

Evaluation of ANGPTL2 for early detection of gastric cancer metastasis and recurrence

JCA



会期 2013年10月3日(木)~5日(土)
会場 パシフィコ横浜
会長 中村 祐輔 (シカゴ大学医学部)

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Introduction

Globally, gastric cancer is one of the most common cancers and the second leading cause of cancer-induced mortality. Because early detection can contribute to a reduction of its mortality, identification of novel biomarkers for gastric cancer is urgently needed. Also, despite advancement in therapeutic modalities for gastric cancer, many gastric cancer patients who have undergone curative surgery suffer from recurrence of cancer because approximately 90% of all cancer-related deaths arise from metastatic spread of primary tumors. Measurement of tumor biomarkers in serum is an alternative screening method for the detection of gastric cancer. However, current gastric cancer biomarkers, such as carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), and C-reactive protein (CRP), have low specificity and low sensitivity for gastric cancer prognosis.

We tried to evaluate as a new suitable marker for early detection of gastric cancer metastasis and recurrence. At first, we evaluated angiopoietin-like protein 2 (ANGPTL2) and the other biomarkers.

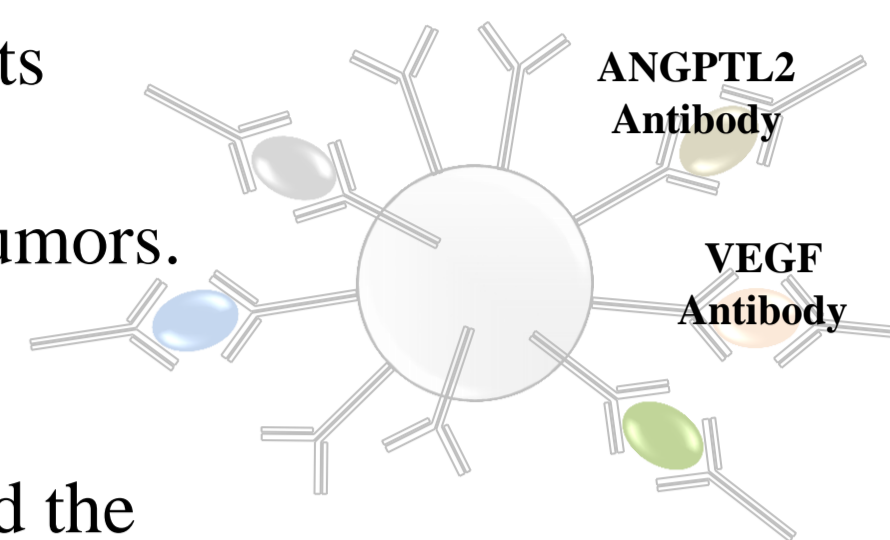


Figure. multiplex antibody's beads model

Result

1. Velocity of cell growth

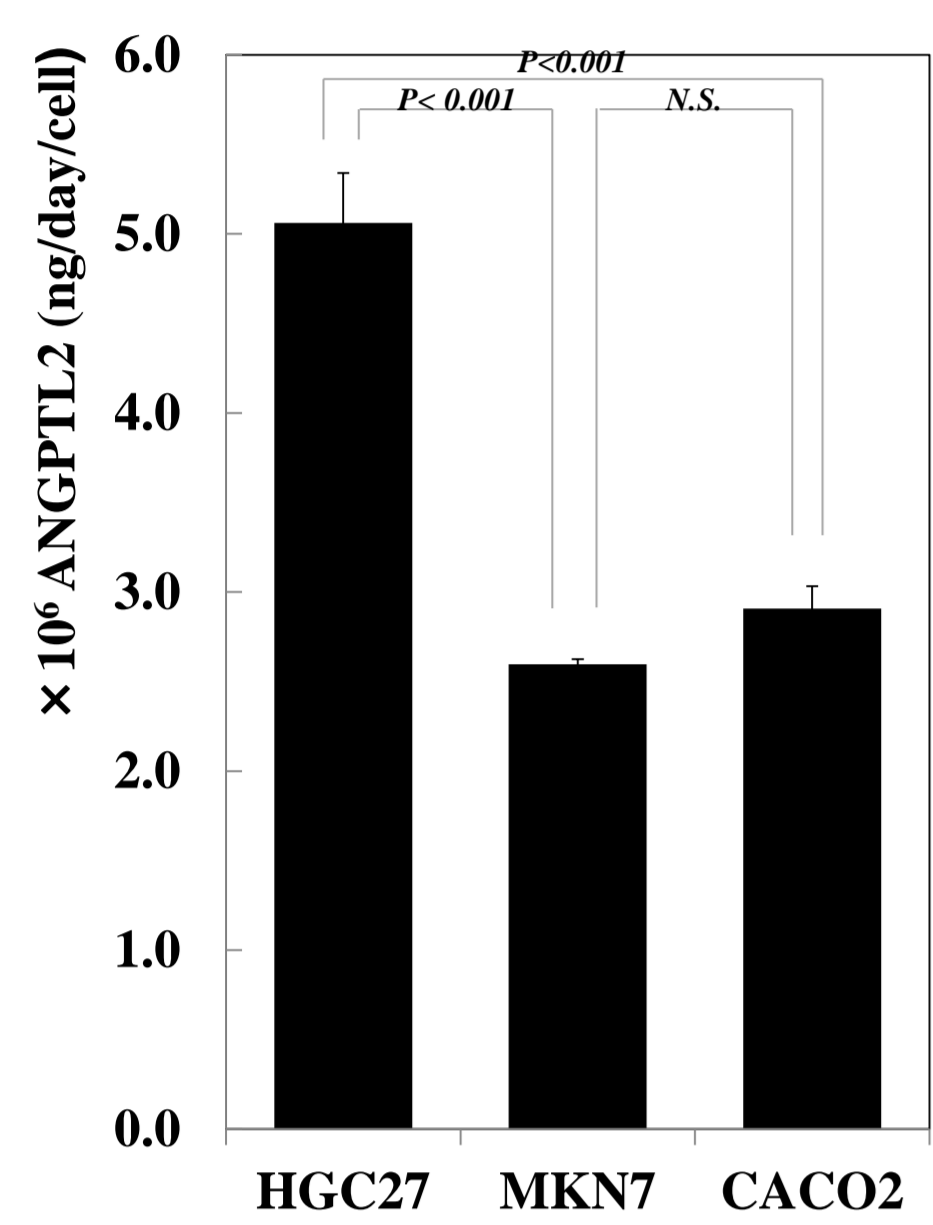


Figure. Growth curves of HGC-27, MKN7 and Caco-2 cells (n = 3). The proliferative rate of HGC-27 cells was markedly higher than that of the other cell lines.

2. ANGPTL2 expression of HGC-27, MKN7 and Caco-2 cells

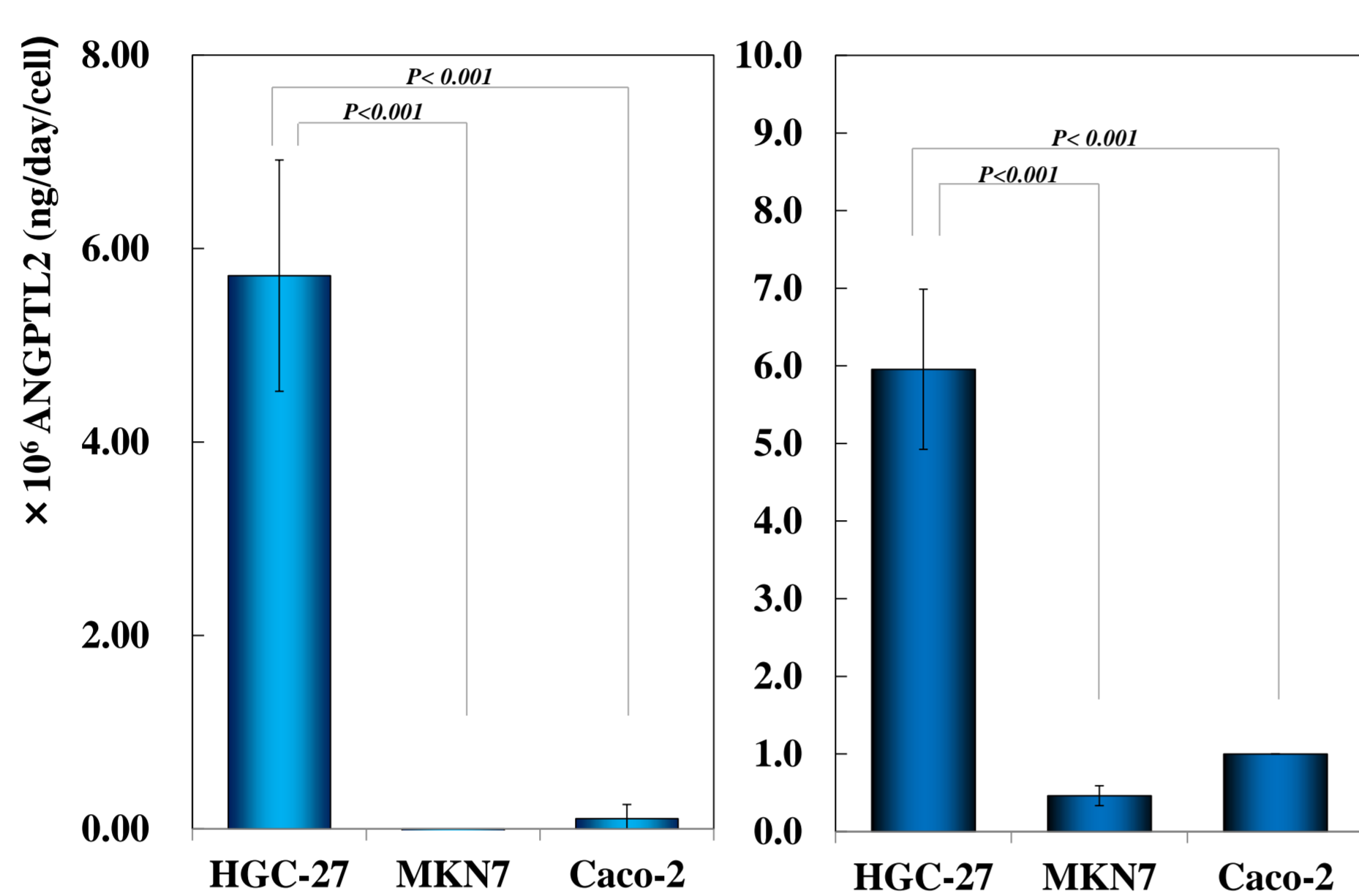


Figure. ANGPTL2 expression in HGC-27, MKN7 and Caco-2 cells at day 2 of cell culture (n = 3). ANGPTL2 was more strongly expressed in HGC-27 cells than in the other cell lines.

3. The expression of angiogenic factors in HGC-27, MKN7 and Caco-2 cells

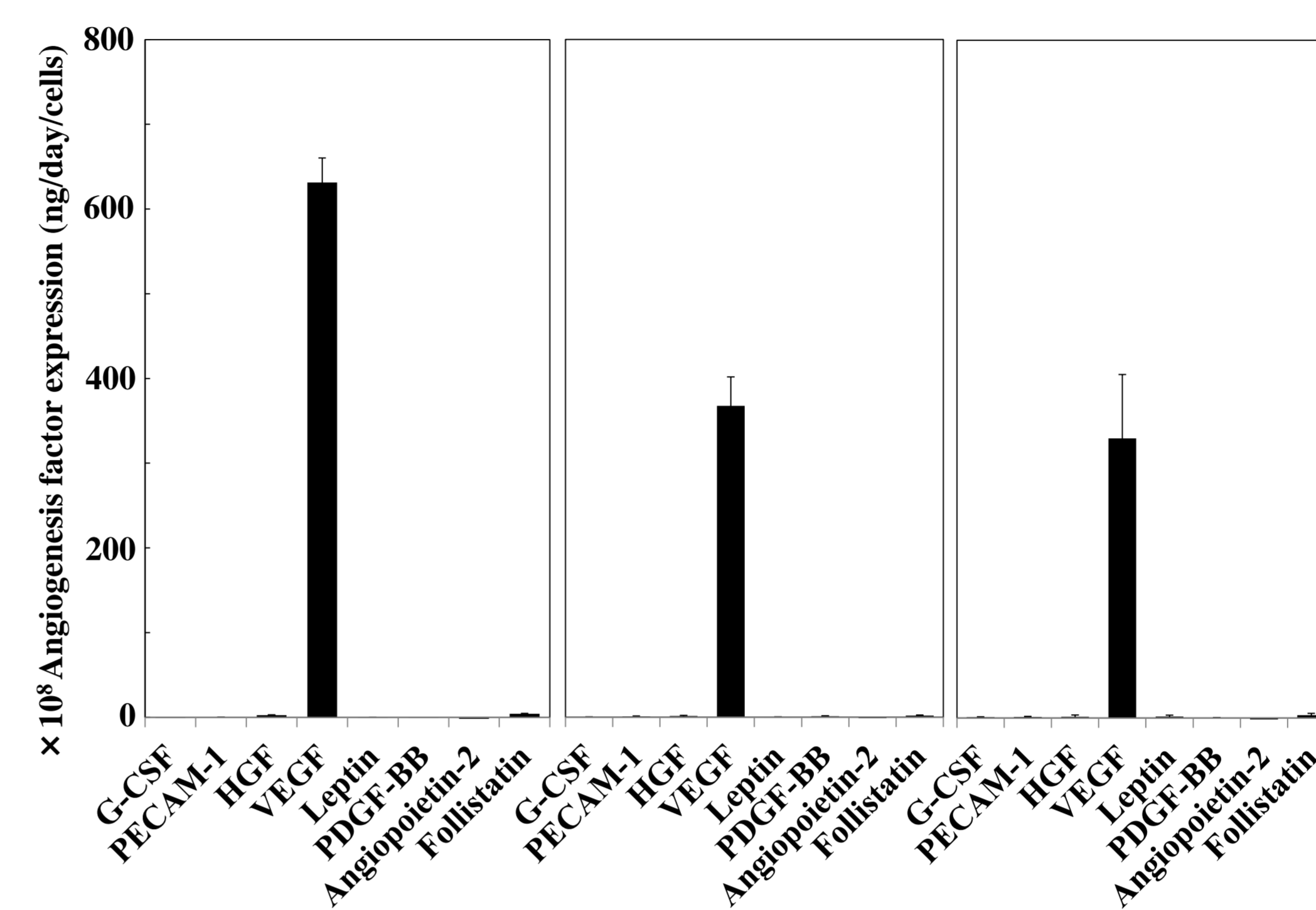
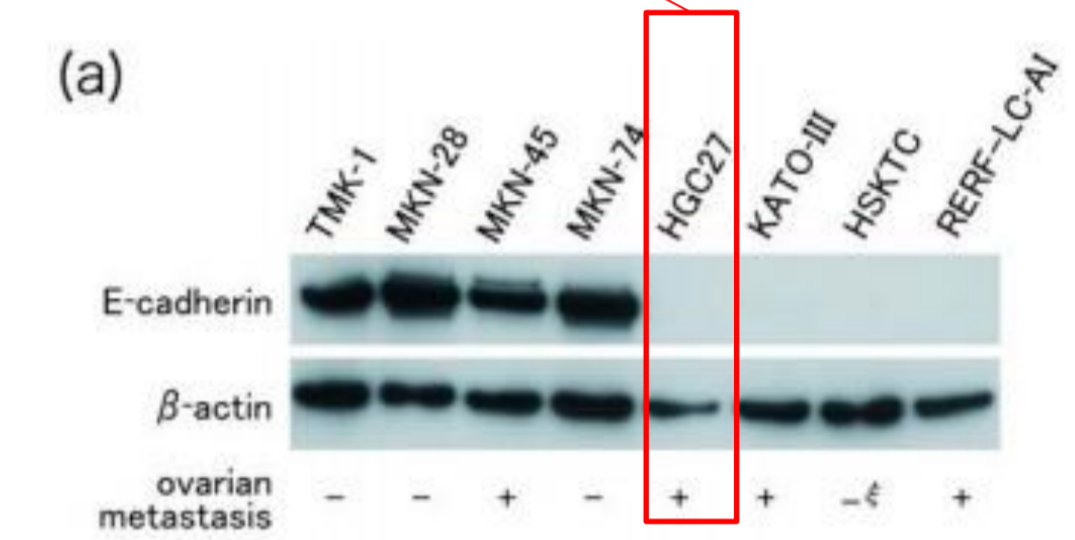


Figure. The expression of angiogenic factors in HGC-27, MKN7 and Caco-2 cells at day 2 of cell culture (n = 3). Only VEGF was found to be expressed by these cell lines, with its expression being notably higher in HGC-27 cells than in the other cell lines.

HGC27 cell line, an undifferentiated gastric cancer cell line, has been reported to lose the expression of E-cadherin



Kawabara Y, Yamada T, Yamazaki K, Du WL, Banno K, Aoki D, Sakamoto M. Establishment of an ovarian metastasis model and possible involvement of E-cadherin down-regulation in the metastasis. Cancer Sci. 2008

4. ANGPTL2 concentration in the plasma samples

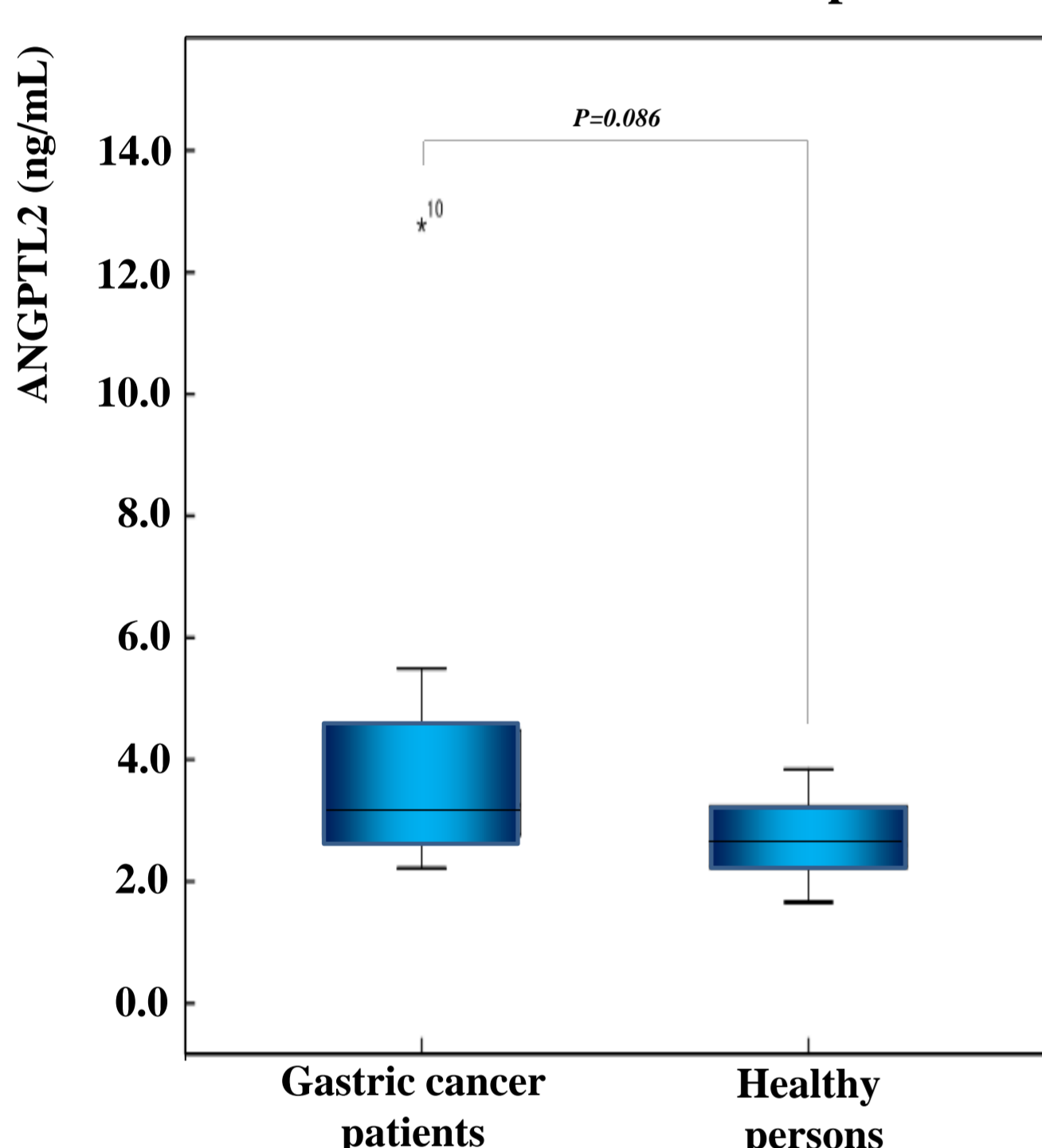
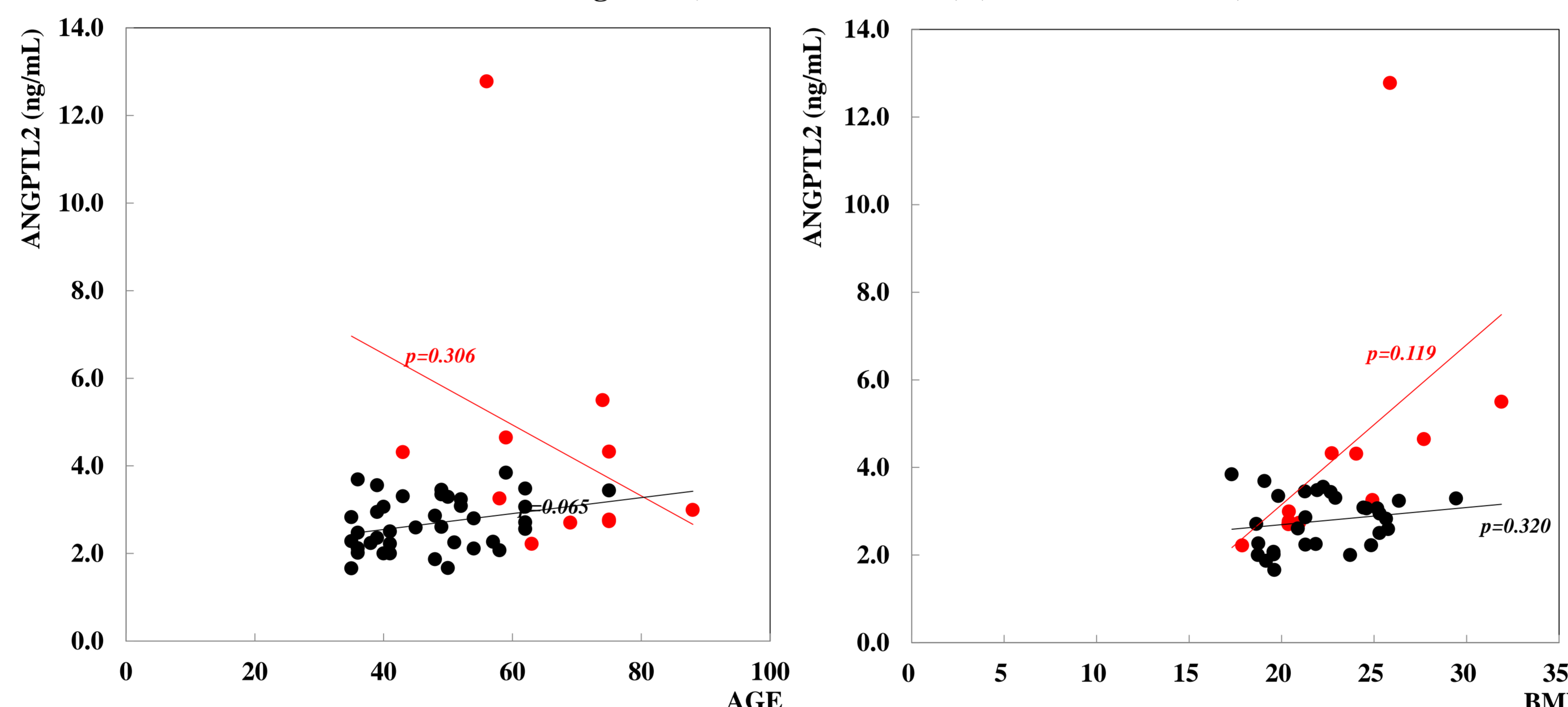


Figure. ANGPTL2 concentration in the serum of gastric cancer patients (n = 11) and healthy controls (n = 38). ANGPTL2 levels were significantly higher in the gastric patients than in healthy participants.

5. Correlation diagram (ANGPTL2 vs AGE) (ANGPTL2 vs BMI)

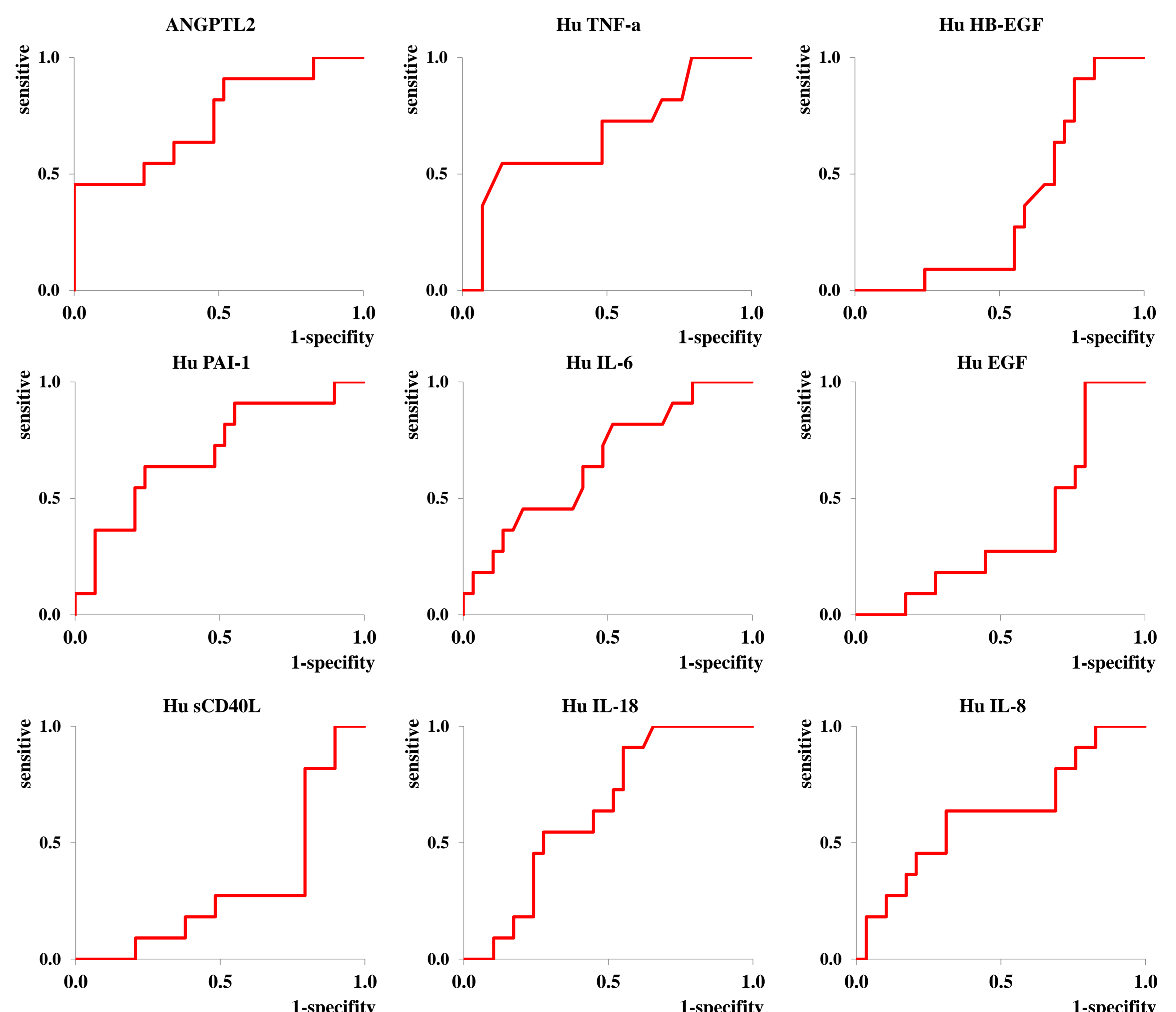


● healthy controls (n = 38) ● gastric cancer patients (n = 11)

	Mean	±	SD	P value
Differentiation				
Well, moderately	5.21	±	3.52	0.334
Poor	3.39	±	0.93	
Depth of tumor invasion				
M, SM,	4.47	±	3.46	0.905
MP, SS, S	4.19	±	1.11	
Ly				0.701
0	4.73	±	3.69	
>=0	3.88	±	1.11	0.893
V	4.46	±	3.23	
0	4.10	±	1.40	

6. Receiver operating characteristic curve

	AUC	SE	p-value	95% CI	
				lower	upper
ANGPTL2	0.737	0.093	0.022	0.554	0.919
Hu Angiopoietin-2	0.589	0.101	0.388	0.391	0.787
Hu sCD40L	0.307	0.090	0.062	0.130	0.484
Hu EGF	0.373	0.093	0.220	0.190	0.556
Hu Endoglin	0.572	0.094	0.486	0.389	0.755
Hu sFASL	0.494	0.092	0.952	0.313	0.674
Hu HB-EGF	0.364	0.087	0.188	0.193	0.534
Hu IGFBP-1	0.420	0.117	0.440	0.191	0.650
Hu IL-6	0.658	0.095	0.126	0.473	0.844
Hu IL-8	0.624	0.102	0.232	0.423	0.824
Hu IL-18	0.638	0.087	0.183	0.467	0.809
Hu PAI-1	0.699	0.095	0.054	0.514	0.884
Hu PLGF	0.553	0.094	0.607	0.369	0.738
Hu TGF-a	0.519	0.100	0.856	0.323	0.715
Hu TNF-a	0.666	0.101	0.108	0.468	0.865
Hu uPA	0.412	0.109	0.396	0.199	0.626
Hu VEGF-A	0.591	0.089	0.380	0.417	0.765
Hu VEGF-C	0.472	0.094	0.785	0.288	0.656
Hu VEGF-D	0.489	0.098	0.916	0.297	0.681



Conclusion

ANGPTL2 is an important key factor to detect gastric cancer metastasis and recurrence. Future work should be focused on how to build up antibody's beads for detecting gastric cancer metastasis and recurrence.

I have no financial relationships to disclose.