CO-EXPRESSION PATTERNS OF TUMOR-ASSOCIATED ANTIGEN GENES BY NON-SMALL CELL LUNG CARCINOMAS: IMPLICATIONS FOR IMMUNOTHERAPY [1]

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Despite the fact that tumor-associated antigens (TAAs) have till now been shown to induce T-cell immune responses in cancer patients, the attempted immunotherapeutic protocols utilizing single TAA vaccine formulations provided poor clinical outcomes. Trying to improve the effectiveness of these formulations [2], recent efforts considered the use of several peptides derived from the same or different TAAs.

AIM

This study aimed to investigate whether a gene expression pattern of tumor-associated antigens (TAA) would exist in Caucasian non-small cell lung carcinoma (NSCLC) patients indicating that their use will be most appropriate for the polyvalent vaccination.

MATERIALS

Tissues were obtained from:

- 12 patients diagnosed with adenocarcinoma (ADC)
- 8 patients diagnosed with squamous carcinoma (SCC)
- 3 patients with bronchoalveolar carcinoma (BAC)
- 2 non-neoplastic patients (hamartoma, lung bullae), served as control

METHODS

Tissue samples were homogenised and the mRNA molecules reversely transcribed to cDNA. The expression analysis was perfomed by the use of relative Real-Time reverse-transcription polymerase chain reaction (RT-PCR) or semi-quantitative RT-PCR [3]. All expression values were normalised with respect to the expression levels of a reference gene (calibrator).

A. The following genes were analysed using semi-quantitative RT-PCR:

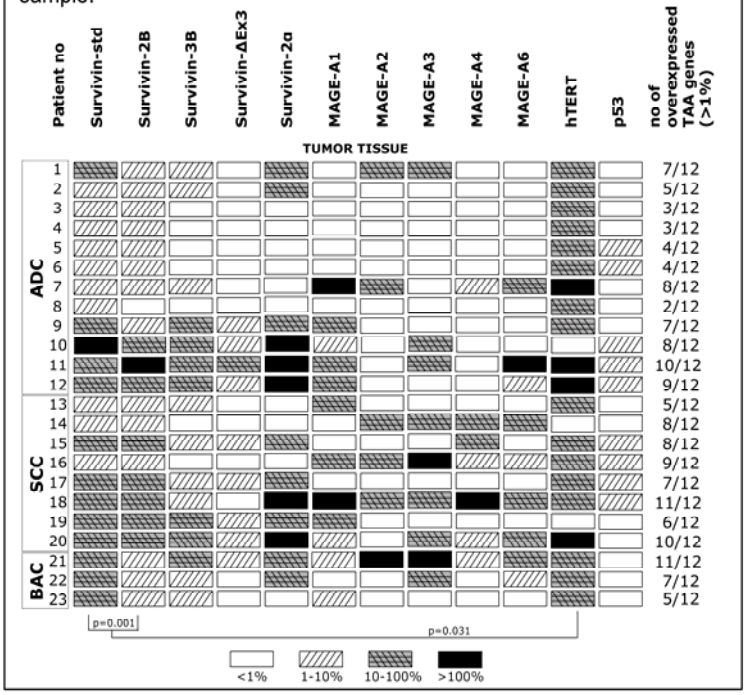
- Survivin-std (standard isoform)
- Survivin-3B
- Survivin-2α
- hTERT
- MAGE-A1
- MAGE-A2
- MAGE-A3
- β-actin (calibrator)

B. The following genes were analysed using relative Real-Time RT-PCR:

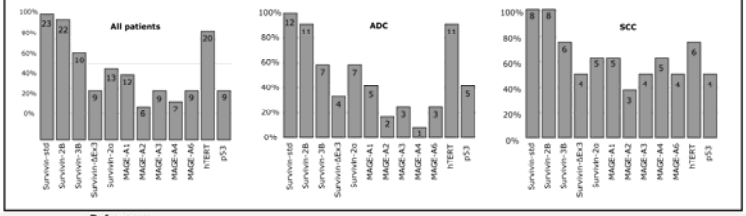
- Survivin-2B
- Survivin-ΔEx3
- p53
- MAGE-A4
- MAGE-A6
- β2-microglobulin (calibrator)

RESULTS

Specific patterns of TAA expression in NSCLC patients. Expression levels (see legend) are presented as a percent expression of a normal testis sample.



Expression frequencies of each TAA, at levels >1% of their expression against the reference testis sample. Within the bars, the absolute number of patients is shown.



mRNA expression levels of the examined TAAs in the tumor samples. (All values are adjusted to the expression of TAAs in a testis sample used as reference)

	All patients (n = 23)	ADC (n = 12)	SCC (n = 8)	BAC (n = 3)
Survivin-std	25.48±34.66	31.19±46.40	13.93±7.05	33.45±19.47
Survivin-2B	17.25±42.51	23.87±58.68	12.82±8.85	2.62±1.83
Survivin-3B	5.65±5.47	5.37±6.34	5.22±5.06	7.92±3.14
Survivin-ΔEx3	3.18±9.53	4.83±13.17	1.70±1.59	0.54±0.41
Survivin-2α	51.07±64.30	53.90±78.82	47.44±50.97	49.41±45.98
MAGE-A1	22.88±41.37	18.07±42.89	36.97±45.50	4.54±4.60
MAGE-A2	19.06±36.40	9.02±25.35	26.70±38.16	38.83±67.26
MAGE-A3	28.00±39.74	11.96±22.59	40.52±48.40	58.80±52.63
MAGE-A4	8.30±29.21	0.17±0.38	22.56±48.14	2.84±4.32
MAGE-A6	11.27±29.12	13.38±39.51	9.88±13.50	6.57±5.84
hTERT	44.42±41.96	47.95±48.87	35.84±37.13	53.14±30.40
p53	1.06±1.14	0.97±0.55	1.39±1.83	0.55±0.21

Correlations of clinical parameters with the expression levels of specific TAAs (TAAs and clinical parameters with statistically not significant correlations were omitted)

	Survivin 2B	Survivin 3B	Survivin ΔEx3	Survivin 2α	MAGE-A1	MAGE-A2	MAGE-A3	MAGE-A4	MAGE-A6	hTERT
All patients										
Age	0.870	0.062	0.530	**0.013**	0.724	0.528	**0.019**	0.090	0.764	0.630
T	0.838	0.256	0.716	0.990	0.087	0.253	0.555	0.782	0.245	**0.017**
Differentiation	0.157	**0.031**	0.319	**0.028**	0.796	0.323	0.503	0.259	0.921	0.412
Tumor size	**0.000**	**0.015**	**0.000**	**0.001**	0.885	0.973	0.191	0.866	**0.000**	0.015
ADC										
T	0.505	0.649	0.463	0.984	**0.004**	**0.040**	0.429	**0.014**	0.199	**0.049**
N	0.957	0.328	0.887	0.947	**0.049**	0.164	0.515	0.084	0.594	0.246
Differentiation	0.854	**0.048**	0.984	0.179	0.815	0.995	0.541	0.987	0.746	0.707
Tumor size	**0.000**	0.176	**0.000**	**0.048**	0.527	0.365	0.630	0.671	**0.001**	0.468

In Caucasian patients with NSCLC the most prevalent TAA expression patterns were those of survivin-std/survivin-2B, survivin-std/survivin-2B/hTERT and survivin-std/survivin-2B/survivin-3B/hTERT observed in 95.5%, 82.5% and 61% of tumor samples respectively.

Compared to ADC, a significantly higher frequency of the co-expression of survivin-std/survivin-2B/MAGE-A4 was found in SCC.

References

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