influence the activity/availability of IKZF3 and promote autoimmunity.

**Funding Source(s):** Versus Arthritis, formerly Arthritis Research UK project grant (20265)

### 241 SINGLE CELL GENOMICS OF SELF-REACTIVE B CELLS REVEALS THE EVOLUTION FROM BENIGN TO PATHOGENIC AUTOANTIBODY AND STRATEGIES FOR EARLY DIAGNOSIS AND PERSONALISED TREATMENT

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10.1136/lupus-2019-lsm.241

**Background** Autoantibodies appear in the serum years before the development of clinical disease in patients ultimately diagnosed with systemic lupus erythematosus (SLE) or Sjögrens syndrome. The transition from benign to pathogenic autoimmunity is not understood. Anti-IgG rheumatoid factors provide an illuminating example of an autoantibody that persists, on average, more than four years prior to the development of systemic vasculitis and type II cryoglobulinemia. The aim of this study was to identify the pathogenic changes occurring in B cells making rheumatoid factor autoantibody during this transition.

**Methods** Massively parallel sequencing of peripheral blood B cell receptors (BCR) was combined with mass spectrometry peptide sequencing of serum rheumatoid factor autoantibodies to identify circulating B cells expressing IgM rheumatoid factor in 4 patients with SLE or Sjögrens syndrome. In a patient presenting with primary Sjögrens syndrome evolving to cutaneous vasculitis, blood samples before and after transition were subjected to single cell analysis of mRNA, genome methylation, and lymphocyte regulatory genes recurrently mutated in lymphoma and leukemia.

**Results** Circulating rheumatoid factor B cell clones and their matched serum autoantibodies were identified in 4 patients, 3 of whom, produced the stereotypic Wa-type rheumatoid factor with IGHV1–69 and IGKV3–20 variable domains. Longitudinal analysis of a patient before and after vasculitis revealed a single Wa-type rogue clone was responsible for the rheumatoid factor over a period of 6 years. Compared to the patients normal memory B cells, the rogue cells had aberrant gene expression corresponding to CD11c+CD21 low B cells observed in autoimmunity, and hypomethylation of gene regions aberrantly hypomethylated in chronic lymphocytic leukemia (CLL). A loss-of-function somatic mutation in a Kelch-like protein gene, KLHL6 identical to recurring CLL and lymphoma mutations was acquired by half of the rheumatoid factor B cells. KLHL6 mutant cells slowly accumulated antibody variable domain replacement mutations that did not alter binding affinity but caused IgM-IgG immune complexes to precipitate at temperatures below 25°C.

**Conclusions** Transition from a benign to pathogenic rheumatoid factor was preceded by a lymphoproliferative disease mutation in the responsible B cells and resulted in accumulation of antibody somatic mutations that diminish immune complex solubility. The ability to detect clones of the rheumatoid factor that are accumulating replacement mutations years prior to the patient developing cryoglobulinemia represents an opportunity to interfere with the conversion from asymptomatic seropositivity to clinical disease.

**Funding Source(s):** Australian National Health and Medical Research Council and New South Wales Department of Health

### 242 ROLE OF STIGMA AND SOCIAL ISOLATION ON DEPRESSION IN PATIENTS WITH CHRONIC CUTANEOUS LUPUS ERYTHEMATOSUS

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10.1136/lupus-2019-lsm.242

**Background** Skin disorders can cause mental health problems associated with stigmatization and social isolation. We found that 26% of individuals with chronic cutaneous lupus erythematosus (CCLE) reported moderate to severe depressive symptoms. While patients perceptions of disrespectful office staff increased the risk of depression, emotional support was associated with a reduction. In this study, we examined the relationships between stigma, social isolation, and depression. We further examined if social isolation mediates the relationship between stigma and depression and whether sociodemographic characteristics may moderate those relationships.

**Methods** We conducted a cross-sectional study in a predominantly African American cohort of patients with primary CCLE from metropolitan Atlanta, Georgia, U.S. Depression, stigma and social isolation were assessed using the NIH PROMIS short forms. Linear and multiple regression were used to examine the relationship between depression, stigma and social isolation. Education attainment, poverty and race were explored as potential moderators.

**Results** Among 118 patients with a documented diagnosis of primary CCLE, 104 (88%) were female, 96 (81%) were African American, 54 (46.2%) completed high school or less, 40 (40.8%) lived in poverty and 34 (28.8%) self-reported moderate to severe depressive symptoms. While patients perceptions of disrespectful office staff increased the risk of depression, emotional support was associated with a reduction. In this study, we examined the relationship between stigma and depression and whether sociodemographic characteristics may moderate those relationships.

**Funding Source(s):** Emory University

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**Abstract 242 Table 1** Multiple linear regression models for predicting depression in CCLE

<table>
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<th>Predictor Variable</th>
<th>β</th>
<th>p-value</th>
<th>β</th>
<th>p-value</th>
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<td>0.08</td>
<td>0.270</td>
<td>0.011</td>
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<tr>
<td>Social isolation</td>
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<td>Education (high school)</td>
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<td>0.004</td>
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</tr>
</tbody>
</table>

*Controlled for age, race, gender and education; **Controlled for age, race and gender.
Abstracts

243 VALIDATION OF PEDANAM AS AN INSTRUMENT OF COGNITIVE EVALUATION IN NEUROPSYCHIATRIC SLE

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10.1136/lupus-2019-lsm.243

Background Translation, validation, and use of a computerized battery for cognitive evaluation of patients with systemic lupus erythematosus (SLE) as part of an investigation of neuropsychiatric manifestations is useful and allows multicenter studies.

Methods This is a quantitative transversal study with control group conducted in pediatric and adult rheumatology clinics. The computer test batteries ANAM (Automated Neuropsychological Assessment Metrics) or PedAnam (Pediatric version) was submitted to the Guidelines for the Process of Cross-Cultural Adaptation. This process has five stages: Initial translation, synthesis of the translations, back translation, harmonization, test of the prefinal version and final version. After the process, we apply the ANAM in 98 SLE patients and healthy age-matched individuals. All individuals underwent an evaluation through the battery tests taking 30 min on average to solve the problems.

Results 98 SLE patients, 69 female and 29 male, ages between 6 and 68 years with mean of 28.6. The control group had 84 people, 73 female and 11 male, ages between 6 and 63 years with mean of 25. For the evaluation was used the Performance Validity Index score, that provides a performance indicator, between 0 and 14, for someone with good effort, or above for someone outside the range of that expected for someone providing good effort. Patients presented an average performance of 8.05, with a minimum of 0 and a maximum of 33, while the control group had a mean of 4.4, minimum 0 and maximum of 27. As the smaller score results in a better effort, it is possible to notice meaningful differences between the groups (p<0.05).

Conclusions Cognitive difficulties are often observed in SLE and practical tools like ANAM and PedAnan should be used to measure the cognitive loss that patients may have; these losses should be monitored more closely if there are other neuropsychiatric symptoms.

Funding Source(s): CNPq CAPES FAPESP

244 POLYMORPHISM OF MICRORNA REGION IN THE TNFA GENE IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2019-lsm.244

Background Studies have implicated microRNAs (miRNAs) in the pathogenesis of systemic lupus erythematosus (SLE). miRNAs regulate approximately 90% of the protein-encoding genes and play a central role in various biological processes, including impairment of cell differentiation and proliferation apoptosis. Polymorphism in miRNA regions of TNFA gene may account for the variations observed in the clinical. The aim of this study was to investigate the presence of polymorphisms of miRNA regions of TNFA gene associated to clinical and laboratory profile of these SLE patients.

Methods Consecutive childhood-onset SLE (cSLE) patients followed at Pediatric Rheumatology Unit of the Unicamp were enrolled in study. Healthy volunteers with were included as control group. A complete clinical, laboratory and neuropsychological was performed in all subjects. cSLE patients were further assessed for clinical and laboratory SLE manifestations, disease activity [SLE Disease Activity Index (SLEDAI)], damage [Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)] and current therapy. Total dose of corticosteroids and other immunosuppressant medications used since the onset of disease were calculated by data obtained by careful review of the medical charts. We investigated miRNA region of the TNFA gene in cSLE compared to healthy volunteers using DNA Sequencing by Capillary Electrophoresis. Data were compared by non-parametric tests.

Results We included 110 cSLE patients [83 women (75.4%)]. The mean disease duration was 13.18±4.32 (1–20 years). We included as a control group 60 healthy individuals [52 women (86.7%)] recruited from the local community. The mean score of cumulative SLEDAI was 2.88 ±2.20 (0.09–12.52). The mean of total corticosteroid dose was 23437.54±16656.55 mg. We identified polymorphism rs3093665 (c.77 A>C) in 8 (7.3%) cSLE patients, polymorphism rs3093666 (c.419 C>T) in 3 (2.7%) patients and polymorphism rs3093667 (c.453 G>T) in 2 (1.8%) cSLE patients. Polymorphism rs3093665 is located in a region of interest, into a miRNA region-binding site of miR-452 and polymorphism rs3093667 into a miRNA