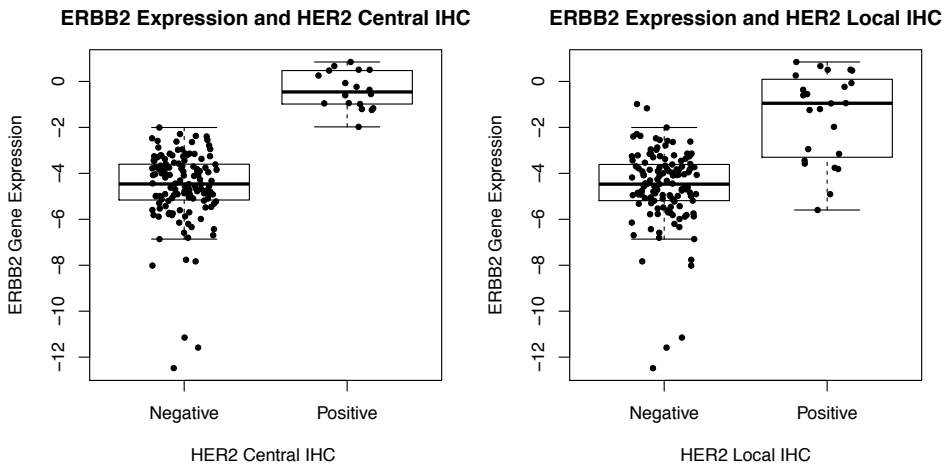
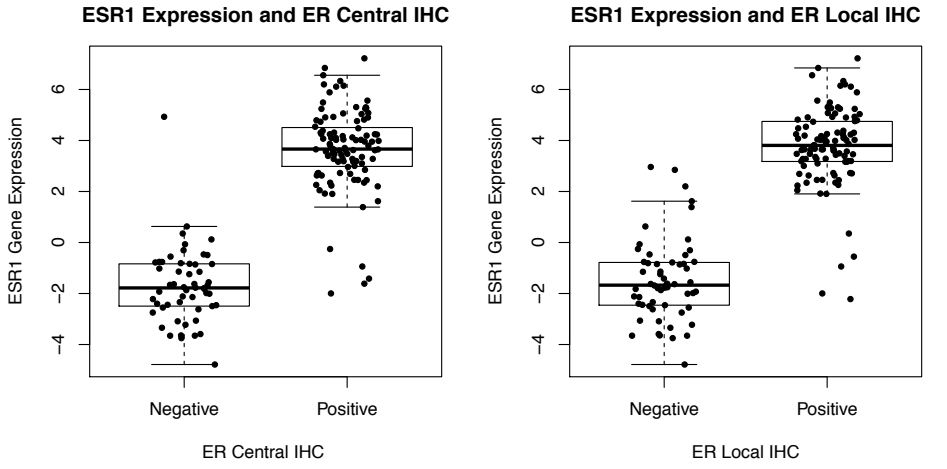
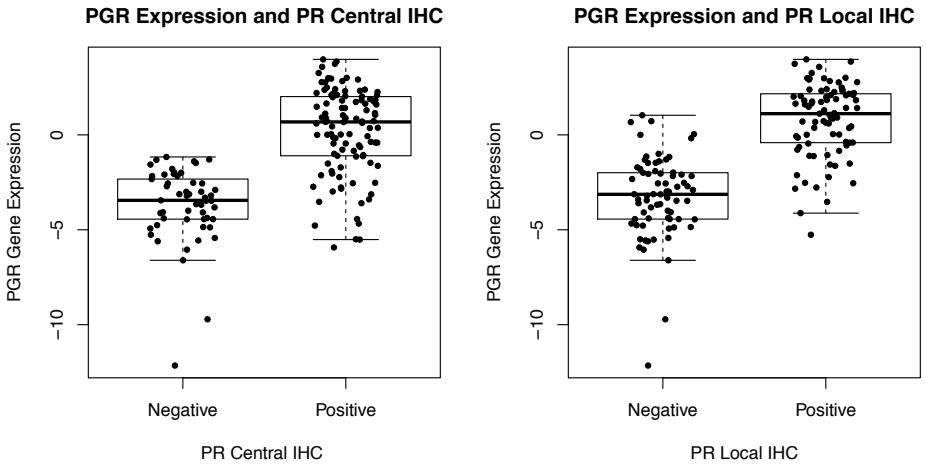
(a)



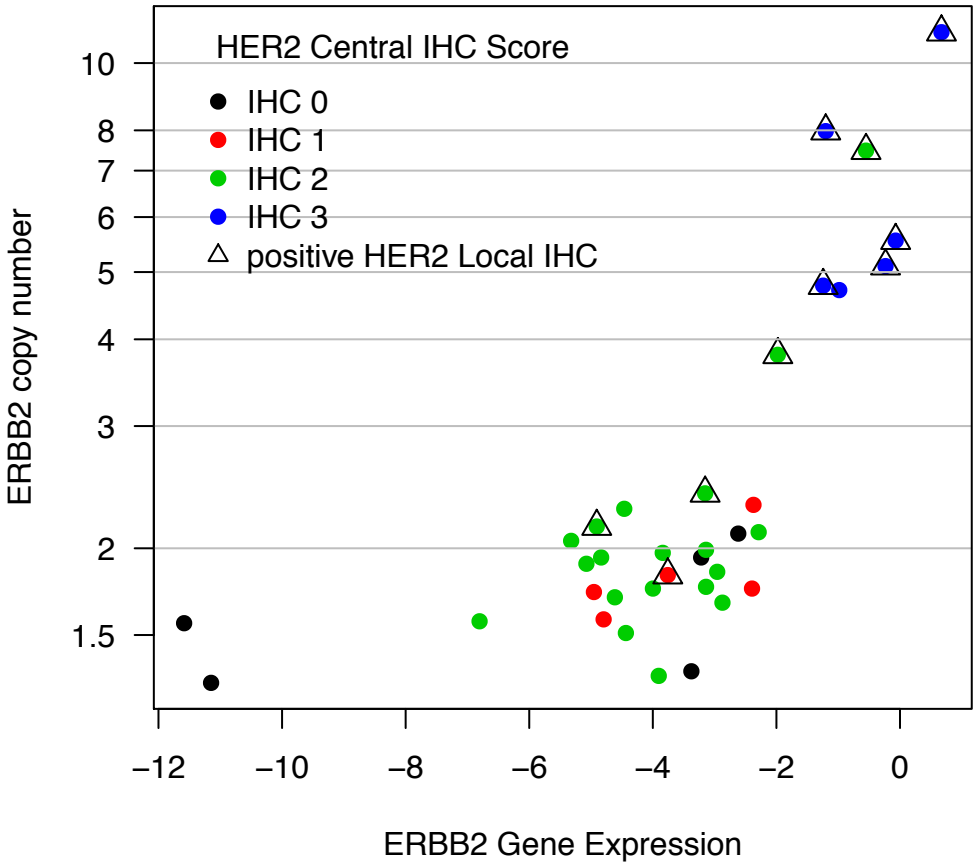
(b)



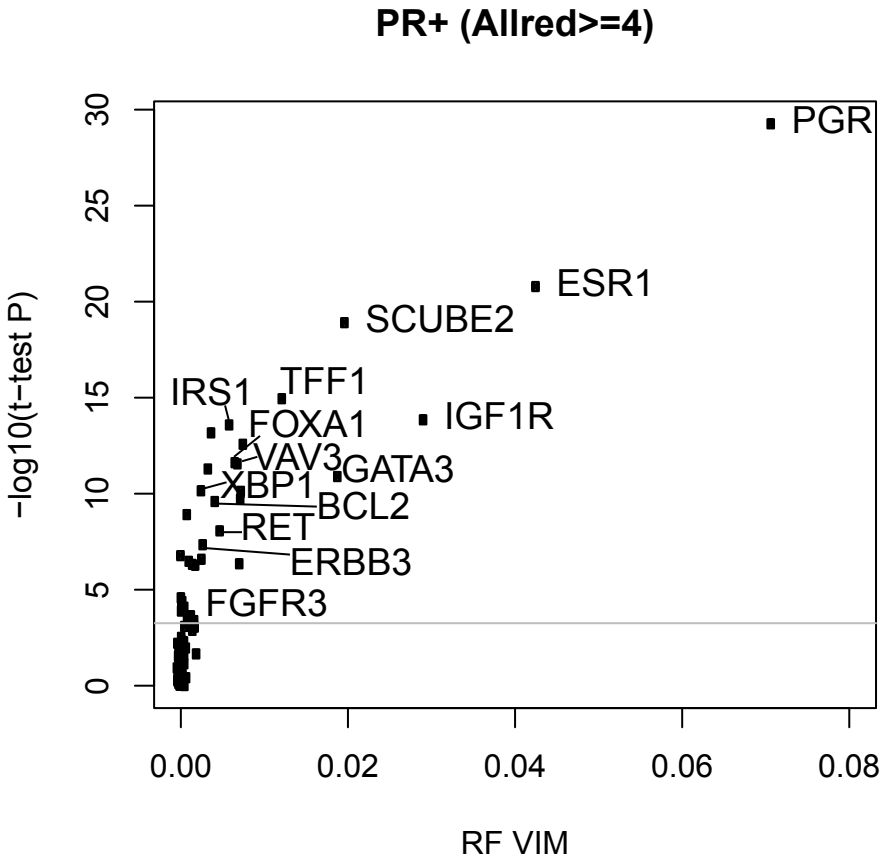
(c)



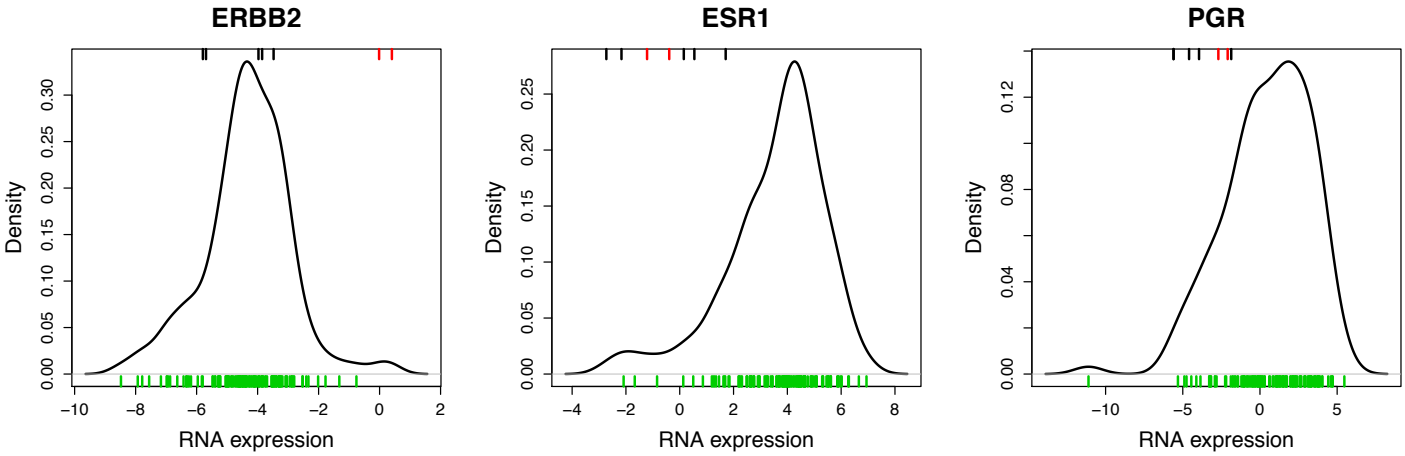
Supplemental Figure 1 Target gene expression of (a) ERBB2 (b) ESR1 (c) PGR by central and local IHC status



Supplemental Figure 2 Comparison of ERBB2 gene expression and ERBB2 copy number from a subset of the 158 training samples for the USO 01062 trial



Supplemental Figure 3 Multivariate variable importance measures (VIM) by random forests for PR prediction. PR positivity was defined as Allred score ≥ 4. Y axes are –log10 based P values of the two group t-test between central IHC positive and negative groups, and (Bonferroni) adjusted P value 0.05 is marked with gray lines. Genes with two sample t-test adjusted p values ≤ 0.05 and fold change ≥ 2 were marked with gene symbols



Supplemental Figure 4 Distribution of *ERBB2*, *ESR1* and *PGR* mRNA of test set 2, a commercially procured sample set of 136 HR+ breast cancers. Black, red and green marks are samples predicted by RFP to be triple negative, HER2+HR-, and HR+ breast cancers

Supplemental Table 1 Performance of the different multivariate prediction methods in terms of predicting local IHC status for an additional set of USO 01062 study samples

	Accuracy	**Specificity**	**Sensitivity**
HER2			
RF	0.92 (579/628)	0.99 (538/545)	0.49 (41/83)
RF+KNN	0.92 (580/628)	0.98 (536/545)	0.52 (43/83)
PAM	0.91(571/628)	0.99 (541/545)	0.36 (30/83)
TGP	0.92 (575/628)	0.99 (540/545)	0.42 (35/83)
ER			
RF	0.92 (586/634)	0.90 (249/277)	0.94 (337/357)
RF+KNN	0.90 (572/634)	0.86 (239/277)	0.93 (333/357)
PAM	0.90 (570/634)	0.84 (232/277)	0.95 (338/357)
TGP	0.93 (591/634)	0.92 (255/277)	0.94 (336/357)
PR			
RF	0.82 (517/634)	0.72(246/340)	0.92 (271/294)
RF+KNN	0.82 (519/634)	0.73 (249/340)	0.92 (270/294)
PAM	0.81 (516/634)	0.72 (244/340)	0.93 (272/294)
TGP	0.82 (571/634)	0.72 (245/340)	0.92 (270/294)

Supplemental Table 2 Prediction performance of test datasets 2 and 3

		Accuracy	TN	HER2+HR-	HR+
HR+ collection	RFP	0.95	5	2	129
	PAM	0.96	4	2	130
	RF-KNN	0.94	6	2	128
	TGP	0.94	8	2	126
Triple negative collection	RFP	0.92	34	2	1
	PAM	0.73	27	2	7
	RF-KNN	0.92	34	2	1
	TGP	0.84	31	2	4