



# Identification of Genes Related to Resistance to Antracyclines and Taxanes in Human Breast Cancers

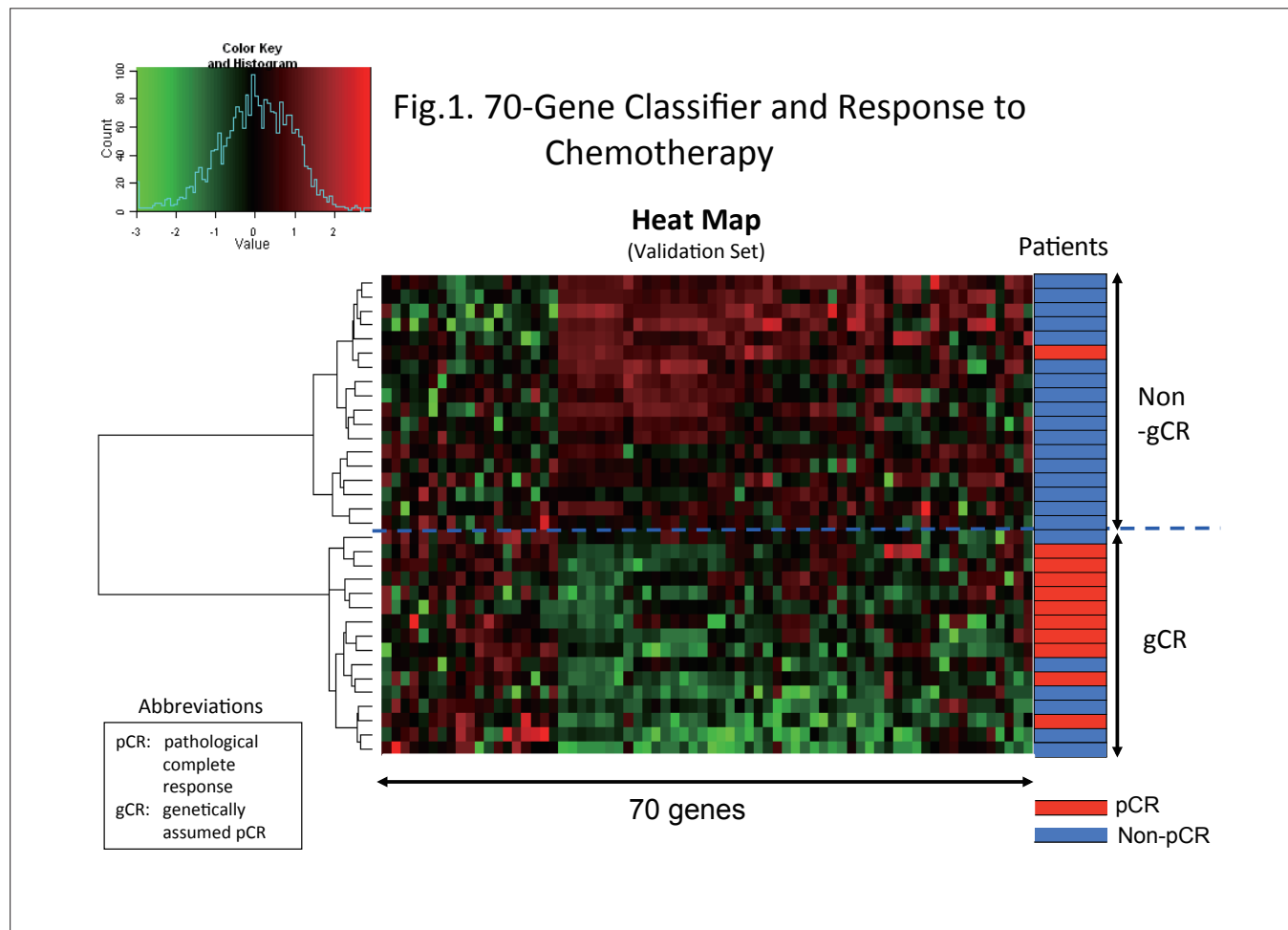
## Outline

- (1) Gene expression profile of tumor samples obtained by a vacuum-assisted core biopsy before Paclitaxel-FEC was analyzed by DNA microarray in breast cancer patients to construct a classifier for predicting pathological complete response (pCR). The 70-probe classifier for predicting pCR to Paclitaxel-FEC was constructed successfully with a high sensitivity of 91% and a high negative predictive value of 93% (Fig. 1., Table 1).
- (2) A diagnostic system comprising a 95-gene classifier was developed for predicting the prognosis of node-negative and ER-positive breast cancer patients by using already published DNA microarray (gene expression) data (n=549) as the training set and the DNA microarray data (n=105) obtained at our institute as the validation set. The 95-gene classifier could classify the 105 patients in the validation set into a high-risk (n=44) and a low-risk (n=61) group with 10-year recurrence-free survival rates of 93% and 53%, respectively ( $p=8.6e-7$ )(Fig. 2).

## Expected Outcome

We have been able to construct the 70-probe classifier for predicting pCR to Paclitaxel-FEC in breast cancers with a high sensitivity and negative predictive value. Because of such a high negative predictive value (>90%), this diagnostic system is expected to be especially useful for the elimination of unnecessary Paclitaxel-FEC.

The 95-gene classifier developed by us can predict the prognosis of node-negative and ER-positive breast cancer patients with high accuracy. The 95-gene classifier seems to perform better than the genomic grade index. As many as 58% of the patients classified into the low-risk group with this classifier could be safely spared adjuvant chemotherapy.



## Table 1. 70-Gene Classifier and Response to Chemotherapy

Training Set

Genetic diagnosis	Pathological diagnosis	
	pCR	Non-pCR
gCR	15	12
Non-gCR	0	23

PPV=55.6% NPV=100%

Validation Set

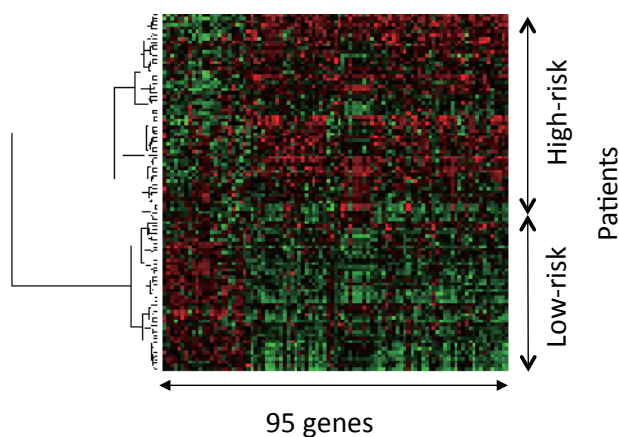
Genetic diagnosis	Pathological diagnosis	
	pCR	Non-pCR
gCR	10	9
Non-gCR	1	14

PPV=52.6% NPV=93.3%

pCR: pathological complete response  
gCR: genetically assumed pCR

## Fig.2. 95-Gene Classifier and Prognosis

Heat Map  
(Validation Set)



ER(+) & n0 Patients (n=105)

