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HIGH ANTI-DSDNA CONTENT IN SLE IMMUNE COMPLEXES IS ASSOCIATED WITH CLINICAL REMISSION FOLLOWING BELIMUMAB TREATMENT

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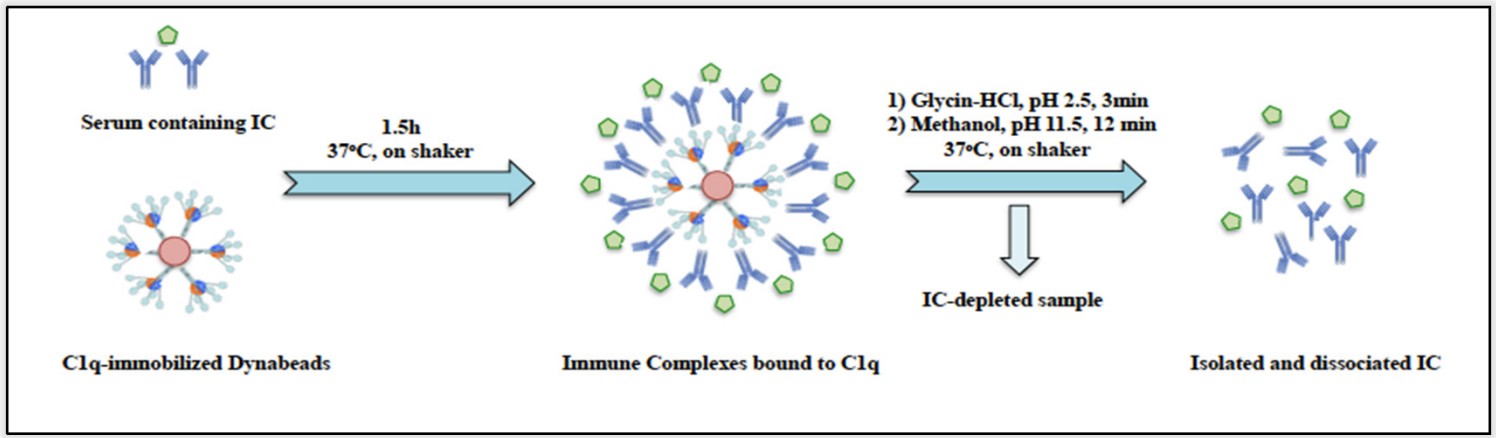
Background:

Systemic lupus erythematosus (SLE) is considered driven by immune complexes (ICs), and autoantibodies are supposed to participate in IC formation.

Thus, the fraction of autoantibodies participating in IC formation merits interest as a diagnostic and/or prognostic marker.

We have developed a technique to quantify autoantibody content in ICs (Sohrabian et al. Ann Rheum Dis 2015;74(Suppl 1):A74).



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Benlysta® (belimumab)

- The first biologic drug approved for treatment of SLE
- IgG1k monoclonal antibody against soluble B L ymphocyte Stimulator (BLyS) a.k.a. B cell Activating Factor (BAFF)
- BLyS/BAFF is implicated in SLE pathogenesis.
- The efficacy of belimumab has been proven in two phase III RCTs (Navarra et al. Lancet 2011; Furie R et al Arthritis Rheum 2011).

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Objective

- To evaluate quantification of autoantibodies in ICs as a measure of disease activity and prognosis for response in belimumab-treated SLE patients.

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Methods:

- 55 patients, 1 year
- Disease activity: SLE Disease Activity Index 2000 (SLEDAI-2K) ≥10, or as low C3/C4.
- Treatment responses: SLE Responder Index (SRI), modified SLEDAI-2K (clinical remission). Low disease activity was recorded as Lupus Low Disease Activity State (LLDAS).
- IC were purified, autoantibody levels determined in serum IC with addressable laser bead immunoassay (FIDIS, Theradiag) :dsDNA, histones, ribosomal P antigen, proliferating cell nuclear antigen (PCNA), SSA/Ro60, SSB/La, SSA/Ro52, Sm, U1RNP and Sm/RNP.

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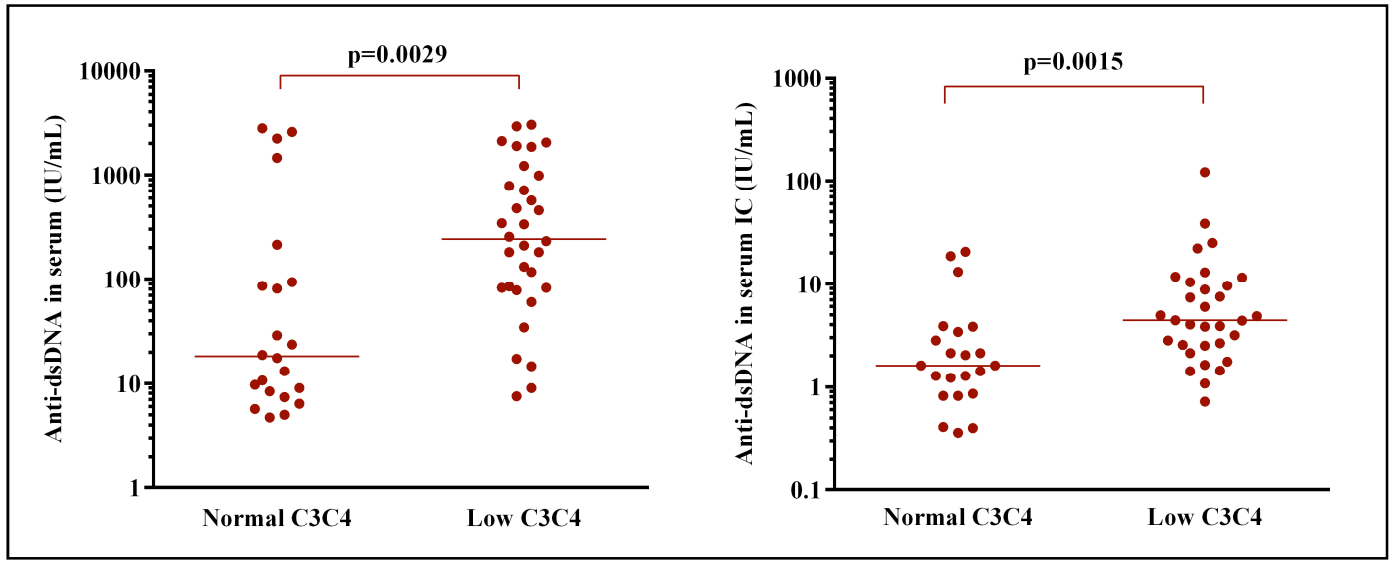
Results, disease activity:

- Antibodies against dsDNA, SSA/Ro60 and Sm/RNP were found in 65%, 54% and 43%, other antibodies with lower percentages.
- Low complement levels were associated with high anti-dsDNA in serum (p=0.0029) and in IC (p=0.0015).



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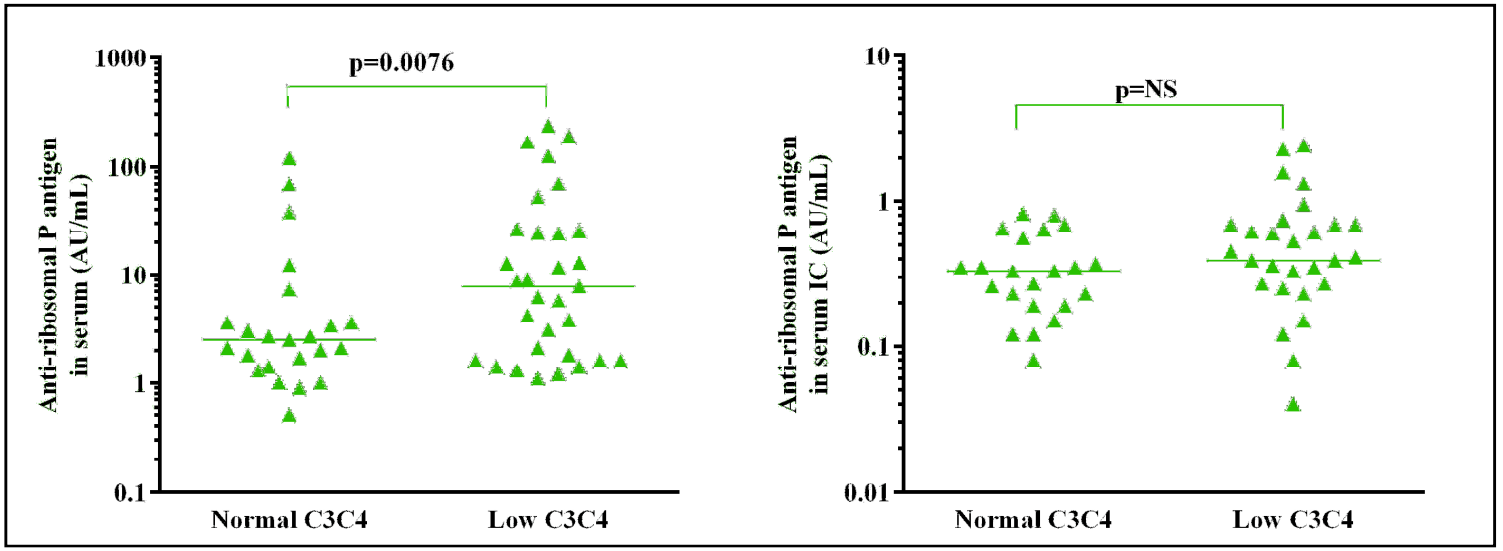
Results, disease activity:

- High anti-ribosomal P antigen levels in serum also associated to low complement, but without any difference in IC levels.



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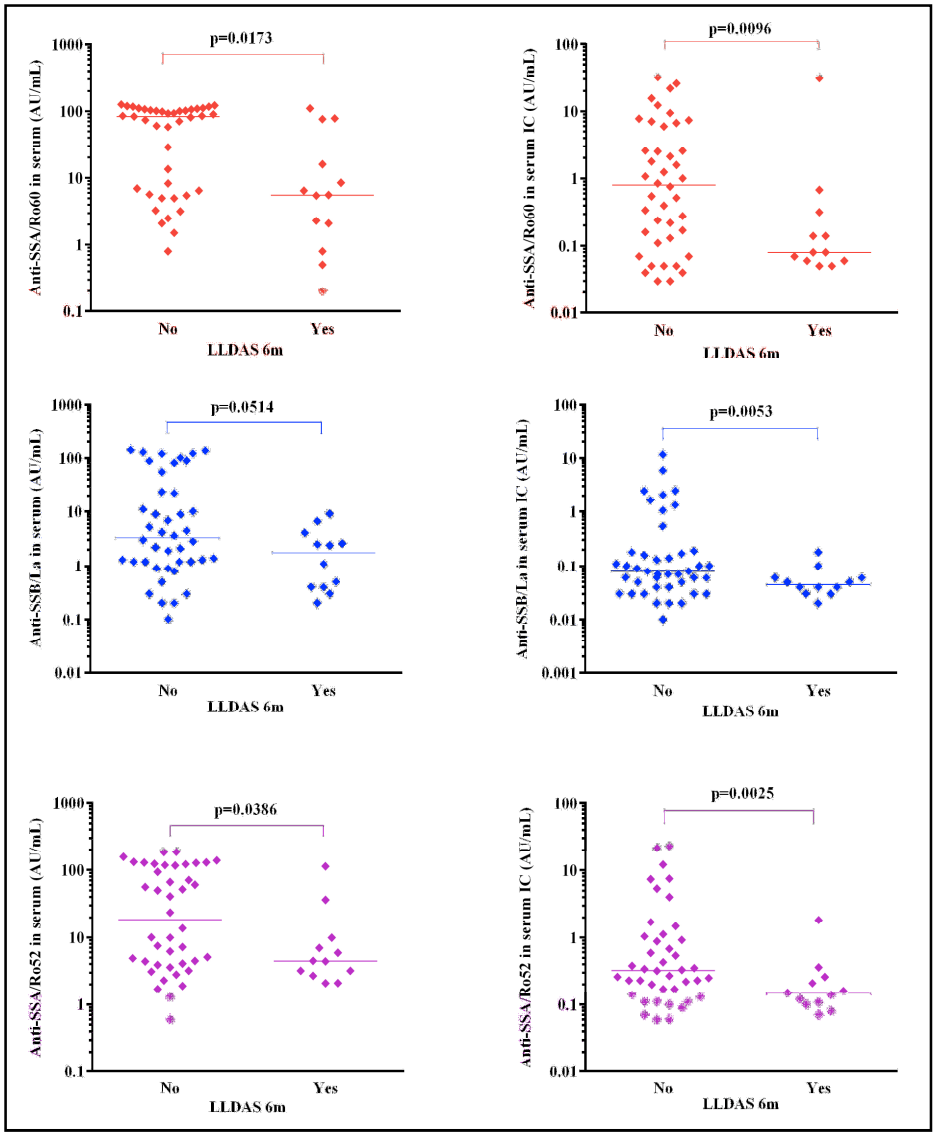
Results treatment responses:

- Baseline serum levels of antibodies against SSA/Ro60, SSB/La and SSA/Ro52 were all lower in patients attaining LLDAS after 6 months; all these associations were stronger for the corresponding IC fractions.



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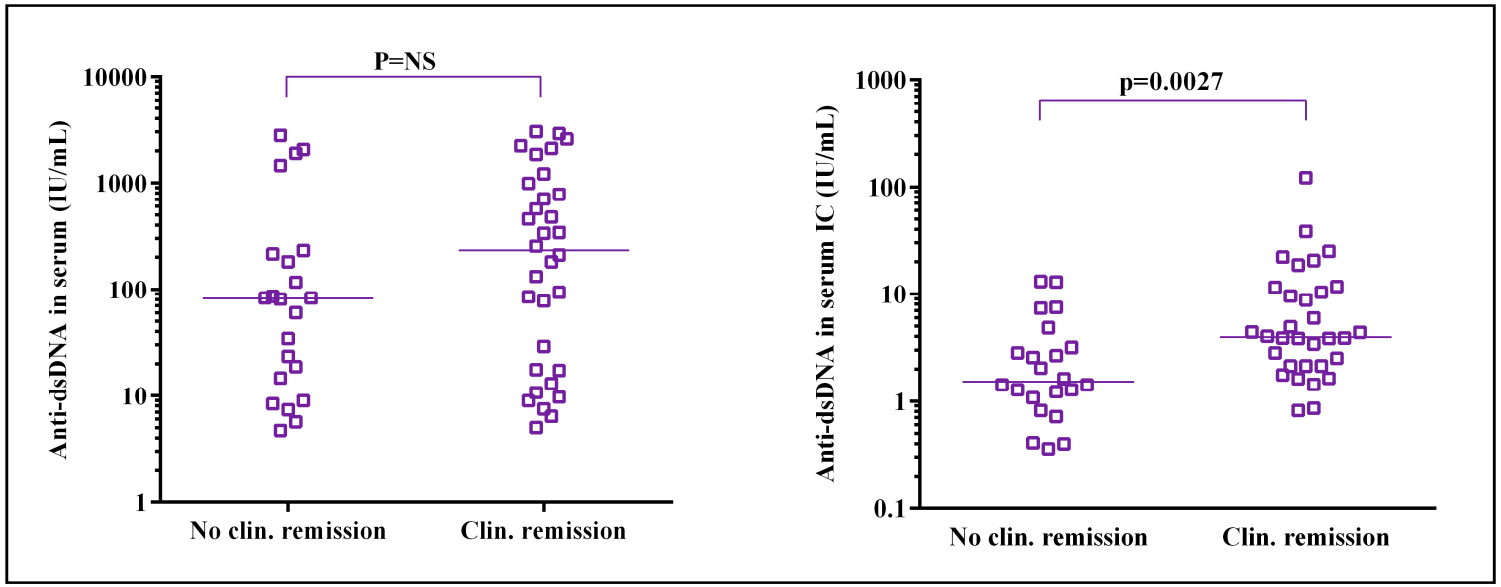
Results, treatment responses:

- Baseline levels of anti-dsDNA and anti-histones in IC associated with clinical remission ever during the follow-up period; no such associations were seen for serum levels.



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Results:

- Low baseline levels of anti-Sm and anti-Sm/RNP in serum but not in IC associated with clinical remission at 6 month ($p=0.0180$ and 0.0403 respectively), and for Sm/RNP also at month 3 ($p=0.0382$).
- Serum levels of all antibodies except SSA/Ro52 declined during the first 6 months, most prominently for dsDNA, histones, ribosomal P, PCNA and Sm/RNP ($p<0.0001$ for all).
- Levels of antibodies in IC declined only for dsDNA ($p=0.048$).

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Conclusions:

- Autoantibody levels in serum and in IC show different associations to disease activity and to treatment responses.
- Whereas IC levels of antibodies against dsDNA and the Ro/La complex seem more closely related to disease activity and/or remission than the corresponding serum levels, the opposite is true for anti-ribosomal P antigen and antibodies against the Sm/RNP complex.
- High baseline anti-dsDNA levels in ICs but not in serum were associated with clinical remission, and anti-dsDNA levels in IC decreased during belimumab treatment.
- The effect of belimumab might primarily relate to autoantibody levels in IC (and not in serum), especially anti-dsDNA.


GOLD HILL
EST. — 1859
ELEV. — 8463
POP. — 118
TOTAL 10440