Identification of Tumor-Associated Autoantibodies in Mesothelioma

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PURPOSE

Malignant pleural mesothelioma (MPM) is a fatal, asbestos-related malignancy arising from the mesothelium, a membrane lining the serosal cavities. A better overall prognosis may be aided by the early identification of such a disease, when the chance of successful treatment may be greater.

A humoral immune response in the form of autoantibodies (AAbs) to tumor-associated antigens (TAAs) has been reported in individuals with evidence of both non-small cell and small cell lung cancer[1-3] compared to at risk controls. Such AAbs have also been described up to 5 years before clinical presentation[4,5].

This study aimed to identify if such AAbs are present in individuals with mesothelioma.

*Early*CDT™-Lung Antigens

Antigen	Role	AAbs reported in:
p53	Tumour suppressor gene	Breast, Lung, CRC, HCC…
SOX2	Onconeuronal antigen	SCLC-PNS
Annexin I	α-phopsholipase	Lung
NY-ESO-1	Cancer-testis antigen	Breast, Lung, Ovarian…
CAGE	Cancer-testis antigen	Lung, Gastric, Pancreatic…
GBU4-5	unknown	Lung

METHODS

Serum from patients with MPM as well as matched normal controls, sera from healthy asbestos-exposed individuals and individuals with asbestos related disease were investigated using the *Early*CDT™-Lung assay.

*Early*CDT™-Lung measures the presence of AAbs to TAAs using a semi-automated enzyme-linked immunosorbent assay[1,2]. The presence of AAbs to mesothelin (a 40kDa mesothelioma-associated antigen) was also investigated.

RESULTS

Raised levels of AAbs were observed, to at least 1 of 7 TAAs, in 13% of individuals with MPM, at a specificity for cancer detection of 92%. Individual sensitivities and specificities of each antigen varied in the panel but raised levels of AAbs were not present to mesothelin when compared to matched control sera.

Elevated levels of AAbs were not seen at higher levels in healthy asbestos exposed individuals (5%) or those individuals with asbestos related diseases (9%) when compared to healthy matched normal controls (8%).

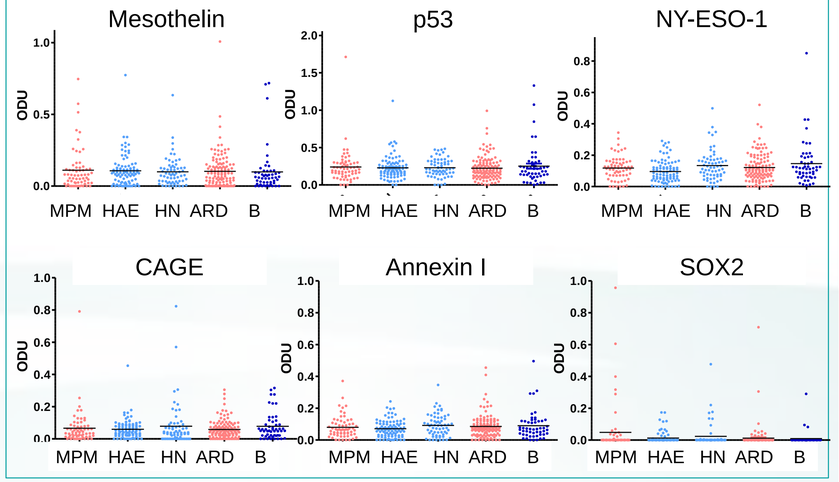
Legend

Group	
Mesothelioma	MPM
Healthy Asbestos Exposed	HAE
Healthy Normal Controls	HN
Asbestos Related Disease	ARD
Benign Lung Disease	B

Chi Squared analysis

Groups	p-value
MPM vs HN	0.38
MPM vs HAE	0.07
MPM vs ARD	0.46
HAE vs HN	0.39
ARD vs HN	0.13

Scatter Plots (OD Values) of AAbs to 6 of the 7 TAAs investigated



Autoantibodies in Mesothelioma and Lung Cancer

Individual and panel percentage positivity (sensitivity) in each patient group shown. Panel: A sample is considered positive when any 1 or more AAb is positive.

	n	p53	SOX2	CAGE	NY-ESO-1	GBU 4-5	Annex I	Meso-thelin	Panel
LCa*	235	11	5	12	12	3	9	ND	**37**
HN-LCa*	235	2	1	2	3	2	5	ND	**10**
SCLC*	243	16	35	7	6	4	2	ND	**51**
HN-SCLC*	243	2	3	2	3	1	2	ND	**10**
MPM	**64**	**3**	**8**	**2**	**0**	**3**	**0**	**0**	**13**
ARD	89	3	2	0	3	2	1	1	**9**
HAE	122	1	0	1	0	2	0	0	**5**
HN-MPM	64	0	2	3	3	0	2	0	**8**

HN-LCa, HN-SCLC and HN-MPM are healthy normal controls matched by age, gender & smoking history to the cancer group. ND: Not done. *Denotes previously published data[2,3]

CONCLUSIONS

Whilst AAbs have been described as being present in 40% of patients with lung cancer of epithelial origin they are only present in 13% of individuals with MPM, at a level not significantly greater than matched normal and at-risk individuals.

The panel of 6 AAbs previously reported[1,2], even with the addition of mesothelin, does not appear to be able to identify individuals with mesothelioma. The main reason is presumed to be the different cell type and etiology of MPM. Further work is required to establish if MPM does induce AAbs to antigens associated with that tumour type.

REFERENCES

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