Oncology

Tissue Polypeptide Antigen - TPA®

A highly sensitive marker

Cytokeratin filaments
All eukaryotic cells have cytoplasmatic cytoskeletal structures known as intermediate filaments. Among the most important of these are the cytokeratin proteins found in epithelial cells. To date the human catalogue of cytokeratins comprises 20 distinct polypeptides[1]. An epithelial cell exhibits a characteristic combination of two or more cytokeratins. The pattern of expression is usually preserved during malignant transformation. The cytokeratins have become well-established markers of epithelial tumours[2].

Tissue Polypeptide Antigen
Tissue polypeptide antigen or TPA is a circulating complex of polypeptide fragments of cytokeratins 8, 18 and 19. These three cytokeratins are characteristic of internal epithelium and are widely distributed in normal tissues and in tumours derived from them[3].
Serum levels of TPA have been shown to correlate well with cell growth rate and tumour burden and are elevated in metastatic and disseminated disease. TPA is therefore valuable as a prognostic marker and for monitoring treatment of patients with different carcinomas[4].

A variety of assays claim TPA®-reactivity
A number of assays for detection of cytokeratins exist on the market **(Table 1)**. These tests vary in reactivity and therefore cannot always be supported by the clinical background for TPA.
The commercial names are very similar and that may pose problems since they do not show identical clinical results [5, 6].

Table 1

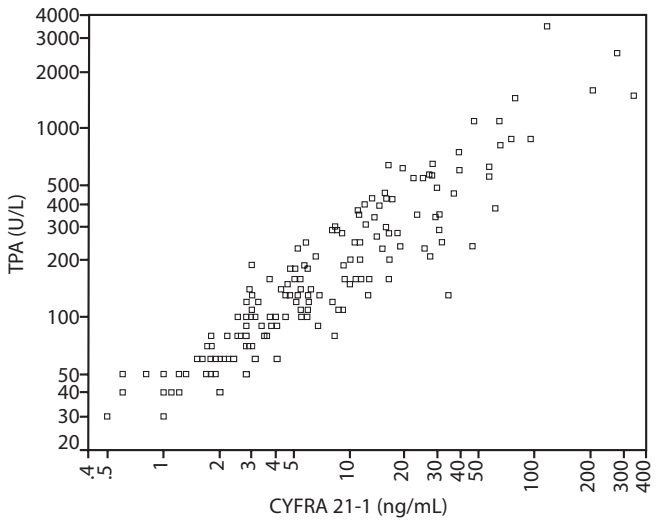
Marker	Cytokeratin 8	18	19
TPA	*	*	*
TPS		*	
CYFRA 21-1			*
TPAcyk	*	*	

Reactivity of commercially available tests for cytokeratins

TPA® in lung cancer

TPA® equals CYFRA 21-1 in lung cancer
The overall sensitivity of TPA in the diagnosis of lung cancer, independent of histotype, is about 70% at 95% specificity level. The sensitivity for non-small cell lung cancer (NSCLC) is about 80%[7, 8]. TPA correlates well with tumour load and the extent of the disease. Furthermore TPA predicts disease progression and is an early indicator of relapse during follow-up in NSCLC. Changes in TPA often precede detection of relapse by conventional methods. Response to treatment can be detected within seven days since the half-life of TPA is less than one day[9].

Fig. 1



Scatter-plot showing pretreatment levels of TPA and CYFRA 21-1, measured, blind of clinical information, in 180 new NSCLC patients (Spearman r coefficient,0.935)

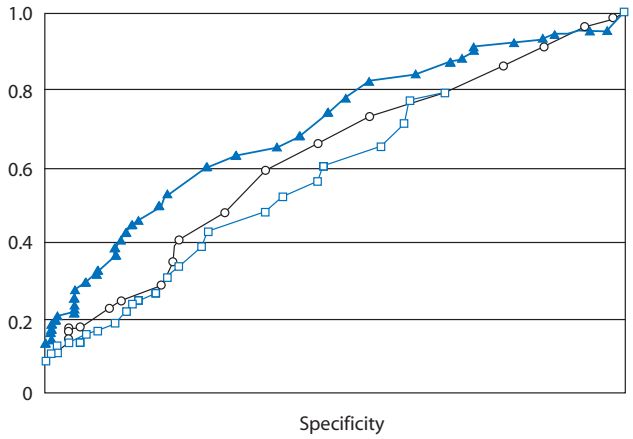
TPA shows an excellent correlation to CYFRA in lung cancer **(Fig. 1)**. Several studies have also demonstrated that TPA and CYFRA show the same clinical sensitivity for lung cancer of different histotypes[10] **(Table 2)**.

Table 2

Tumour marker	Sensitivity (%)					
	SCLC	NSCLC	SCC	AC	ICC	Others
TPA	**27**	**51**	**64**	36	53	44
CYFRA	26	51	68	35	29	44
CEA	28	22	16	31	12	33
NSE	56	25	33	16	24	22
SCC	8	30	45	20	18	11
TPS	17	19	20	18	24	22

Clinical sensitivity at 95% specificity for the most frequently used lung cancer markers related to histology

Fig. 2



Receiver operating characteristic of curves of (–o–) CA 15-3, (–□–) CEA AND (–▲–) TPA. Calculations based on values of the breast cancer group (n = 240) and the control group (n = 86). Area under the ROC curves: CA 15-3 = 0.623; CEA = 0.588; TPA = 0.702

TPA® in breast cancer

TPA and CA 15-3 the ideal combination for monitoring and follow-up of breast cancer

Several studies showed that TPA has the highest sensitivity for breast cancer[11] **(Fig. 2)**. In a recent study different combinations of tumour markers were assayed in all stages of breast cancer. The combination of a tumour marker with high specificity for breast cancer, CA 15-3, with the less specific but highly sensitive TPA increased the sensitivity by approximately 25% at all stages – a greater increase than for any other combinations tested[12].

TPA has been used in the therapeutic monitoring of breast cancer for several decades. A raise in serum TPA values has been shown to precede the clinical symptoms by several months.

The combination of cytokeratin markers and CA 15-3 provides additive diagnostic information. Using changes of marker levels, an increase of > 25% was judged as progressive disease and a decrease of > 50% as tumour response. This demonstrated that the cytokeratin markers are superior to CA 15-3 in follow-up of chemotherapy **(Table 3)**[13]. The combination of CA 15-3 and TPA is therefore a valuable supplement to the conventional methods and the best combination of markers for evaluation of breast cancer patients.

Table 3

Tumour marker	Sensitivity (%)	
	CR, PR	PD
TPS	84	82
TPA	97	82
CA15-3	68	66

Correlation between clinical response according to UICC and tumour marker changes

Conclusions

- TPA® discriminates between localised and metastatic disease
- TPA® values normally decrease in response to successful treatment. If TPA® values remain unaffected or increased, a change of treatment should be considered
- Increased TPA® values during follow-up of treatment may indicate relapse