Supplementary Method 1: Power calculation for survival analysis in SGCTG cohort

We estimated the average power of the analysis in SGCTG cohort using the formula 1 and 2 described before (1, 2).

$$N = \frac{(\mu_{1-\alpha/2} + \mu_{1-\beta})^2}{(\log\theta)^2 \varphi(1-p)p} \quad (1)$$

$$FDR = \frac{\pi_0 \alpha}{\pi_0 \alpha + (1-\pi_0)(1-\beta)} \quad (2)$$

Here, μ_γ indicates the γ-quantile of the standard normal distribution; θ is the hazard ratio; φ is the probability of an uncensored observation; p is the methylation frequency of loci in ovarian cancer; π_0 is the proportion of true null hypotheses; α is the significant level and 1-β is the average power expected on the microarray.

power (β)	FDR	true positive ($1-\pi_0$)	significant level (α)	uncensored (φ)	hazard ratio (θ)	methylation frequency (p)	Sample size (N)
0.75	0.10	0.05	0.0044	0.9	2	0.25	150
0.83	0.10	0.1	0.0102	0.9	2	0.25	150
0.89	0.10	0.05	0.0052	0.9	2	0.50	150
0.93	0.10	0.1	0.0115	0.9	2	0.50	150

Reference

1. Schmoor C, Sauerbrei W, Schumacher M. Sample size considerations for the evaluation of prognostic factors in survival analysis. Stat Med 2000;19: 441-52.
2. Tong T, Zhao H. Practical guidelines for assessing power and false discovery rate for a fixed sample size in microarray experiments. Stat Med 2008;27: 1960-72.

Supplementary Method 2: Logistic regression analysis

Construction of response model using forward stepwise likelihood ratio algorithm

The methylation of *VEGFB, PRM2, CD82, TR2IT1, GPX4, RAD54L* and *EME2* was used as categorical variables in the multivariate logistic regression model construction. 20% of the patients with highest methylation were defined as the 'high methylation group'. Otherwise they were in the 'low methylation group'. Forward stepwise likelihood ratio algorithm was used in the model construction, where the variables with significance level less than 0.05 to enter the model, and with significance level larger than 0.1 to be removed from the model. The variables included and excluded from the model were shown in M2.Table 1 and M2.Table 2 below, respectively. Only methylation of *VEGFB* and *GPX4* were included in the final model.

Validation of the biomarkers associated with response in TCGA cohort

The patients collected by TCGA study were used as the validation cohort for the association between response and methylation of *VEGFB* and *GPX4* identified from SGCTG cohort. As shown in M2.Table 4, batch effect was a confounding factor in the response analysis, especially in a group of the patients from batch 14. Therefore, the patients in batch 14 were excluded in the analysis. In the following logistic regression analysis in TCGA cohort, methylation was used a categorical variable. The patients with higher methylation (top 20% of patients) of *VEGFB* (cg05492845, chr11: 63758874-63758875) or *GPX4* (cg17812013, chr19: 1055136-1055137) were categorised as 'poor response group'. This group of patients was more likely to have poor response to chemotherapy in this cohort (OR: 2.06, 95% CI 0.96-4.42, p=0.064). After adjusted batch effect in the model, this trend became clearer (adjusted OR: 4.24, 95% CI 1.21-14.84, p=0.024).

M2.Table 1: Variables in the multivariate logistic regression model

		B	S.E.	Wald	df	Sig.	Exp(B)	95% CI.for EXP(B)	
								Lower	Upper
Step 1[a]	VEGFB group (high methylation)	1.779	.593	8.989	1	.003	5.921	1.851	18.937
	Constant	-.274	.215	1.626	1	.202	.760		
Step 2[b]	VEGFB group (high methylation)	1.644	.608	7.319	1	.007	5.176	1.573	17.035
	GPX4 group (high methylation)	1.387	.569	5.935	1	.015	4.001	1.311	12.210
	Constant	-.509	.239	4.538	1	.033	.601		

a. Variable(s) entered on step 1: VEGFB group.

b. Variable(s) entered on step 2: GPX4 group.

M2: Table 2: Variables not in the multivariate logistic regression model

			Score	df	Sig.
Step 1	Variables	RRM2 group	3.712	1	.054
		CD82 group	2.643	1	.104
		TR2IT1 group	.648	1	.421
		GPX4 group	6.502	1	.011
		RAD54L group	3.399	1	.065
		EME2 group	4.500	1	.034
	Overall Statistics		12.815	6	.046
Step 2	Variables	RRM2 group	1.696	1	.193
		CD82 group	1.973	1	.160
		TR2IT1 group	.003	1	.960
		RAD54L group	1.796	1	.180
		EME2 group	2.288	1	.130
	Overall Statistics		7.042	5	.218

M2.Table 3: Classification Table[a]

Observed			Predicted from multivariate model		
			Response		
			Good response	Poor response	Percentage Correct
Step 1	response	Good response	50	4	92.6
		Poor response	38	18	32.1
	Percentage		56.8	81.8	61.8
Step 2	response	Good response	46	8	85.2
		Poor response	27	29	51.8
	Percentage		63.0	78.3	68.2

a. The cut value is .500

M2.Table 4: batch effect in the logistic regression analysis in TCGA cohort

		B	S.E.	Wald	df	Sig.	Exp(B)	95% CI.for EXP(B)	
								Lower	Upper
Step 1[a]	Batch			12.733	7	.079			
	batch(12)	-.634	.683	.860	1	.354	.531	.139	2.025
	batch(13)	-.411	.646	.404	1	.525	.663	.187	2.352
	batch(14)	**-2.325**	**1.099**	**4.478**	**1**	**.034**	**.098**	**.011**	**.842**
	batch(15)	-19.891	8770.825	.000	1	.998	.000	.000	.
	batch(17)	-.154	.622	.061	1	.804	.857	.253	2.899
	batch(18)	-.228	.619	.136	1	.713	.796	.236	2.680
	batch(19)	.877	.575	2.323	1	.128	2.403	.778	7.423
	Constant	-1.312	.426	9.496	1	.002	.269		

a. Variable(s) entered on step 1: batch. Reference is batch 9