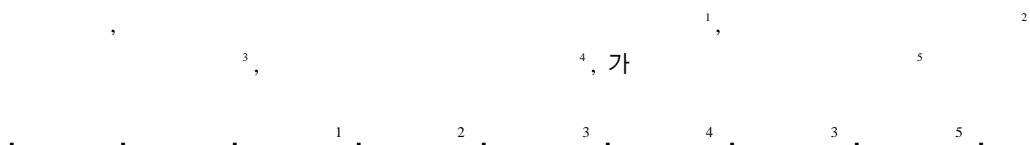


Transforming Growth Factor- β 1



Study of plasma transforming growth factor- β 1 level as a useful tumor marker in various cancers

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Background : Many investigators have found transforming growth factor- β 1 (TGF- β 1) to be elevated in tumors. Changes in responsiveness to TGF- β 1 have been linked to malignant transformation, tumor progression and tumor regression. Many malignant cell lines of epithelial or hematopoietic origin are refractory to the antiproliferative effects of TGF- β 1. However, a little is known about the association of TGF- β 1 with progression of malignant tumor. **Methods** : In this study, we measured the plasma level of TGF- β 1 in various cancer patients and evaluated the utility of plasma TGF- β 1 as a possible tumor marker. Plasma TGF- β 1 levels were measured using enzyme-linked immunosorbent assay in cancer patients and normal controls. Carcinoembryonic antigen (CEA) and alpha-fetoprotein (AFP) as tumor marker were compared with TGF- β 1 in the aspects of sensitivity and specificity. **Results** : The mean of plasma TGF- β 1 levels was 1.219 ± 0.834 ng/ml in normal controls, 5.491 ± 3.598 ng/ml in breast cancer, 12.670 ± 10.386 ng/ml in lung cancer, 5.747 ± 3.228 ng/ml in hepatocellular carcinoma and 10.854 ± 7.996 ng/ml in cervical cancer. In comparison with CEA and AFP, TGF- β 1 is more sensitive. **Conclusion** : We conclude that the high levels of TGF- β 1 are common in the plasma of cancer patients. These results suggest that the plasma TGF- β 1 level can be a potent tumor marker in various cancer patients.

Key Words: carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), cervical cancer, enzyme-linked immunosorbent assay (ELISA), transforming growth factor- 1 (TGF- β 1), tumor marker

, TGF- β 가 (13,14). TGF- β
 (1,2), TGF- β (15-17).
 (3,4). transforming growth factor- β TGF- β 1 (18-23)
 1(TGF- β 1) 25 kDa , TGF- β 1
 (homodimer) 가 .
 . TGF- β 1 TGF- β 1
 TGF- β 1 .
 in vitro (latency
 associated peptide) (,) 가 TGF- β 1
 . TGF- β 1
 TGF- β 가 .
 가 가 .
 carcinoembryonic antigen
 (CEA) alpha-feto protein
 (AFP), prostate-specific
 antigen (PSA)
 TGF- β 1
 75 kDa TGF- β 1
 (TGF- β RII) -
 (serine-threonine kinase) .
 TGF- β 1 TGF- β RII DNA-
 53 kDa (TGF- β RII) .
 . TGF- β RII (kinase) .
 , 가 ,
 . TGF- β 1 ,
 G1
 (5) . ,
 (6-8). , ,
 , TGF- β 1
 AFP CEA
 TGF- β 1
 (9,10). .
 TGF- β 1
 (11), TGF- β 1 DNA
 (12) 가
 1. TGF- β 1
 , ,
 TGF- β TGF- β .

121 dish peroxidase) conjugate well 1 30
 conjugate TGF-β1 -HRP
 84 20
 45 가
 190 450 nm
 가 2 well
 coefficient of variance (%) 10
 290
 EDTA CEA Solid phase ELISA
 assay kit(S-RAM Inc.,)
 , 3000 g 20 4
 1.5 ml -70 가 CEA -HRP conjugate 가
 2. TGF-β1, AFP, CEA
 TGF-β1 human TGF-β1 immunoassay 450nm
 kit (R&D Systems, Minneapolis, MN, USA) CEA
 enzyme-linked immunosorbent assay (ELISA) AFP AFP assay kit(S-RAM Inc.
 . TGF-β1) Monoclonal AFP 가
 well 가 HRP가
 TGF-β1 latency associated peptide(LAP), latent TGF-β AFP 가
 1 binding protein (LTBP) 3 가
 . LAP TGF-β1 N 450nm
 , LTBP AFP
 120 180 kD . TGF-
 β1 3.
 ROC (Receiver Operating Characteristic) curve
 cut-off value (sensi-
 tivity) 1- (specificity)
 TGF-β1 (24).
 ROC curve TGF-β1
 ,
 latent TGF-β1 가
 100 μl 2.5 N
 acetic acid/10 M urea () 2.7 N
 NaOH/1 M HEPES
 TGF-β II 가
 coating 96 well 4.
 (20 - 25 , , 50 45
) 3 , 49 TGF-β1
 TGF-β1 -HRP (horsera-

alpha-fetoprotein(AFP) , , 2.5 ng/mL 가
carcinoembryonic antigen(CEA) .

(CAP) SCL(3.
Table III TGF-β1
TGF-β1 , , AFP
McNemar .
CEA TGF-β1 가
McNemar p-value가 0.0015
p-value가 0.00001
TGF-β1

1. TGF - β1
TGF-β1 Table I , Fig. 1
TGF-β1

2. TGF - β1 ROC
Table II ROC curve
TGF-β1
2.0 ng/mL, 1.5 ng/mL,

Table . Cut-off value of TGF-β1 concentrations in various cancer patients using ROC curve analysis.

	TGF-β1 Cut-off value (ng/ml)	Sensitivity	Specificity
Breast cancer	1.5	0.868	0.817
Lung cancer	2.5	0.978	0.952
Cervical cancer	2.0	0.963	0.934
Hepatocellular carcinoma	2.0	0.952	0.934

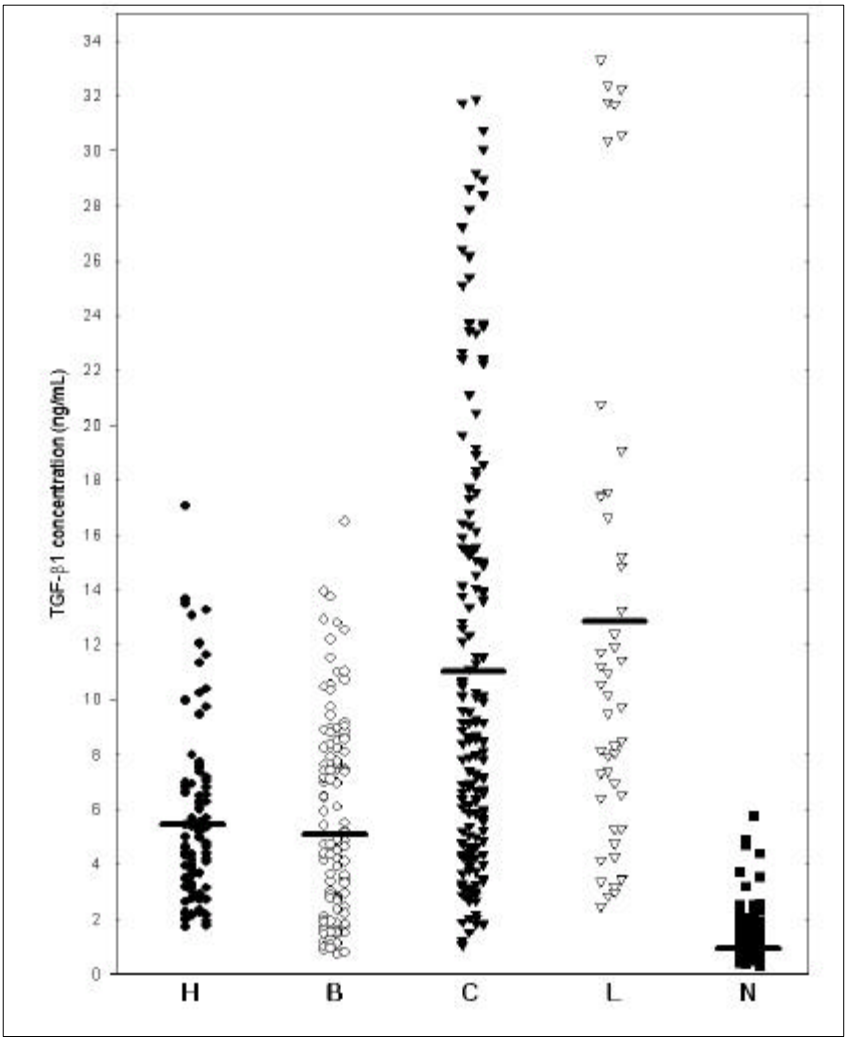
Table . TGF-β1 concentrations in the plasma of various cancer patients and normal controls.

	Plasma TGF-β1 concentration (Mean ± Standard Deviation, ng/ml)	Number of patients
Breast cancer	5.491 ± 3.598	121
Lung cancer	12.670 ± 10.386	45
Cervical cancer	10.854 ± 7.996	190
Hepatocellular carcinoma	5.747 ± 3.228	84
Normal	1.219 ± 0.834	290

Table . Comparison of sensitivity and specificity with CEA and AFP in various cancer patients and normal controls.

Tumor marker	CEA	AFP	TGF- β1
Breast cancer (50 case)	1/50 (2.0%)	-	50/50 (100.0%)
Lung cancer (45 case)	11/45 (24.4%)	-	44/45 (97.8%)
Cervical cancer (49 case)	2/49 (4.1%)	-	49/49 (100.0%)
Hepatocellular carcinoma (50 case)	-	38/50 (76.0%)	50/50 (100.0%)
Specificity (Normal 50 case)	50/50 (100.0%)	50/50 (100.0%)	50/50 (100.0%)

Cut-off value : CEA < 4.5 ng/ml, AFP < 15 ng/ml, TGF-β1 < 2.0 ng/ml



H : Hepatocellular carcinoma, B : Breast cancer, C : Cervical cancer, L : Lung cancer, N : Normal control

Fig. 1. Distribution of TGF-β1 concentration in the plasma of various cancer patients and normal controls. Solid bars represent mean values.

가 . Fig. 2

TGF-β1

가

TGF-β1

Table III

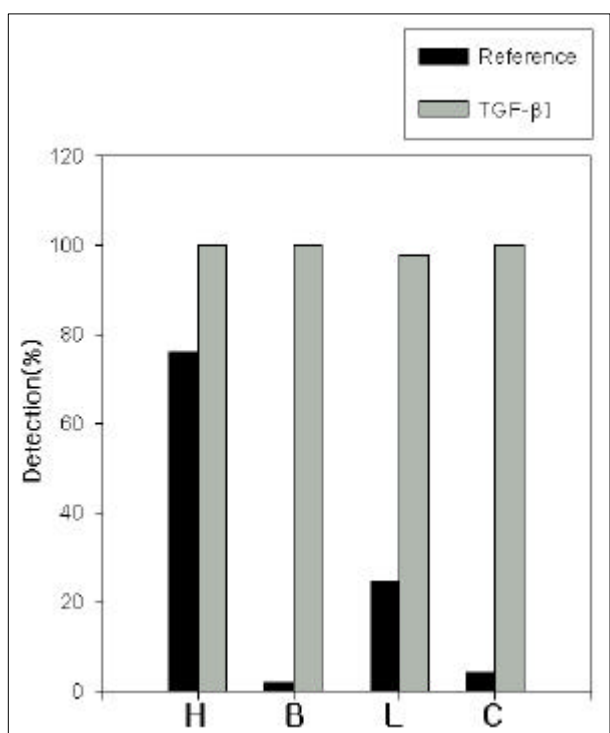
(22,25).

TGF-β1

Shirai (26)

100%

TGF-β1



H : Hepatocellular carcinoma, B : Breast cancer,
C : Cervical cancer, L : Lung cancer
Cut-off value : CEA < 4.5 ng/ml, AFP < 15 ng/ml,
TGF- β 1 < 2.0 ng/ml

Fig. 2. Comparison of sensitivity with other tumor marker proteins in various cancer patients.

AFP (alpha-fetoprotein)

TGF- β 1 가 2 가

TGF- β 1 가

가 (27-29). Shim (30) -

TGF- β 1 가

가 -

가

가

CEA, AFP, PSA

TGF- β 1

(CEA, AFP)

P value <0.05

가

Table II

87% 98%

TGF-β1

-

(29,30)

가

. Fig. 1

TGF-β1

.

TGF-β1

가

TGF-β1

,

가

, TGF-β1

.

TGF-β1

가

가

TGF-β1

,

가

TGF-β1

가

가

가

(stage of disease)

TGF-β1

(28).

TGF-β1

50%

TGF-β1

가

가

TGF-β1

가

TGF-β1

(29). -

TGF-β1

가

TGF-β1

가

(30,31).

TGF-β1 mRNA

가

가

TGF-β1

(23)

가

TGF-β1

TGF-β1

가

가

.

,

TGF- β 1 가
가
가
TGF- β 1
CEA, AFP
CEA, AFP TGF- β 1 가
TGF- β 1 가
가

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