Adipose Tissue, Appetite, and Obesity

CNS, INFLAMMATORY, AND THERMOGENIC INFLUENCES OF BODY WEIGHT

Identification of a Novel Transcriptional Regulator of Metabolic Disease in Circulating and Central Myeloid Cells

David R. Sweet, BS, Neelakantan T. Vasudevan, PhD, Liyan Fan, BS, BA, Chloe E. Booth, BS, Komal S. Keerthy, BS, Mukesh K. Jain, MD.
Case Western Reserve University, University Hospitals Cleveland Medical Center, Cleveland, OH, USA.

OR04-04

Derangement in systemic metabolic homeostasis is tightly associated with widespread activation of resident and circulating immune cells, a phenomenon known as 'metaflammation'. Numerous studies have explored the role of tissue resident and circulating macrophages in contributing to metaflammation, obesity, and their sequelae; however, there is a dearth of information regarding targetable transcriptional regulators of the genesis and persistence of metabolic disease. Here, we identify myeloid Krüppel-like factor 2 (KLF2) as a novel regulator of metabolic disease. Previous reports demonstrate that KLF2 serves as a critical regulator of myeloid cell quiescence and is downregulated in numerous acute and chronic inflammatory states. Specifically in the context of chronic metaflammation, we note that KLF2 expression is decreased in circulating immune cells of obese patients and in adipose tissue macrophages of high fat diet (HFD) fed mice, which is consistent with the hypothesis that KLF2 regulates metaflammation. To explore this further, we utilized mice with myeloid cell-specific deletion of KLF2 (K2KO) which exhibit accelerated obesity and insulin resistance. K2KO mice have widespread central (i.e. CNS) and peripheral metaflammation both in the basal and HFD-stimulated states. To discern whether the effect of myeloid deletion of KLF2 on metabolism is due to deletion in microglia in the feeding centers of the hypothalamus or in peripheral immune cells, bone marrow chimeras with head shielding were created. 50% reconstitution of circulating immune cells with K2KO cells in wildtype (WT) mice was sufficient to maintain the metabolic disease phenotype, while mice with K2KO microglia + WT circulating cells had only slightly improved outcomes compared to K2KO mice. Conversely, ablation of microglia in K2KO mice using PLX5622 formulated in HFD also successfully attenuated the aberrant feeding behavior, weight gain, and glucose dyshomeostasis seen in K2KO mice. Together, these data demonstrate a role for loss of KLF2 in hematopoietic and CNS resident cells in causing metabolic disease. Given that myeloid KLF2 expression decreases under metabolic stress in WT mice and humans, we sought to explore whether maintenance of KLF2 expression in these cells would be protective against diet-induced metabolic disease. Indeed, mice with myeloid-specific overexpression of KLF2 demonstrated a markedly improved metabolic phenotype when challenged with HFD, providing evidence that targeting KLF2 expression in myeloid cells may prove to be a therapeutic option against metaflammation.

Adipose Tissue, Appetite, and Obesity

OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Anthropometric Parameters, Body Fat Percentage and Metabolic Profile in Sarcopenic Women with Recommendation for Bariatric Surgery

Nara Nóbrega Crispim Carvalho, Mrs., MSc[1], Caio Chaves de Holanda Limeira, Mr., Student[2], Heloisa Calegari Borges, Ms., Student[2], Débora Nóbrega Lima, Student[3], Patricia Nunes Mesquita, Mrs, MD[4], Gitana Silva Rego, RN[5], Narriane Chaves Pereira Holanda, Mrs, MSc[5], Vinícius José Baccin Martins, Mr, PhD[5], João Modesto Filho, Mr, PhD[5], Flávia Cristina Fernandes Pimenta, Mrs, PhD[5], José Luiz de Brito Alves, Mr, PhD[5].
[1]Hospital Universitário Lauro Wanderley, João Pessoa, Brazil, [2]Universidade Potiguar, Natal, Brazil, [3]Universidade Federal de Pernambuco, Natal, Brazil, [4]Universidade de Pernambuco, Recife, Brazil, [5]Universidade Federal da Paraíba, João Pessoa, Brazil.

MON-588

INTRODUCTION: Sarcopenia (SARC) is a musculoskeletal disorder that predisposes several complications, including metabolic ones. Obesity also provides higher risk for metabolic complications, however, there is lack of evidences regarding the association of obesity with SARC on metabolic parameters in non-elderly individuals. **OBJECTIVE:** To evaluate anthropometric parameters, body fat percentage (BFP) and metabolic parameters in women with and without SARC preceding Bariatric Surgery (BS). **METHODS:** A cross-sectional study involving 60 obese women in the outpatient care in a public Brazilian University Hospital between March to September 2018. Body composition was given by bio-impedance (inbody-370), multifrequency (5, 50, 250Hz) with 12 hours fasting, dominant Handgrip Strength (HS) was evaluated by Jamar dynamometer (3 measurements; 30 sec interval). Were also evaluated fasting blood glucose, HbA1c, homeostatic model assessment-insulin resistance (HOMA-IR), total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides and high-sensitive C-reactive protein (hs-CRP). SARC was defined by the association of a low muscle mass index (weight-adjusted appendicular skeletal muscle mass: ASMM/weight x 100%) and decreased HS, using as cutoff points the smallest quintile for each variable. Data were expressed as mean ± standard deviation and independent t-test was used for comparison between groups. Statistics were made by SPSS software, 20th version (IBM Corp., Armonk, NY). **RESULTS:** The mean age, weight, body mass index and BFP of sarcopenic and non-sarcopenic women were: 40.75 ± 11 x 39.23 ± 8.92 years old (p=0.665), 102.93 ± 9.58 x 109.19 ± 14.25 Kg (p=0.237), 44.88 ± 2.7 x 42.24 ± 4.79 Kg/m^2 and 54.12 ± 1.11 x 51.44 ± 3.43% (p=0.052), respectively. Regarding the laboratory parameters of women with and without SARC: fasting blood glucose 89.25 ±