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Autoantibody detection by arrays

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Keywords

autoantibodies, lupus, rheumatoid arthritis, scleroderma, Sjogren

Context

A wide variety of autoantibodies are of diagnostic importance in rheumatic diseases. In addition to this clinical aspect, autoantibody patterns and their development in early disease help improve our understanding of disease pathogenesis. While microarrays are already widely used for nucleic acid screening, a related technique may be very useful for rapidly detecting multiple autoantibodies with small amounts of serum.

Significant findings

With a robotic arrayer, 1152 feature arrays were fabricated that carried 196 distinct autoantigens in replicate sets on poly-L-lysine coated glass slides. These arrays were tested with well-characterized sera of patients with autoimmune diseases, mixtures of these sera and sera of healthy individuals. The autoantibodies were scanned after being made visible with fluorochrome-labeled secondary reagents specific for different immunoglobulin subclasses. By this approach, antibodies to most autoantigens were detectable, including antibodies to post-translational modifications and to linear peptides, but there were some exceptions (e.g. for Sm proteins). The technique was shown to be specific, more sensitive than ELISA, and capable of quantifying autoantibody concentrations. In an alternative approach, with more technical problems due to staining variations, patient and control sera were directly labeled with the fluorochromes Cy3 and Cy5, respectively, and the resulting color (green, red, or yellow for the addition of both) was assayed, as in other arrays.

Comments

Using tiny amounts (as low as 0.2 ?l) of serum, autoantigen microarrays are a powerful tool to investigate the often complex autoantibody pattern of rheumatic (and other autoimmune) diseases. The authors of this paper mention several possible scientific applications of the new technique, including the assessment of epitope spreading, investigations of the role of immunoglobulin isotypes or testing for novel autoantigens. They also discuss a possible role in clinical decision making through better knowledge of the consequences of different autoantibody patterns, as well as a major role in diagnostic screening. The latter point is of tremendous economic interest. Indeed, such tests may be very helpful if the autoantibody patterns derived distinguish between significant autoantibodies and irrelevant findings. Otherwise, cheap and simple all-antigen testing may increase a present diagnostic problem; if high throughput testing leads to high numbers of false positive results, unacceptable frequencies of additional diagnostic tests could be a costly consequence.

Methods

Roboter-fabricated autoantigen arrays, ELISA

References

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