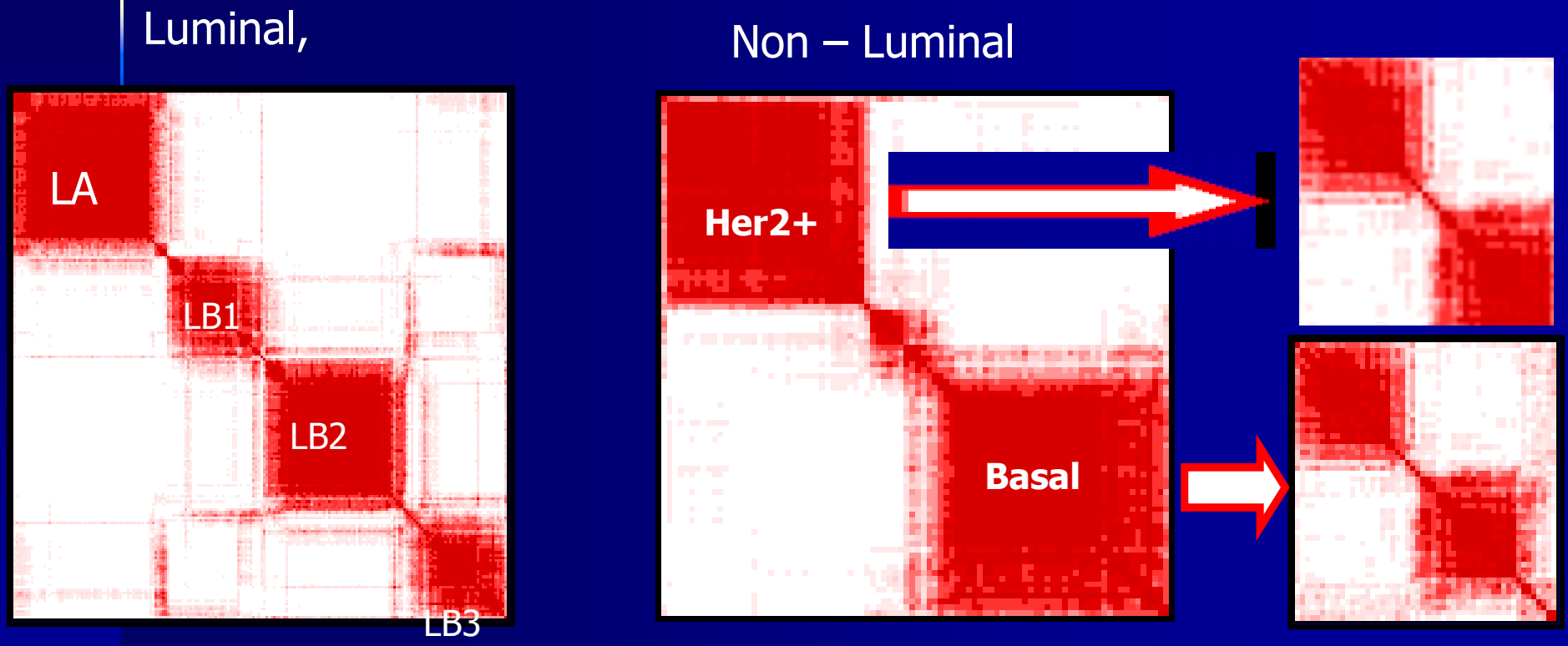
**286 patients** (1980-1995)
- no systemic therapy
- 219 patients: conservative surgery
- 67 patients: mastectomy
- 248 patients: radiotherapy

**Affymetrix U133a** mRNA microarrays

**Clinical information**
- ER status: 209 ER+, 77 ER-
- time to follow up: median 101 months
- relapse status within 5 years: 93 yes, 183 no
- median age 52 (range 26-83)

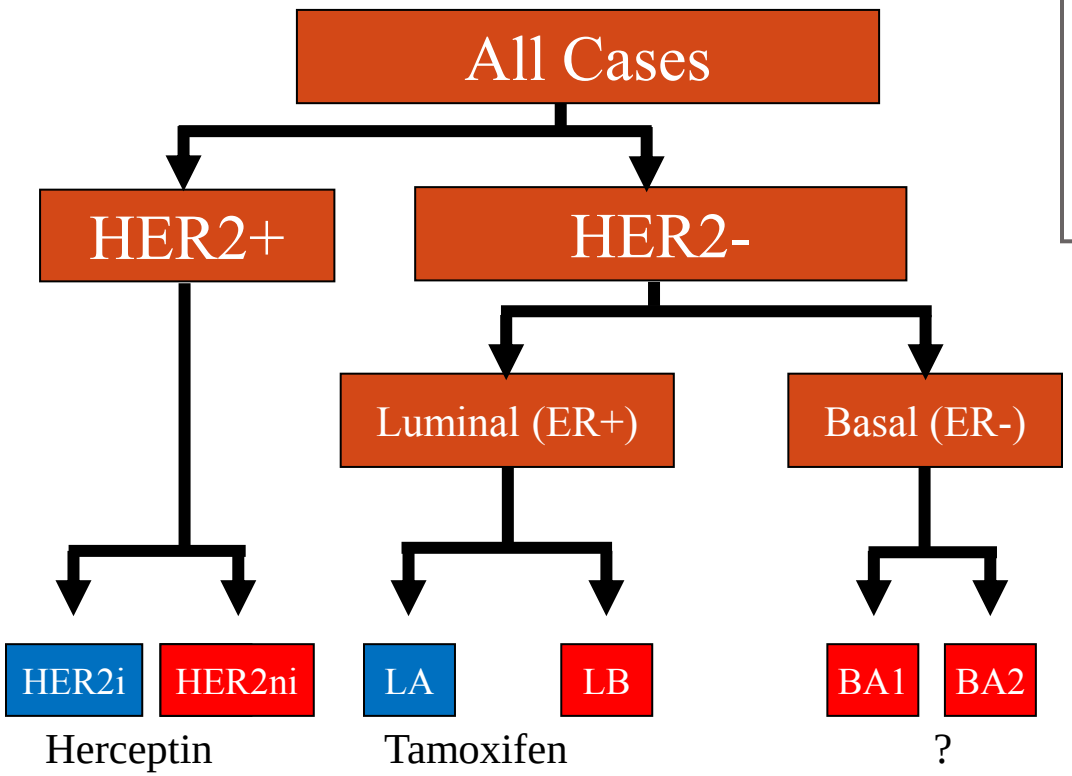
Alexe et al Cancer Research, 67, 10669-10676, 2007.

# Clusters in dataset from Wang et al, 2005, Lancet




*G. Alexe, G.S. Dalgin, D. Scanfeld, P. Tamayo, J. Mesirov, C. DeLisi, L. Harris, N. Barnard, M. Martel, A.J. Levine, S. Ganesan, G. Bhanot,* 'High Expression of Lymphocyte Associated Genes in Node Negative HER2+ Breast Cancer correlates with lower Recurrence rates.' Cancer Research, 67, 10669-10676, 2007.

# Breast cancer subtypes



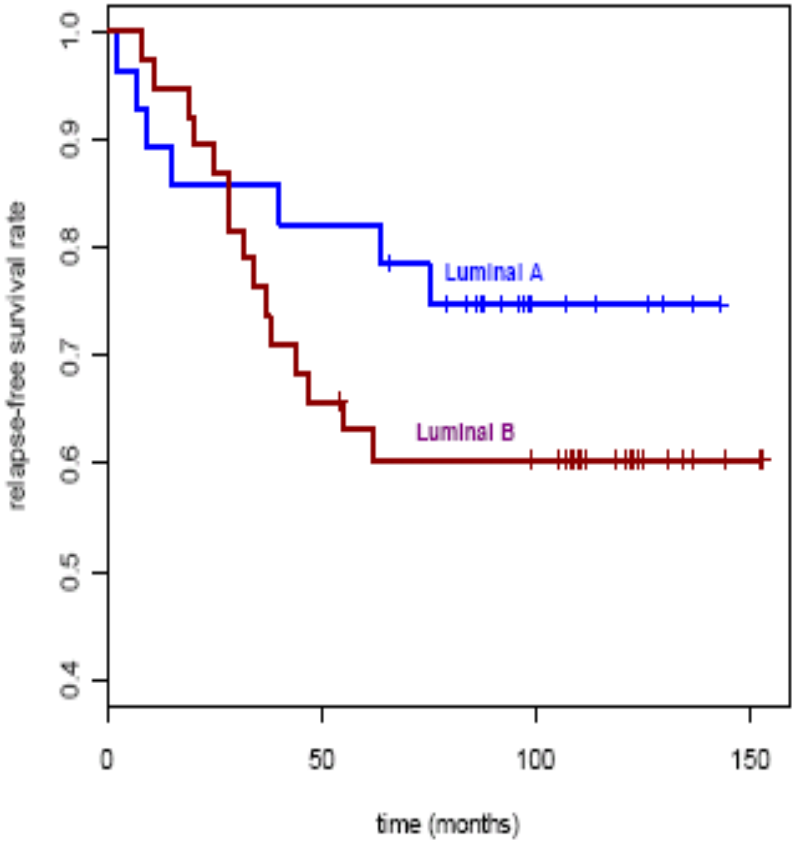

**Discovery Data Set: (Wang et al. 2005) - 286 early stage (LN) breast cancers treated with surgery + RT. Long term follow-up (7.1 years median)**

**Validation Data Set: 249 primary invasive breast tumors (Ivshina et al. 2006)- Long term follow-up ~ 9 years.**

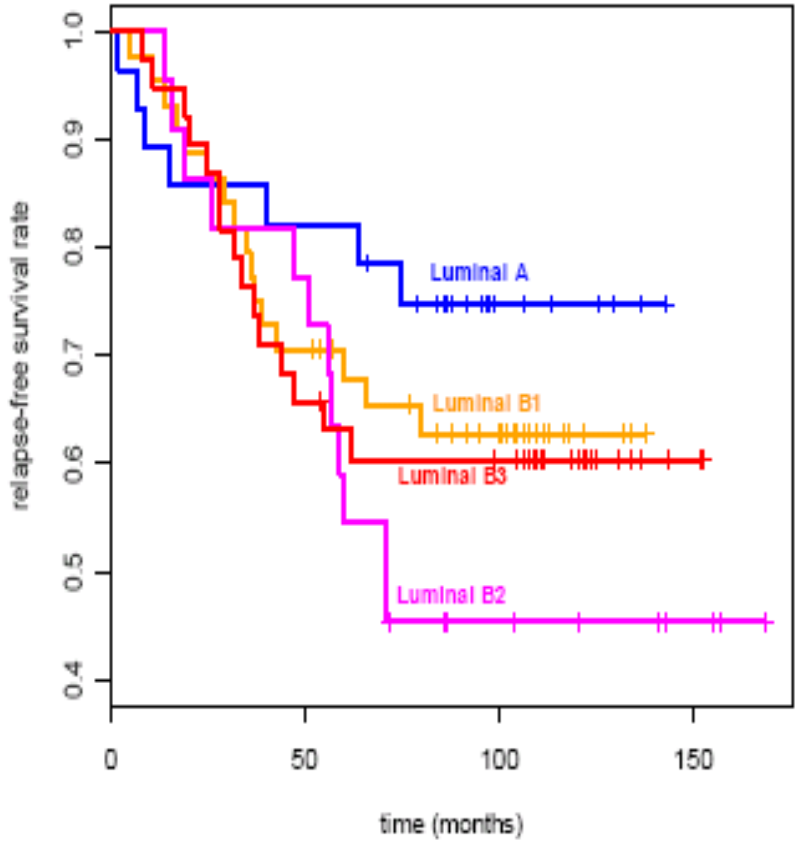
**Alexe et al, (2007) Cancer Research, 67, 10669**
**Dalgin et al, (2007) BMC Bioinformatics 8:291**

# Recurrence free survival in the Luminals

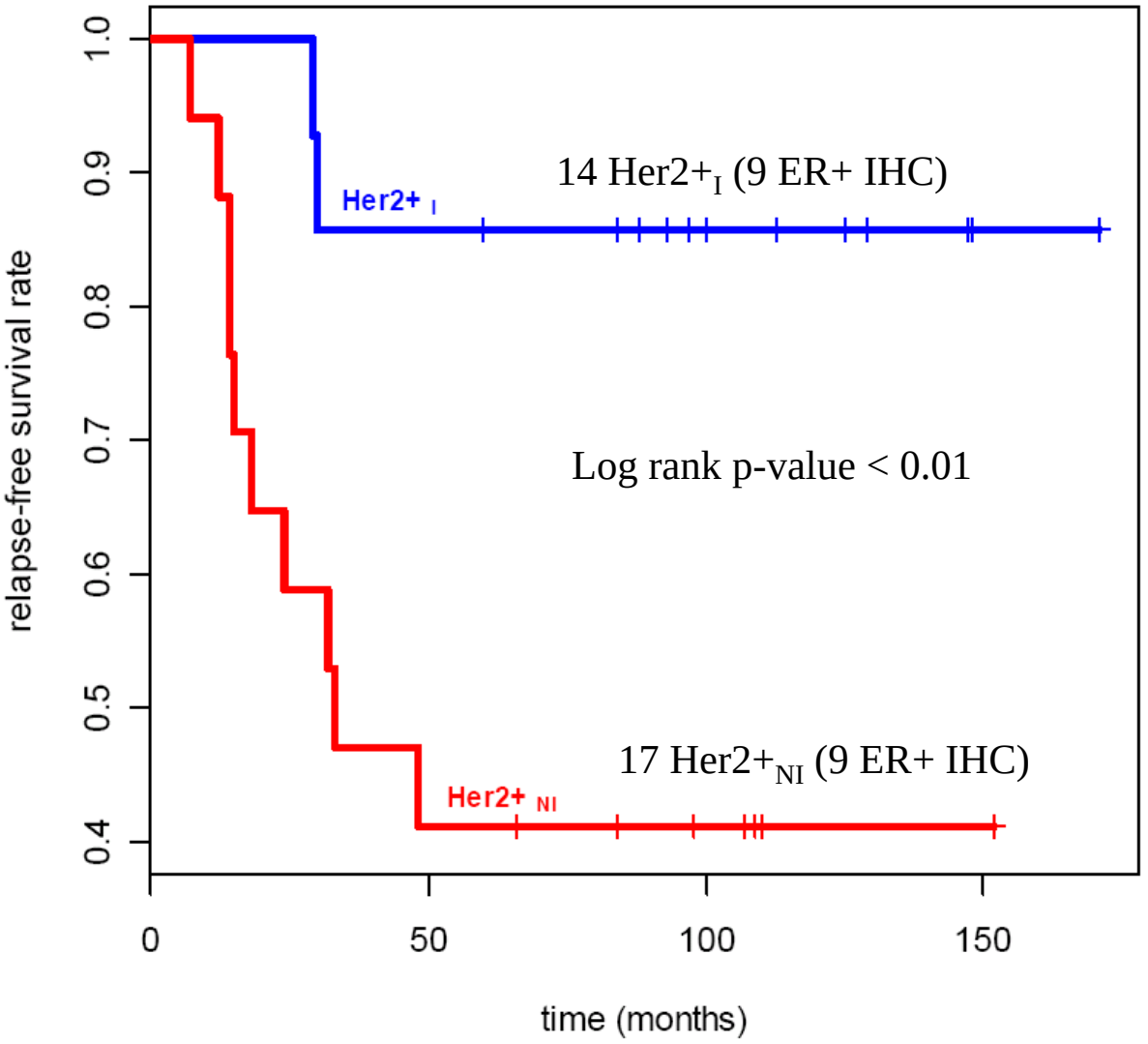
**44 core Luminal A, 88 core Luminal B**



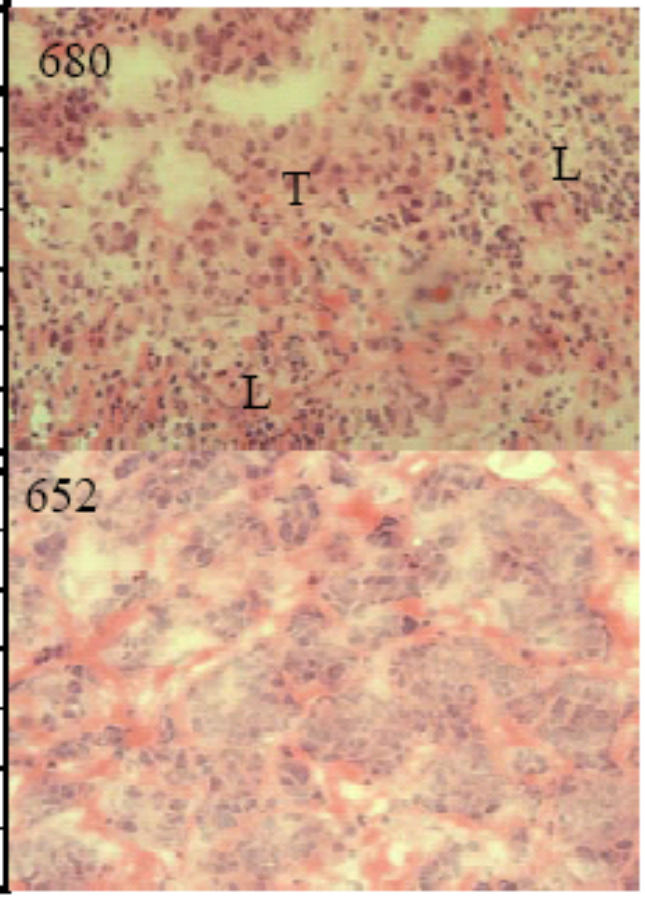

**44 LA, 22 LB1, 38 LB2, 28 LB3**



# Recurrence free survival in HER2+$_I$ and HER2+$_{NI}$



| Tumor | Path CR | Subtype by gene expression | Lymphocytic infiltration | |
|---|---|---|---|---|
| | | | Pathologist 1 | Pathologist 2 |
| 680 | No | HER2+$_I$ | 2 | 2 |
| 568 | No | HER2+$_I$ | 2 | 3 |
| 334 | Yes | HER2+$_I$ | 3 | 3 |
| 438 | No | HER2+$_I$ | NE | NE |
| 422 | Yes | HER2+$_I$ | 3 | 3 |
| 611 | No | HER2+$_I$ | NE | NE |
| | | | | |
| 514 | No | HER2+$_{NI}$ | 1 | 1 |
| 652 | No | HER2+$_{NI}$ | 1 | 1 |
| 405 | No | HER2+$_{NI}$ | 1 | 2 |
| 512 | No | HER2+$_{NI}$ | NE | NE |
| 278253 | No | HER2+$_{NI}$ | 1 | 1 |
| 641 | No | HER2+$_{NI}$ | 1 | 1 |
| 637 | No | HER2+$_{NI}$ | 1 | 1 |



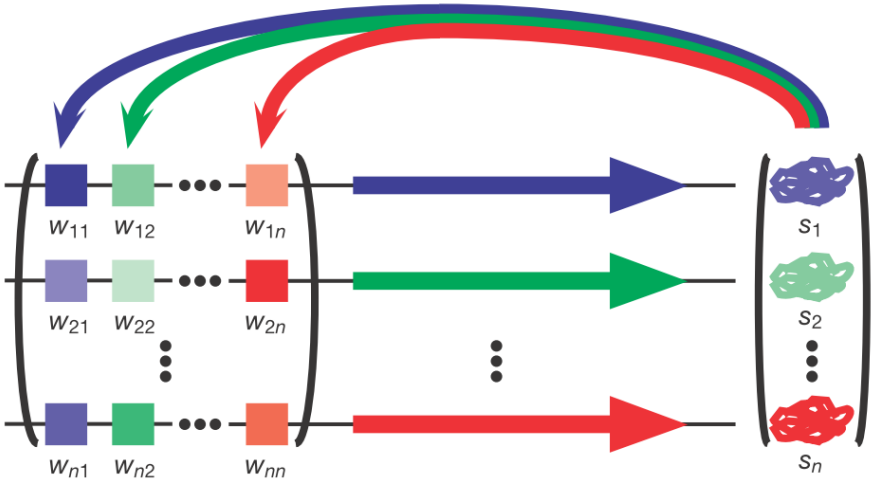

**Lymphocytic Infiltration in HER2+$_I$ subtype from a neoadjuvant phase II trial of trastuzumab and vinorelbine.. H&E sections were independently scored for lymphocytes by two pathologists. NE specimen quality was insufficient for proper evaluation. The score difference had p<0.0001 by the Fisher exact test.**

# Therapeutic Targets in Triple Negative Breast Cancer

Erhan Bilal (Rutgers/IBM)

**Bilal E, et al, Genes and Cancer (2010), 1(10): 1063-73.**

# Artificial gene networks




$$S(t+1) = f(W*S(t)),\ f(x) = 1/(1+e^{-ax})$$

$$F(\hat{S}) = e^{-D/\sigma}$$

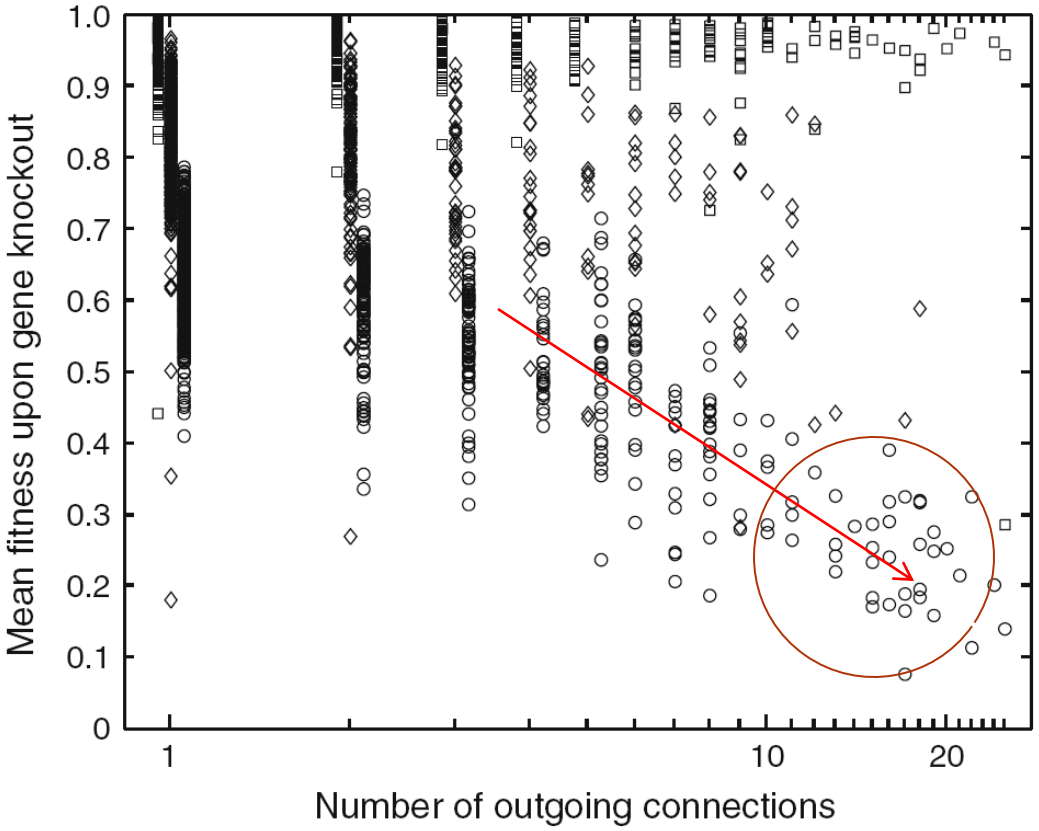
$$D = \frac{1}{N}\sum(\hat{s}_k - s_k^{OPT})^2$$

Simulation:

- Evolve 100 networks of 25 genes for 1000 generations under strong selection σ = 0.1
- Evolution occurs by mutation and recombination of *W* matrices
- Relevance of a gene is change in fitness on knocking it down.

***Bergman et al., Genetica (2007) 129:83–103***

# Node degree and essentiality



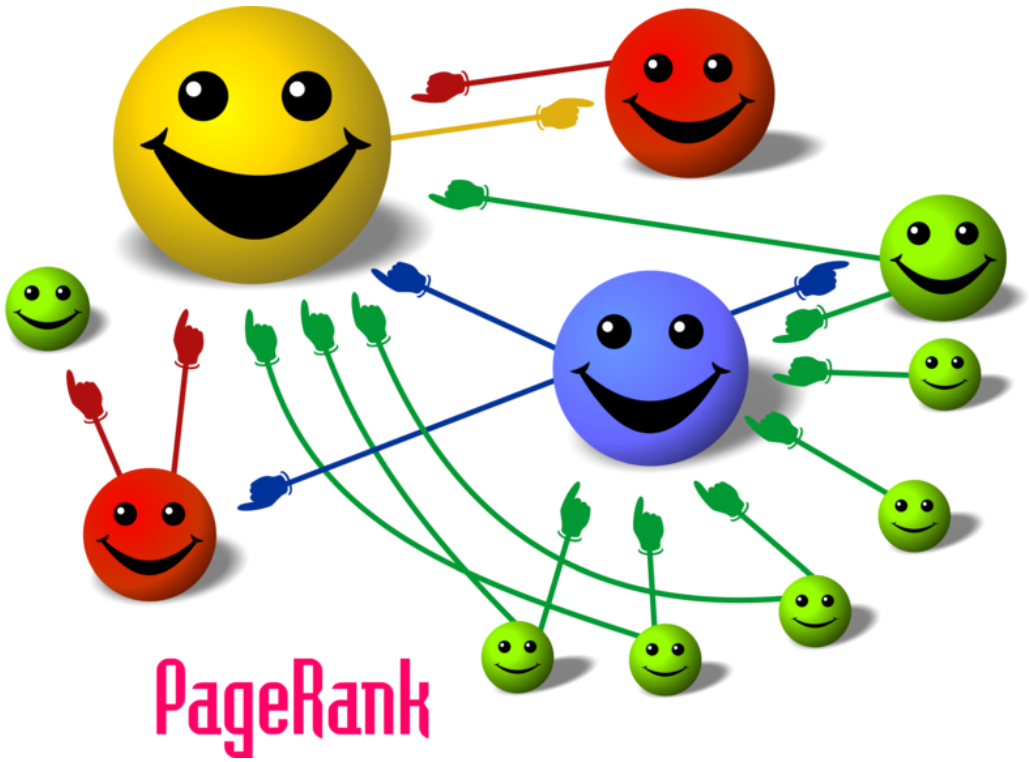

Discovered Hypothesis:

Knocking out genes that are *over-expressed and correlated with a large number of other genes* should have a big impact on the fitness of the cell

**Data are divided into three classes based on the equilibrium expression level of the knocked out gene: s >0.75 (circles), 0.75 <s < 0.25 (diamonds), and s <0.25 (squares).**

**Bergman et al., *Genetica* (2007) 129:83–103**

# Google PageRank Algorithm

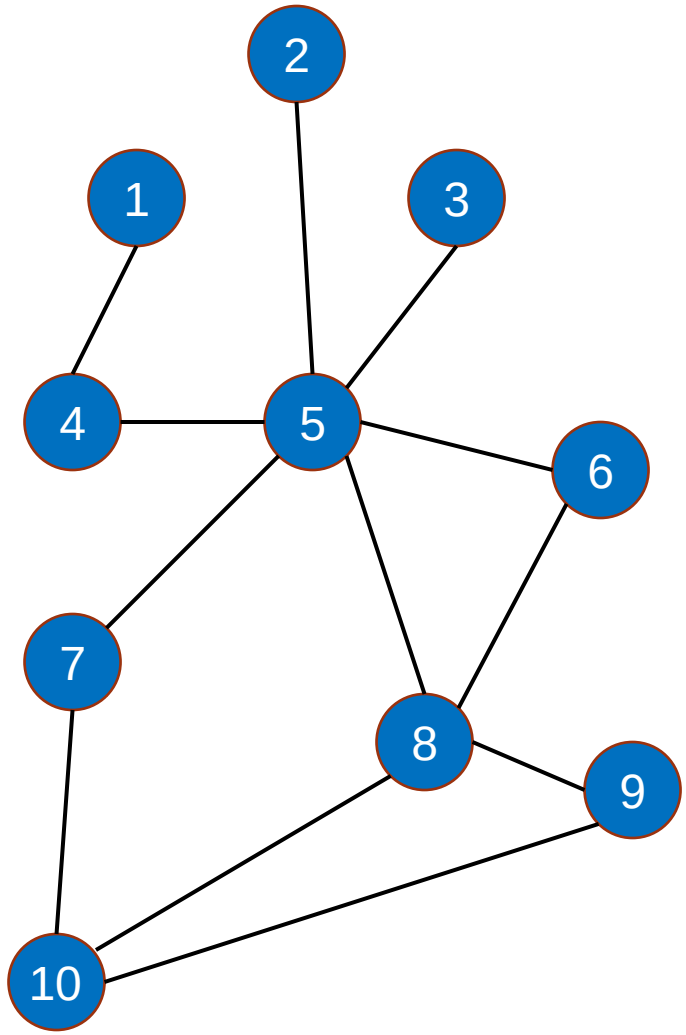


# Eigenvector centrality

$$\mathbf{A} = \begin{bmatrix} 1 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 1 & 1 & 1 & 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 1 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 & 1 & 0 & 1 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 \end{bmatrix}$$

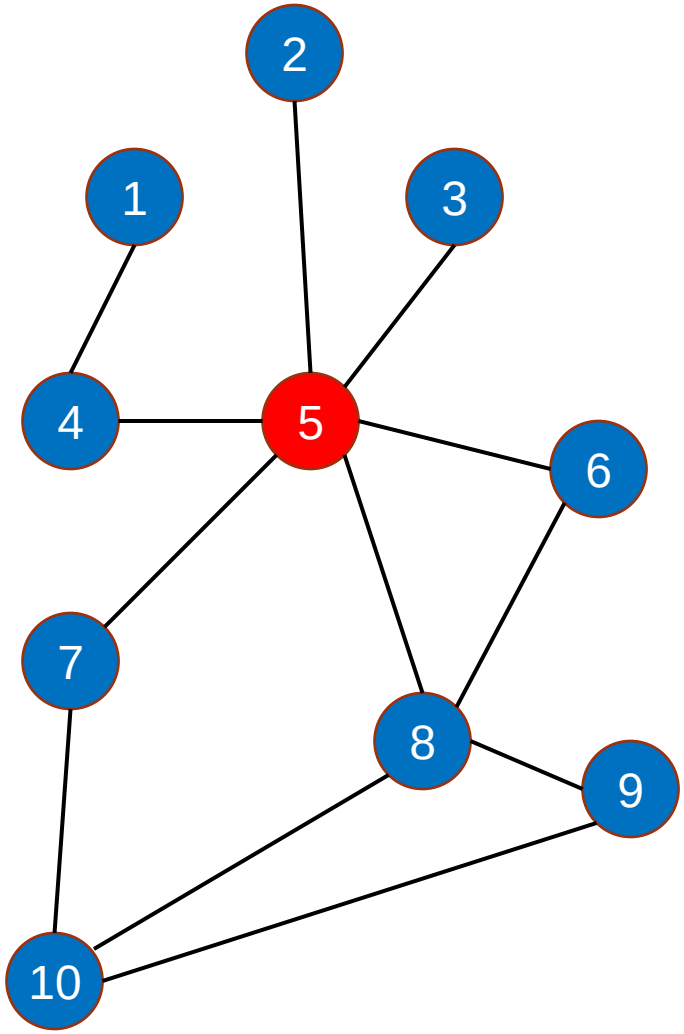
$$s_i = \frac{1}{\lambda} \sum_j a_{ij} s_j, \quad s \text{ centrality score}$$

$$\mathbf{As} = \lambda \mathbf{s}, \quad \text{eigenvector equation}$$



# Gene centrality measure

| Node | Centrality |
|---|---|
| 1 | 0.065 |
| 2 | 0.175 |
| 3 | 0.175 |
| 4 | 0.196 |
| 5 | 0.537 |
| 6 | 0.332 |
| 7 | 0.285 |
| 8 | 0.481 |
| 9 | 0.267 |
| 10 | 0.337 |



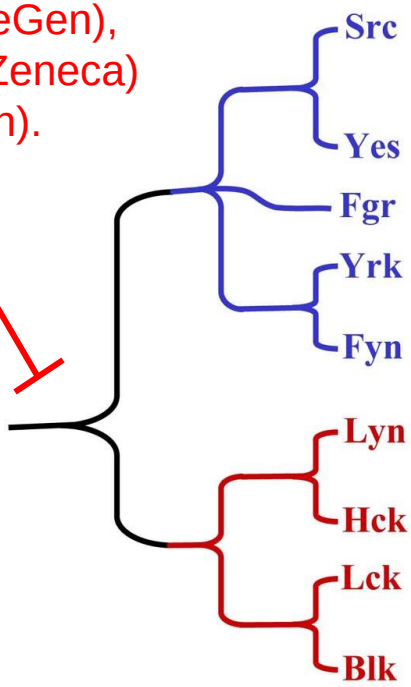
# Centrality and Outlier scores for top oncogenes in Breast Cancer subtypes:

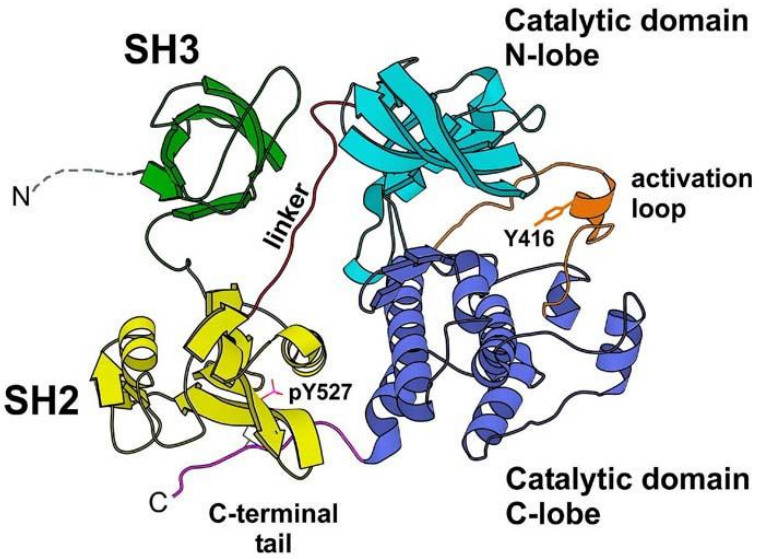
| W+I | BA1 | | BA2 | | HER2I | | HER2NI | | LA | | LB | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Gene | Centrality | Outlier score θ | Centrality | Outlier score θ | Centrality | Outlier score θ | Centrality | Outlier score θ | Centrality | Outlier score θ | Centrality | Outlier score θ |
| LYN | 4.35 | 80% | 1.9 | 39% | 3.32 | 29% | 0.21 | 5% | 0 | 0% | 0 | 0% |
| YES1 | 3.67 | 70% | 1.82 | 52% | 0 | 0% | 1.24 | 25% | 0 | 0% | 0.24 | 6% |
| HCK | 3.82 | 63% | 0.38 | 10% | 4.36 | 47% | 0.21 | 6% | 0.59 | 6% | 0.31 | 8% |
| FYN | 2.43 | 41% | 0.92 | 31% | 7.59 | 55% | 0.38 | 7% | 1.65 | 13% | 0.43 | 8% |
| LCK | 3.1 | 52% | 0.5 | 15% | 11.9 | 87% | 0 | 0% | 0.91 | 10% | 0.39 | 7% |
| PIM2 | 4.11 | 65% | 0.29 | 10% | 5.87 | 79% | 0 | 0% | 0.6 | 9% | 0.43 | 13% |
| HER2 | 0 | 0% | 0 | 0% | 6.5 | 100% | 4.52 | 100% | 0.01 | 0% | 0.05 | 2% |
| TGFBR2 | 0.04 | 1% | 0.72 | 9% | 3.39 | 42% | 0.83 | 13% | 13.51 | 66% | 0.45 | 9% |
| ERG | 0 | 0% | 0.73 | 12% | 1.67 | 21% | 2.09 | 32% | 10.5 | 64% | 1.19 | 26% |
| FOS | 0 | 0% | 0.11 | 2% | 1.5 | 28% | 0.96 | 21% | 5.74 | 77% | 0.76 | 34% |
| ETS2 | 0.46 | 11% | 1.6 | 32% | 2.36 | 27% | 0.71 | 19% | 5.83 | 34% | 0.49 | 11% |
| ESR1 | 0 | 0% | 0 | 0% | 0.82 | 14% | 1.56 | 26% | 7.12 | 71% | 3.48 | 83% |
| EGFR | 0.75 | 11% | 2.34 | 38% | 1.25 | 18% | 1.32 | 24% | 1.56 | 19% | 5.07 | 41% |

$$g'_{ij} = \frac{g_{ij} - median(g_i)}{MAD(g_i)} \qquad \theta = \frac{1}{N}\sum_j^N \Delta_j \text{ , where } N = 10, \Delta_j = 1 \text{ if } g'_j > 1, \text{ and } \Delta_j = 0$$

# SRC kinase family and its inhibitors

Dasatinib® (Bristol-Myers Squibb),
AP 23846 (Ariad),
TG 100598 (TargeGen),
AZD 0539 (AstraZeneca)
or SKI-606 (Wyeth).




SRC pathway involvement

- Development
- Cell growth
- Immune response
- DNA damage
- …

The Engen Laboratory
http://www.hxms.neu.edu/srcfam.htm

**Validation: YES1 levels in public BC datasets GSE2034 and GSE4922 (upper)**

**IF Staining on 13 FFPE samples (lower) shows high (left), medium (middle) and low(right) levels of YES1**

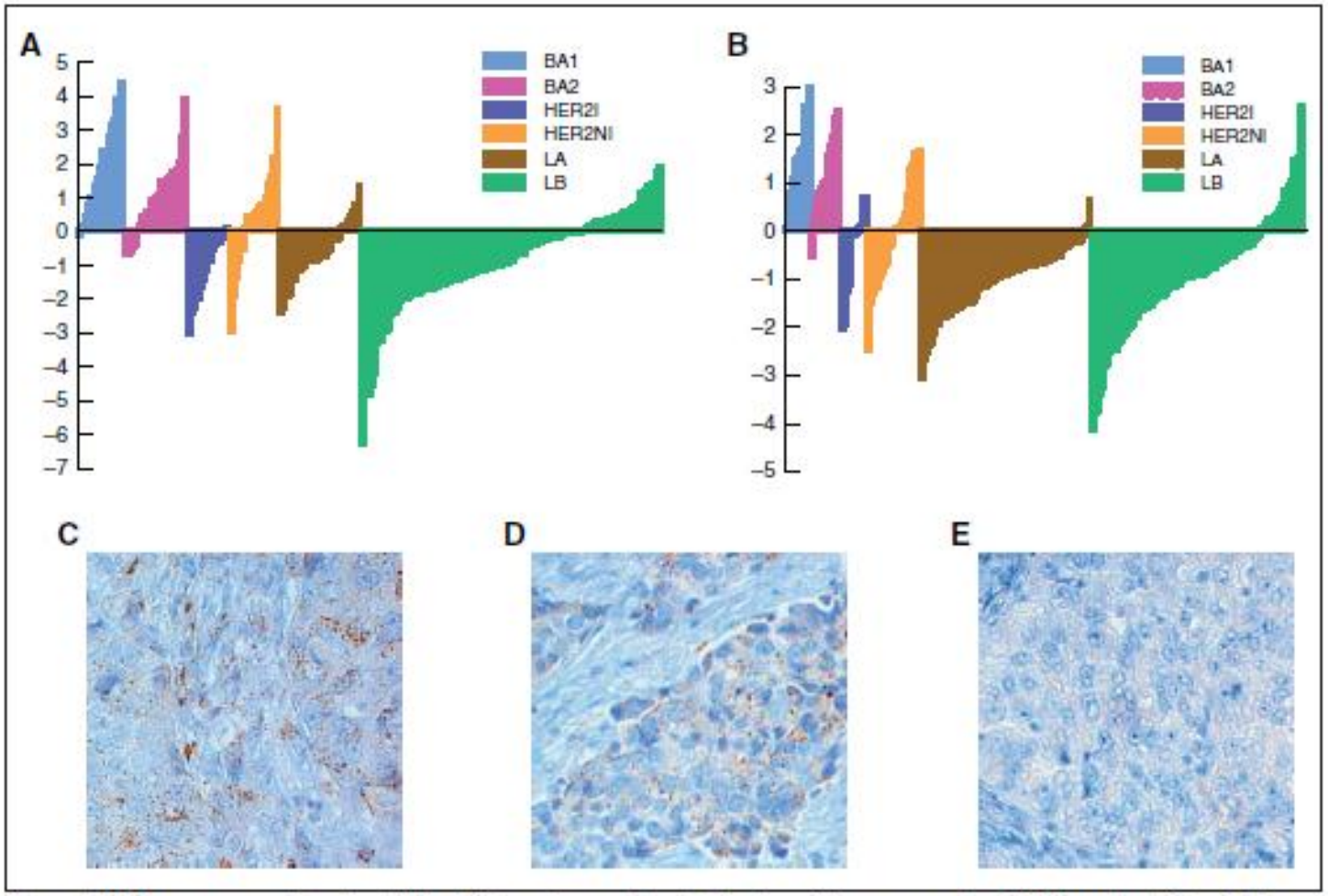
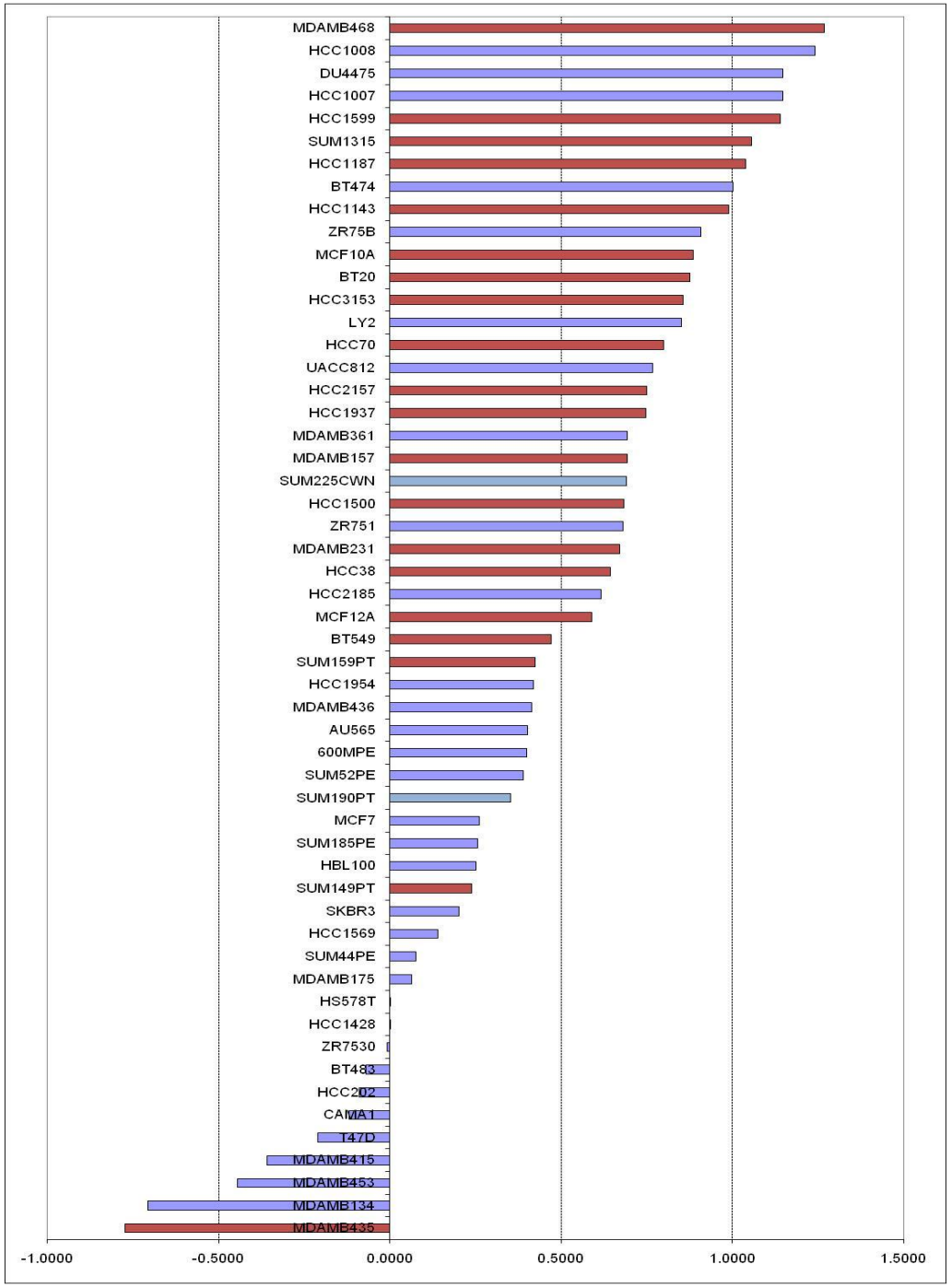
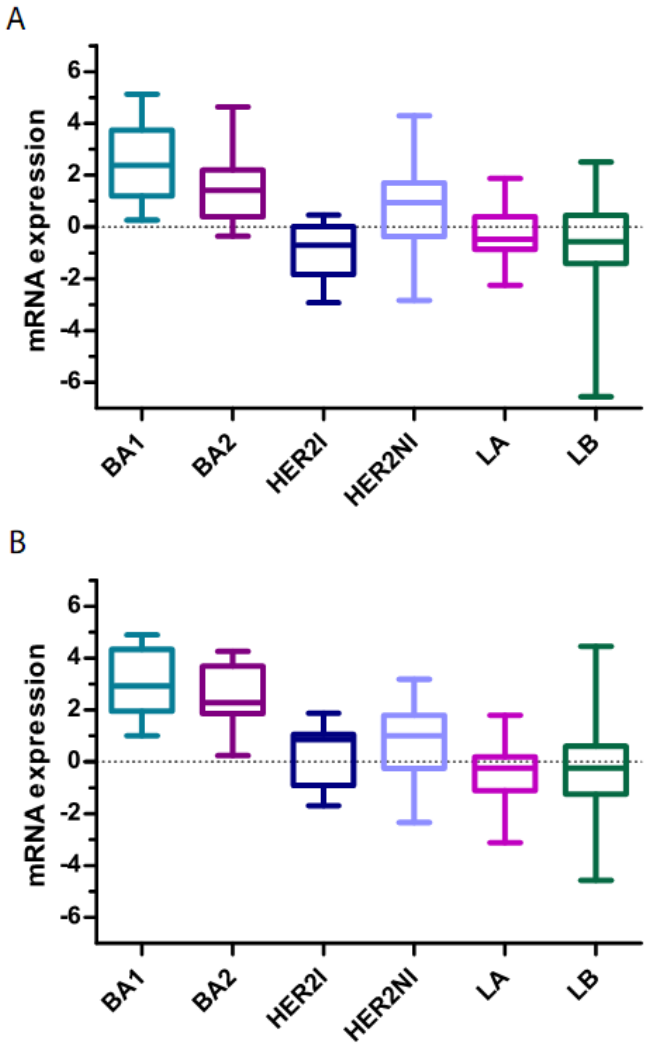



**Figure 1.** YES1 is overexpressed in a subset of basal-like breast tumors. Bar plots showing relative overexpression of YES1 in a subset of basal-like breast tumors in the GSE2034 (**A**) and GSE4922 (**B**) gene expression datasets. To confirm this, 13 ER−/PR−/HER2− paraffin-embedded breast cancer tissue slides were probed for expression of YES1 by immunohistochemistry with an appropriate YES1-specific antibody. Of the 13 samples, 2 had high expression levels of YES1, 6 had medium expression, and 5 had low or no expression. Shown are examples of the staining protocol on slides showing high (**C**), medium (**D**), and low/zero (**E**) expression of YES1 in cancer cells on the slides.

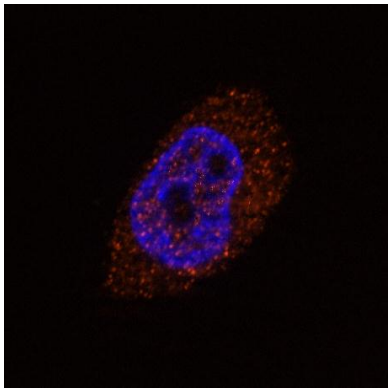


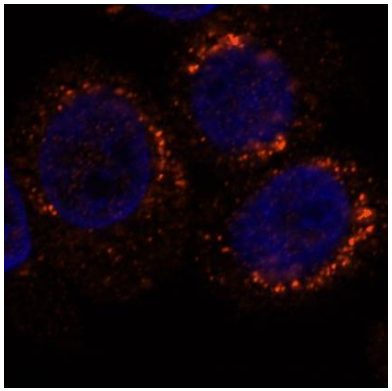

Neve et al, Cancer Cell (2006)

# YES1 expression

MDAMB231

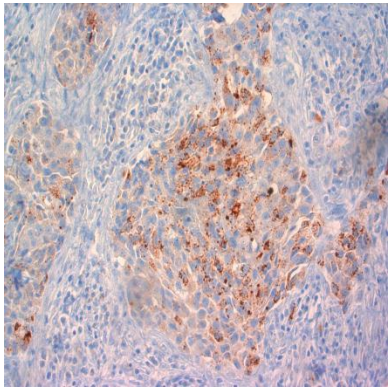


MDAMB468

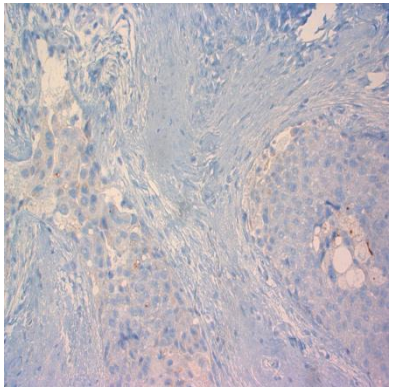


IF staining with anti-Yes1 antibody of two ER-/PR-/HER2- breast cancer cell lines.

ER-/HER2-/YES1+



ER-/HER2-/YES1-

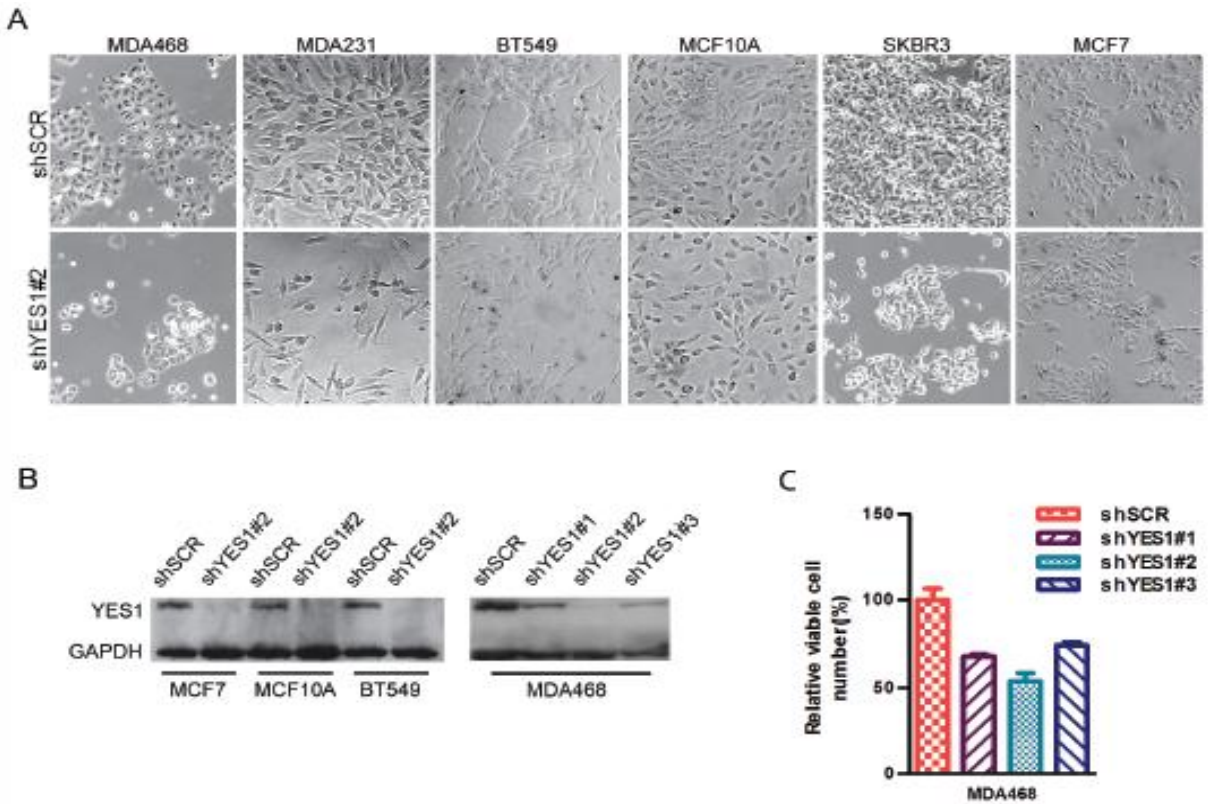


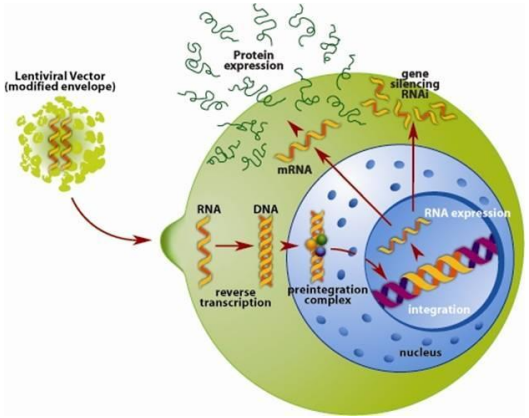
13 ER-/PR-/HER2- breast cancer tissue samples:

- 6 samples with LOW/NO Yes1 expression
- 5 samples with MEDIUM Yes1 expression
- 2 samples with HIGH Yes1 expression

# YES1 is a drug target in Triple Negative Breast Cancer

Cell fitness upon silencing YES1 with RNAi using a lentivector




Bilal E, et al, Genes and Cancer (2010), 1(10): 1063-73.

# Amplicons and Recurrence in ER+ Breast Cancer

Erhan Bilal

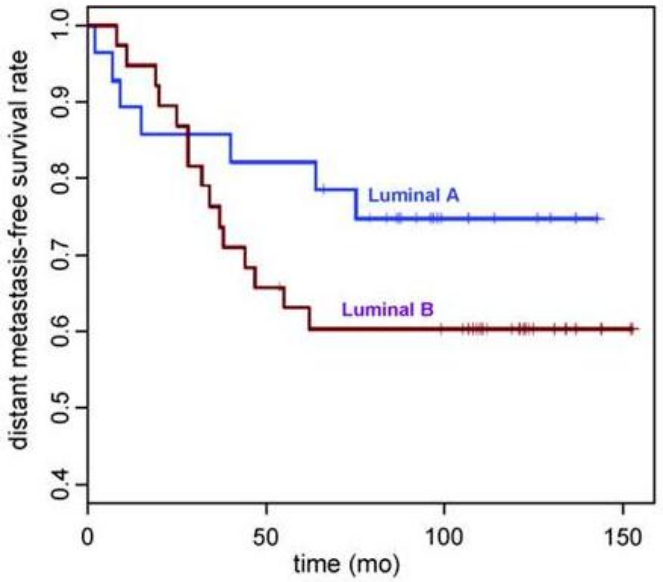
Hege Russnes (OUH)

Vanessa Almendro (Dana Farber)

**Bilal E, et al, PLoS One 2012, in press**

# Tamoxifen resistance in ER+ breast cancers

- **Pathways associated with Tamoxifen resistance in vitro:**
  - **Estrogen associated transcription factors and activators (Erα/β, NF-kB, NCOA1, NCOA3, PELP1, CBP and p300)**
  - **Growth factor receptors (ERBB2, EGFR, EGF1R, FGFR)**
  - **MAPK signaling (MEK, ERK, CDK10)**
  - **PI3K signaling (AKT, PTEN)**
  - **SRC interacting proteins (BCAR1, BCAR3)**
  - **Cyclins, MYC, CDK inhibitors**
  - **BCL-2 family members (BCL-2, BIK, BAD)**
  - **Survival signaling (XBP1)**
- **Signatures predicting response to endocrine therapies:**
  - **Breast cancer subtypes (LB)**
  - **Oncotype Dx (21 genes)**
  - **Genomic grade signature**
  - **HOXB13/IL17RB expression ratio**
  - **TuM1 (33 genes), etc.**




**~ 30% of ER+ patients on Tamoxifen suffer early relapse.**

Musgrove et al, *Nature reviews* (2009)

# Outlier analysis

$$g'_{ij} = \frac{g_{ij} - median(g_i)}{MAD(g_i)}$$

$$\text{High/low outlier} => 90\% \text{ or} < 10\% \text{ quantile}$$

$$\text{for each sample.}$$

**Three gene expression datasets from Desmedt et al (*Lancet* 2005) GSE 6532**

**81, 109 and 87 ER+ Affymetrix samples treated with Tamoxifen**

**Long term follow-up (9 years median)**

$$\mathbf{B} = \begin{bmatrix} 1 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & 0 & 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 & 1 & 0 & 1 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 \end{bmatrix}$$

bad prognosis

good prognosis

**Only genes associated with differential expression were kept (logrank test, p<0.05)**

Let $\mathbf{C}_{1,2}$ be covariance matrices between rows of $\mathbf{B}_{1,2}$

$$\mathbf{R}_{1,2}(i,j) = \mathbf{C}_{1,2}(i,j) \Big/ \sqrt{\mathbf{C}_{1,2}(i,i)\mathbf{C}_{1,2}(j,j)}$$

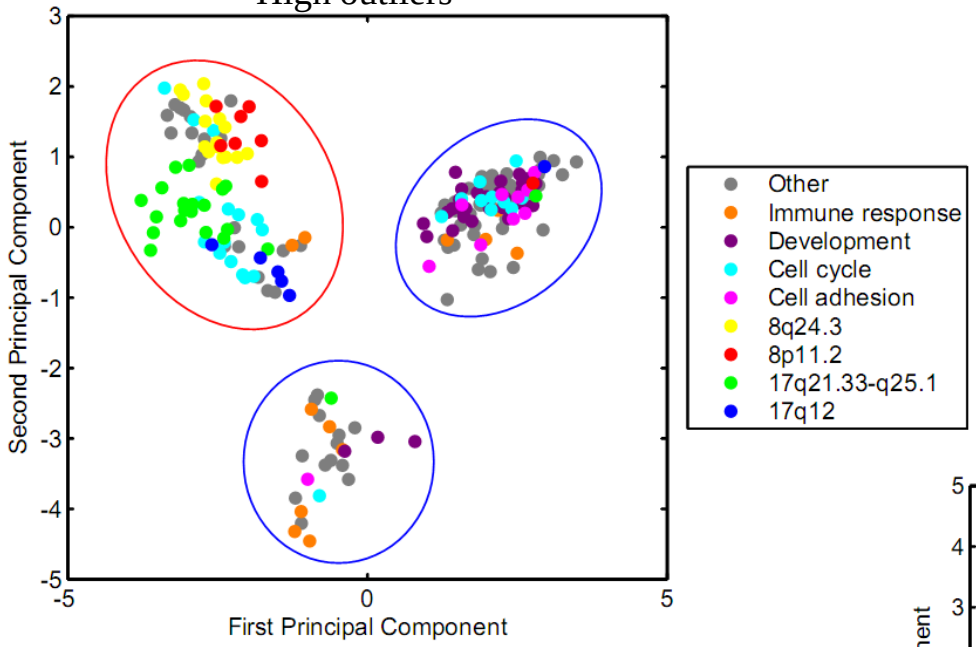
Clusters of tightly correlated genes identified by iteratively removing row/column *i* if

$\sum_j \Delta_{ij} \le 1$, where $\Delta_{ij} = 1$ if $\mathbf{R}_{1,2}(i,j) > 0.5$ and $\Delta_{ij} = 0$ otherwise

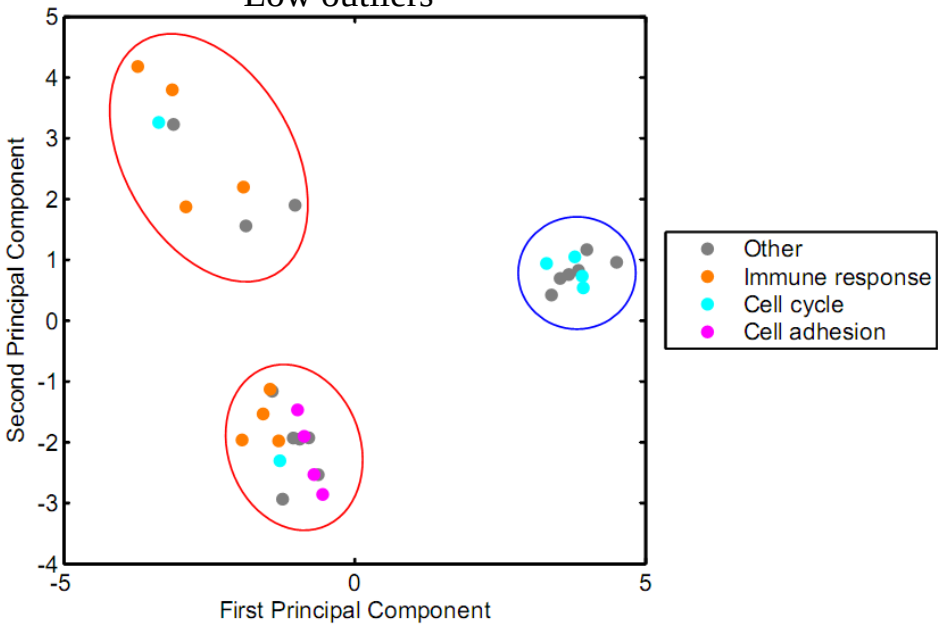
# Gene patterns associated with Tamoxifen resistance in dataset GSE6532

| | Over-expression | p-values | Under-expression | p-values |
|---|---|---|---|---|
| Good Prognosis with Tamoxifen treatment | Immune response | 1.61E-05 | Cell cycle | 1.10E-03 |
| | Development | 7.56E-08 | | |
| | Cell adhesion | 1.68E-04 | | |
| Poor outcome with Tamoxifen treatment | Cell cycle | 9.12E-07 | Immune response | 1.36E-05 |
| | 17q21.33-q25.1 | 3.87E-05 | Cell adhesion | 2.01E-08 |
| | 17q12 | 1.39E-08 | | |
| | 8p11.2 | 1.11E-16 | | |
| | 8q24.3 | 2.22E-16 | | |

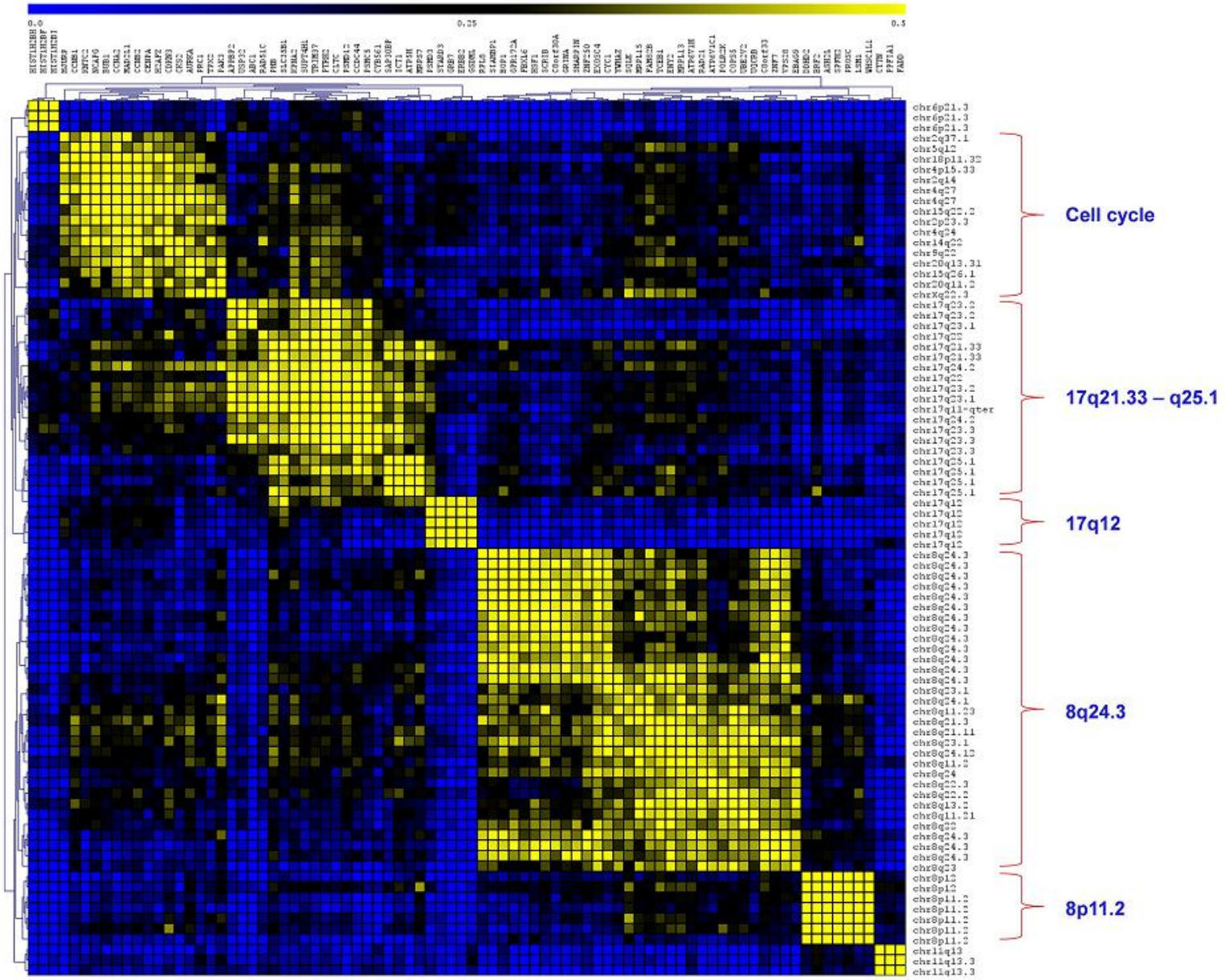
High outliers



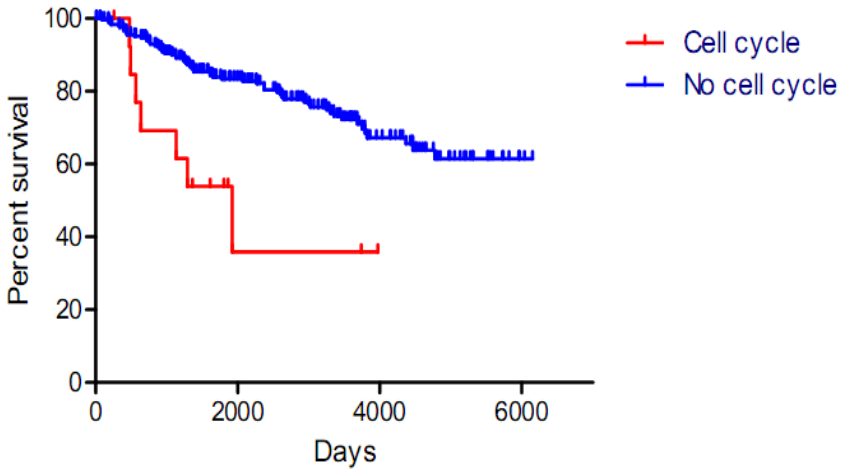

Low outliers

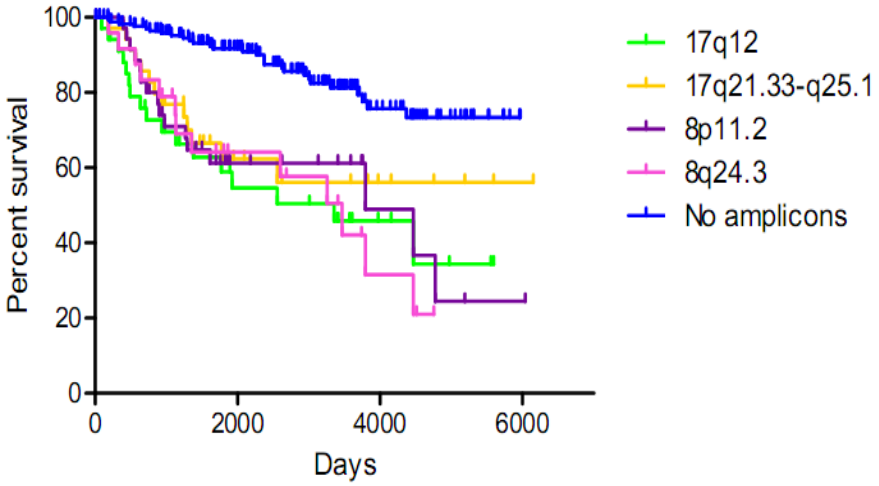


# Overexpressed genes associated with poor prognosis



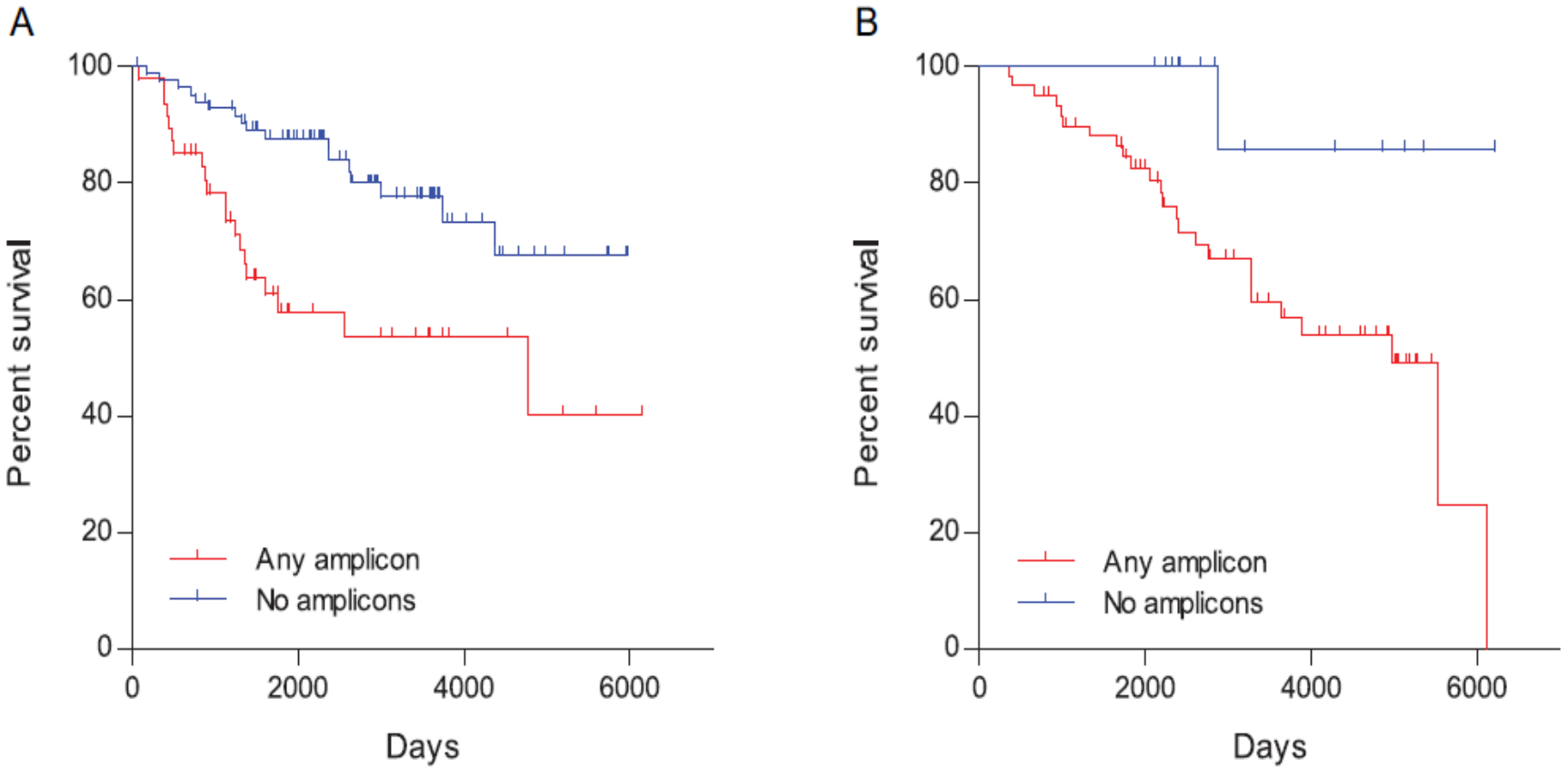
# Survival Differences between classes



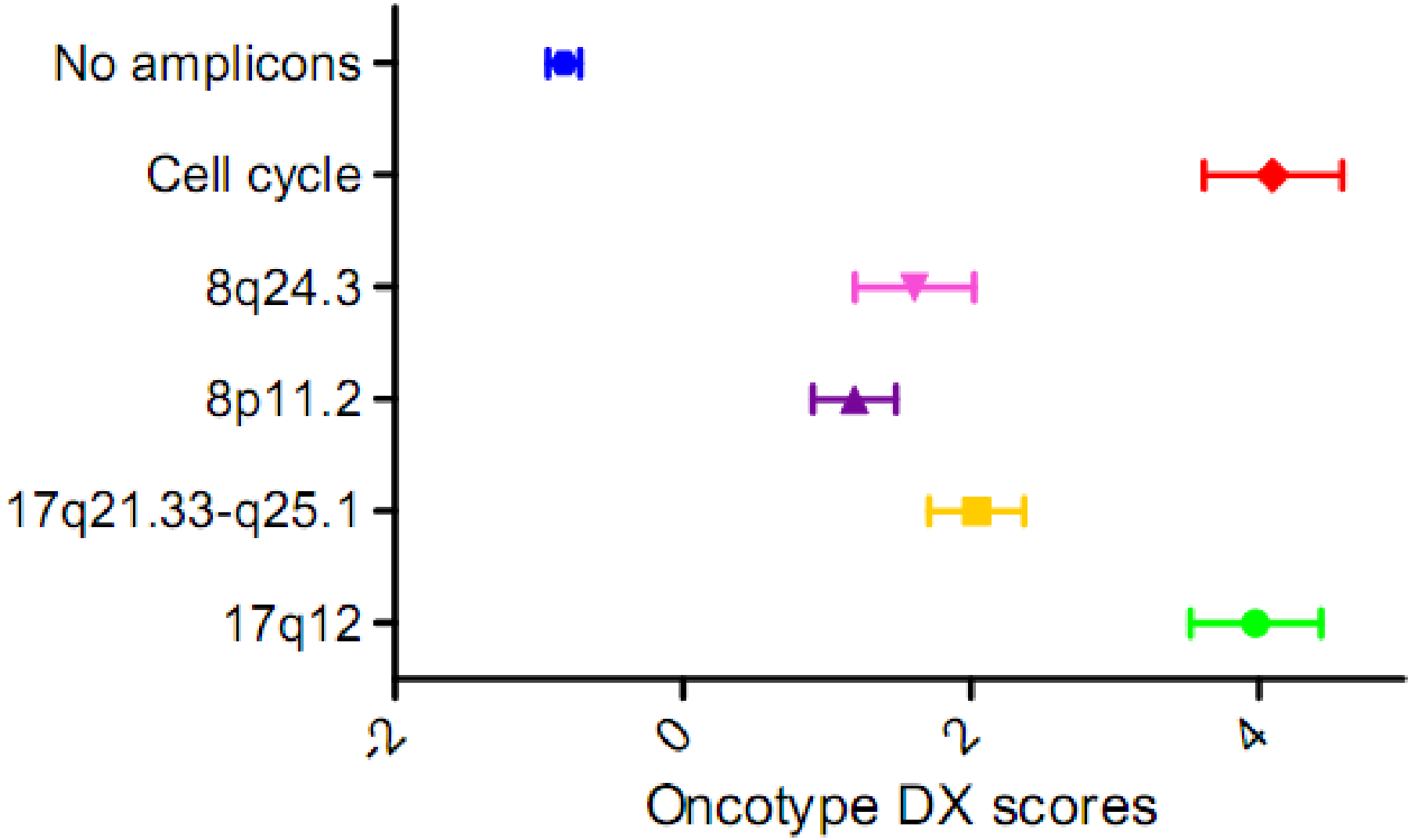




| Amplicon | Med survival (days) | Hazard ratio | 95% CI | p-value | H-Grade tumor enrich. p-value | Node stat association p-value | Oncogene |
|---|---|---|---|---|---|---|---|
| 17q12 | 3355 | 4.1 | 3.8 – 21.0 | <0.0001 | 0.0002 | 0.85 | ERBB2 |
| 17q21.33-q25.1 | — | 3.1 | 2.2 - 13.6 | 0.0003 | 0.2 | 0.86 | ? |
| 8p11.2 | 3795 | 3.8 | 3.2 - 18.3 | <0.0001 | 0.04 | 0.83 | ? LSM1 |
| 8q24.3 | 3468 | 4.3 | 4.3- 34.1 | <0.0001 | 0.002 | 0.86 | ? HSF1 |

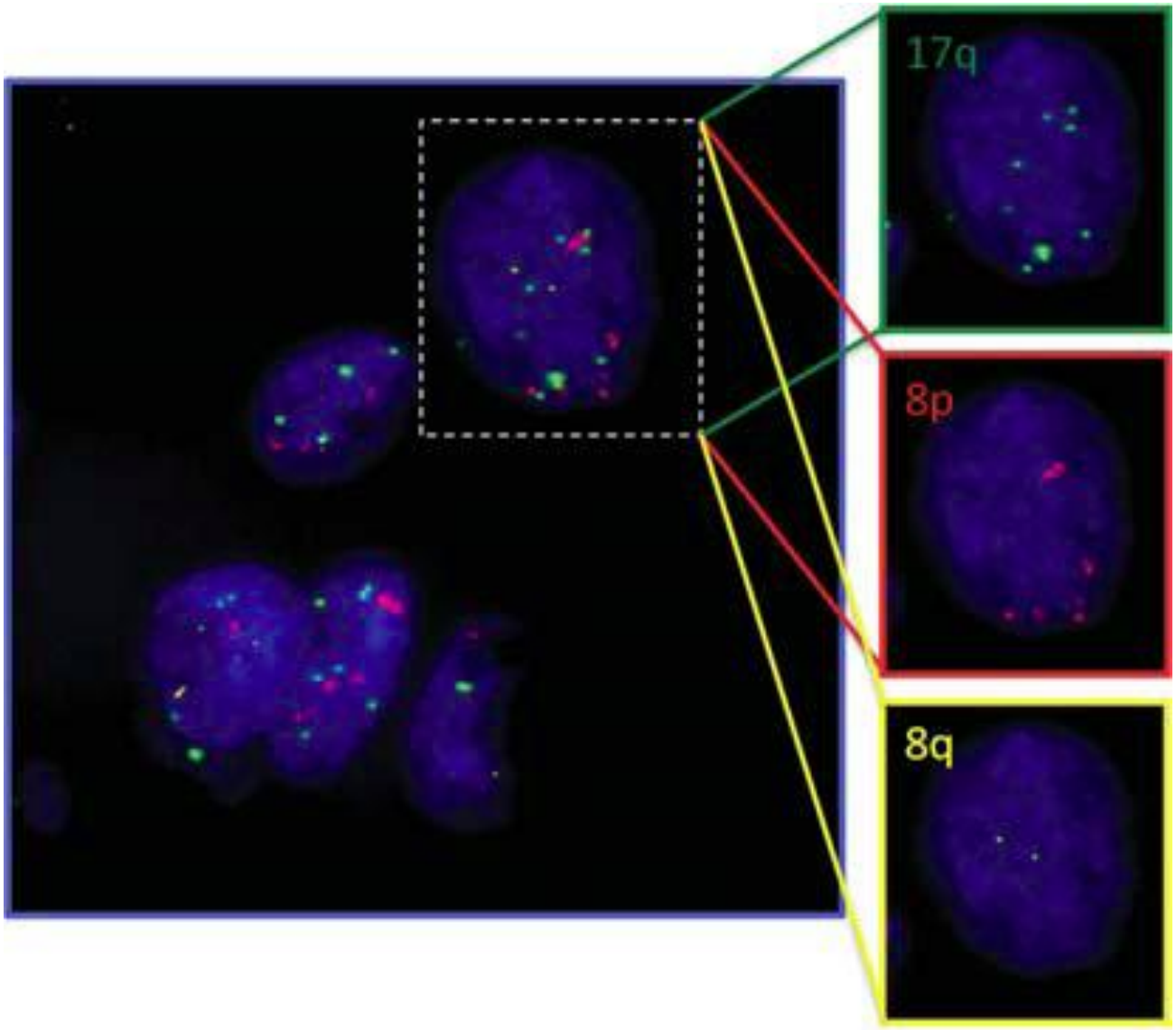
# Survival for intermediate grade tumors in GSE6532 (gene expression) and GSE22133 (CGH array) datasets

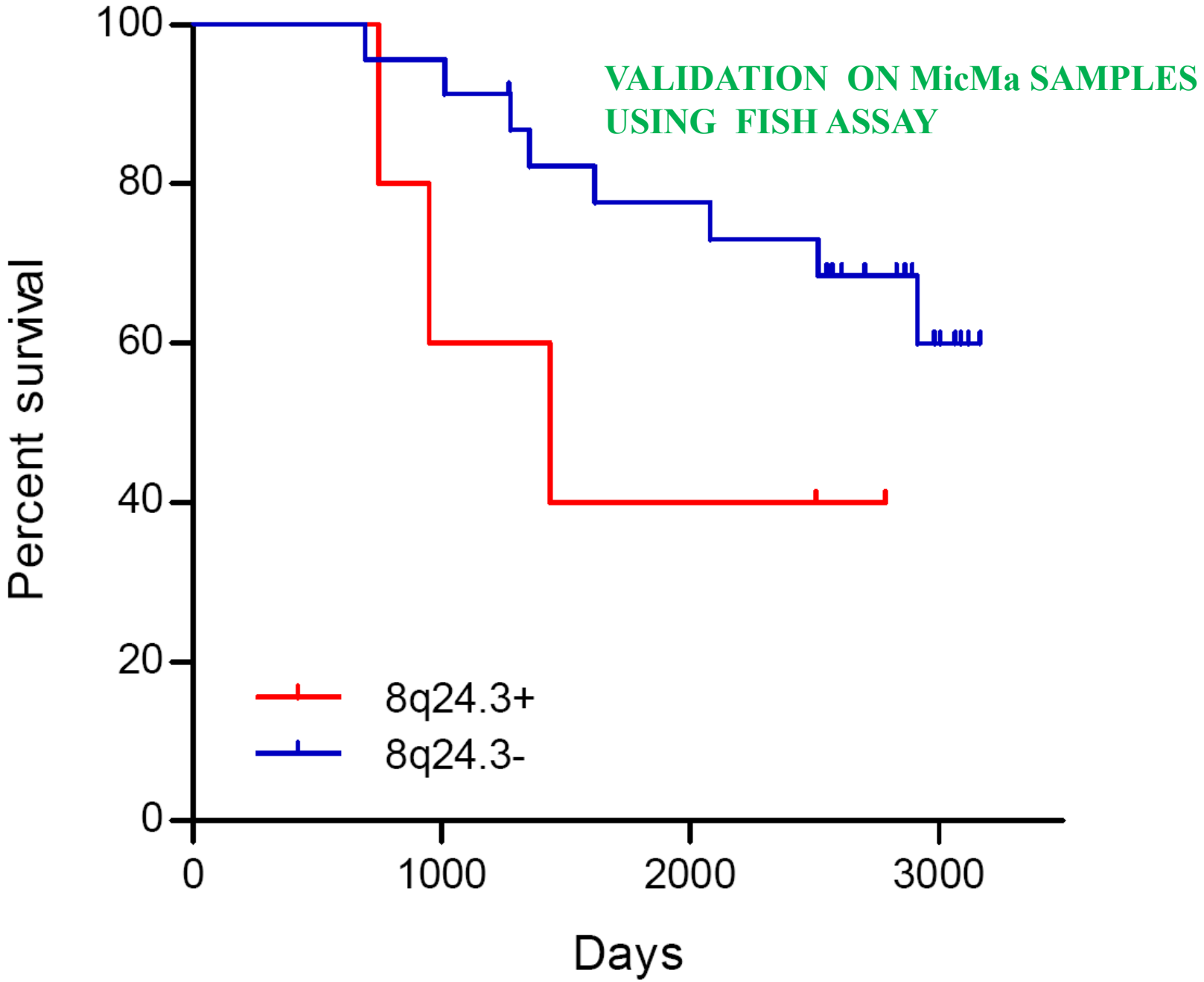


# Amplicons and Inferred Oncotype Dx Score



# Multiplex FISH Assay to detect Amplicons




VALIDATION ON MicMa SAMPLES
USING FISH ASSAY
Percent survival
100
80
60
40
20
0
0
1000
2000
3000
Days
8q24.3+
8q24.3-

# Acknowledgments

Erhan Bilal
Rutgers/IBM

Gabriela Alexe
MIT/Harvard

Michael Seiler
Rutgers

Vanessa
Almendro
DFCI

Hege Russnes
DFCI/OUH

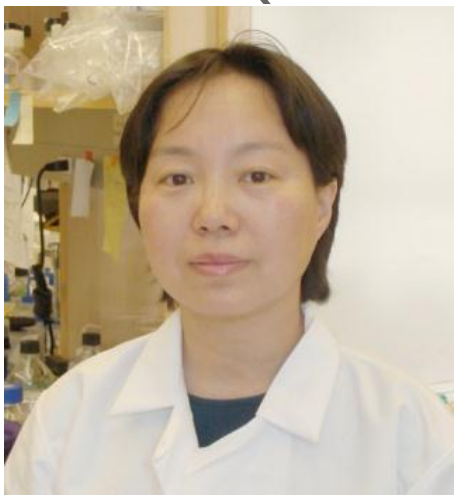
Arnie Levine
IAS/CINJ

Shridar Ganesan
CINJ

Anne-Lise
Børresen-Dale
OUH

Vessela
Kristensen
OUH

# The Ganesan Lab
# (Where The Real Biology Happens)



Ming Yao

Shridar Ganesan

Sunniva Bjorklund

Vasudeva Ginjala

Atul Kulkarni

Jay Oza