Supplementary Figure 1. Analysis ROC of FF3 and CEA diagnostic evaluation for discriminating the CA and CRC groups in the training group. A: TFF3 for discriminating CA and CRC; B: TFF3 for discriminating CA and early stage CRC; C: TFF3 for discriminating CA and advanced stage CRC; D: CEA for discriminating CA and CRC; E: CEA for discriminating CA and early stage CRC; F: CEA for discriminating CA and advanced stage CRC; G: The multivariate model for discriminating CA and CRC; H: The multivariate model for discriminating CA and early stage CRC; I: The multivariate model for discriminating CA and advanced stage CRC. Abbreviation: TFF3: Trefoil

factors family; ROC: receiver operating characteristic; CA: colorectal adenoma;

CRC: colorectal cancer

Supplementary Table 1 Diagnostic evaluation of TFF3, CEA alone or combination for discriminating HC and CRC in the training group

Indicator	Groups	AUC (95% CI)	Cutoff Value	Sensitivity	Specificity
TFF3	HC *vs* CRC	0.930 (0.903, 0.958)	21.30	94.86%	73.91%
	HC *vs* early stage CRC	0.892 (0.849, 0.935)	21.30	92.68%	73.91%
	HC *vs* advanced CRC	0.954 (0.931, 0.977)	31.77	81.82%	95.65%
CEA	HC *vs* CRC	0.850 (0.809, 0.890)	3.09	70.56%	92.17%
	HC *vs* early CRC	0.814 (0.745, 0.882)	3.00	69.51%	90.43%
	HC *vs* advanced stage CRC	0.872 (0.828, 0.917)	3.09	72.73%	92.17%
TFF3+CEA	HC *vs* CRC	0.968 (0.951, 0.984)	0.60	92.99%	91.30%
	HC *vs* early stage CRC	0.953 (0.926, 0.981)	0.60	91.46%	91.30%
	HC *vs* advanced stage CRC	0.976 (0.961, 0.992)	0.72	93.18%	93.91%

Abbreviation: TFF3: Trefoil factors family; HC: healthy control; CC: colorectal cancer; AUC: area under curve

Supplementary Table 2 Diagnostic evaluation of the multivariate model for discriminating HC and CC, CA and CC in the validation group

Groups	AUC (95% CI)	Cutoff Value	Sensitivity	Specificity
HC *vs* CC	0.941 (0.912, 0.970)	0.60	89.39%	87.85%
HC *vs* early stage CC	0.910 (0.856, 0.965)	0.60	85.71%	87.85%
HC *vs* advanced CC	0.961 (0.938, 0.991)	0.72	90.79%	92.52%
CA *vs* CC	0.850 (0.799, 0.902)	0.57	72.73%	87.50%
CA *vs* early CC	0.814 (0.741, 0.887)	0.41	71.43%	80.77%
CA *vs* advanced stage CC	0.877 (0.824, 0.929)	0.57	78.95%	87.50%

Abbreviation: TFF3: Trefoil factors family; HC: healthy control; CA: colorectal adenoma; CC: colorectal cancer; AUC: area under curve