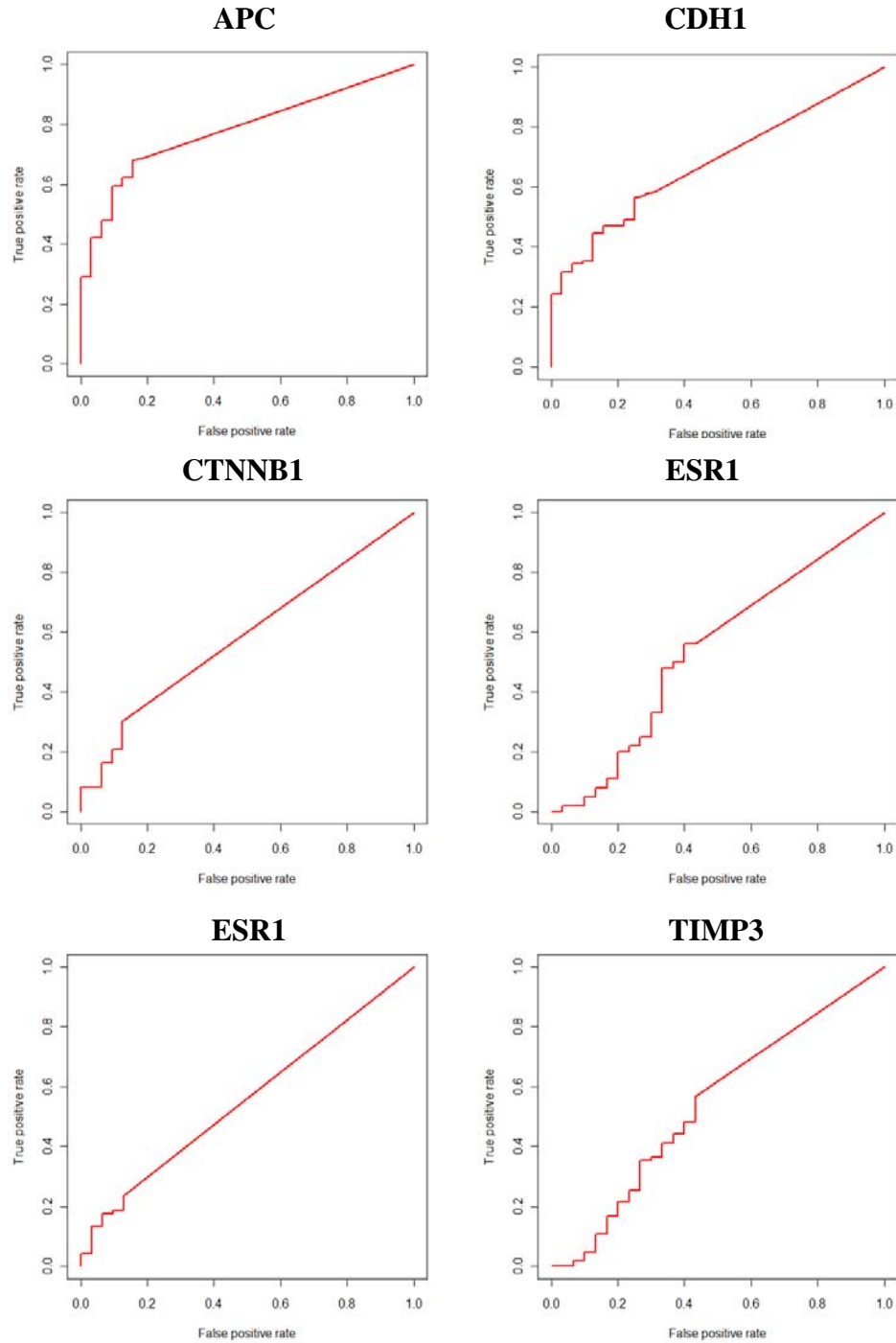
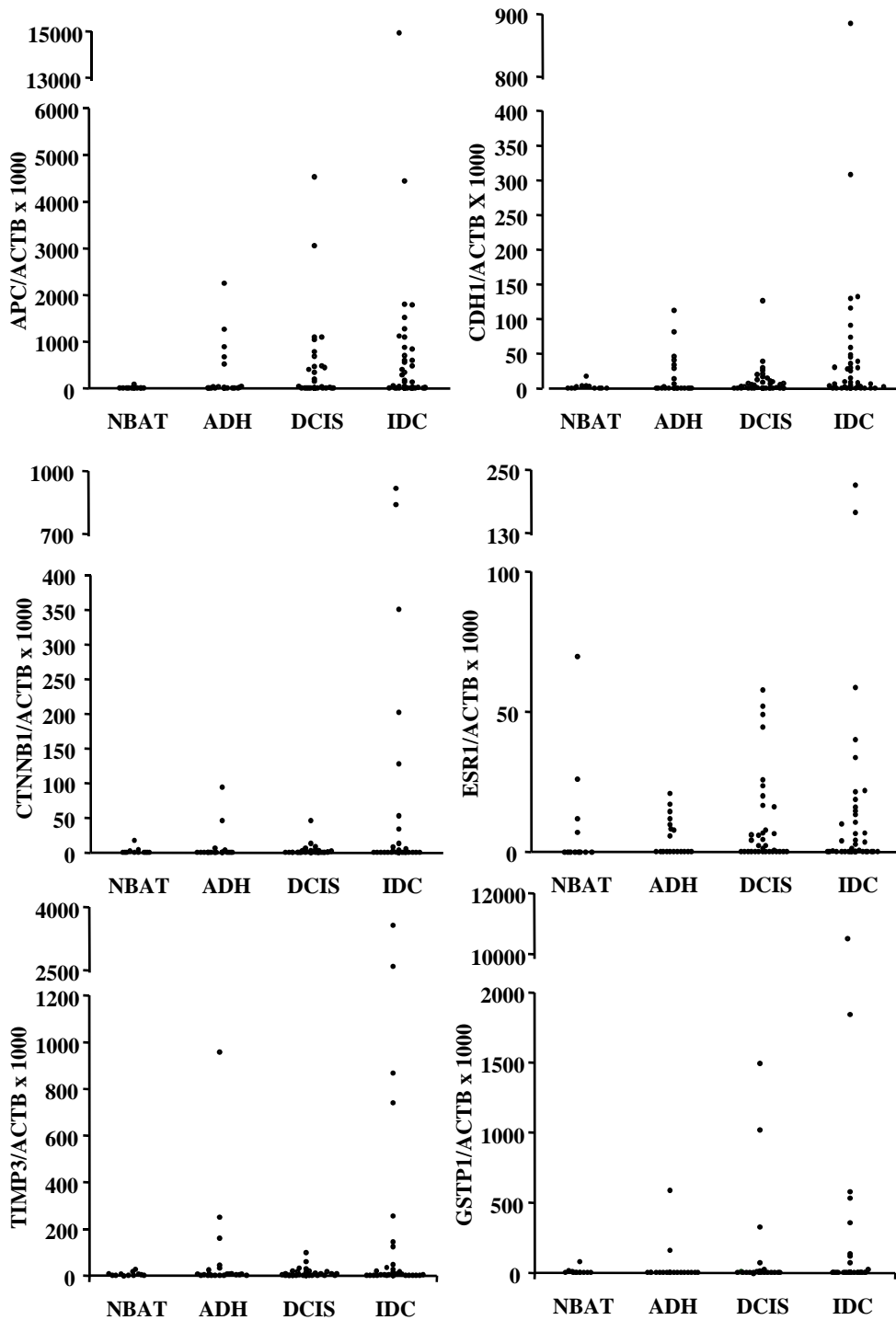


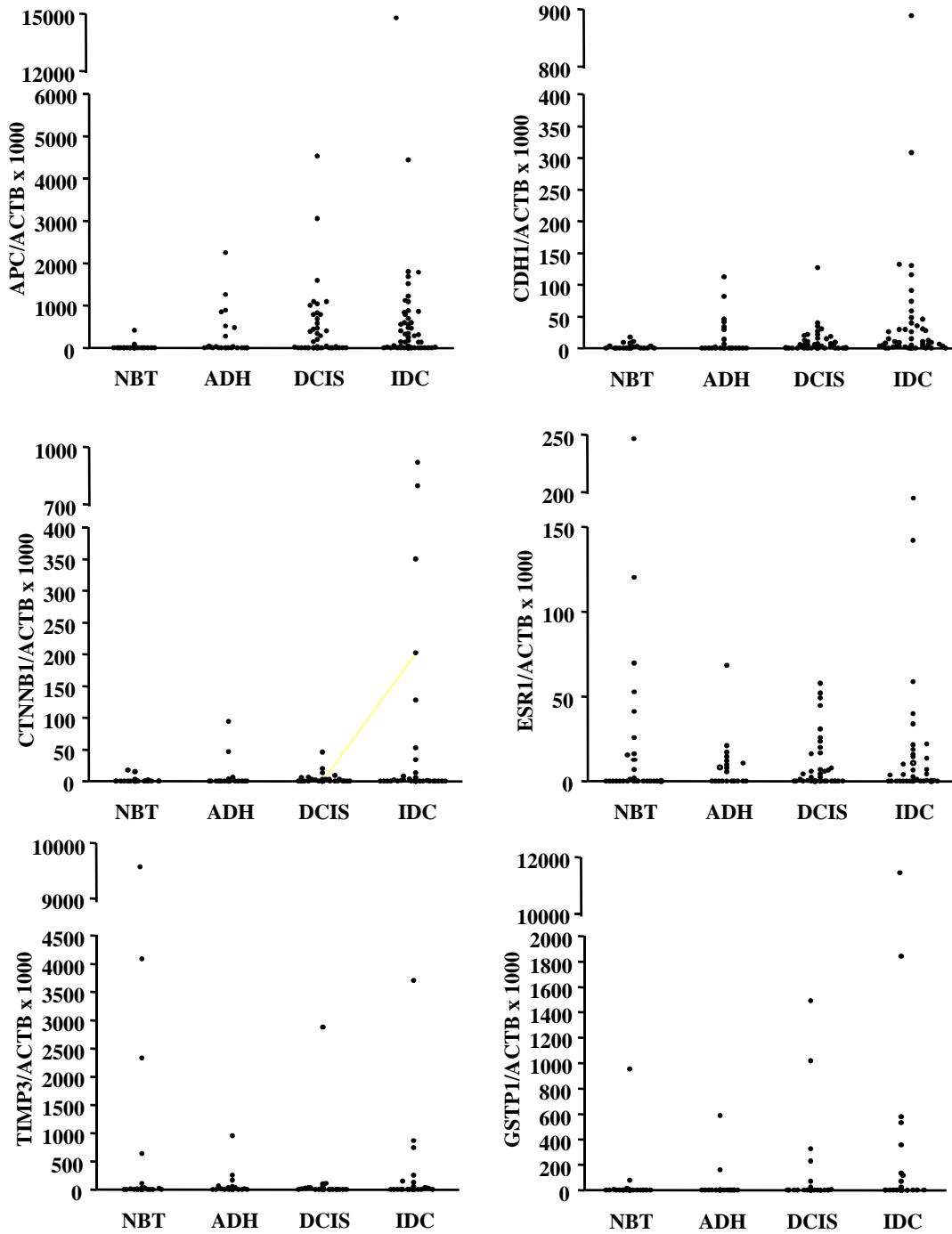
Supplemental Figure 1. Methylation levels for the six genes showing methylation in the 12 cases for which paired Normal Breast tissue Adjacent to Tumour (NBAT) was available. ADH, Atypical Ductal Hyperplasia, DCIS, Ductal carcinoma in situ, IDC Invasive Ductal Carcinoma. Methylation levels are expressed as the ratio of the quantity mean value of the target gene to the quantity mean value of the reference gene (ACTB) multiplied by 1000.



Supplemental Figure 2. ROC curve analysis of Quantitative Methylation specific PCR results. ROC curve for QMSP assay were designed on the basis of *target gene/ACTB* ratios determined in normal breast tissues (n=32) and pathological samples (n=138). The area under the curve (AUC) was 0.77 for APC, 0.68 for CDH1, 0.75 for CTNNB1, 0.54 for ESR1, 0.56 for GSTPI, 0.54 for TIMP3



Supplemental Figure 3. Scatter plot representation of promoter methylation distribution in synchronous NBAT, Normal Breast tissue Adjacent to Tumor (n=12), ADH Atypical Ductal Hyperplasia (n=24), DCIS, Ductal Carcinoma in situ (n=40) and IDC Invasive Ductal Carcinoma (n=45). Methylation levels are expressed as the ratio of the quantity mean value of the target gene to the quantity mean value of the reference gene (ACTB) multiplied by 1000.



Supplemental Figure 4. Scatter plot representation of promoter methylation distribution in Normal Breast Tissue (NBT) (N=32), Atypical ductal Hyperplasia (ADH) (n=26), Ductal Carcinoma in situ (DCIS) (n=50) and Invasive Ductal Carcinoma (IDC) (n=62). Methylation levels are expressed as the ratio of the quantity mean value of the target gene to the quantity mean value of the reference gene (ACTB) multiplied by 1000.