protein (CRP). Additionally we aimed to examine whether diet mediates the association between muscle mass and CRP. Methods: In a cross sectional study in 2570 women aged 18-79 years from the TwinsUK cohort, body composition was measured using dual-energy X-ray absorptiometry. Indexes of muscle mass, fat free mass (FFM, kg) and fat free mass index (FFMI – lean mass in kg/height2), were compared between quartiles of the diet scores after adjustment for age, physical activity, smoking, energy intake and total body mass. In a subgroup analysis (1658 women), CRP was measured and the potential attenuation of diet on the relationship between CRP and muscle mass was determined. Ethical approval and informed consent were obtained from all participants. Analyses were performed in STATA version 11.0 (STATA Corp, USA). Results: Mean age was 49.7 years, FFM 39.6 kg, FFMI 15 kg/m2, and CRP 2.49 mg/L. Higher adherence to the three diet scores was positively associated with muscle mass. The magnitude of associations ranged from 1-3% between extreme quartiles of diet scores. Higher CRP levels were also associated with lower indexes of muscle mass with between quintile differences of 2%. The MDS and AHEI scores attenuated the association between muscle mass and CRP by 1-8%. Conclusions: In adult women, a healthier dietary pattern high in fruit and vegetables, whole grains, dietary fiber, nuts and legumes and low in saturated fat and processed meats may be important in reducing the negative impact of CRP levels on muscle mass.

IDENTIFICATION OF GENETIC MARKERS OF SUSCEPTIBILITY TO FRAILTY SYNDROME IN OLDER MEXICAN COMMUNITY-DWELLING ADULTS: PRELIMINARY RESULTS. T.G. Pérez-Suárez, M. Escamilla-Tilch, L.M. Gutiérrez-Robledo, J.A. Ávila-Funes, J.F. Muñoz-Valle, J.R. Padilla-Gutiérrez, N. Torres-Carrillo, N.M. Torres-Carrillo *(Mexico City, Mexico)*

Background: Frailty is a late-life syndrome of unknown etiology, characterized by muscle weakness, weight loss and fatigue. Even though the knowledge of the pathophysiological mechanisms underlying frailty syndrome remains limited, evidence suggests that inflammation has a major role in the pathophysiology of frailty. Taking into account the current knowledge about the biological basis of frailty, we hypothesize that genetic variants within genes that encode for molecules involved in the regulatory patter of the inflammatory response, would associate with frailty syndrome. Methods: Genomic DNA was extracted from the peripheral blood of all subjects (n=630). The genotyping of the variable number of tandem repeat (VNTR) polymorphisms of IL-1RN and IL-4 genes was carried out by the polymerase chain reaction (PCR) technique. The statistical analysis was performed using SPSS v18.0 and Genetic Data Analysis. Results: Mean age was 77.7±6.0 years, 52.5% were women. Prevalence of frailty was 11.6%. Frail subjects were older, had lower MMSE scores, 86.3% had disability for IADL, and 67.6% had disability for ADL. We did not observed a significant difference in the distribution of genotypic frequencies between frail, pre-frail and robust groups for IL-4 and IL-1RN gene polymorphisms ($p>0.05$); but when we compared the allelic frequencies for both polymorphisms, we observed a significant difference for allele A2 of IL-1RN gene polymorphism (frail vs robust; OR 1.84, 95% CI 1.08-3.12, $p=0.02$). Likewise, we analyzed the combined effect of IL-4 and IL-1RN gene polymorphisms and their possible association with frailty, we identified the IL-4low-IL-1RNhigh combined genotype as a haplogroup of risk to frailty syndrome (OR 7.86, 95% CI 1.83-33.69, $p=0.006$). Conclusions: Our results suggest that A2 allele of IL-1RN gen polymorphism and IL-4low-IL-1RNhigh haplogroup are genetic markers of susceptibility to frailty in older Mexican adults. However, further studies are required to evaluate the actual mechanism of these associations in frailty syndrome. Funding: The present study is supported by a grant no. DI-PI-003/2012 to Dra. Nora Magdalena Torres-Carrillo of the National Institute of Geriatrics (Instituto Nacional de Geriatría, México, D.F.)

MITOCHONDRIAL DYSFUNCTION AND MOTOR NEURON DEGENERATION IN SARCOPENIA. K.A. Rygiel, J.P. Grady, D.M. Turnbull *(Newcastle Upon Time, United Kingdom)*

Sarcopenia, a natural age-related process of muscle mass and strength decline, is complex like all ageing phenomena. It appears that both the affected muscle and the nervous system are involved. Evidence supporting denervation has been provided previously and it includes fibre type grouping, angular fibres expressing denervation markers, larger but fewer motor units and reduction in lower motor neuron population (around 30% in human and rodents). We were interested to investigate mechanisms driving motor neuron (MN) degeneration and we hypothesized that one of them could involve mitochondrial dysfunction. We assessed 14 post mortem lumbar spinal cord tissue samples obtained from individuals with no known neuromuscular disease (68-99 years). Histochemical (COX/SDH) analysis revealed only one cytochrome c oxidase-deficient MN throughout the cases. Immunohistochemistry to subunits of mitochondrial respiratory chain complexes demonstrated normal levels of complex II or IV but marked downregulation or absolute loss of complex I subunits in a proportion of cells (around 20 and 10% respectively). This phenomenon was restricted to aged individuals as a similar observation was not made for young controls. Complex I-deficient MNs were laser microdissected (LMD) from the tissue sections and mitochondrial DNA (mtDNA) was analysed. We found a significant reduction in mitochondrial copy number in complex I-deficient MNs versus MNs with maintained complex I expression (P-value = 0.02). Importantly, MNs with complex I-deficiency were significantly smaller than complex I-normal cells (P-value < 0.0001). This study demonstrates that mtDNA copies decrease in MNs with age. Reduction in copy numbers is likely to cause the downregulation of complex I subunits which may further lead to MN size reduction. It is possible that complex I deficiency is an initial step in mitochondrial dysfunction and further accumulation of mtDNA damage over a certain threshold causes the cell to degenerate. This study was supported by the Centre for Brain Ageing and Vitality, Medical Research Council UK

SARCOPENIC OBESITY IN OLDER PERSONS: MODIFICATIONS OF BODY COMPOSITION, MUSCULAR STRENGTH AND PHYSICAL PERFORMANCE DUE TO RESISTANCE TRAINING. K. Stoever, A. Heber, S. Eichberg, W. Zijlstra, K. Brixius *(Cologne, Germany)*

Background: At present, it is unclear whether obese older persons with and without signs of sarcopenia respond differently to resistance training. Therefore, the objective of this study is to investigate the influence of resistance training on physical parameters of obese men with and without sarcopenia. Methods: The participants were 33 physically inactive and obese older men (≥ 65 years, BMI ≥ 30 kg/m2), without diabetes mellitus and other serious diseases. Sarcopenia was assessed using the Short Physical Performance Battery (SPPB), handgrip strength, skeletal muscle index (SMI) by bioelectrical impedance analysis, and gait speed at a 6 meter walkway. Subjects were divided into group 1 (no or presarcopenia, n= 15) or group 2 (sarcopenia, n= 18). Furthermore, the one-repetition maximum (1 RM) and isometric muscular strength were assessed by leg and chest press. The intervention consisted of a progressive resistance training, twice a week for 16 weeks with 80-85% of 1 RM and three sets with 8-12 repetitions. Cohens 'd' was calculated to evaluate effect size of different variables. Results: At baseline, the two groups differed significantly in SMI, SPPB-score, handgrip strength, 1 RM and isometric strength. After training, the results displayed an increase in isometric strength of lower (d=0.73, group 1: 22%, group 2: 34%) and upper limbs (d=0.19, 4%, 6%), the 1 RM at the lower limbs (d=0.73, 18%, 38%) and the upper limbs (d=0.16, 12%, 14%). Also, the SPPB-score (d=0.38, 11%, 15%) and the 6m-gait speed (d=0.4, 5%, 10%) increased. Group 2 was able to increase its right hand grip strength by 12%, whereas group 1 maintained its initial high strength values. SMI remained constant in both groups. Conclusions: Both groups show improvements after the resistance training with slightly more benefits for persons with sarcopenia, but the two groups did not differ significantly after training. Funding: The present study is supported by the German Sport University Cologne.

SUSTAINED ATTENTION CORRELATES WITH TWO MODELS OF FRAILTY AT BASELINE AND FOLLOW-UP: THE IRISH LONGITUDINAL STUDY OF AGEING. A.M. O'Halloran, B.L. King-Kallimanis, M.D.L. O'Connell, I.H. Robertson, R.A. Kenny *(Dublin, Ireland)*

Background: Frail older adults perform poorly on tasks placing high demands on resources of attention, a fundamental aspect of executive function. We investigated the relationships between two models of frailty and sustained attention, at baseline and follow-up, in a cognitively intact cohort of community-living adults aged 50+ years. Methods: 4,229 participants completed a comprehensive health assessment at Wave 1 and home interviews at Waves 1 (2010) and 2 (2012) of The Irish Longitudinal Study on Ageing (TILDA). Frailty index (FI) scores from 0 -1 were calculated from 40 self-report items (Rockwood et al, 2007). The FRAIL scale was also used to defined frailty or pre-frailty as the presence of 3+ or 1–2 items respectively, from fatigue, resistance, ambulation, illness and loss of weight (Morley et al, 2012). Multivariate and multinomial regression analyses computed associations between measures from the Sustained Attention to Response Task (SART) and the frailty models at baseline and at follow-up. Results: Respectively, the prevalence of frailty and pre-frailty increased from 1.1% (FI score: 0.38, ±0.10), and 17.9% (FI score: 0.19, ±0.11) at baseline, to 1.4% (FI score: 0.40, ±0.10), and 18.6% (FI score: 0.19, ±0.11) at follow-up. Declining sustained attention was associated with pre-frailty ($p<0.01$), frailty ($p<0.05$) and higher FI scores ($p<0.01$) in this cohort aged 50 years and older at baseline. This was indexed by slower mean reaction time (RT), greater RT variability, and more SART errors. Correlations between the measures of sustained attention and pre-frailty, frailty and FI scores were strengthened at a follow-up of 2 years. All correlations were adjusted for age, gender and education. Conclusions: Sustained attention is significantly correlated with two models of frailty at baseline and at a follow-up of 2 years, suggesting an objective and modifiable cognitive marker of frailty progression. Funding: The present study is supported by the Department of Health and Children, the Atlantic Philanthropies and Irish Life plc.

INCIDENCE AND PREVALENCE OF SARCOPENIA AND SARCOPENIC OBESITY IN A COHORT OF ELDERLY BRAZILIANS: SABE SURVEY – HEALTH, WELL-BEING AND AGING. M.F.N. Marucci, M.A. Roediger[1], D.R. Bueno[1], L.S. Ferreira[2], L.A. Gobbo[1], Y.A.O. Duarte[1], M.L. Lebrão[1] *(1. São Paulo, Brazil; 2. Rio de Janeiro, Brazil)*

Background: The prevalence of sarcopenia and sarcopenic obesity has increased in elderly, however the knowledge of incidence rate are still scarce. This study verified the incidence and prevalence of sarcopenia and sarcopenic obesity in cohort of elderly in community-dwelling. Methods: It was analyzed elderly (≥ 60 years), of SABE Survey, in 2000 (n=2,143) and 2006 (n=1,115), carried out in the city of São Paulo, Brazil. The analyzed variables were: prevalence in 2000 of sarcopenia and sarcopenic obesity; and incidence in 2006, by gender and age groups (60-74 and ≥ 75). Sarcopenia was identified considering: low performance in the sit and rise from a chair test - S&R (time ≥ 75th percentile); low handgrip strength-HS (≤ 25 percentile); and low muscle mass-MM (≤ 20th percentile), using percentile of this study population; where diagnosed sarcopenic elderly who had both poor performance and low MM or, normal performance, but low HS and MM. It was considered to be Sarcopenic Obese-SO if the elderly, besides having the sarcopenia, showed waist circumference ≥ 80 cm for women and ≥ 94 for men. It was used the Rao & Scott test and software Stata/SE 10.1. Results: In six years of study the incidence rate of sarcopenia and obesity sarcopenic were 12/1.000 person-years (14 for

women and 11/1.000 person-years for men; 11 for 60-74 and 14/1.000 person-years for ≥ 75 years) and 2/1.000 person-years (4 for women and 0/1.000 person-years for men; 0 for 60-74 and 7/1.000 person-years for ≥ 75 years), respectively. The prevalence of sarcopenia and sarcopenic obesity in 2000 was 10% (58% in women and 55% in the age group ≥ 75) and 3% (91% in woman and 71% in the age group ≥ 75), respectively. Conclusion: The incidence and prevalence of sarcopenia and sarcopenic obesity presented different values considering sex and age group. Funding: FAPESP - Foundation for Research Support of the State of São Paulo and CAPES - Coordination for the Improvement of Higher Level

MMP-2 MEDIATED DEGRADATION OF TITIN IN MUSCLE ATROPHY STUDY. S. Sun[1], A. Nedergaard[1], M.A. Karsdal[1], K. Henriksen[1], G. Armbrecht[2], D.L. Belavý[2], J. Rittweger[3], D. Felsenberg[2] *(1. Herlev, Denmark; 2. Berlin, Germany; 3. Cologne, Germany)*

Background: Muscle loss is a problem which is getting increased clinical awareness, as loss of muscle mass and function are important predictors of mortality, morbidity and quality of life. In muscle loss syndromes, there is a pronounced lack of biochemical biomarkers that can predict or monitor pathological progress. In order to identify novel biomarkers of muscle loss, we set out to test if a cleavage fragment of the muscle protein titin identified in urine could be used as such a marker and we raised an antibody and constructed an ELISA assay for serum detection of said fragment. Methods: A competitive ELISA assay measuring the titin fragment was developed. For biological validation of the assay, it was measured in rat tissue extractions and in vitro rat muscle enzymatic cleavage model, in order to characterize how the fragment is produced in vivo. Then the titin degradation marker was validated in a human 56-day bed rest study. Results: The ELISA measuring titin fragment was technically robust and the fragment was shown to be produced by MMP-2 cleavage. This titin-MMP2 degradation fragment had higher expression in rat EDL muscle extraction compared to extractions from soleus and cardiac muscle. In a human bed rest study, the titin-MMP2 fragment was initially decreased about 10% after 1 day of bed rest, and then gradually increased until day 47, up to an average of 17% increase. On the last day of bed rest, the concentration did not significant differ to day 47. Conclusions: We developed an ELISA measuring titin-MMP2 degradation fragment in human serum. We proposed that the titin-MMP2 marker during bed rest process may potentially reflect compensatory mechanisms to the catabolic immobilization stimulus. The gradually increased titin-MMP2 may reflect aspects of the catabolic processes in human long-term bed rest-induced muscle loss.

NEUROPHYSIOLOGICAL DETERMINANTS OF MUSCLE WEAKNESS IN AGING. B.C. Clark, T.D. Law, R.L. Hoffman, J.T. Gau, D.W. Russ *(Athens, USA)*

Background: Muscle weakness predisposes seniors to a 4-fold increase in functional limitations. The potential for age-related degradation in nervous system function to contribute to muscle weakness and physical disability has garnered much interest of late. We have reported that experimentally-induced weakness in young adults results in impairments in voluntary (neural) activation (VA), and that this impairment is associated with increases in indices of motor cortex GABAergic inhibition assessed using transcranial magnetic stimulation (TMS). In this study we tested the hypothesis that weaker seniors have impairments in VA and increases in cortical inhibition. Methods: Young adults (n=46; 21.2±3.4 yrs; 20 women; 23.8±3.7 kg/m2) and seniors (n=42; 70.8±5.9 yrs; 27 women; 24.3±3.4 kg/m2) had their wrist flexion muscle strength quantified along with VA capacity (by comparing voluntary and electrically-evoked forces). Additionally, single-pulse TMS was used measure motor evoked potential (MEP) amplitude and silent period duration during isometric wrist flexion contraction tasks equal to 15% and 30% of strength. Paired-pulse TMS was used to measure intracortical facilitation and short-interval and long-interval intracortical inhibition. Seniors were divided into stronger (top two tertiles) and weaker (bottom tertile) cohorts based on wrist flexion strength relative to body weight. Results: The most novel findings are: 1) weaker seniors exhibit a 20% deficit in VA, which was a significantly greater impairment when compared to the stronger seniors; 2) the weakest tertile of seniors demonstrated ~20% smaller MEPs during the 30% contraction task when compared to the stronger seniors suggesting reduced corticospinal excitability associated with increasing contraction intensity; and 3) the weaker seniors demonstrated nearly 2-fold higher levels of long-interval intracortical inhibition compared to the stronger seniors upon resting conditions. Conclusions: These findings indicate that weaker seniors exhibit significant impairments in voluntary (neural) activation, and that this impairment may be mechanistically associated with increased motor cortex GABAergic inhibition. Funding Source: This work was supported in part by grant R15HD065552 from the National Institutes of Health's Eunice Kennedy Shriver National Institute of Child Health and Human Development to B. C. Clark.

CROSS-SECTIONAL ASSOCIATIONS BETWEEN DIFFERENT MEASURES OF OBESITY AND MUSCLE STRENGTH IN MEN AND WOMEN FROM A BRITISH COHORT STUDY. V.L. Keevil[1], R. Luben[1], N. Dalzell[1], S. Hayat[1], A.A. Sayer[2], N.J. Wareham[1], K.T. Khaw[1] *(1. Cambridge, United Kingdom; 2. Southampton, United Kingdom)*

Background: Obesity is a modifiable risk factor for poor health but its relationship with grip strength, a marker of sarcopenia, has been inconsistently reported. Therefore, we examined the cross-sectional associations between grip strength and both body mass index (BMI), an indicator of total adiposity, and waist circumference (WC), an indicator of central adiposity. Methods: 8,441 community-based participants enrolled in the European Prospective Investigation into Cancer-Norfolk study (aged 48-92 years old) underwent assessment of maximum grip strength (Smedley dynamometer), WC (measured at the natural waist) and BMI (weight/height^2). Associations between grip strength and adiposity measures were explored using linear regression. Analyses were performed separately for men and women and adjusted for age, height, social class, physical activity, co-morbidity, smoking and alcohol intake. Results: Mean BMI was 27.1 kg/m2 (+3.6 kg/m2) for men and 26.6 kg/m2 (+4.8 kg/m2) for women. Grip strength increased across quartiles of BMI. Men and women in the upper quartile of BMI were 2.70kg (95%CI 2.07, 3.33) and 1.46kg (95%CI 1.05, 1.86) stronger respectively than those in the bottom quartile. Grip strength also increased weakly across quartiles of WC. However, including both BMI and WC in the same model (as continuous measures) revealed an inverse association between grip strength and WC, whilst the positive associations with BMI strengthened. For every 10cm increase in WC, grip strength was 3.56kg (95%CI 3.04, 4.08) lower in men and 1.00kg (95%CI 0.74, 1.24) lower in women. Conclusions: Higher WC and lower BMI were associated with lower grip strength. In this context, BMI likely indicates lean mass reserves and WC levels of abdominal fat, the type of fat most associated with the adverse metabolic consequences of obesity. This provides intriguing insights into possible mechanisms linking obesity and sarcopenia and reinforces the need to measure WC in older people with normal or low BMI.

NO PROTECTION OF MUSCLE MITOCHONDRIAL FUNCTION IN ELITE OCTOGENARIAN MASTER ATHLETES. S. Spendiff, M.-E. Filion, G. Gouspillou, K. Wright, M. Vuda, J. Morais, R.T. Hepple, T. Taivassalo *(Montreal, Canada)*

Background: Muscle exhibits a progressive deterioration with advancing age. Clinical impact is most severe in those > 75 y and mitochondrial functional alterations are hypothesized to play a causal role. As such, we reasoned that elite octogenarian Master Athletes (MAs), as individuals who exhibit remarkable physical function at an age typically associated with marked muscle deterioration, would exhibit superior retention of mitochondrial function. Method: 15 elite MAs and 14 age-sex matched non-athlete (NA) controls (≥75years) underwent assessment of thigh muscle cross sectional area (CSA) and a needle biopsy of the vastus lateralis. Mitochondrial respiration, reactive oxygen species emission and calcium retention capacity were assessed in saponin-permeabilized myofibres. Mitochondrial content was assessed by Western blotting for mitochondrial proteins and biochemical measurement of citrate synthase (CS) activity. The combined cytochrome c oxidase/succinate dehydrogenase stain was performed to provide an indication of the number of fibres with severe respiratory chain defects (RCD). Results: MAs had a greater thigh CSA (NAs 89±18 vs MAs 111±33cm2), a lower abundance of fibres with RCD (NAs 5±4.7 vs MAs 2±2.6%) and a greater CS activity (NAs 4±1.5 vs MAs 7±2.5μmol/min/g) when compared to NAs. However, there were no differences in mitochondrial protein contents or in any aspect of mitochondrial function in permeabilized myofibres. Conclusions: Despite the markedly superior physical function and muscle content in elite octogenarian MAs and higher muscle CS activity, this translated only to a reduced abundance of RCD fibres with no other protection of mitochondrial function. Whilst this may be counter to the proposed impact of mitochondrial dysfunction in aging muscle, our analyses cannot rule out whether mitochondria from MAs are more resistant to stressors, which in turn may impart greater resilience in their muscles against age related deterioration. Funding: The present study was supported by operating grants from the Canadian Institutes of Health Research (MOP to R.T.H, MOP to T.T). M.V. is funded by SNSF.

SHORTER TELOMERES IN PERIPHERAL BLOOD LYMPHOCYTES FROM OLDER COMMUNITY-DWELLERS WITH SARCOPENIA. M. Lorenzi, G. Onder, D.L. Vetrano, F. Landi, R. Bernabei, E. Marzetti *(Rome, Italy)*

Background: Telomere shortening in peripheral blood lymphocytes (PBLs) has been associated with chronological age and several disease conditions. However, its association with sarcopenia has never been investigated. The aim of the present study was to determine whether telomeres of PBLs obtained from older community-dwellers with sarcopenia were shorter relative to non-sarcopenic peers. We further explored if PBLs telomere length correlated with muscle mass. Methods: Analyses were conducted in 107 consecutive persons aged > 65 years referred to the outpatient clinic of our Geriatric Center. The presence of sarcopenia was established according to the European Working Group on Sarcopenia in Older People (EWGSOP) criteria, with bioimpedance analysis (BIA) used for muscle mass estimation. Telomere length, defined as Telomere-Single copy gene ratio (T/S), was determined in PBLs by quantitative real-time polymerase chain reaction (PCR). Results: Among 107 outpatients (mean age 75.1 ± 6.6 years, 61.7% women), sarcopenia was diagnosed in 18 individuals (16.8%).PBL telomeres were significant shorter in sarcopenic subjects (T/S = 0.226 ± 0.09) relative to non-sarcopenic individuals (T/S = 0.263 ± 0.20; p = 0.038), independent of age. Age-adjusted linear regression analysis showed a positive correlation between telomere length and muscle mass (Beta = 0.23; 95% CI = 0.72-7.56; p = 0.01). Conclusions: Telomere shortening in PBLs is associated with sarcopenia and correlates with muscle mass in community-dwelling older adults. PBL T/S may therefore serve as a novel biomarker for sarcopenia. Funding: Intramural grant from Catholic University; Centro Studi Achille e Linda Lorenzon

INCIDENCE, RISK FACTORS AND THE PROTECTIVE EFFECT OF HIGH BODY MASS INDEX AGAINST SARCOPENIA IN COMMUNITY-LIVING OLDER CHINESE PEOPLE. R. Yu, M. Wong, J. Leung, J. Lee, T.W. Auyeung, J. Woo *(Hong Kong)*

Background. There are few studies relating to the incidence of sarcopenia. We examined the incidence of sarcopenia and its risk factors over a 4-year period using the European Working Group on Sarcopenia in Older People (EWSOP) criteria. Methods.