Autoantibodies to Novel Cytoplasmic Structures (GW bodies) Involved in mRNA Processing

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INTRODUCTION

This particular cytoplasmic discrete speckled pattern [1,2] is quite unique as the structures observed are a new entity named GW bodies (Figure 1), abbreviated GWBs (also known as mammalian P bodies or processing bodies). Functionally, GWBs are involved in the process of RNA interference (RNAi), mRNA degradation and/or mRNA storage. A subset of mRNAs are targeted to these cytoplasmic structures, therefore GWBs play a central role in the cell by influencing the fate of mRNAs. GWBs are ubiquitous and present in many tissues and cell lines as well as normal cells but appear to be more highly expressed in cancer cells such as HEp-2 (laryngeal carcinoma) and HeLa (cervical carcinoma) that are now routinely used to screen human sera for the presence of autoantibodies.

To date, five target autoantigens in GWBs have been published. They include GW182, a unique protein characterized by a numerous glycine (G) and tryptophan (W) repeats[3], Ge-1/hedls [4,5], RAP-55[6], diacyl-phosphatidyl ethanolamine[2], and Su/hAgo2[7].

The clinical diagnosis of patients with autoantibodies to GWBs can be divided into four main groups. In a study from the University of Calgary, the most common diagnosis is Sjögren's syndrome, systemic lupus erythematosus (SLE), and the third group has neurological disease[3]. In another study from Brazil[2] there was no clear cut clinical associations, although 3 patients with SLE were noted, but the majority comprise the fourth category of other conditions[2]. The difference between the clinical profiles in these two centers may be explained on the basis of different clinical referral patterns. For example, in Calgary, serum samples of patients with suspected autoimmune neurological disease (ataxia, motor and sensory neuropathy) are routinely evaluated. Examination of 5000 patient serum samples received during 2000-2001, by ANA at the Mitogen Advanced Diagnostics Laboratory at the University of Calgary, demonstrated that the prevalence

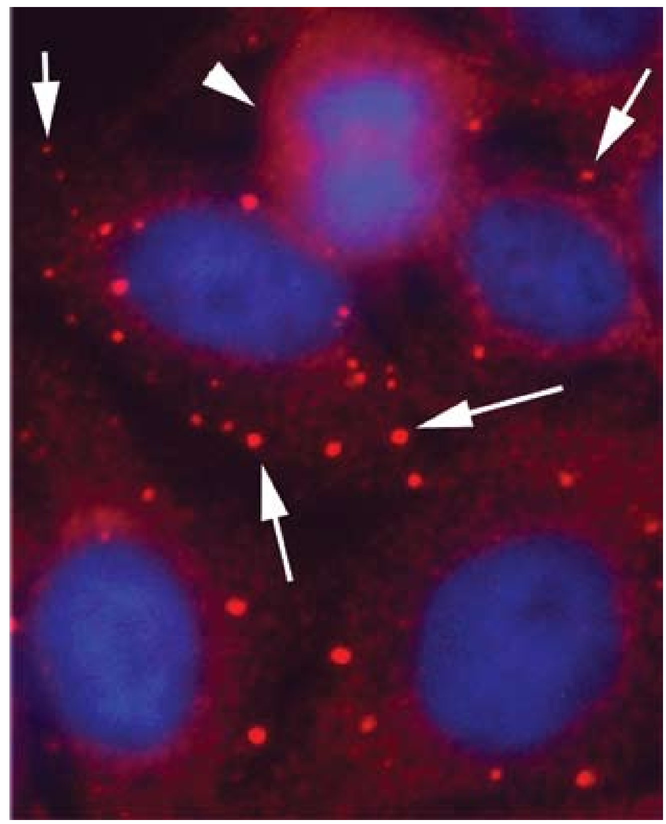

Figura 1 – Hep2000 cells stained with patient serum containing autoantibodies to GWBs (red). The nuclei are stained with DAPI (blue). Arrows are pointing to different sized GWBs while the arrowhead marks a cell undergoing mitosis.

of autoantibodies to GWBs was approximately 0,36%, similar to that observed for anti-Sm antibodies (0,4%), and higher than anti-PCNA antibodies (0,1%)[1]. The specificity of anti-GWB antibodies in the aforementioned diseases, in addition the prognostic, diagnostic value and pathogenic role of these autoantibodies remains to be determined. In addition, autoantibodies to components of the RNA interference and mRNA processing pathway represents an additional unique subset of autoantibodies to a family of macromolecuales characterized as RNA-protein complexes[8].

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