selection. The novel in silico framework identified SLE as a prime potential indication for cenerimod and supported the cenerimod phase 2b clinical trial in patients with SLE (CARE study, NCT03742037).

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THU0009 SYSTEMIC DEREGULATION OF LONG NON-CODING RNAs IN PATIENTS WITH SYSTEMIC SCLEROSIS AND THEIR ASSOCIATION WITH REGULATORS OF FIBROSIS.

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Background: Microvascular dysfunction is one of the major clinical challenges in systemic sclerosis (SSc) and mesenchymal transformation of the major event for microvascular dysfunction. Recent studies have shown epigenetic regulation of long non coding RNAs (lncRs) in different disease pathophysiology.

Objectives: To study the differential expressions of lncRs in patients with SSc and to study their associations with regulatory molecules of fibrosis

Methods: Peripheral Blood were collected from 15 diffused cutaneous SSc patients (dSSc) [ACR, 2013] and 10 age-sexes matched healthy controls. RNA was isolated from the peripheral blood & cDNAs were prepared and the Relative mRNA expressions were measured with respect to an endogenous control gene by real-time PCR. Protein expressions were measured by ELISA.

Results: Increased expression of MEG3, MALAT1 and NEAT1 (3.5, 3, 4fold respectively) has been found in SSc patients with respect to healthy individuals and they are mutually correlated (MEG3 and NEAT1: $r=0.9$, $p<0.0001$; MALAT1 and NEAT1: $r=0.7$, $p<0.0001$; MEG3 and MALAT1 $r=0.7$, $p<0.0001$). The expression of NEAT1 is significantly higher ($p=0.0009$) in case patients with disease duration (DD) >5 years compare to the patients with DD≤5 years. No significant difference was found in the expression of MEG3 and MALAT1 between these two subpopulations. Modified Rodnan's skin score (mRDSS): the clinical parameter of measuring fibrosis, was significantly up regulated ($p=0.004$) in patients with long disease duration (>5 years) and also have a positive correlation with DD ($r=0.2$, $p=0.2$) and the regulatory RNAs: MEG3 ($r=0.4$, $p=0.003$), MALAT1 ($r=0.2$, $p=0.2$), and NEAT1 ($r=0.3$, $p=0.009$).

The master regulator of fibrosis TGFβ which is significantly up regulated at both transcriptional ($p<0.0001$) and translational ($p=0.0009$) level has significant positive correlation with MEG3 ($r=0.3$, $p=0.02$), MALAT1 ($r=0.5$, $p=0.0005$), and NEAT1 ($r=0.3$, $p=0.006$). MEG3, MALAT1 and NEAT1 also have significant high correlation ($r=0.7$, $p<0.0001$; $r=0.6$, $p<0.0001$ and $r=0.7$, $p<0.0001$ respectively) with αSMA: the marker of fibroblast activation and the collagen-I ($r=0.3$, $p=0.03$; $r=0.3$, $p=0.03$ and $r=0.3$, $p=0.03$ respectively).

In multivariate analysis MEG3 and NEAT1 together could explain 37.5% variability of fibrotic marker and NEAT1 alone could explain 35.5% of the same.

Conclusion: mRDSS probably does not reflect the underlying fibrotic process occurring sub-clinically, as no significant correlation was observed either with the disease duration or with the pro-fibrotic molecules (TGFβ, αSMA, and collagen1). The strong inter-correlation of NEAT1, MALAT1 and MEG3 suggest that any one of them might well be studied as specific marker of sub-clinical fibrosis. The long non coding RNAs (MALAT1, MEG3, NEAT1) better reflects the sub-clinical fibrosis occurring in the patients, suggested by strong correlation with fibrotic markers (TGFβ, αSMA, collagen1). The linear regression values suggest that NEAT1 could be an important biomolecule in SSc pathogenesis.

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THU0010 GENES ASSOCIATED WITH NUCLEOTIDE OLIGOMERIZATION DOMAIN-LIKE RECEPTOR SIGNALING PATHWAY ARE UPREGULATED IN CUTANEOUS LUPUS ERYTHEMATOSUS

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Background: Cutaneous Lupus Erythematosus (CLE) is a disfiguring autoimmune skin disorder with several subtypes: discoid lupus, subacute cutaneous lupus, and acute cutaneous lupus. CLE is associated with defects in the adaptive immune system, and, at times, systemic involvement. The innate immune system is likely involved as seen in the presence of interface dermatitis, which is observed in viral exanthems, and improvement of CLE using inhibitors to membrane-bound Pattern Recognition Receptors.

Objectives: Compare the expression of genes associated with the innate immune system in active CLE skin lesions of different subtypes compared to normal skin controls.

Methods: Five datasets selected from the Gene Expression Omnibus (GEO) were analyzed using GEO2R to compare the gene expressions between different subtypes of CLE. Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database, Gene Card, and Kyoto Encyclopedia of Genes and Genomes (KEGG) Pathway analysis were used to identify the interaction and function of specific genes.

Results: There were a total of 147 CLE skin samples and 52 normal controls. Genes associated with the Nucleotide-Binding Oligomerization Domain-Like Receptor (NLR) signaling pathway were upregulated in CLE skin samples (adjusted p-value < 0.001). Five genes associated with the NLR signaling pathway, STAT1, OAS1, OAS2, OAS3, and AIM2, were found to be upregulated in skin samples of CLE patients in all datasets, regardless of type, compared to normal controls in all datasets. These five genes are associated with transcription activation, regulation of viral infection, and interferon response.

Conclusion: Genes associated with the NLR signaling pathway are upregulated in the skin lesions of CLE patients compared to normal controls, supporting the role of the innate immune system in CLE. Further validation studies using experimental methods are needed.

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THU0011 ANALYSIS OF METABOLIC STATUS IN CYBRIDS REVEALED IMPAIRED METABOLIC FLEXIBILITY IN OA PROCESS.

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Background: There are several metabolic pathways involved in cell metabolism, including glycolysis, tricarboxylic acid (TCA) cycle and fatty acid (FA) oxidation. Metabolic flexibility has previously described as the ability to respond or adapt to changes in metabolic demand; assessed by the ability to switch from fat to carbohydrate oxidation. In the last years there is a growing interest to assess the influence of metabolic flexibility, as a mechanism to explain how lipids can accumulate in the tissue. During OA, it has been established a relationship between mitochondrial dysfunction and cellular damage due to impairments in mitochondrial function and metabolic flexibility. Several studies have suggested that fatty acids may play an important role in OA development and progression.

Objectives: The aim of this work was to examine the differences in glucose and fatty acid metabolism, with special focus on metabolic flexibility, in cybrids from healthy (N) or OA donors.