Autoantibodies against Nucleolin

Nucleolin, one of the major and most studied nucleolar proteins, was first described by Orrick *et al.* (1973). In humans it is encoded by the NCL gene. Nucleolin is a nucleolar phosphoprotein implicated in the synthesis, processing, and transport of ribosomal RNA and gene transcription. The association of several structural domains allows the interaction of nucleolin with DNA and RNA sequences and nucleic acid-binding proteins. More precisely, nucleolin has been implicated in chromatin structure, rDNA transcription, rRNA maturation, ribosome assembly, and nucleocytoplasmic transport. Furthermore, it is a target of granzyme A of cytotoxic T cells.

The development of distinct combinations of autoantibodies has been recognized as an important characteristic of certain systemic autoimmune diseases. Nucleolin was identified as an autoantigen in systemic lupus erythematosus (SLE) and certain other systemic autoimmune diseases by Minota *et al.* (1991). Depending on the study, the reported prevalence of autoantibodies in the serum of SLE patients ranges from 17 to 64% (Sherer *et al.*, 2004). A strong association of IgM autoantibodies to nucleolin and histone H1 in the serum of patients with SLE was also shown earlier (Jarjour *et al.*, 1992). SLE is a debilitating and chronic life threatening tissue disease that can virtually affect any organ. Early diagnosis is essential to alleviate the progression of SLE. As reviewed by Sherer at al. (2004), more than 100 autoantibodies have been reported to be associated with SLE making its diagnosis a mosaic of several parameters.

Data recorded in a mouse model indicate that nucleolin is one of the immunodominant molecules that break down self-tolerance and initiate autoantibody-spreading (Hirata *et al.*, 2000). Autoantibodies against DNA, one of the major autoantigens reported to be associated with SLE, occurred almost simultaneously with or after those against nucleolin. The number of antigens reactive with autoantibodies in immunoblots increased gradually with age. Two sets of immunogenic regions at amino acids 314–389 and 387–461 were identified; each contained overlapping discontinuous epitopes and a centrally located RNA recognition motif (Valdez *et al.*, 1995).

Ordering Information		
19700	Nucleolin	0.1 mg
19701		1.0 mg

DIARECT produces nucleolin in the baculovirus/insect cell expression system as a truncated version lacking the N-terminal chromatin/histone-binding domain.

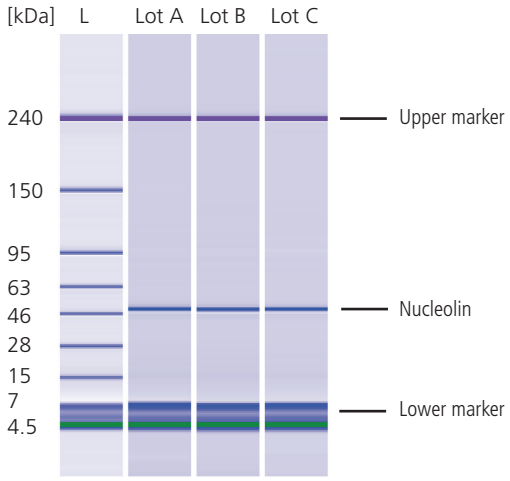

Figure: Electrophoretic analyses of three independent lots (Lot A-C) of recombinant nucleolin. The loading buffer added to the individual protein preparations contained an upper and lower marker. The molecular weight of the protein standards included in the size ladder (L) are indicated on the left.

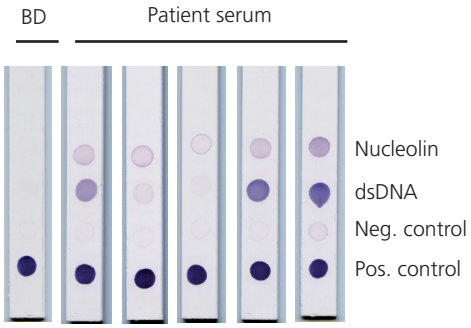

Figure: Immunodot analyses of sera from a blood donor (BD) and patients with presumed systemic lupus erythematosus for autoantibodies against nucleolin and double stranded DNA (dsDNA).

References:
Ginisty *et al.* (1999) J Cell Sci. 112:761-772
Hirata *et al.* (2000) Clin Immunol. 97:50-58
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Orrick *et al.* (1973) PNAS. Sci. USA 70:1316-1320
Sherer *et al.* (2004) Semin Arthritis Rheum. 34:501-537
Srivastava et al. (1999) FASEB J. 13:1911-1922
Valdez *et al.* (1995) Mol. Immunol. 32:1207-1213

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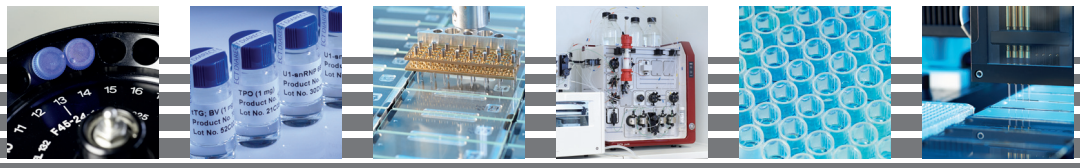

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