THE JOURNAL OF
Allergy AND Clinical Immunology

VOLUME 139 • NUMBER 2

American Academy of Allergy Asthma & Immunology

AMERICAN ACADEMY OF ALLERGY, ASTHMA & IMMUNOLOGY

2017 AAAAI Annual Meeting

Atlanta, GA

March 3-6, 2017

Program and abstracts of papers to be presented during scientific sessions

Abstract sessions programmed by the AAAAI

663 Neuroinflammatory biomarkers in Chronic Fatigue Syndrome (CFS)

James N. Baraniuk, MD[1], Rakib U. Rayhan, MD, PhD[2], Amber Surian, MS[3], Madison Keefe, BSc[3], Emma Ordway, BSc[4], Flo M. Addiego[3], and Narayan Shivapurkar, PhD[3]; [1]Georgetown University Medical Center, Washington, DC, [2]Howard University, Washington, DC, [3]Georgetown University, Washington, DC, [4]Georgetown, Washington, DC.

RATIONALE: Neuroinflammation provides a unifying mechanism for fatigue, exertional exhaustion, cognitive, sleep, nociceptive (pain, tenderness) and interoceptive (migraine, dyspnea, nonallergic rhinitis, irritable bladder and bowel) dysfunction in CFS. Hypotheses of causation include central sensitization; chronic or noncytolytic neurotrophic infections; autoreactive immune dysfunction with neural targets; brainstem atrophy with autonomic dysfunction; metabolic; mitochondrial and psychosomatic dysfunction.

METHODS: Sedentary control (SC) and CFS subjects were diagnosed by history and physical (1994 CDC criteria) before submaximal bicycle exercise testing on 2 days, fMRI before and after exercise, lumbar puncture, and heart rate variability testing.

RESULTS: Ceiling and floor effects significantly distinguished CFS from SC on SF-36, McGill Pain, Fatigue, depression, anxiety, catastrophizing, and other psychometric instruments. CFS and SC had comparable performance on exercise DAYs 1 and 2 with no incremental deficits in VO2, peak heart rate, or post-exercise fatigue. Cerebrospinal fluid (csf) metabolomes and proteomes showed subtle variations between SC and CFS, but csf and plasma cytokines, and csf microRNA profiles were equivalent. Exercise caused transient postural orthostatic tachycardia in half of CFS, but sympathetic (low frequency) and parasympathetic (high frequency) heart rate variability were not altered. CFS had lower thresholds for pain with normal stimuli such as light (photophobia), sound (phonophobia), hyperventilation (dyspnea), orthostasis (vestibular intolerance), light pressure (systemic hyperalgesia) and nasal irritation (nonallergic rhinopathy).

CONCLUSIONS: Neural mechanisms of central sensitization modulate the amplitude of sensory inputs and enhance conscious perception of nociceptive and interoceptive stimuli. Objective biomarkers and mechanisms remain elusive for explaining the disabling fatigue, exertional exhaustion and cognitive incapacitation. R01NS085131.

664 Yellow Nail Syndrome Associated with Lymphopenia

Pamela P. Tongchinsub, MD; University Of Arizona, Tucson, AZ.

BACKGROUND: Yellow nail syndrome (YNS) is a rare condition of unknown etiology that is characterized by yellow dystrophic nails, lymphedema, and recurring respiratory conditions, including pleural effusions, bronchiectasis, and sinusitis. Despite chronic sinopulmonary manifestations, specific associations with immune dysfunction have not been well-described.

RATIONALE: To present a case of a patient with YNS complicated by recurrent pulmonary effusions and empyema in the setting of marked lymphopenia.

METHODS: A 63 year old male noted a 6 year history of yellow nails, edema, and the onset of pulmonary infections. Immunological evaluation included measurement of serum total lymphocyte count, immunoglobulins, and functional assays.

RESULTS: Complete blood counts revealed absolute lymphopenia since 2012, with range of 200-500 lymphocytes/μL for the past year. Flow cytometry confirmed absolute CD4 count 156 (normal >533/uL), CD8 109 (normal 240-1046/uL), CD19 59 (normal 83-809/ul) and CD16/56 70 (normal 90-571/uL). Lymphocyte mitogen response was impaired. Complement level was normal and HIV screening was negative. Quantitative immunoglobulin levels were within normal limits; IgG1 and IgG2 subclasses were low.

CONCLUSIONS: This case report outlines a patient with YNS and recurrent respiratory infections who was found to have pan-lymphopenia and impaired lymphocyte function. This finding suggests a possible correlation between the chronic sinopulmonary infections characteristic of YNS and immune dysfunction, underscoring the importance of immune evaluation for recurrent infection in this population.

665 Immunophenotype and Subsets of Synoviocytes in Patients with Osteoarthritis

O. V. Degtereva[1], Andrei Hancharou[2], I. U. Ramanava[2], A. U. Duzh[1], and Lawrence M. DuBuske, MD, FAAAAI[3,4]; [1]Belarusian Medical Academy of Post-Graduate Education, Minsk, Belarus, [2]Republican Research and Practical Center for Epidemiology and Microbiology, Minsk, Belarus, [3]George Washington University School of Medicine, Washington, DC, [4]Immunology Research Institute of New England, Gardner, MA.

RATIONALE: Osteoarthritis (OA) is a chronic progressive disease, characterized by degradation of joint cartilage, synovial inflammation and joint dysfunction. Initiation and maintenance of inflammation may be related to fibroblast-like synoviocytes (FLS) and macrophage-like synoviocytes (MLS).

METHODS: Samples of synovial fluid (SF) from 12 patients with the OA (ICD-10 codes: M15, M16 and M17) were assessed for FLS and MLS by flow cytometry. Adherent SF cells were also cultured for 5 days in serum-free media. The immunophenotypes of cells were analyzed.

RESULTS: CD90+CD45- FLS were absent in the specimens. Among CD45+ cells, 26.3% (range 15.4% – 45.2%) expressed CD14. More than 98% of CD14+ cells expressed HLA-DR. The expression of CD16 was greater than 80%, but the number of CD80+ cells did not exceed 10%. Cultured adherent SF cells formed clusters, being polygonal in shape with long processes (median – 78.5 micrometer). No CD90+ cells were identified. More than 98% of cells expressed CD45 and CD14 markers. The immunophenotype of the MLS was typical for the M1-macrophages, with high expression of CD16, CD86, CD284 and HLA-DR, and low expression of CD206. Cells expressed ICAM-1 and VCAM-1 molecules. Expression of CD273 was seen in greater than 70% of cells.

CONCLUSIONS: Absence of FLS in the SF of patients with OA was indicative of the integrity of the synovial membrane. There was polarization of the MLS into the cells with pro-inflammatory function, able to support the inflammatory reaction in OA.

MONDAY

844 Glycerol Monolaurate (GML) Inhibits Human T Cell Signaling, Metabolism, and Function By Disrupting Lipid Dynamics

Michael S. Zhang[1], Aline Sandouk[1], and Jon C. D. Houtman, PhD[2]; [1]University of Iowa, Iowa City, IA, [2]University of Iowa, Iowa City, IA.

RATIONALE: Glycerol Monolaurate (GML) is a naturally occurring fatty acid with potent antimicrobial properties. Interestingly, GML suppresses lymphocyte proliferation and inositol triphosphate production, suggesting that GML has immunomodulatory functions. In this study, we have mechanistically examined if GML affects the signaling, metabolism, and functional output of human primary T cells.

METHODS: Primary human peripheral blood T cells were isolated and expanded from blood cones and treated with GML dissolved in ethanol or ethanol vehicle control. Cytokine production was measured by ELISA. Protein phosphorylation was detected using immunoblotting. Membrane clustering of signaling proteins was imaged using total internal reflection fluorescence microscopy. Flow cytometry assays measuring calcium influx and ordered lipid domains were done by detecting cells stained with the calcium chelator dye, Fluo-4M, and the membrane intercalating dye, Di-4-ANEPPDHQ, respectively. T cell metabolism was assessed using Seahorse XF-96 Extracellular Flux Analyzer.

RESULTS: GML potently altered the lipid order and disorder dynamics in the plasma membrane that resulted in reduced membrane localized clustering of the proteins LAT, PLC-γ, and AKT. Altered membrane signaling events induced decreased phosphorylation of PI3K and AKT as well as abrogated calcium influx. In addition to signaling defects, GML treated cells have profoundly altered metabolism profiles characterized by suppressed oxidative phosphorylation and increased glycolysis. Functionally, GML treatment potently reduced TCR-induced production of the cytokines IL-2, IFN-γ, TNF-α, and IL-10.

CONCLUSIONS: Our data reveal that the widely used anti-microbial agent GML alters the lipid dynamics of human T cells, leading to their defective signaling, metabolism, and function.

845 Mesenchymal Stem Cell Induce Tolerogenic Dendritic cells which Inhibit Proliferation of Autologous T-cells

Andrei Hancharou[1], N. H. Antonevich[1], and Lawrence M. DuBuske, MD, FAAAAI[2,3]; [1]Republican Research and Practical Center for Epidemiology and Microbiology, Minsk, Belarus, [2]George Washington University School of Medicine, Washington, DC, [3]Immunology Research Institute of New England, Gardner, MA.

RATIONALE: Human olfactory epithelium-derived stem cells (hOE-MSC) inhibit proliferation of T-cells and induce a tolerogenic profile of co-cultured dendritic cells (DC). This study assesses the effects of the hOE-MSC-induced DC on proliferation of autologous T-cells.

METHODS: hOE-MSC were generated from 5 patients with non-inflammatory diseases of the nasal cavity. hOE-MSC were CD45-CD90+CD73+CD105+CD31-. Dendritic cells were obtained from blood monocytes. DC were cultured over hOE-MSC monolayer for 3 days. The obtained tolerogenic DC (tDC) were collected and further co-cultured with CFSE-loaded blood T-cells for 3 days with PHA (1ug/mL). The cell proliferation index was assessed.

RESULTS: The obtained hOE-MSC-induced tDC, which were assessed for hOE-MSC contamination, were negative for CD90+ cells (<0.1%). tDC expressed high levels of CD273 and CD85k molecules, indicative of tolerogenic properties. hOE-MSC-induced tDC exerted a strong immunosuppressive effect on autologous T-cells, significantly ($p<0.02$) reducing the proliferation index: T-cells alone – 1.53 (range 1.44-1.56) ; T-cells and immature DC – 1.44 (range 1.32-1.47); T-cells and mature DC – 1.9 (1.87-2.44); and T-cells and tDC – 1.18 (1.13-1.27).

CONCLUSIONS: Generated hOE-MSC-induced tDC have strong immunosuppressive properties making them candidates in treatment of autoimmune diseases.

846 Mavs Mediates a Senescence Associated Secretory Phenotype By Inducing Interferon Beta Expression in Human SLE Bone Marrow Stromal Cells

Richard J. Looney, MD, FAAAAI[1,2], Jennifer Anolik[3], and Lin Gao[3]; [1]University of Rochester School of Medicine and Dentistry, Rochester, NY, [2]University of Rochester, Rochester, NY, [3]University of Rochester School of Medicine and Dentistry, Rochester.

RATIONALE: Bone marrow mesenchymal stromal cells (MSCs) display robust immunomodulatory properties which are impaired in lupus patients, but the underlying mechanisms are unknown. This study was undertaken to address defects in human SLE BM-MSC and the potential role of these defects in SLE pathogenesis.

METHODS: Patients fulfilling SLE classification criteria and healthy controls were recruited under an Institutional Review Board approved protocol (n=6 each). BM-MSCs were isolated with low density Ficoll/Hypaque (1.073 g/mL) and grown in tissue culture. MSC phenotype was verified by flow cytometry. MSCs were studied using immunocytochemistry, real-time PCR, western blotting, comet assay for DNA damage, beta-galactosidase assay, and RNA interference.

RESULTS: SLE BM-MSCs displayed significantly reduced proliferation rate, increased production of reactive oxygen species, increased DNA damage and repair, and senescence associate secretory phenotype (SASP) as evidenced by increased cytokine production. The expression of IFNb was increased 5 folds ($p<0.05$) and genes specifically induced by IFNβ were elevated in SLE MSCs. The expression of immunomodulatory factors was significantly reduced. Level of MAVS, also known as Interferon Beta Promoter Stimulator Protein 1, was positively correlated with the level of IFNb ($r > 0.9$, $p < 0.01$). Silencing MAVs inhibited IFNb expression and rescued the SASP in SLE MSCs.

CONCLUSIONS: SLE BM-MSCs have a senescent phenotype and display impaired immunomodulatory function. This phenotype is dependent on elevated levels of MAVS, an essential component of innate immune responses to cytoplasmic nucleic acids. Thus, a MAVS-IFNb positive feedback loop appears to play a key role in the defects seen in human SLE BM-MSC.