

genotype phase. Our analysis showed that somatic mCAs increase with older age up to approximately 102 years, but the prevalence of the subjects with mCAs tend to decrease after that age, thus suggesting that accumulation of mCAs is less prevalent in long-lived individuals. We also used Poisson regression to show that centenarians and their offspring tend to accumulate less mCA (RR = 0.63, p=0.045) compared to the controls.

#### IMMUNE CELL AND ADIPOSE GENE EXPRESSION REPROGRAMMING IN JUVENILE MONKEYS BORN TO HEALTH AND WEIGHT-DIVERSE MOTHERS

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Over 93 million Americans are obese and 66 million suffer from metabolic disease. Roughly 40% of obese people do not have metabolic abnormalities (metabolically health obese [MHO]), while approximately 15% of lean do (metabolically unhealthy lean [MUL]). African green monkeys (AGMs) demonstrate naturally occurring obesity and metabolic syndrome (MetS) without diet manipulation, and MetS criteria are heritable. Age-matched maternal AGMs were classified by adjusted MetS criteria ([n=44]; waist >40cm, fasting glucose (FG) >100 mg/dL, SBP/DBP >135/85mmHg, and HDL-c <50mg/dL) and classified as metabolically healthy lean (MHL), MHO, MUL or metabolically unhealthy obese (MUO). Age, weight and sex-matched pre-pubertal juvenile offspring from these mothers were additionally selected (n=9-11/group; ages=1.1-3.4years) for evaluation. We assessed monocyte subtypes by flow cytometry, and subcutaneous adipose gene expression patterns by RNAseq. Non-classical monocytes were increased in obese and unhealthy mothers (MHO p=0.02, MUL p=0.003, MUO p=0.00002) compared to MHL. MUL and MUO juvenile offspring also had more non-classical monocytes compared to MHL (p=0.05 and p=0.07). Monocyte chemoattractant protein-1 (MCP)-1 was measured in plasma and found to be elevated in MUO juveniles (p=0.02). Patterns of increased cytokine and extracellular matrix gene expression were seen in MUL and MUO juveniles' adipose (6-7/group), mirroring obese and unhealthy mothers' adipose gene expression patterns. Maternal health and obesity influence offspring immune cells and adipose gene expression prior to weight gain and metabolic disease onset. Our data underscore maternal monocyte and adipose profiles as inherited phenotypes that present prior to adipose expansion and may be targets to improve intergenerational health trajectories.

#### THE ROLE OF THE HUMAN IMMUNE SYSTEM IN THE AGING PROCESS: A MATHEMATICAL MODEL OF CELL AND CYTOKINE ACTIVATION

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The role of the human immune system as a factor in the aging process has led to extensive research in the field of infection biology and bioinformatics. Cell-based mathematical models have previously been used to simulate the immune system in response to pathogens. A variety of cells, such as activated and resting macrophages, plasma cells, antibodies, helper T cells, T-lymphocytes, and B-lymphocytes, have already been simulated by mathematical models. This work aims to incorporate cytokines in these mathematical models to create a more comprehensive simulation that can predict cytokine levels in response to a Gram-positive bacterium, *S. aureus*. To accomplish this, the cytokines Tumor Necrosis Factor Alpha (TNF- $\alpha$ ), Interleukin 6 (IL-6), Interleukin 8 (IL-8), and Interleukin 10 (IL-10) were studied to quantify the relationship between cytokine release from macrophages and the concentration of the pathogen, *S. aureus* ex vivo. The results of the simulation were compared to ex vivo human whole blood data to test its accuracy. The future expansion of this model may provide a clearer image of the various interactions within the immune system and this improved model of the immune system may also facilitate a better understanding of the mechanisms that lead to the degradation of the immune system during the aging process.

### Session 9105 (Poster)

#### Biology of Aging: Interventions

##### 3-HYDROXYANTHRANILIC ACID ADMINISTRATION DID NOT PREVENT AGE RELATED BONE LOSS

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Aging is associated with accumulation of various tryptophan degradation products that may having either bone anabolic or catabolic effects. In epidemiologic studies, elevated levels of 3-hydroxyanthranilic acid (3-HAA) are associated with a higher bone mineral density (BMD). We have previously shown that the C57BL/6 mouse loses bone mass with age. Thus, we hypothesized that administering 3-HAA via a daily intraperitoneal (IP) injection would result in preserved or increased BMD. In an IACUC-approved protocol, we injected 26-month-old C57BL/6 mice with either a low dose (0.5 mg) or high dose (5 mg) of 3-HAA IP five days a week for eight weeks. At the end of this time mice were sacrificed and body composition and bone mineral density measured by DigiMus. BMD was significantly lower in the high dose 3-HAA group: 0.0570 + 0.004 vs 0.0473 + 0.006 vs 0.0432 + 0.0075 gm/cm<sup>2</sup>, (means+SD, Control vs 0.5 mg 3HAA vs 5 mg 3HAA, p=0.004, 0 vs 5.0 mg, n=6-9/group). 3-HAA had no significant impact on body composition (lean body mass: 86.7 + 1.7% vs 86.2 + 2.7% vs 86.1 + 2.0%, Control vs 0.5 mg vs 5.0 mg 3-HAA, p=ns; and fat mass 12.6 + 2.0% vs 13.8 + 2.7% vs 13.9 + 2.0% vs 0.2%,