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## **Humoral Autoimmunity In Patients With Breast Cancer**

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The objective of the present study was to analyze several parameters of humoral autoimmunity such as ANA, ANNA, anti-p53 and anti-Her-2/neu in patients with breast cancer in early as well as in advanced stages and to correlate the results with established prognostic factors of the disease. In addition, an IFT-method for the detection of anti-p53 autoantibodies in clinical samples was established and compared with several commercially available assays, to investigate a possible bias caused by the assay chosen for the measurement of anti-p53 autoantibodies. Finally, the target antigens of ANAs were examined to identify if the specificities of ANAs in patients with breast cancer are similar to those seen in "classical" autoimmune diseases.

We were not able to detect any positive results in the sera of 154 patients with breast cancer for antineuronal nuclear antibodies. On the basis of these results it appears inappropriate to look for ANNA in all breast cancer patients. However, we would recommend that it should be performed in patients with breast cancer suffering from neurological symptoms, since the detection of ANNA in neurologically symptomatic patients can be taken as a good evidence for an underlying tumor as has previously been reported.

In the IFT for the detection of p53 autoantibodies two cell lines were used - one expressing the p53 antigen and one not expressing the p53 antigen. This approach allowed to draw some conclusions concerning the specificities of the anti-p 53 autoantibodies detected in patients with breast cancer.

Firstly, we could show that high-titer anti-p53 responses could be detected by this approach, and that in the group of IFT-positive sera, the presentation of the p53-antigen in the test was not relevant for the positive result, as demonstrated by positivity of all IFT positive also in both anti-p53 ELISA formats tested. These results mainly argued for conformation independent, linear epitopes on p53. This was an interesting finding, particularly in view of the data describing a lower efficiency of a peptide based screening approach for anti-p53 by comparison to full-length antigen preparations.

Secondly, we were alerted to the fact that there was also a comparatively high rate of other nuclear autoantibodies in this patient group, which were subsequently further investigated.

Thirdly, the comparison of signal intensity of the ANA- and anti-p53 antibodies further highlighted the potential importance of other nuclear antigens: the highest anti-p53 titers detected were in the lower range of the titers of the anti-nuclear antibodies seen in our patient group.

Interestingly, the prevalence of ANA in our study patients was 43% by using a cutoff of 1:80 and 31% by cutoff of 1:160, which was obviously higher than in the healthy population and higher than results reported in previous studies.

The correlation of the results for ANAs with other known prognostic factors in breast cancer indicated that ANAs had no prognostic significance in the study group.

The characterization of ANAs according to their fluorescence patterns identified specificities only in 3 sera. This finding indicated that ANAs found in malignancy are different from classical ANAs found in autoimmune diseases. Analyzing the antibodies profile seen in individual patients showed that ANAs and other tumor specific autoantibodies mostly occurred independently from each other in breast cancer patients. This would support the hypothesis that a far higher rate of tumors is autoimmunogenic than has previously been reported. In the light of these data, more studies should be undertaken to identify new tumor-associated autoantigens, and to further elucidate the induction of autoimmunogenic mechanisms by tumor growth and possibly tumor development. Increasing knowledge about the serologically detectable autoimmune parameters might be a gateway for the identification of tumor specific T lymphocytes, and a possible molecular basis for the development of new immunological therapeutic strategies in a wide variety of human neoplasms.