# Supplementary Material: Enhancing Prediction Performance by Add-on Combining Circulating Tumor Cell Count, CD45^{neg} EpCAM^{neg} Cell Count on Colorectal Cancer, Advance, and Metastasis

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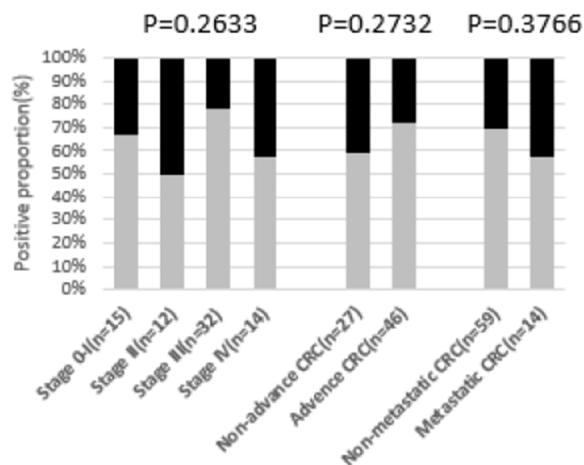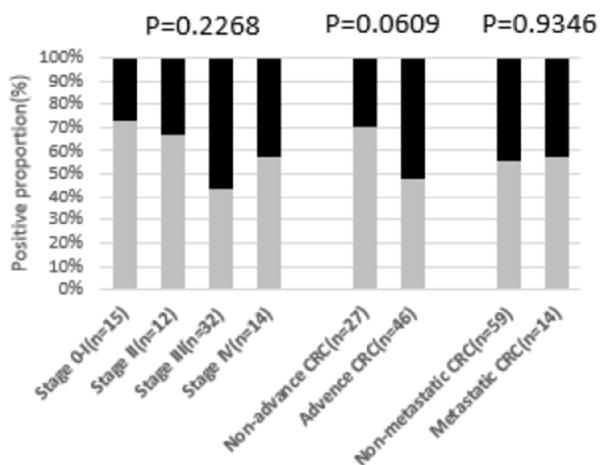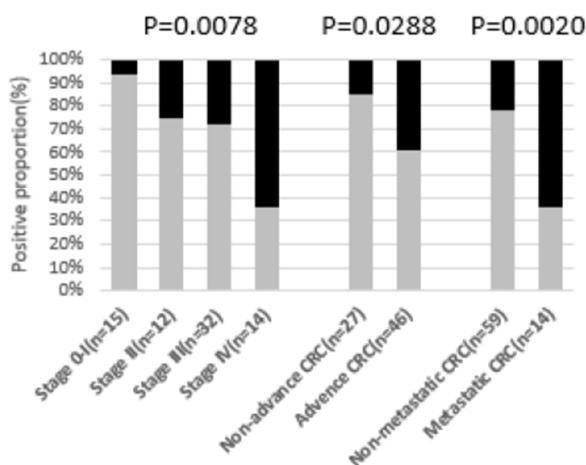
(E) CD45^{neg} EpCAM^{pos} CTCs $\geqq$3/7ml and/or CEA>5ng/ml

P=0.0072   P=0.4887   P=0.0010

Positive proportion(%)

Stage 0-I(n=15), Stage II(n=12), Stage III(n=32), StageIV(n=14), Non-advance CRC(n=27), Advence CRC(n=46), Non-metastatic CRC(n=59), Metastatic CRC(n=14)

(F) CD45^{neg} EpCAM^{neg} cells $\geqq$500/7ml and/or CEA>5ng/ml

P=0.0416   P=0.0066   P=0.0765

Positive proportion(%)

Stage 0-I(n=15), Stage II(n=12), Stage III(n=32), Stage IV(n=14), Non-advance CRC(n=27), Advence CRC(n=46), Non-metastatic CRC(n=59), Metastatic CRC(n=14)
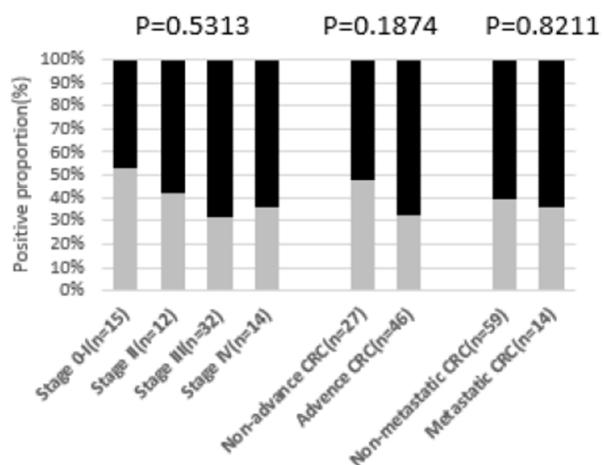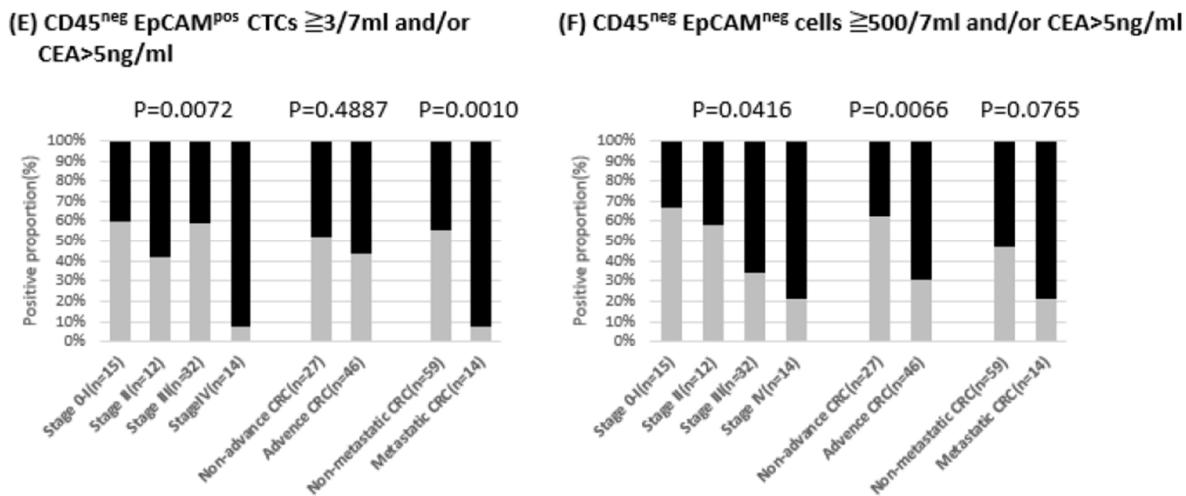
Figure S1. The proportional distribution comparison by advanced or metastasis statuses using single or combing different biomarkers.

Table S1. Performance of CEA, CD45neg EpCAMpos CTCs (continuous), CD45neg EpCAMneg ($\geqq$400) cell counts, and combined biomarkers predicting advanced or metastasis CRCs.

Biomarker(s)	Predictor(s)*			Advanced vs. Non-advanced CRC AUROC (95%CI)	Metastasis vs. Non-metastasis CRC AUROC (95%CI)
	CD45^{neg}EpCAM^{pos} CTCs (continuous)	CD45^{neg} EpCAM^{neg} cells $\geqq$400/7ml	CEA>5ng/ml		
1-type	√			0.561 (0.424, 0.699)	0.664 (0.497, 0.831)
		√		0.635 (0.491, 0.779)	0.630 (0.475, 0.784)
			√	0.643 (0.515, 0.771)	0.780 (0.645, 0.914)
2-type	√	√		0.638 (0.494, 0.781)	0.662 (0.495, 0.830)
		√	√	0.712 (0.587, 0.836)	0.786 (0.661, 0.911)
	√		√	0.635 (0.506, 0.763)	0.837 (0.740, 0.934)
3-type	√	√	√	0.710 (0.586, 0.835)	0.837 (0.739, 0.935)

* all analysis was adjusted age (continuous) and gender. AUROC: area under the receiver operating characteristic. CEA: Carcinoembryonic Antigen.

Table S2. Performance of CEA, CD45neg EpCAMpos CTCs (continuous), CD45neg EpCAMneg (≧500) cell counts, and combined biomarkers predicting advanced or metastasis CRCs.

Biomarker(s)	Predictor(s)*			Advanced vs. Non-advanced CRC AUROC (95%CI)	Meta vs. Non-meta CRC AUROC (95%CI)
	CD45^{neg} EpCAM^{pos} CTCs (continuous)	CD45^{neg} EpCAM^{neg} cells ≧500/7ml	CEA>5ng/ml		
1-type	√			0.561(0.424, 0.699)	0.664(0.497, 0.831)
		√		0.658(0.518, 0.798)	0.627(0.478, 0.777)
			√	0.643(0.515, 0.771)	0.780(0.645, 0.914)
2-type	√	√		0.658(0.519, 0.797)	0.668(0.504, 0.833)
		√	√	0.709(0.584, 0.834)	0.782(0.650, 0.914)
	√		√	0.635(0.506, 0.763)	0.837(0.740, 0.934)
3-type	√	√	√	0.710(0.585, 0.835)	0.826(0.706, 0.945)

* all analysis was adjusted age (continuous) and gender. AUROC: area under the receiver operating characteristic. CTC: Circulating Tumor Cells.

Table S3. Performance of CEA, CD45neg EpCAMpos (≧3) CTCs, CD45neg EpCAMneg (≧400) cell counts, and combined biomarkers predicting advanced or metastasis CRCs.

Biomarker(s)	Predictor(s)*			Advanced vs. Non-advanced CRC AUROC (95%CI)	Meta vs. Non-meta CRC AUROC (95%CI)
	CD45^{neg} EpCAM^{pos} CTCs ≧3/7ml	CD45^{neg} EpCAM^{neg} cells ≧400/7ml	CEA>5ng/ml		
1-type	√			0.614(0.478, 0.749)	0.642(0.487, 0.797)
		√		0.635(0.491, 0.779)	0.630(0.475, 0.784)
			√	0.643(0.515, 0.771)	0.780(0.645, 0.914)
2-type	√	√		0.672(0.542, 0.803)	0.639(0.473, 0.805)
		√	√	0.712(0.587, 0.836)	0.786(0.661, 0.911)
	√		√	0.677(0.554, 0.800)	0.815(0.710, 0.920)
3-type	√	√	√	0.727(0.609, 0.845)	0.818(0.714, 0.922)

* all analysis was adjusted age (continuous) and gender. AUROC: area under the receiver operating characteristic. CTC: Circulating Tumor Cells.

Table S4. Performance of CEA, CD45neg EpCAMpos (≧3) CTCs, CD45neg EpCAMneg (≧500) cell counts, and combined biomarkers predicting advanced or metastasis CRCs.

Biomarker(s)	Predictor(s)*			Advanced vs. Non-advanced CRC AUROC (95%CI)	Meta vs. Non-meta CRC AUROC (95%CI)
	CD45^{neg} EpCAM^{pos} CTCs ≧3/7ml	CD45^{neg} EpCAM^{neg} cells ≧500/7ml	CEA>5ng/ml		
1-type	√			0.614(0.478, 0.749)	0.642(0.487, 0.797)
		√		0.658(0.518, 0.798)	0.627(0.478, 0.777)
			√	0.643(0.515, 0.771)	0.780(0.645, 0.914)
2-type	√	√		0.680(0.553, 0.807)	0.639(0.484, 0.794)
		√	√	0.709(0.584, 0.834)	0.782(0.650, 0.914)
	√		√	0.677(0.554, 0.800)	0.815(0.710, 0.920)
3-type	√	√	√	0.713(0.594, 0.833)	0.812(0.700, 0.925)

* all analysis was adjusted age (continuous) and gender. AUROC: area under the receiver operating characteristic. CTC: Circulating Tumor Cells.

Table S5. Performance of CEA, CD45neg EpCAMpos (≧3) CTCs, CD45neg EpCAMneg (≧600) cell counts, and combined biomarkers predicting advanced or metastasis CRCs.

Biomarker(s)	Predictor(s)*			Advanced vs. Non-advanced CRC AUROC (95%CI)	Meta vs. Non-meta CRC AUROC (95%CI)
	CD45^{neg} EpCAM^{pos} CTCs ≧3/7ml	CD45^{neg} EpCAM^{neg} cells ≧600/7ml	CEA>5ng/ml		
1-type	√			0.614(0.478, 0.749)	0.642(0.487, 0.797)
		√		0.666(0.529, 0.803)	0.617(0.459, 0.776)
			√	0.643(0.515, 0.771)	0.780(0.645, 0.914)
2-type	√	√		0.681(0.557, 0.805)	0.628(0.467, 0.790)
		√	√	0.709(0.584, 0.833)	0.785(0.652, 0.917)
	√		√	0.677(0.554, 0.800)	0.815(0.710, 0.920)
3-type	√	√	√	0.717(0.598, 0.836)	0.816(0.705, 0.928)

* all analysis was adjusted age (continuous) and gender. AUROC: area under the receiver operating characteristic. CTC: Circulating Tumor Cells.