The Presence of Autoantibodies to Tumour-Associated Antigens can Predate Clinical Diagnosis of Lung Cancer

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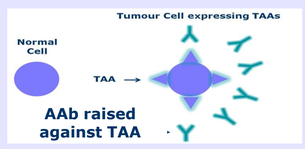
Aim

Autoantibodies (AAbs) to tumour-associated antigens (TAAs) are often described as being present in individuals with cancer [1-4] but there are fewer studies which report AAbs prior to diagnosis.

The presence of AAbs to TAAs in individuals with autoimmune diseases (Rheumatoid arthritis (RA) and Systemic Lupus Erythematosus (SLE)) with and without cancer was investigated.

Background

Mutated, over-expressed, aberrantly expressed or post-translationally modified tumour associated antigens (TAAs) in cancer can often elicit a detectable autoimmune response.



AAbs can provide an *in vivo* amplification of carcinogenesis, in some cases months to years before the tumour becomes otherwise clinically detectable.

AAbs have been reported as being of diagnostic potential in a range of solid tumours.

Autoantibody testing is ideally suited to 'at-risk' groups in the population who are pre-disposed to developing cancer.

SLE is an autoimmune disease which is often characterised by the presence of AAbs to DNA and proteins such as Ro, La and other nuclear antigens, although such individuals are not at an increased risk of developing a cancer (with the exception of non–Hodgkin's lymphoma).

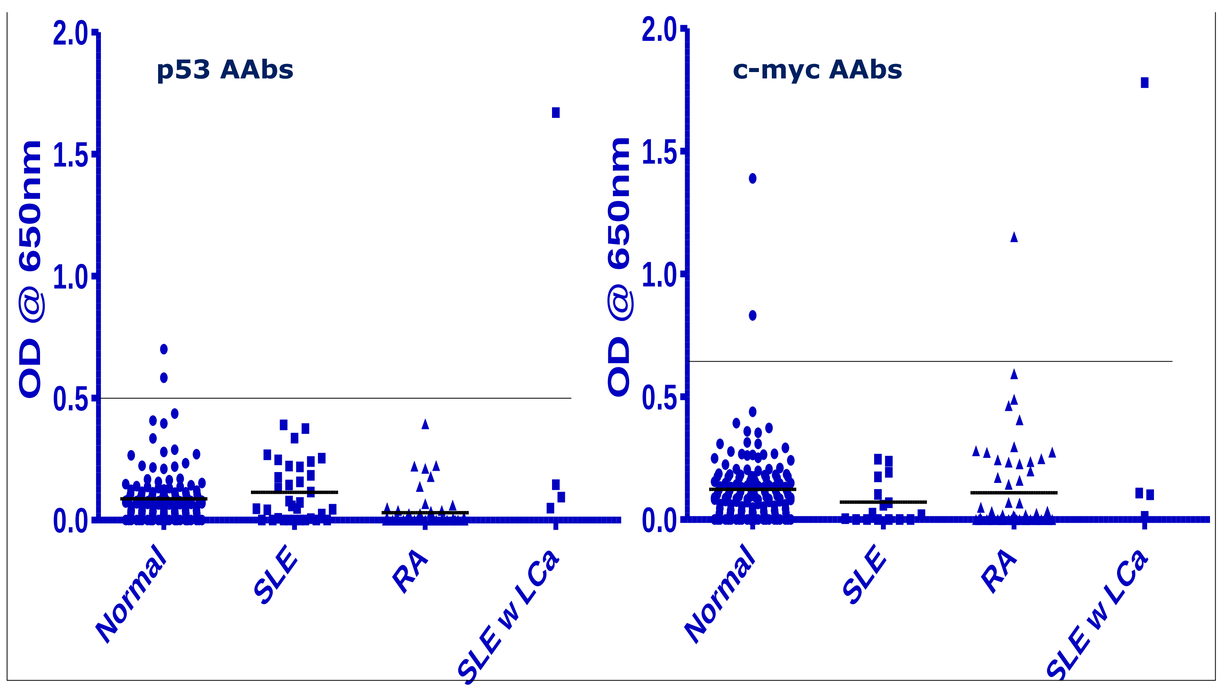
Methods

Recombinant TAAs p53 and c-myc as well as a control protein (VOL) were produced in *E.coli* and purified according to in house protocols. Semi-automated ELISA was used to analyse the IgG AAb response to a titrated concentration range of these antigens.

AAbs were measured in sera from individuals with RA (n=59), with SLE (n=24), with SLE and lung cancer (n=4), and individuals with no evidence of disease (n=146). Serum samples were also available from the 4 individuals with lung cancer up to 10 years before the cancer was diagnosed.

Results

Figure 1. Scatter plots showing AAb responses to p53 and c-myc in normal individuals as well as individuals with SLE, RA, and both SLE and lung cancer



- The specificity was >98% for either p53 or c-myc in the normal cohort
- The positivity in the SLE and RA groups was 0% and 2% respectively

Figure 3. Time course of p53 AAbs in a patient with SLE. LCa developed in 2002.

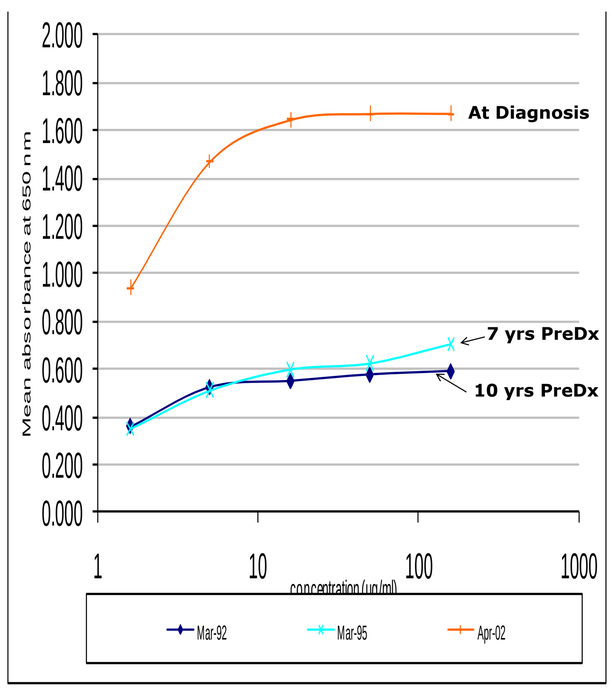
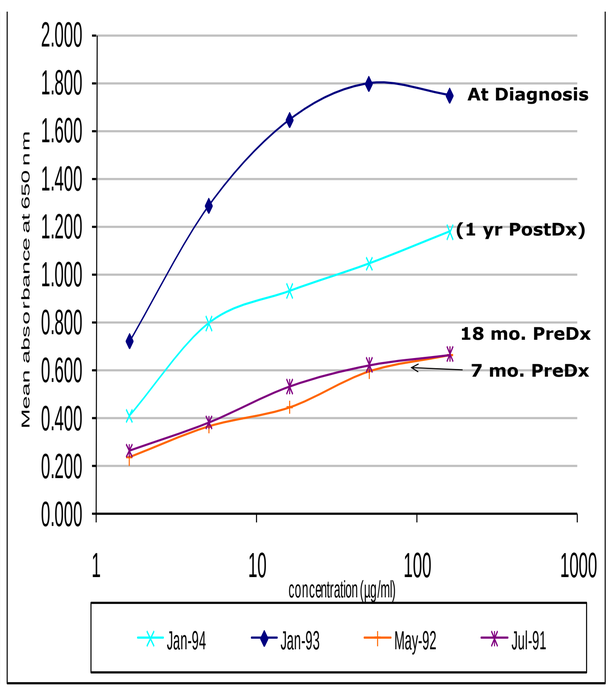


Figure 2. Time course of c-myc AAbs in a patient with SLE. LCa developed in 1993.



- Levels of AAbs were beginning to rise before the clinical diagnosis of lung cancer

- AAbs to p53 or c-myc were present at diagnosis in 50% of the individuals with lung cancer and SLE, but not in the age and SLE matched control sera.
- These antibodies were also detectable in the same individuals 1.5-10 years prior to the diagnosis of cancer, where samples were present.

Discussion and Conclusion

AAbs to TAAs antigens are not present in individuals with RA or SLE at a level higher than in the general population, but exist in some individuals who have a lung cancer and SLE at a frequency similar to that published[3-4].

Where present AAbs to TAAs were also present at a stage before a cancer was confirmed.

It is therefore possible that some individuals with lung cancer are capable of triggering an early measurable autoimmune response to their disease, at a time when the therapeutic options for treatment are greatest.

References

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Acknowledgments

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