the Aβ-expressing strain is a progressive paralysis that can be halted with treatment of known effectors of Alzheimer's disease. As such, we screened our battery of compounds with this strain to determine which compounds have a significant affect on delaying Aβ-associated paralysis. Lastly, using the WormBot's ability to capture video recording, we examine how each compound affects mobility as animals age.

SESSION 835 (POSTER)

BIOLOGY OF AGING IV

EFFECT OF CALORIC RESTRICTION AND RAPAMYCIN ON OVARIAN AGING IN MICE

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The ovarian follicular reserve of primordial follicle declines with aging in female mammals. Caloric restriction (CR) has been shown to increase the preservation of the ovarian follicular reserve. Likewise, rapamycin has similar effects to CR on the ovarian reserve. Therefore, the aim of our study was to evaluate the effects of rapamycin and CR on the metabolism and ovarian follicular reserve and gene expression in mice. Thirty-six female mice were used, and allocated into 3 groups: control, rapamycin (4mg/kg body weight every other day) and 30% CR. At 85 days of treatment, an insulin tolerance test (ITT) and glucose tolerance test (GTT) was performed. At 93 days ovaries were collected for analysis. CR females had lower body weight ($P<0.05$) and were more insulin sensitive ($P=0.003$), while rapamycin treated females did not change body weight ($P>0.05$) and were more resistant to insulin ($P<0.05$). Females from the CR and rapamycin groups had a twice higher number of primordial follicles ($P=0.02$ and 0.04) and half the number of primary, secondary and tertiary follicles ($P<0.05$). Both CR and rapamycin females had increased ovarian gene expression of Foxo3a mRNA ($P<0.05$). In conclusion, female mice from rapamycin and CR groups had an increased ovarian follicular reserve associated to higher expression of Foxo3a mRNA, despite divergent metabolic effects of the treatments.

LATE-LIFE TIME-RESTRICTED FEEDING AND EXERCISE DIFFERENTIALLY ALTER HEALTHSPAN IN OBESITY

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Aging and obesity increase multimorbidity and disability risk, and determining interventions for reversing healthspan decline is a critical public health priority. Exercise and time restricted feeding (TRF) benefit multiple health parameters when initiated in early-life, but their efficacy and safety when initiated at older ages are uncertain. Here, we tested the effects of exercise versus TRF in diet-induced obese, aged mice from 20 to 24 months of age. We characterized healthspan across key domains: body composition, physical, metabolic, and cardiovascular function, activity of daily living (ADL) behavior, and pathology. We demonstrate that both exercise and TRF improved aspects of body composition. Exercise uniquely benefited physical function, and TRF uniquely benefited metabolism, ADL behavior, and circulating indicators of liver pathology. No adverse outcomes were observed in exercised mice, but in contrast, lean mass and cardiovascular maladaptations were observed following TRF. Through a composite index of benefits and risks, we conclude the net healthspan benefits afforded by exercise are more favorable than those of TRF. Extrapolating to obese older adults, exercise is a safe and effective option for healthspan improvement, but additional comprehensive studies are warranted before recommending TRF.

GROWTH DIFFERENTIATION FACTOR 15 IS CORRELATED TO MARKERS OF IMMUNOSENESCENCE IN MONOCYTES

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Immunosenescence is an age-associated decrease in function of immune cells precipitated by a variety of mechanisms and affecting nearly every immune cell subset. In myeloid cell subsets, aging reduces numbers of phagocytes and impairs their functional abilities, including antigen presentation, phagocytosis, and bacterial clearance. Recently, we have described an aging effect on several functions indicating immunosenescence in monocytes, including impaired mitochondrial function and reduced inflammatory cytokine gene expression during stimulation with lipopolysaccharide (LPS). We hypothesized that circulating factors altered by the aging process underly these changes. Growth/differentiation factor-15 (GDF-15) is a distant member of the transforming growth factor-beta superfamily that has known anti-inflammatory effects in macrophages and has recently been shown to be highly differentially expressed during aging. We used biobanked serum and plasma samples to assay circulating GDF-15 levels in subjects from our previous studies and examined correlations between GDF-15 levels and monocyte mitochondrial function and inflammatory responses. Monocyte interleukin-6 production due to LPS stimulation was negatively correlated to plasma GDF-15 levels ($p = 0.046$). Additionally, serum GDF-15 was positively correlated to circulating CD16+ monocyte proportions ($p = 0.021$) and negatively correlated to monocyte mitochondrial respiratory capacity ($p < 0.001$). Therefore, our data suggest that GDF-15 is a potential circulating factor affecting a variety of monocyte functions and promoting monocyte immunosenescence, and thus is an attractive candidate for therapeutic intervention to ameliorate this.

AGE-RELATED DIFFERENCES IN IMMUNO-HEMATOLOGIC PROFILES AND THEIR ASSOCIATION WITH ALL-CAUSE MORTALITY

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Immuno-hematologic function (IHF) is increasingly being recognized as a central component of health status in older age. In this study, we sought to identify homogeneous IHF profiles regarding their relationship to all-cause mortality. We then studied the distribution of these profiles among individuals over age 65. We used data on 30,828 NHANES participants, including 10 baseline complete blood count with differential components [e.g., lymphocytes, leukocytes, red cell distribution width (RDW)] and all-cause mortality. We used latent profile analysis (LPA) to simultaneously optimize intra-cluster homogeneity on CBC components and inter-cluster survival differences. LPA (using MPlus 8.2) allowed for the empirical comparison of different solutions based on goodness-of-fit criteria. After LPA model convergence, a 9-class solution balanced goodness-of-fit criteria and interpretability of the resulting classes. The largest 3 classes accounted for 83.7% of the sample, with classes 1, 2 and 3 comprising 32.1%, 28.6% and 23.6%. Class 2 had lower lymphocytes, monocytes, neutrophils and platelets relative to classes 1 and 3. Survival rates were different between classes 1 and 2 (Cox model hazard ratio, HR=0.85; P=0.012) and 2 vs 3 (HR=1.18; P=0.001). The remaining 6 classes, which generally shared in common characteristics of higher RDW and lower hemoglobin, also were involved with significant survival differences. Multinomial logistic regression revealed that, among the subset of 7,173 participants over 65, older age was significantly associated with membership in class 1 relative to classes 2 (P<0.001) and 3 (P<0.001). These results point toward the possibility of developing immune marker profile indicative of accelerated aging.

EARLY TIME RESTRICTED FEEDING IMPROVES HIGH DENSITY LIPOPROTEIN FUNCTION IN GERIATRIC MONKEYS

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Ageing conveys the greatest risk for cardiovascular disease (CVD) development, which is the dominant cause of mortality in developed nations. High density lipoprotein (HDL) particles mediate reverse cholesterol transport, are anti-inflammatory and their function predicts CVD. We observed lower plasma cholesterol efflux capacity in geriatric vervet monkeys (p=0.03) when consuming either healthy or Western diets. Adult (n=16) and geriatric (n=19) monkeys were stratified into groups fed Western diet on ad libitum (Ad Lib) or early time restricted feeding (eTFR) schedules. eTRF supplied excess food only between 6am to 2pm. Housing, seasonality and fasting conditions for data and sample collections were equivalent. After 6 months, cholesterol efflux to HDL was greater in eTRF monkeys (p=0.01), with no age by group interaction. Efflux media and plasma was chromatographically separated to confirm labelled cholesterol, and enzymatically measured cholesterol, respectively, was affiliated with HDL particles. eTRF monkeys had higher total plasma cholesterol levels (p=0.03) which was due to greater cholesterol amounts associated with only HDL, and resulted in HDL particles that were larger. eTRF resulted in robustly better HDL function such that measures from geriatric individuals were comparable to younger adults. Additionally, no differences in adiposity was observed in eTRF monkeys. Few interventions are known to raise HDL levels, and more importantly, are confirmed to improve HDL function. Our study is to date the largest, longest, controlled eTRF evaluation in primates and we show that positive biological effects are observable in HDL isolated from both adult and geriatric individuals independently of weight change.

DEVELOPING THE COMMON MARMOSET AS A TRANSLATIONAL MODEL OF AGE-RELATED OSTEOARTHRITIS

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Age is a primary risk factor for osteoarthritis (OA). The mechanisms that contribute to OA are poorly understood and disease modifying treatments have not been identified. A critical shortcoming in developing therapies is the limited number of translational models available to identify the causes of naturally occurring OA. Our goal is to use the common marmoset as a non-human primate (NHP) model of age-related OA. NHP are the closest evolutionary relative to humans and share many characteristics of human aging. The marmoset has advantages over other NHP for aging research because of their relatively short maximal lifespan and small size. Micro-computed tomography (uCT) was performed on whole-knee joints obtained from young (10 yrs, n=3) marmosets at necropsy. OA was evaluated using a clinical uCT scoring system and quantitative assessments of subchondral bone structure and ossified meniscal volume. Advancing age was positively correlated to increased uCT OA score (p<0.05, r=0.59), mainly through increased number and size of osteophytes and progressive subchondral bone sclerosis from the medial to both medial and lateral compartments. For marmosets displaying meniscal ossification, older marmosets had greater (p<0.05) ossified meniscal volume than middle-aged and younger marmosets, respectively. Trabecular (p=0.05) and cortical bone thickness (p<0.05) were also lower in older marmosets. These data are the first to indicate that the marmoset develops naturally occurring, age-related OA and support the pursuit of additional studies using the marmoset to identify OA mechanisms and test potential interventions.

LIFETIME EXERCISE ATTENUATES AGE- AND WESTERN DIET-RELATED DECLINES IN PHYSICAL FUNCTION IN MICE

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Aging is associated with progressive declines in physical function. However, it is unknown if consumption of a western-style diet (WD; high-fat and sucrose, low fiber),