

## Autoantibodies in Overlapping Systemic Sclerosis and Primary Biliary Cirrhosis Autoimmune Diseases

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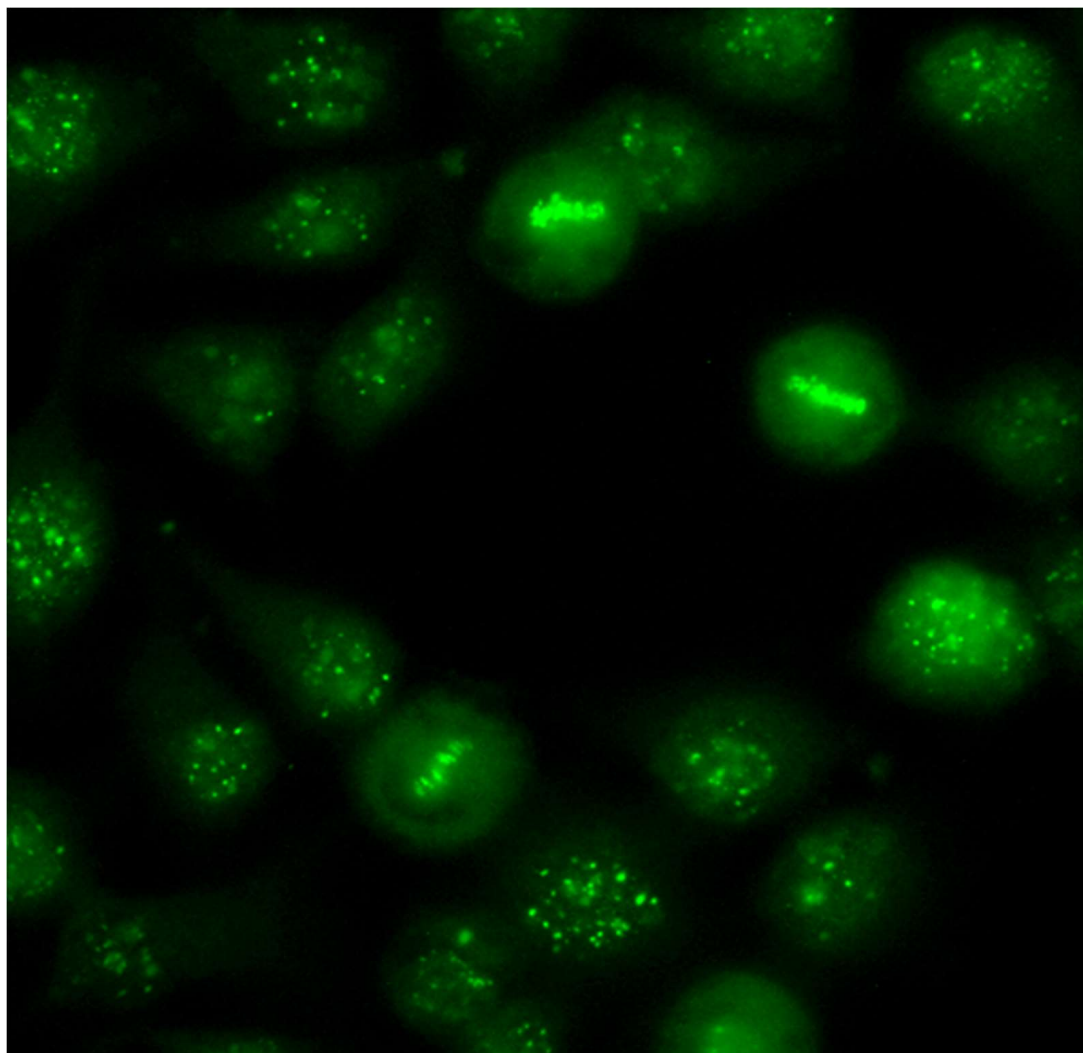
Anticentromere antibodies (ACA) are considered an important diagnostic marker of scleroderma or systemic sclerosis (SSc), being CENP-B the major centromere auto-antigen recognized by sera from SSc patients [1]. However, ACA can also be detected in patients with other connective tissue diseases [2]. Significantly the prevalence of organ-specific antibodies in SSc patients is relatively high [3]. Thus, primary biliary cirrhosis (PBC) is the most frequent autoimmune liver disease described in SSc patients and more often complicated specifically with limited cutaneous SSc (lcSSc) [4]. It is also well recognized that PBC is an overlapping condition between the autoimmune hepatology and rheumatology [5].

In PBC patients anti-mitochondrial auto-antibodies (AMA) are considered a hallmark of the disease and usually occurred in 80-95% of them [6]. In an original report, the AMA and ACA autoantibodies were demonstrated not presented any cross-reactivity between mitochondrial and centromere autoantigens [7]. Both AMA and ACA present discrete autoantibody populations which may coexist in the same patient, although the coexistence of primary biliary cirrhosis and systemic sclerosis is rare [8].

During past years, many studies have described the presence of PBC antibodies in SSc. Illustrative examples of recent studies are: in a large cohort of Italian patients with systemic sclerosis, PBC antibodies were detected in 20% of patients [9]. The prevalence of AMAs was higher in patients with lcSSc than in those with diffuse cutaneous SSc (dcSSc) and is strongly associated with the presence of ACAs. Interestingly, higher prevalence

of both PBC-associated autoantibodies and PBC in the Japanese SSc population was found than in the Caucasian SSc population [10]. In a Belgian population, a wide range of PBC-Ab is detectable in SSc in the absence of cholestatic liver enzyme elevations [11]. Further, auto-antibodies to Nt-CENPB in patients with scleroderma and AMA positive were found in a Spanish population [12], and a recent report in a Moroccan population, SSc patients with positive Nt-CENPB antibodies also showed reactivity against AMA-M2 antibodies [13]. Thus, the co - appearance of anti-centromere antibodies with others in SSc patients at different stages of disease may suggest some putative significance for the evaluation and development of this disorder [14].

Although a significant number of reports in the bibliography suggest that SSc and PBC may have a common immunological or pathophysiological link it needs to be properly investigated [4-7,15]. Testing for autoantibodies against centromeric antigens (Figure 1) and the AMA may help to define the prognosis of both autoimmune disorders. Base for the balance of both types of autoantibodies, a distinct weight could be given to the anti-CENPB and anti-mitochondria specificities in the SS classification criteria and the development of PBC in SSc patients [16,17]. Besides all previous clinical evidences, it remains to be established if AMA could be a serological marker to suspect the occurrence and development of PBC disease in patients with scleroderma. In any case, a large cohort of systemic sclerosis and PBC patients should be studied to establish any significant immunological link between both autoimmune disorders.



**Figure 1:** Immunofluorescence staining of HeLa cells with a human autoimmune ACA serum. Cells were fixed in methanol for 10 min at  $-20^{\circ}\text{C}$ , washed in PBS, stained with ACA serum diluted 1:200 in PBS, followed by anti-human IgG FITC labeled diluted 1:200 in PBS. Both sera incubations were for 30 min at  $37^{\circ}\text{C}$  with 10 min interval washes with PBS. Labeling of centromere regions of interphase and mitotic cells is shown.

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