ABSTRACT

Title of dissertation: DOES THE ALPHA-ACTININ-3 (*ACTN3*) POLYMORPHISM INFLUENCE KNEE EXTENSOR PEAK POWER RESPONSE TO STRENGTH TRAINING IN OLDER ADULTS?

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Recent reports suggest that a polymorphism of the alpha-actinin-3 gene (*ACTN3*) is associated with muscle power. Homozygosity for the R577X single nucleotide polymorphism (SNP) at the ACTN-3 gene locus results in the absence of ACTN-3 expression. To examine the influence of this polymorphism on baseline peak power (PP) and PP changes with strength training (ST), we studied 53 older men (64 (9) yr) and 65 older women (65 (9) yr) before and after a 10-week single leg knee extension strength training (ST) program. At baseline, when men and women were combined, the XX group had a relative PP (tested at 70% of 1 RM) that was 36 ± 17 watts (W) higher than the RR group (279 ± 12 W, $P < 0.05$), and the RX group was 43 ± 17 W higher than the RR group ($P < 0.05$), when age and sex differences were used as covariates. As a result of the ST program, change in absolute PP in the RR group was significantly higher than in the XX group (48 ± 7 W vs. 26 ± 7 W, $P < 0.05$), when the data were adjusted for age,

sex, and changes in the untrained leg. Separate analyses by sex found that in women the XX group had a significantly higher baseline absolute PP than the RR (240 ± 11 W vs. 208 ± 9 W) and RX groups (240 ± 11 W vs. 208 ± 10 W, both $P < 0.05$), when age and baseline fat-free mass were covaried. The change in absolute PP in the RR group was significantly higher than in the XX group (63 ± 14 W vs. 25 ± 9 W**,** $P < 0.05$) with ST in men, when the data were adjusted for age and changes in the untrained leg. There were no differences among genotype groups in women for change in absolute PP. These results suggest that the *ACTN3* R577X polymorphism may influence peak power at baseline and in response to ST in older adults, but this relationship is strongly dependent on the sex of the group studied.

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INTRODUCTION

The loss of muscle mass, strength, and power with advanced age (sarcopenia) is associated with dysfunction and poor health status in older adults (140, 141). For this reason, interventions designed to prevent and treat of sarcopenia should positively affect muscle mass, strength, and power without adverse side effects. The administration of growth hormone and testosterone have been recommended for this, but the efficacy and untoward side effects of these agents have been questioned (18). Therefore, strength training (ST) is becoming the intervention of choice for sarcopenia due to the substantial evidence for its efficacy and safety (77, 148). However, muscle mass and strength responses to ST vary widely even among people of similar characteristics performing the same training program (26, 81).

ST-induced changes in peak power and movement velocity are also highly variable in older adults. For example, we have recently observed changes in peak power with ST of the knee extensors for men and women ranging from – 19 to 126 W at the same absolute resistance, and peak movement velocity changes ranging from -1.1 to 2.7 rad/sec at the same absolute resistance (37). Additionally, in a previous investigation from our laboratory, we found considerable inter-individual variability in muscle quality (MQ, strength per unit of muscle) (81). These large inter-individual differences among older men and women, along with the fact that twin studies suggest that a major portion of the variance in skeletal muscle phenotypes can be accounted for by heredity (6), suggest that genetic factors may explain a large portion of these inter-individual differences in responses to ST. However, polymorphisms within specific genes that could potentially explain the genetic differences between responders and non-responders

to a ST intervention have not been clearly identified. Obtaining this information would have important clinical implications because it could aid in identifying the optimal manner of stratifying ST to those who benefit the most and least in each component (muscle mass, strength, and muscle power) of sarcopenia.

Recent reports have suggested that a polymorphism of the alpha-actinin-3 gene (*ACTN3*) may be associated with muscle power and may at least partially explain the inter-individual variability in power (198). Alpha-actinins (ACTN) are cytoskeletal proteins that are encoded by the spectrin superfamily genes and are present in both non-muscle and muscle tissues. They are the primary constituent of the Z-disks in skeletal and cardiac muscle (39). The function of ACTN heterodimers is to cross-link and bind with actin, along with preserving a spatial association among myofilaments (119). While ACTN-2 expression occurs in all skeletal muscle fiber types, ACTN-3 expression is restricted to type 2 fibers (131).

A single nucleotide polymorphism (SNP) has been identified in exon 16 of the ACTN-3 gene and is associated with a complete absence of ACTN-3 protein (131). This SNP is a C to T transition at position 1,747, which causes a change in the 577 amino acid residue from arginine, resulting in a premature stop codon (R577X) (131). Homozygosity of 577X results in an absence of ACTN-3 protein, although the individuals affected appear phenotypically normal. Approximately 19% of Caucasians are ACTN-3 deficient, indicating that this SNP is a common polymorphism among this racial group (119). The absence of ACTN-3 due to the X-allele of the R577X SNP has raised questions regarding its potential effects on muscle function and athletic performance. In this regard, recent cross-sectional data suggest that a deficiency of

ACTN-3 is associated with an enhancement of athletic power performance (202). Elite power athletes, such as sprinters, have a significantly lower X-allele frequency than other types of athletes or controls (129, 198). Recent ST data with younger adults showed that women who are X homozygotes have lower baseline isometric arm strength compared to heterozygotes, but had significantly greater increases in strength compared to heterozygotes, and displayed additive effects when all three groups were compared (31). However, we are not aware of any information available on the influence of the *ACTN3* R577X polymorphism on peak power and peak movement velocity responses to ST in older adults. These components of sarcopenia may be even more important than strength for influencing functional abilities in the elderly (34). Therefore, the purpose of this study was to determine the influence of the *ACTN3* R577X polymorphism peak muscle power at baseline and in response to ST in older adults. We hypothesize that women X homozygotes will have lower knee extensor absolute peak power at baseline when compared to the RR and RX genotype groups, but the increase in absolute peak power with ST will be greater in the X homozygotes than in the RR and RX genotype groups.

METHODS

Subjects. One-hundred fifty-one relatively healthy, inactive, Caucasian men and women volunteers between the ages of 50 and 85 yrs were recruited as subjects in this study. All subjects underwent a phone-screening interview, received medical clearance from their primary care physician and completed a detailed medical history prior to participating in this study. All subjects were nonsmokers, and were free of significant cardiovascular, metabolic, or musculoskeletal disorders that would affect their ability to safely perform heavy resistance exercise. Subjects who were already taking medications

for at least three weeks prior to the start of the study were permitted into the study as long as they did not change medications or dosages at any time throughout the study. After all methods and procedures were explained, subjects read and signed a written consent form, which was approved by the Institutional Review Board of the University of Maryland, College Park. All subjects were continually reminded throughout the study not to alter their regular physical activity levels or dietary habits for the duration of the investigation, and body weight was measured weekly throughout the study to help confirm compliance to maintaining a stable diet.

Genotyping. Genomic DNA, isolated from white blood cells, was prepared from EDTA-anticoagulated whole blood samples by standard salting-out procedures (Puregene DNA Extraction, Gentra Systems Inc.). Genotyping for the *ACTN3* R577X polymorphism was carried out following the procedures described by Mills et al. (119). Briefly, DNA was amplified via polymerase chain reaction (PCR) using flanking primers designed specifically for the R577X polymorphism. A restriction fragment length polymorphism (RFLP) procedure was used to identify genotypes for each subject at this locus. PCR was performed by 40 cycles of denaturation at 94°C for 30 sec, annealing at 58°C for 30 sec, and extension at 72°C for 30 sec, and a final extension step of 72°C for 5 min. The amplified fragment subsequently underwent digestion by *Dde* I. Agarose gel electrophoresis was then performed using a 3% gel at 150V. Digested products were stained with ethidium bromide, and then examined under UV light for genotype identification.

Body Composition Assessment. Body composition was estimated by dual-energy x-ray absorptiometry (DXA) using the fan-beam technology (model QDR 4500A,

Hologic, Waltham, MA). A total body scan was performed at baseline and again after the ST program. A standardized procedure for patient positioning and utilization of the QDR software was used. Total body fat-free mass (FFM), fat mass, and % fat were analyzed using Hologic version 8.21 software for tissue area assessment. Total body FFM is defined as lean soft tissue mass plus total body bone mineral content (BMC). The coefficients of variation (CV) for all DXA measures of body composition were calculated from repeated scans of 10 subjects who were scanned three consecutive times with repositioning. The CV was 0.6 % for FFM and 1.0% for % fat. The scanner was calibrated daily against a spine calibration block and step phantom block supplied by the manufacturer. In addition, a whole body phantom was scanned weekly to assess any machine drift over time.

Body weight was measured to the nearest 0.01 kg with subjects dressed in medical scrubs, and height was measured to the nearest 0.1 cm using a stadiometer (Harpenden, Holtain, Wales, UK). Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared.

Muscular Strength. One-repetition maximum (1 RM) strength tests were assessed on the knee extension exercise before and after the ST program using an air-powered resistance machine (Keiser Sports/Health Equip. Co., Inc., Fresno, CA). This exercise was chosen because it could easily be tested in a standardized way using objective criteria. The 1 RM test was defined as the maximal resistance that could be moved through the full range of motion with proper form one time. Approximately the same number of trials (6-8) and the same rest periods between trials (~ 1 min) were used to reach the 1 RM after training as before training. Before the regular ST program, 1 RM

testing, and power testing were performed, subjects underwent at least two familiarization sessions in which the participants completed the training program exercises with little or no resistance and were instructed on proper warm-up, stretching and exercise techniques. These low-resistance training sessions were conducted in order to familiarize the subjects with the equipment, to help control for the large 1 RM strength gains that commonly result from skill (motor learning) acquisition during the initial stages of training, and to help prevent injuries and reduce muscle soreness following the strength testing protocol. The same investigator conducted strength tests for each subject both before and after training using standardized procedures with consistency of seat adjustment, body position, and level of vocal encouragement. When appropriate, straps and/or belts were used to stabilize the subject so that recruitment of outside muscle groups was minimized. The 1 RM was achieved by gradually increasing the resistance from an estimated sub-maximal load after each successful exercise repetition until the maximal load was obtained.

Muscle Volume. To quantify quadriceps muscle volume (MV), computed tomography (CT) imaging of the trained and untrained thighs was performed (GE Lightspeed Qxi, General Electric, Milwaukee) at baseline and during the last weeks of the 10-week unilateral ST program. Axial sections of both thighs were obtained starting at the most distal point of the ischial tuberosity down to the most proximal part of the patella while subjects were in a supine position. Measurements of MV in the untrained leg served as a control for seasonal, methodological, and biological variation of MV, by comparing the changes in the control leg to the training-induced changes in the trained leg. This also has the advantage over using a separate group of subjects as controls, by

controlling for attention effects and genetic differences between treatment and control groups. Section thickness was fixed at 10 mm, with 40 mm separating each section, based on previous work in our laboratory by Tracy et al. (177). Quadriceps MV was estimated based on using a 4 cm interval between the center of each section. Each CT image was obtained at 120 kVp with the scanning time set of 1 s at 40 mA. A 48-cm field of view and a 512 X 512 matrix were used to obtain a pixel resolution of 0.94 mm. Two technicians performed analyses of all images for each subject using Medical Image Processing, Analysis, and Visualization (MIPAV) software (NIH, Bethesda). Briefly, for each axial section, the cross-sectional area (CSA) of the quadriceps muscle group was manually outlined as a region of interest. The quadriceps CSA was manually outlined in every 10 mm axial image from the first section closest to the superior border of the patella to a point where the quadriceps muscle group was no longer reliably distinguishable from the adductor and hip flexor groups. The same number of sections proximal from the patella were measured for a particular subject before and after training, to ensure within subject measurement replication. Investigators were blinded to subject identification, date of scan, and training status, for both baseline and after training analysis. Repeated measurement coefficient of variation were calculated for each investigator based on repeated measures of selected axial sections of one subject on two separate days. Average intra-investigator CV was 1.7% and 2.3% for investigator one and two respectively. The average inter-investigator CV was < 4.3%. Final MV was calculated using the truncated cone formula as reported by Tracy et al. (177) and described by Ross et al. (147).

Peak Muscle Power. Determination of peak knee extensor peak power and movement velocity were performed on a customized Keiser pneumatic resistance knee extension (K410) machine (Keiser Sports/Health Equip. Co., Inc., Fresno, CA), specifically designed for muscle power assessment. The K410 machine was equipped with load cell force transducers and position sensors to detect rotary motion at the joint. The K410 hardware was connected to a PC and used an industrial data collection expansion card to digitize data at 400 times $\cdot$ s^{-1} from the force sensors and position sensors. This speed was configured and set by the K410 software. Movement velocity assessment was derived from a crystal oscillator on the data collection board.

Prior to testing, seated blood pressure was measured after five minutes of rest, and then a one-minute warm-up was performed on a stationary cycle ergometer. Subjects were then positioned on the K410 with the medial condyle aligned with the axis of rotation of the machine arm. Subjects were instructed to cross their arms across their chest, and a seat belt attached to the machine was then securely fastened around the waist to help isolate the knee extensor muscle group. Subjects were instructed to perform a knee extension with each leg unilaterally at a resistance of ~ 30% of their measured 1 RM and at ~ 50% of their maximal velocity, as a warm-up trial. Following a 30 s rest period, subjects performed three power tests on each leg alternating between right and left at 50%, 60%, and 70% of their 1 RM, with a 30 s rest period between each of the three trials and 2 min rest periods between each increase in resistance. The tester offered standardized oral encouragement to each subject to extend his or her knee as quickly and forcefully as possible during each trial. The highest peak power value of the three trials for each % of 1 RM and the highest (peak) movement velocity attained during this same

trial was selected. Although peak movement velocity was selected from the same test trial as peak power, it was measured separately from peak power as the highest velocity obtained during the trial, independent of where peak power was obtained. The entire procedure was repeated 48-72 h later and the peak power values at each resistance level for both baseline tests was averaged in an effort to establish a more stable baseline assessment. This test was repeated during the last week of the 10-week unilateral ST program for the after ST test. During this latter test, an attempt was made to find a load that could be replicated from baseline testing that represented 50% or 60% of the after ST 1 RM for testing at the same absolute load. When a replicable load could not be found that fell at one of these relative loads (i.e., 50% or 60% of the after ST 1 RM), the load that was used at 50% of the baseline 1 RM value was used for the after ST same absolute load (regardless of the % of after ST 1 RM that the load represents) during the after ST test. The 70% of the after ST 1 RM was compared to 70% of 1 RM at baseline for assessing the effects of training on peak power and movement velocity at the same relative load. This relative load was chosen because it is the approximate load where the highest peak power was found at baseline and after training in our pilot data and from another investigation (34, 49). Data for each repetition was passed through a zero-phase forward and reverse digital filter designed using MatLab version 6.0.5 (Math Works Inc., Natick, MA) to remove sensor noise prior to determining the peak power and movement velocity. A low-pass, 10^{th} order Butterworth filter with a cutoff frequency of 10 Hz was used. A simple point-to-point search of the power and movement velocity data was conducted to determine the peaks because the resulting power and movement velocity curves were unimodal throughout a single repetition. The power machine was calibrated

daily against a standardized weight supplied by the manufacturer. The CV for the force and machine arm position were calculated from ~ 35 calibration data points, measured at evenly spaced time intervals during the duration of the study. The CVs were < 5% for force at all positions and for both the right and left sides.

Training Program. The training program consisted of unilateral (one-legged) training of the knee extensors of the right leg, three times per week, for ~ 10 weeks. Training was performed on a Keiser A-300 air powered leg extension machine. It allowed ease of changing the resistance without interrupting the cadence of the exercise. The untrained control leg was kept in a relaxed position throughout the training program.

Subjects warmed-up on a bicycle ergometer for approximately two minutes prior to each training session. Following the two familiarization training sessions previously described, the training consisted of five sets of knee extension exercise for those < 75 yrs of age and four sets for those ≥ 75 yrs of age. We did not have those ≥ 75 perform the last set because of our concern that performing 50 repetitions at near maximal effort for this age group might have caused overtraining, which has been shown to result in a reduction in strength gains with training (133). The protocol was designed to include a combination of heavy resistance and high volume exercise. The first set was considered warm-up and consisted of five repetitions at 50% of the 1 RM strength value. The second set consisted of five repetitions at the current 5 RM value, which was initially estimated based on our previous data showing that it corresponds to ~ 85% of 1 RM in most people. Adjustments were made as needed during each training session so that the resistance used resulted in failure to complete a 6^{th} repetition. The 5 RM value was increased continually throughout the training program to reflect increases in strength

levels. The first four or five repetitions of the third set were performed at the current 5 RM value, then the resistance was lowered just enough to complete one or two more repetitions before reaching muscular fatigue. This process was repeated until a total of 10 repetitions were completed. This same procedure was used in the fourth and fifth sets, but the total number of repetitions was increased in each set to 15 and 20 reps, respectively. This procedure allowed subjects to use near maximal effort on every repetition while maintaining a relatively high training volume. The second, third, fourth, and fifth sets were preceded by rest periods lasting 30, 90, 150, and 180 seconds, respectively. The shortening phase of the exercise was performed in approximately two seconds, and the lengthening phase lasted approximately three seconds. Subjects performed supervised stretching of the knee extensors and hip flexors following each training session.

Statistical Analyses. All statistical analyses as described below were performed using SAS software (SAS version 9.1, SAS institute, Inc., Cary NC).

Tests for differences among means. Differences in means for baseline variables among genotype groups were determined using three level two-way analysis of covariance (ANCOVA), covarying for age, body mass, height, BMI, percent fat, fat free mass, and medication use where appropriate for the model. The use of medications was classified into the following categories: diuretics, ACE inhibitors, hormone replacement therapies (HRT), and anti-inflammatory/pain reducers. These categories were selected because of their potential for having physiological effects on muscle mass. Using the muscle change with training in the trained leg and the change or drift in the control leg during this same time period (for power and velocity data), as the dependent variables,

primary hypotheses were tested by three level two-way ANCOVAs. Adjusting (when appropriate in the model) for appropriate covariates including age*genotype (when age was centered) and sex*genotype interactions, changes were compared among the three levels: R homozygotes, heterozygotes, and X homozygotes for the R577X polymorphism. However, these interactions were not significant and were dropped from all models. Analyses were also done on men and women separately following the whole group analyses using three level one-way ANCOVAs. To reduce experiment-wise error rate, contrast comparisons for pairwise comparisons that were not pre-planned were analyzed only when a significant global F ($P < 0.05$) was found. Because it is possible that several of the dependent variables were highly correlated, a multivariate analysis of variance (MANOVA) was conducted to determine the influence of genotype on the variables of interest. Additionally, contrasts were used to determine if there was a dominant, recessive, or additive effect of the X allele on the primary variables. Tests of normality of the data indicate that the baseline and after training values for PP and MQ are normally distributed in men and women (Shapiro-Wilk $P > 0.05$). Although the data for men and women were normally distributed, the residual plots suggest that the variances between men and women are not homogeneous.

Hardy-Weinberg equilibrium. The *ACTN3* genotype distribution was evaluated for conformity with Hardy-Weinberg equilibrium using a chi-square test using one degree of freedom.

Statistical power analyses. Statistical power for the three primary genotype comparisons described in the primary hypotheses were estimated for the genotype influence on each variable. These analyses were performed using a standard deviation

(SD) obtained from our pilot data of ~ 20 subjects, which employed the identical training and testing protocol, and an estimated effect size (unit difference between groups). The effect size for absolute peak power change approximates the magnitude of changes in muscle power with aging that is associated with changes in functional ability (164). These estimates also assumed an attrition rate of ~ 20% during the study. Statistical power for changes in baseline absolute peak power, absolute PP change, and MQ change *a-priori* was estimated to be > 0.80 with alpha set at 0.05 (in men, critical effect size baseline absolute PP = 110 W, SD = 79; absolute PP change = 32 W, SD = 24; MQ change = 1.9 kg/cm^3 x 10^{-2}, SD = 1.3; in women, baseline absolute PP = 52 W, SD = 47; absolute PP change = 26 W, SD = 21; MQ change = 1.6 kg/cm^3 x 10^{-2}, SD = 1.4) and accounting for genotype distribution. Power calculations were based on estimations from previous reports (164) and our preliminary data of a genotype distribution of ~ 40%, ~ 40%, and ~ 20% for the RR, RX, and XX genotypes, respectively.

RESULTS

Subject characteristics and muscle function measures at baseline and after ST for men (n = 69) and women (n = 82) are shown in Table 1. There was a significant increase in 1 RM strength in both men (n = 55) and women (n = 57) with ST (both $P < 0.001$), but men had a significantly greater increase than women ($P < 0.05$) when baseline differences, age, and FFM were covaried. Muscle volume (MV) also increased significantly in both men (8.9 ± 1%) and women (9.0 ± 1%; both $P < 0.001$). There were no significant changes in BMI, body weight, % body fat, or FFM in either men or women with ST. There were also no significant differences by *ACTN3* R577X genotype group in men or women at baseline for age, height, weight, BMI, % body fat, or FFM. Moreover,

there were no significant differences in these subject characteristics at baseline among genotype groups in men or women for the analyses of absolute peak power (n = 53, 65), change in absolute peak power with ST (n = 37, 43), or change in muscle quality with ST (n = 49, 51).

Table 2 shows that 1 RM strength increased significantly in the trained leg in men (25.6 ± 2%) and in women (28.9 ± 2%, both $P < 0.001$) with ST, irrespective of *ACTN3* genotype. These increases are likely reduced by our familiarization procedures performed prior to baseline strength testing (see methods for explanation). Moreover, there were significant changes in MV in the trained leg in men and women with ST (both $P < 0.001$). Table 2 also shows a significant increase in knee extensor absolute PP (PP at the same absolute resistance at both baseline and after ST) in both men (10.3 ± 2%) and women (15.7 ± 2 %, both $P < 0.001$) with ST. However, relative PP (PP at 70% of baseline 1 RM and 70% of the improved 1 RM after ST) increased significantly only in women (10.0 ± 2%; $P < 0.001$) with ST (Table 2). Table 2 also shows that there was a significant increase in absolute peak movement velocity (PV) in men (9.7 ± 1%) and in women (12.1 ± 2%, both $P < 0.001$) with ST. Additionally, there was a significant decrease in relative PV in men ($P < 0.001$), but not in women. Muscle quality increased significantly in the trained leg in both men and women with ST (both $P < 0.001$). Furthermore, there was a significant increase in absolute muscle power quality (MPQ) in women with ST ($P < 0.05$), but there was no significant change in men. Finally, there was a significant decrease in relative PV quality in men (-17.3 ± 4%) and women (- 13.3 ± 3%) in the trained leg with ST (both $P < 0.001$). The only variables that changed significantly in the untrained leg in men were 1 RM strength (due to the cross education

effect), MQ (both $P < 0.001$), and absolute MPQ ($P < 0.05$). The changes in 1RM, muscle volume, MQ, absolute PP, absolute PV, and relative PV quality in men were significantly different than the changes or drift in the untrained leg. The only variables that changed in the untrained leg in women were 1 RM ($P < 0.001$) and MV ($1.2 \pm 0.5\%$, $P < 0.01$). However, this absolute change in MV was very small and not likely to be physiologically meaningful. The changes in 1RM, MV, PP, absolute PV, and MQ were significantly different than the changes or drift in the untrained leg in women. The changes in 1RM and absolute PP with ST were greater in men than in women when baseline differences, age, and FFM were covaried ($P < 0.05$).

Genotype results. Due to the longitudinal design of the investigation and multiple variables examined within each genotype group, most of the measures have some missing data points. The minimum number of subjects for any of the main variables with ST is in men with 13, 17, and 7 subjects for the RR, RX, and XX *ACTN3* genotype groups, respectively (absolute PP change). In women, the minimum number of subjects is 19, 14, and 10 for the RR, RX, and XX *ACTN3* genotype groups, respectively (absolute PP change). Chi square analysis shows that the genotype distribution of the *ACTN3* R577X polymorphism in this cohort did not fit the expectations of Hardy-Weinberg equilibrium ($\chi^2 = 4.99$, $P = 0.03$). Genotype distributions for the *ACTN3* R577X genotype groups were 62 (41%), 59 (39%), and 30 (20%) for the RR, RX, and XX genotype groups, respectively.

One-way multivariate analyses of variance (MANOVAs) were conducted to determine the influence of *ACTN3* genotype on 1 RM strength, absolute PP, and absolute PV at baseline and in response to ST. Significant differences were found among the three

genotype groups at baseline for these dependent variables (Wilks' L = 0.89, F (6, 218) = 2.25, $P < 0.05$). In addition, there were significant differences among genotype groups in changes in these same variables with ST (Wilks' L = 0.83, F (6, 142) = 2.37, $P < 0.05$). Table 3 shows the follow up ANCOVAs to the baseline MANOVA results for differences in muscle function variables by *ACTN3* R577X genotype group when men and women were combined. The XX group had a baseline relative PP that was 36 ± 17 W higher than the RR group ($P < 0.05$), and the RX group was also higher than the RR group 43 ± 17 W ($P < 0.05$) when age and sex differences were covaried. In addition, the XX group had a significantly higher relative MPQ than the RR group (0.28 ± 0.11 W/cm^3, $P < 0.05$), and the RX group was also greater than the RR group (0.20 ± 0.1 $W/cm^3 \times 10^{-1}$, $P < 0.05$). Furthermore, the XX group had a higher baseline relative PV than the RR group (0.37 ± 0.17 rad/sec, $P < 0.05$), and the RX group was also greater than the RR group (0.28 ± 0.14 rad/sec, $P < 0.05$). These variables (PP, MPQ, PV) were strongly correlated (r = + 0.67 to + 0.83, $P < 0.001$), which may explain why they are all significantly different by *ACTN3* genotype. There were no significant differences at baseline between *ACTN3* R577X genotype groups for 1 RM, MV, muscle quality, absolute PP, MPQ, PV, or PV quality when age and sex differences were covaried (Table 3). There were no age-genotype interactions for any of the analyses performed at baseline.

Because a previous report suggests that the influence of *ACTN3* R577X genotype on muscle function may depend on what sex group is studied (31), and because sex was a significant covariate in the model for the variables shown in Table 3 at baseline, separate analyses were performed for the baseline values and training response of each sex group

by *ACTN3* genotype. Table 4 shows the difference in muscle function measures by *ACTN3* genotype in women. There was a significantly greater baseline 1 RM in the RR group than in the RX group (2.9 ± 1 kg, $P < 0.01$) when age and hormone replacement therapy (HRT) were included as covariates. In addition, the XX group had a significantly higher baseline absolute PP than the RR (32 ± 14 W) and RX groups (32 ± 15 W, both $P < 0.05$) when age and baseline FFM were included as covariates. Contrasts indicate that there is a significant dose response (additive) effect of the X allele on absolute PP at baseline in women ($P < 0.05$). Furthermore, the XX group had a significantly greater relative PP than the RR group (35 ± 14 W) and the RX group (35 ± 15 W, both $P < 0.05$) when age, baseline FFM, and HRT were covaried. Furthermore, the XX group had a significantly greater relative MPQ than the RR group (0.31 ± 0.14 $W/cm^3 \times 10^{-1}$) and the RX group (0.28 ± 0.12 $W/cm^3 \times 10^{-1}$, both $P < 0.05$) when age and baseline FFM were covaried. There were no baseline differences by *ACTN3* genotype in men for any of the muscle function measures shown in Table 4. Usage of ACE inhibitors, diuretics, or anti-inflammatory medications were not significant covariates in any of the models of baseline muscle function measures by *ACTN3* genotype group.

Figure 1 shows that when men and women are combined and grouped by *ACTN3* genotype, the change in absolute PP with ST in the RR group was significantly greater than in the XX group (22 ± 11 W, $P < 0.05$) with ST. There was a trend toward significantly greater absolute PP change in the RR group than in the RX group (19 ± 10, $P = 0.07$) with ST, when the data were adjusted for age, sex, and changes in the untrained leg. Contrasts also indicate that there is a significant dose response (additive) effect of the X allele on change in absolute PP with ST ($P < 0.05$). There was a significant within

group increase in the RR, RX (both $P < 0.001$), and XX ($P < 0.01$) groups from baseline with ST. Figure 1 also shows that there was a borderline significantly greater change in relative PP in the RR group than in the XX group (26 ± 13 W, $P = 0.05$) when the data were adjusted for age, sex, and changes in the untrained leg. In addition, there was a significantly greater change in absolute MPQ in the RR group than in the XX group (0.20 ± 0.08 $W/cm^3 \times 10^{-1}$, $P < 0.01$) when the data were adjusted for age, sex, and changes in the untrained leg. There were no significant differences in 1 RM, MV, MQ, PV, absolute MPQ, or PV quality with ST among genotype groups when men and women were combined.

Figure 2 shows that in men grouped by *ACTN3* genotype, the change in the RR group was significantly higher than the XX group (38 ± 17 W, $P < 0.05$) in absolute PP with ST, when the data were adjusted for age and changes in the untrained leg. Contrasts also indicate that there is a significant additive effect of the X allele on change in absolute PP with ST in men ($P < 0.05$). There was a significant within group increase in the RR group from baseline ($P < 0.01$), but the XX group did not increase their absolute PP significantly. There were no differences in the change in the relative PP in men by *ACTN3* genotype with ST (Figure 2). Figure 3 shows that the increase in absolute MPQ with ST in the RR group was significantly higher than the change in the XX group (24 ± 10 $W/cm^3 \times 10^{-3}$, $P < 0.05$) when age and changes in the untrained leg were included as covariates. In addition, there was a within group trend toward a significant increase in absolute MPQ in the RR group ($P = 0.09$) with ST, but not in the RX or XX groups. There was no difference between genotype groups for change in relative MPQ with ST (Figure 3). There was a trend toward a significantly higher change in absolute PV in the

RR group than in the XX group (2.8 ± 1.5 rad/sec x 10^{-1}, $P = 0.06$). Furthermore, there was a significant within group increase in absolute PV in the RR ($P < 0.01$) and RX ($P < 0.001$) groups in men with ST, but there was only a trend toward a significant increase in the XX group ($P = 0.09$). There were no differences among *ACTN3* genotype groups for change in relative PV with ST. Absolute PP, MPQ, and PV are strongly correlated ($r = +0.77$ to $+0.91$, $P < 0.001$), which may, once again, explain why there was a significantly lower change in the XX group when compared to the RR group for these muscle function variables. There were no significant differences in men by *ACTN3* R577X genotype for change in 1 RM strength, MV, MQ, absolute PV quality, or relative PV quality with ST. In women there was a significant within group increase in muscle volume in the RR, RX, and XX genotype groups (all $P < 0.001$). Furthermore, the increase in muscle volume was significantly greater in the XX group (123 ± 13 cm^3) than in the RR group (88 ± 11 cm^3; $P < 0.05$) when age and change in the untrained leg were covaried. However, there were no significant differences among genotype groups in women for changes in 1 RM strength, PP, MQ, PV, MPQ, or PV quality with ST. There were no age-genotype interactions for any of the analyses performed with ST.

DISCUSSION

The results of the present study demonstrate for the first time, and contrary to our hypothesis, that increases in knee extensor peak power with ST are significantly influenced by *ACTN3* R577X genotype in men, but not in women, such that men who are R homozygotes have significantly greater peak power response to ST than X homozygotes. This difference was observed when subjects were tested for peak power at

the same absolute load before and after ST (i.e., absolute peak power), and when this peak power was normalized for the entire volume of trained musculature (i.e., absolute muscle power quality). Also contrary to our hypothesis, the data demonstrate that baseline absolute peak power in women is significantly greater in X homozygotes than in R homozygotes and heterozygotes. Although these results need to be confirmed in an independent cohort before any definitive conclusions can be made, they do provide support for the hypothesis that the *ACTN3* R577X genotype influences baseline peak power and the effectiveness of ST for increasing peak power and muscle power quality in older adults.

The finding of an ~ 15% training-induced increase in absolute peak power in men R homozygotes, but no significant increase in men X homozygotes, is in contrast to the conclusions of a previous report (31) that women X homozygotes have a greater strength response than heterozygotes with ST. In that report, it was suggested that one explanation for *ACTN3* genotype influencing strength response to ST in women, but not in men, could be the potential of steroid hormones in masking the effects of ACTN-3 expression on muscle structure differences. However, that conclusion was based on young adults undergoing arm training rather than leg training and for strength changes rather than peak power changes. We did not observe any differences in the changes in muscle volume in men among genotype groups, suggesting neuromusculature adaptation differences as a potential mechanism for peak power differences among *ACTN3* genotype groups in men. Nevertheless, the specific mechanisms responsible for these findings will require many more studies.

The ACTN-3 protein may allow skeletal muscle to have a greater capacity for the conduction of force at the Z line during a rapid contraction (198). Given that ACTN-3 expression is limited to type II fibers, those most involved in maximal force, contractile speed, and power production, our measurement of peak muscle power might be a better indicator of the influence of the *ACTN3* polymorphism with ST than strength measures. In an earlier investigation, we found that there was significant variability in PP response to ST (37), and the results of the present investigation suggest that at least part of this inter-individual variability in men may be explained by *ACTN3* R577X genotype. Thus, there are likely many other unidentified genes influencing such a complex phenotype as muscle power.

Our data also suggest that the increase in absolute PP with ST follows a dose-response (additive) relationship by *ACTN3* genotype, with the R allele appearing to be associated with the generation of greater muscle power response to training. This is supported by the work of Yang et al. (197) who observed that ACTN-3 expression in skeletal muscle may be positively correlated with the number of R alleles present. Furthermore, our finding of *ACTN3* genotype influencing increases in absolute peak power with ST at relatively low loads (~ 50% of 1 RM after training), may have important implications for functional abilities. This conclusion is based on recent data suggesting that selected functional ability performance in older adults may be more dependent on peak power and movement velocity at lower external loads than high loads (34).

It is unclear why baseline relative PP and MPQ were higher in the XX group than in the RR and RX genotype groups in women. Data from a previous investigation found

that women X homozygotes had a lower maximal isometric voluntary contraction strength (MVC) at baseline than heterozygotes (31). Our results may also appear to be in contrast to an earlier case-control study that found no X homozygous women in a cohort of 35 elite women sprint athletes (198). However, young women (~ 25 yrs) were studied in the first investigation and arm flexor MVC was measured, so these results are not necessarily generalizable to older women and to different phenotypes (strength vs. power) assessed in different muscle groups. In the second investigation (198), the subjects were highly trained young women and these findings may not correspond to the muscle function values observed in older, sedentary women as were studied in the current investigation. One possible explanation, although highly speculative, for our finding of differences in relative PP and MPQ at baseline among genotype groups in women, may be differences in the coactivation of the antagonist muscle groups (68), but future studies would be required to provide more definitive explanations for this. The finding of a significantly greater increase in absolute MPQ in men R homozygotes than in X homozygotes with ST, further demonstrates that there are factors other than muscle hypertrophy that are responsible for genotype differences in peak power. Further evidence for this comes from the finding that there were no significant differences in muscle volume change between genotype groups. Earlier reports estimate that ~ 60% of the increase in muscular power with ST is due to factors other than muscle hypertrophy (46). There are no data in the current study to determine what factor(s) this might be, but it is likely due to some neuromuscular adaptation that produces an increased peak power in R homozygotes without a concomitant increase in muscle mass, resulting in a greater increase in power per unit of trained muscle. Although we are not aware of any data to

support these genotype differences, there is support for the conclusion that increases in power and strength with ST in older adults can be influenced substantially by neural adaptations (68). Additionally, a previous report from our laboratory showed that women have a significant increase in absolute muscle power quality with ST, but men do not (37). However, the subjects in that study were not stratified by genotype, which might explain why no overall MPQ increase with ST was found in men.

The use of the untrained leg also adds a unique level of experimental control by controlling for normal drift in values due to variations in methodology, biology, season of the year, genetic differences between groups, and differences in attention between experimental and control groups. This, in combination with our data showing that unlike strength there is no cross-education effect on absolute PP in men, minimizes the level of variance due to experimental error.

Nevertheless, there are limitations in the current investigation. For example, subjects in this investigation were trained using a moderate velocity training protocol (~ 2 seconds during the shortening phase and ~ 3 seconds during the lengthening phase). A higher velocity training protocol would likely produce greater gains in power (49). We chose a ST protocol that is more commonly used, with a well-established track record for being safe and effective in older adults for producing substantial improvements in all the major components of sarcopenia (i.e., muscle mass, strength, and muscle quality, as well as power) (37, 81, 102, 176). It is still not well established whether a high velocity training program, with a heavy enough resistance for optimal strength gains, is well tolerated by older subjects (44). Another limitation was that there was a relatively wide range of ages. It is conceivable that the youngest subjects in the study may have slightly

different training responses than the older ones, but age was included as a covariate in our analyses and there were no significant age differences between genotype groups. Finally, this investigation shows the relationship between only one polymorphism in only one gene at only one locus. Muscle power is a complex phenotype, which is probably influenced by numerous genes and polymorphisms, as well as other environmental factors that may be interacting with these genes in unknown ways. The limited sample size in the current investigation, especially when stratifying by sex, does not allow for the analysis of the interaction of multiple loci.

Future studies will need to not only use much larger homogenous sample sizes, but will need to carefully develop research designs to accommodate the limitations of this study and the ones highlighted by Clarkson et al. (31). Although there was a significant influence of the *ACTN3* polymorphism on PP at baseline in women and with ST in men, there was no statistically significant sex-genotype interaction with regard to baseline PP or change in PP with ST. Future studies might need to consider the magnitude of the influence of the *ACTN3* polymorphism on this phenotype and adjust for the numbers of men and women to account for this difference. Age might also be an effect modifier with regard to the influence of this SNP, as there are significant structural changes (e.g. loss of type II fibers, fiber type grouping) that occur in elderly skeletal muscle. Although there was no age-genotype interaction for PP at baseline or change in PP with ST, the sample size in the current investigation likely limited the statistical power to detect this relationship. Having enough subjects evenly distributed throughout the adult age range might allow for the group to be broken up into tertiles, quartiles, or even quintiles to make comparisons of relative changes in PP with ST regarding the R577X SNP. In

addition, perhaps an analysis of fiber type proportion and the relative change in strength, power, muscle mass, velocity, and various muscle quality measures would be a more sensitive model for detecting changes resulting from the presence or absence of ACTN-3 in skeletal muscle. Establishing the influence of the *ACTN-3* R577X SNP on functional abilities, likely an even more complex phenotype, in elderly populations, is necessary in order to determine if this genotype is of importance for targeting individuals who may be more susceptible to the effects of sarcopenia and who may need specific interventions. In addition, this technique needs to be applied to measure the peak power in other movements, such as upper leg extension used in the leg press exercise, as previously reported with average peak power (41, 49), and how these different muscle groups respond to ST by *ACTN3* genotype. Finally, an increased sample size is needed in order to study gene x gene interactions that explain a greater proportion of the variance of these complex phenotypes.

Table 1. *Physical characteristics at baseline and after strength training (ST) in men and women.*

	Men		Women	
	Baseline	After ST	Baseline	After ST
N	69	55[1]	82	57[2]
Age (yr)	64 (9)	--	65 (9)	--
Height (cm)	174.5 (6.9)	--	161.5 (6.6)	--
Weight (kg)	85.6 (13.2)	85.8 (12.7)	72.3 (15.1)	72.5 (14.1)
BMI (kg/m^2)	27.9 (3.5)	28.0 (3.5)	27.8 (5.9)	27.9 (5.2)
Body Fat (%)	28.4 (5.2)	28.2 (4.6)	39.4 (5.5)	39.1 (5.5)
Fat-Free Mass (kg)	60.4 (8.4)	60.8 (7.6)	42.6 (6.5)	42.9 (5.9)
1-RM (kg)	32.0 (8.8)	40.2 (9.5)*†	16.6 (4.5)	21.4 (5.2)*
Muscle Volume[3] (cm^3)	1,756 (278)	1,913 (313)*	1,083 (197)	1,180 (209)*

Values are means (SD). Data presented are for all subjects with baseline and after ST measurements.
BMI = body mass index; 1-RM = knee extension one-repetition maximum; kg = kilograms.
[1]There were 51 subjects for weight & BMI, 49 for body fat %, 46 for FFM, 55 for 1 RM, and 49 for muscle volume that had both baseline and after ST values.
[2]There were 53 subjects for weight, BMI, FFM, and body fat %, 57 for 1 RM, and 51 for muscle volume that had both baseline and after ST values.
[3]Muscle volume of the knee extensors.
*Significantly different than baseline ($P < 0.001$).
†Significantly greater change than women when covarying for baseline differences, age, and FFM ($P < 0.05$).

Table 2. *Changes in 1 RM knee extensor strength, muscle volume, peak power, peak movement velocity, muscle quality, muscle power quality, and movement velocity quality with strength training (ST) in the trained and untrained leg in men and women.*

	Men		Women	
	Trained Leg	Untrained Leg	Trained Leg	Untrained Leg
1 RM (kg)	8.2 ± 0.5[c,f,g]	3.5 ± 0.6[c]	4.8 ± 0.4[c,f]	1.5 ± 0.3[c]
Muscle Volume (cm^3)	157 ± 10[c,f]	3 ± 7	97 ± 7[c,f]	13 ± 5[b]
Absolute Peak Power[1] (W)	47 ± 9[c,e,g]	13 ± 7	34 ± 5[c,f]	- 2 ± 4
Relative Peak Power[2] (W)	23 ± 12	0.3 ± 7	21 ± 5[c,e]	- 2 ± 6
Absolute Peak Movement Velocity[1] (rad/s) x 10^{-1}	5.2 ± 0.8[c,e]	0.9 ± 1.1	5.3 ± 0.7[c,f]	0.2 ± 0.7
Relative Peak Movement Velocity[2] (rad/s) x 10^{-1}	- 4.9 ± 1.2[c]	- 3.3 ± 1.2	- 2.0 ± 1.0	- 1.6 ± 1.1
Muscle Quality[3] (kg/cm^3) x 10^{-3}	3.1 ± 0.3[c,d]	2.0 ± 0.3[c]	2.9 ± 0.4[c,f]	1.2 ± 0.3
Absolute Muscle Power Quality[1] (W/cm^3) x 10^{-3}	4.2 ± 5.7	11.0 ± 4.9[a]	11.1 ± 4.8[a]	- 2.1 ± 3.7
Relative Muscle Power Quality[2] (W/cm^3) x 10^{-3}	- 3.5 ± 7.4	4.2 ± 4.4	- 0.1 ± 5.2	- 4.4 ± 5.8
Absolute Movement Velocity Quality[1] ($rad/s/cm^3$) x 10^{-4}	0.4 ± 0.6	1.1 ± 0.7	1.3 ± 0.9	- 0.01 ± 1.0
Relative Movement Velocity Quality[2] ($rad/s/cm^3$) x 10^{-4}	- 4.5 ± 0.8[c,e]	- 1.3 ± 0.7	- 5.0 ± 1.0[c]	- 2.2 ± 1.0

Values are means ± SEM; W = watts; rad/s = radians · sec^{-1}; kg = kilograms.
[1]The same absolute resistance at both baseline and after ST.
[2]70% of 1-RM at baseline and 70% of the improved 1-RM after ST.
[3]1-RM/Muscle Volume.
[a]Significantly greater than baseline ($P < 0.05$).
[b]Significantly greater than baseline ($P < 0.01$).
[c]Significantly different than baseline ($P < 0.001$).
[d]Significantly different than the untrained leg ($P < 0.05$).
[e]Significantly different than the untrained leg ($P < 0.01$).
[f]Significantly different than the untrained leg ($P < 0.001$).
[g]Significantly greater change than the other sex when covarying for baseline differences, age, and FFM ($P < 0.05$).

Table 3. *Baseline differences in 1 RM knee extensor strength, muscle volume, muscle quality, peak power, muscle power quality, peak movement velocity, and movement velocity quality in the trained leg by ACTN3 R577X genotype in men and women combined.*

	ACTN3 R577X Genotype		
	RR	RX	XX
1 RM (kg)	25.6 ± 0.6 (61)	23.3 ± 0.9 (59)	24.6 ± 1.1 (30)
Muscle Volume[1] (cm^3)	1477 ± 26 (53)	1401 ± 32 (49)	1466 ± 41 (24)
Muscle Quality[2] (kg/cm^3) x 10^{-2}	1.7 ± 0.04 (53)	1.6 ± 0.04 (49)	1.7 ± 0.06 (24)
Absolute Peak Power[3] (W)	315 ± 12 (44)	331 ± 15 (47)	338 ± 13 (27)
Relative Peak Power[4] (W)	279 ± 12* (44)	322 ± 11 (47)	315 ± 15 (28)
Absolute Muscle Power Quality[3] (W/cm^3) x 10^{-1}	2.1 ± 0.1 (38)	2.3 ± 0.1 (38)	2.3 ± 0.1 (22)
Relative Muscle Power Quality[4] (W/cm^3) x 10^{-1}	2.0 ± 0.1* (38)	2.2 ± 0.1 (38)	2.3 ± 0.1 (22)
Absolute Peak Movement Velocity[3] (rad/s)	4.7 ± 0.2 (44)	5.0 ± 0.1 (47)	5.0 ± 0.2 (27)
Relative Peak Movement Velocity[4] (rad/s)	4.0 ± 0.1* (44)	4.3 ± 0.1 (47)	4.4 ± 0.1 (28)
Absolute Movement Velocity Quality[3] ($rad/s/cm^3$) x 10^{-3}	3.4 ± 0.1 (38)	3.8 ± 0.2 (38)	3.5 ± 0.2 (22)
Relative Movement Velocity Quality[4] ($rad/s/cm^3$) x 10^{-3}	3.0 ± 0.1 (38)	3.3 ± 0.1 (38)	3.2 ± 0.2 (22)

Values are least-square means ± SEM (*n*) when covarying for age and sex; RM = repetition maximum; W = watts; rad/s = radians · sec^{-1}; kg = kilograms.

[1]Muscle volume of the knee extensors.

[2]1-RM/muscle volume.

[3]The same absolute resistance at both baseline and after ST.

[4]70% of 1-RM at baseline.

*Significantly less than the RX and XX groups when covarying for age and sex ($P < 0.05$).

Table 4. *Baseline differences in knee extensor strength, muscle volume, muscle quality, peak power, muscle power quality, peak movement velocity, and movement velocity quality by ACTN3 R577X genotype in women.*

	ACTN3 R577X Genotype		
	RR	RX	XX
1 RM (kg)	18.4 ± 0.7 (35)	15.5 ± 0.9**‡ (29)	17.8 ± 1.2 (18)
Muscle Volume[1] (cm^3)	1,146 ± 36 (32)	1,047 ± 29 (24)	1,135 ± 53 (14)
Muscle Quality[2] (kg/cm^3) x 10^{-2}	1.6 ± 0.05 (32)	1.4 ± 0.06 (24)	1.6 ± 0.08 (14)
Absolute Peak Power[3] (W)	208 ± 9 (27)	208 ± 10 (21)	240 ± 11*† (17)
Relative Peak Power[4] (W)	205 ± 10 (27)	205 ± 11 (21)	240 ± 12*†‡ (17)
Absolute Muscle Power Quality[3] (W/cm^3) x 10^{-1}	1.9 ± 0.1 (24)	2.0 ± 0.1 (16)	2.2 ± 0.1* (13)
Relative Muscle Power Quality[4] (W/cm^3) x 10^{-1}	1.9 ± 0.1 (24)	1.9 ± 0.1 (16)	2.2 ± 0.1*† (13)
Absolute Peak Movement Velocity[3] (rad/s)	4.4 ± 0.2 (27)	4.5 ± 0.2 (21)	4.7 ± 0.2 (17)
Relative Peak Movement Velocity[4] (rad/s)	3.9 ± 0.1 (27)	3.8 ± 0.1 (21)	4.2 ± 0.2 (17)
Absolute Movement Velocity Quality[3] ($rad/s/cm^3$) x 10^{-3}	4.2 ± 0.2 (24)	4.3 ± 0.3 (16)	4.2 ± 0.3 (13)
Relative Movement Velocity Quality[4] ($rad/s/cm^3$) x 10^{-3}	3.7 ± 0.2 (24)	3.7 ± 0.2 (16)	3.8 ± 0.2 (13)

Values are least-square means ± SEM (*n*); 1 RM = One repetition maximum; W = watts; rad/s = radians · sec^{-1}; MV = muscle volume; HRT = hormone replacement therapy.

There were no significant baseline differences between genotype groups in men.

[1]Muscle volume of the knee extensors.

[2]1-RM/MV.

[3]The same absolute resistance at both baseline and after ST.

[4]70% of 1-RM at baseline.

*Significantly different than the RR group when covarying for age and baseline FFM ($P < 0.05$).

**Significantly different than the RR group when covarying for age and HRT ($P < 0.01$).

†Significantly different than the RX group when covarying for age and baseline FFM ($P < 0.05$).

‡HRT was a significant covariate in the analysis.

FIGURE LEGENDS:

Figure 1. Changes in knee extensor absolute (same absolute resistance before and after ST) and relative (70% of 1 RM at baseline and after ST) peak power (PP) with ST by *ACTN3* R577X genotype in men and women combined. When covarying for age, sex, and changes in the untrained leg, there was a significantly greater increase in absolute PP in the RR group than in the XX group (*$P < 0.05$) and a trend toward a significantly greater increase than the RX group ($P = 0.07$) with ST. When covarying for age, sex, and changes in the untrained leg, there was a borderline significantly greater increase in the RR group than in the XX group ($P = 0.05$). Values are least-square means ± SEM.

Figure 2. Changes in knee extensor absolute (same absolute resistance before and after ST) and relative (70% of 1 RM at baseline and after ST) peak power (PP) with ST by *ACTN3* R577X genotype in men. When covarying for age and changes in the untrained leg, there was a significantly greater increase in absolute PP in the RR group than in the XX group with ST (*$P < 0.05$). There were no significant differences in relative PP change among genotype groups. Values are least-square means ± SEM.

Figure 3. Changes in knee extensor absolute (same absolute resistance before and after ST) and relative (70% of 1 RM at baseline and after ST) muscle power quality (MPQ) with ST by *ACTN3* R577X genotype in men. When covarying for age and changes in the untrained leg, there were significantly greater increases in absolute MPQ in the RR (*$P < 0.05$) than in the XX group with ST. There were no significant differences in relative MPQ change among genotype groups. Values are least-square means ± SEM.

Figure 1.

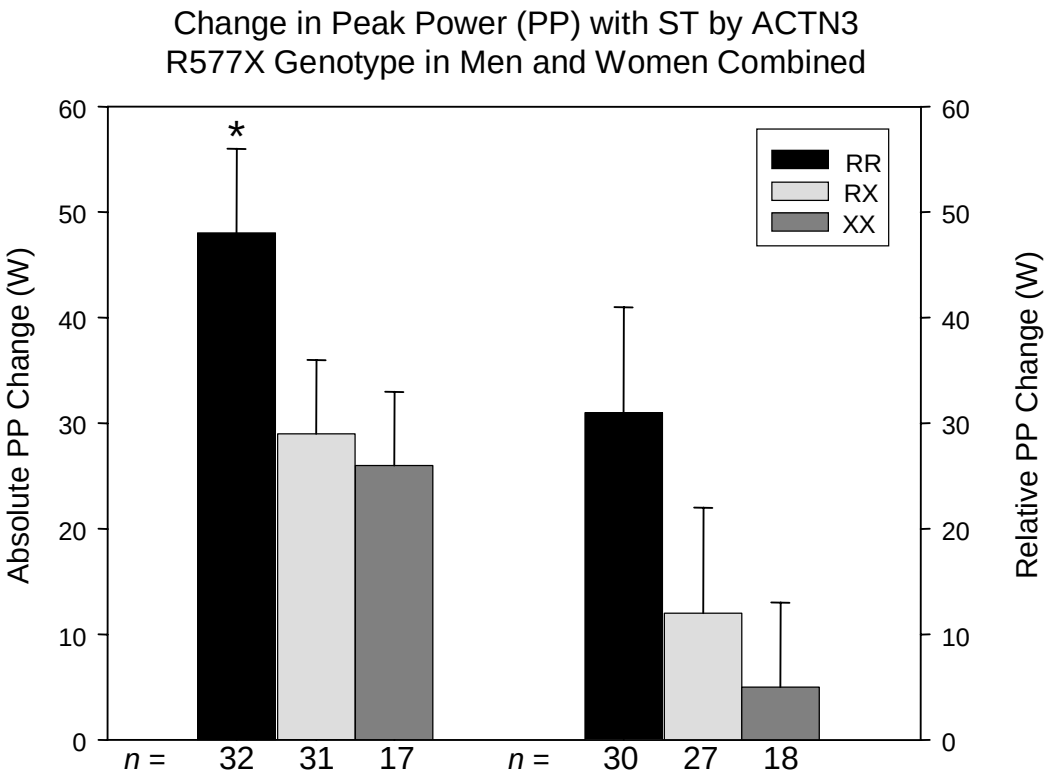

Change in Peak Power (PP) with ST by ACTN3
R577X Genotype in Men and Women Combined
Absolute PP Change (W)
Relative PP Change (W)
RR
RX
XX
*
0
10
20
30
40
50
60
n = 32 31 17
n = 30 27 18

Figure 2.

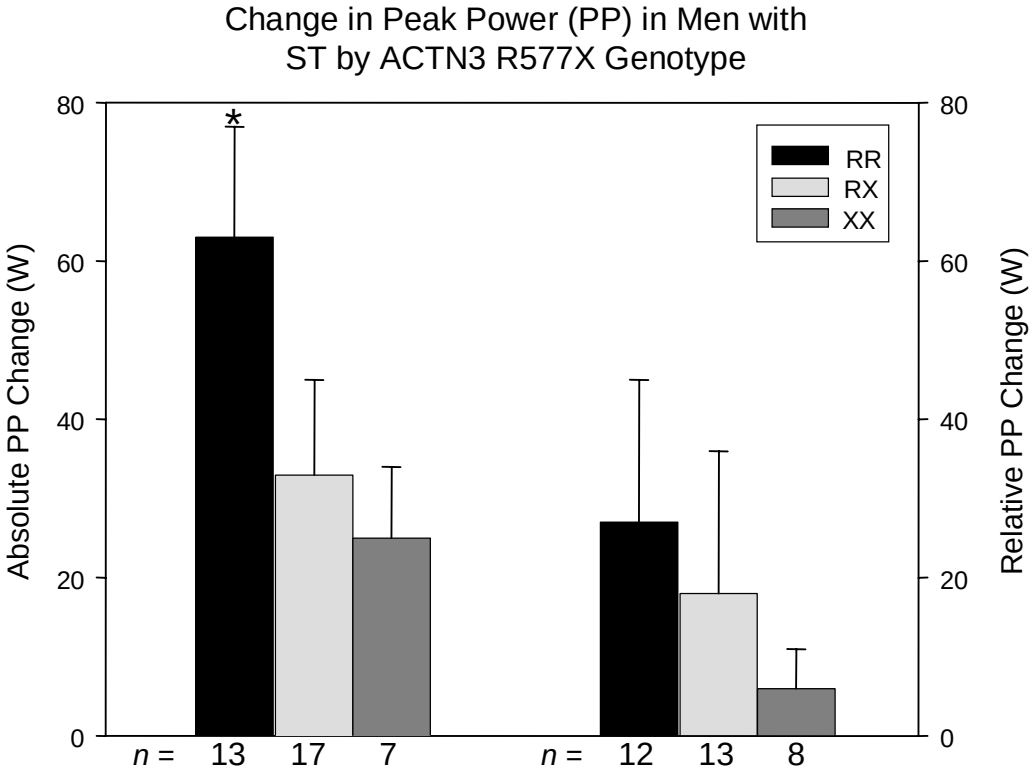
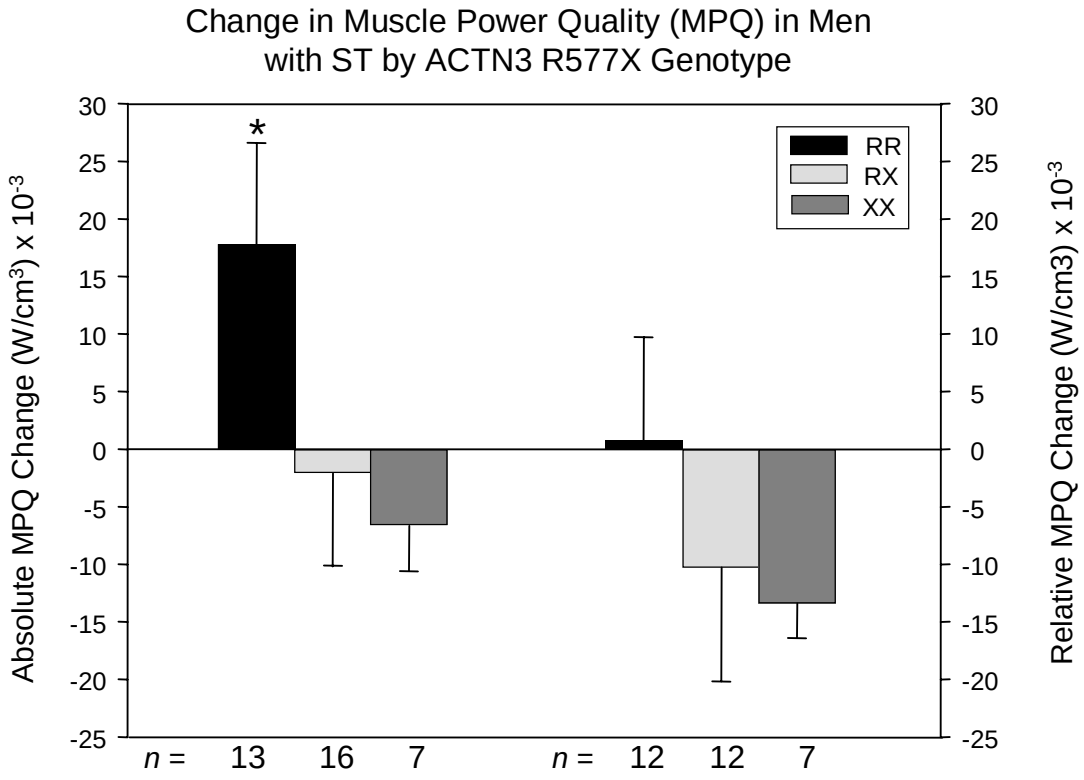

Change in Peak Power (PP) in Men with
ST by ACTN3 R577X Genotype
Absolute PP Change (W)
Relative PP Change (W)
RR
RX
XX
*
0
20
40
60
80
n = 13 17 7
n = 12 13 8

Figure 3.


Change in Muscle Power Quality (MPQ) in Men
with ST by ACTN3 R577X Genotype
Absolute MPQ Change (W/cm3) x 10-3
Relative MPQ Change (W/cm3) x 10-3
RR
RX
XX
*
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
n = 13 16 7 n = 12 12 7

APPENDIX A

Research Hypotheses
Delimitations
Limitations
Operational Definitions

APPENDIX A

Research Hypotheses, Delimitations, Limitations, and Operational Definitions

Research Hypotheses

1. Women X homozygotes at the *ACTN3* gene locus of the R577X polymorphism will demonstrate significantly greater absolute peak knee extensor muscular power change with strength training when compared to RX and RR genotype groups.

2. Women X homozygotes at the *ACTN3* gene locus of this same polymorphism will demonstrate significantly lower absolute peak knee extensor muscular power at baseline when compared to RX and RR genotype groups.

3. Women X homozygotes at the *ACTN3* gene locus of this polymorphism will demonstrate significantly greater increases in muscle quality change with ST when compared to RX and RR genotype groups.

4. There will be no association in men between the *ACTN3* R577X polymorphism and absolute peak knee extensor power at baseline or change in peak power with ST.

Delimitations

1. The scope of this study will be delimited to 110 men and women between the ages of 50 and 85 yrs who volunteer as study participants.

2. Participation in the study will be limited to healthy participants free of musculoskeletal or cardiovascular disease.

3. Based on previous research, subjects will be divided into three groups in determining the effect of this genotype. The groupings will be based on homo- and heterozygosity for the R577X polymorphism.

Limitations

1. The participants will be volunteers and not randomly selected from the general population. Therefore, the results of this study cannot be generalized to individuals who do not possess characteristics such as age, body size, physical activity, etc. similar to those of subjects in the study.

2. Subjects will self-report many factors related to health and lifestyle such as physical activity habits, dietary habits, medication regimens, and medical conditions. Because the accuracy of these reports cannot be verified, it is possible that inaccurate self-reports may occur, which could adversely affect the results of this study.

3. It will not be possible to verify compliance of factors that are not being self reported, but are part of what subjects are asked to do outside of training during the study period (e.g. maintain diet and activity patterns and not change their medications).

4. Genotypes other than the *ACTN3* R577X polymorphism will not be assessed in the proposed study. It is possible that the *ACTN3* polymorphism effects are present only in the presence of a specific, but unknown, genetic background (epistasis).

5. Polymorphisms in the regions flanking the ACTN-3 gene will not be identified or assessed in the genomic material for this study. It is therefore possible that any reported genotype effect is due to linkage disequilibrium between the R577X polymorphism and a distinct and putative polymorphism at another locus within the same chromosome.

Operational Definitions:

5-RM: Refers to the maximum amount of resistance an individual can move through a complete range of motion only five times.

R577X polymorphism (ACTN-3 gene): Results from a C to T transition at position 1,747, which causes a change in the 577 residue from arginine, resulting in a premature stop codon (R577X). Homozygosity of R577X results in an absence of α-actinin-3 expression, although the individuals affected typically appear phenotypically normal. Genbank accession number M86407.

Computed tomography (CT): A technique for assessing regional muscle size based on the examination of axial scans of the thigh. Visual images are created from the measurement of the intensity of x-rays and analyzed to measure cross-sectional area. The images are based on the attenuation of x-rays as they pass through the body. Attenuation scores are measured in Hounsfield units, which depend upon the level of absorption of emitted x-ray beams, -1000 air to +1000 bone. Skeletal muscle is typically 0 to 100 and adipose tissue is usually -190 to -30.

Dual-energy x-ray absorptiometry (DXA): A technique for assessing whole and regional body composition that considers the body to be composed of three

compartments: bone mineral mass, soft tissue, and lean tissue. Tissue amounts are based on the attenuation of x-rays as they pass through the body.

ACTN-3 protein: Cytoskeletal protein that is present in both non-muscle and muscle tissues. ACTN-3 is the primary constituent of the Z-disks in skeletal muscle and is only expressed in type II skeletal muscle fibers.

ACTN-3 gene: *ACTN3* is located on chromosome 11 (11q13-q14), spans ~17 kbp, and contains 21 exons.

Muscle Power: Calculated as the product of torque and angular velocity and reported in watts. Torque is calculated by multiplying the force exerted by the distance from the knee joint to the force sensor (0.34925 m) and reported in N-m. Angular velocity is reported as rad $\cdot$ s^{-1}.

Muscle Power Quality: Calculated as the peak muscle power (watts) of the knee extensors divided by the muscle volume (cm^3) of the knee extensors.

Muscle quality: Also known as specific tension or specific force is the strength of a muscle divided by the cross-sectional area to estimate the amount of force production per unit area of muscle tissue. This has been shown to decrease with age and increase with resistance training.

Muscle volume: Muscle volume will be determined by the MIPAV software and equations used by Tracy et al. (20). Briefly, this involves an equation that utilizes the 8-10 axial thigh slices that are obtained from the CT scan.

Sarcopenia: A condition characterized by the loss of muscle size, quality, and function that occurs with aging. This typically leads to or exacerbates ailments such as osteoporosis and loss of functional independence.

Sedentary: A description for individuals who are not physically active. In the proposed study this term describes individuals who, on average, have exercised aerobically for less than 20 minutes per day less than 2 times per week and have not performed any type of regular resistance training over the past six months.

APPENDIX B: FORMS

Consent form

CONSENT TO PARTICIPATE IN A RESEARCH PROJECT

Project Title: Effects of Gene Variations on Age- and Strength Training-Induced Changes in Muscular Strength, Body Composition, Blood Pressure, Glucose Metabolism, and Lipoprotein-lipid Profiles

I state that I am over 18 years of age, in good physical health, and have elected to participate in a program of research being conducted by Dr. Ben Hurley in the Department of Kinesiology at the University of Maryland, College Park, MD 20742.

I understand that the primary purpose of this study is to assess the role that genetics may play in causing losses of muscular strength and muscle mass with age and gains in strength and muscle mass as a result of strength training. I understand that another purpose of the study will be to assess the influence of genes on changes in body composition, blood pressure, blood sugar metabolism, blood fats muscle power, and performance of common physical tasks with age and strength training.

I understand that the procedures involve three phases. During the first phase, I will undergo testing, which will include a blood draw to analyze my DNA (genetic material), blood sugar and fats, and other blood proteins. My blood pressure, body composition, bone mineral density, leg muscle volume, muscle strength, muscle power, and ability to complete selected tasks similar to common activities of daily living will also be assessed during this first phase. The second phase of the study involves my participation in a strength training program three times a week for approximately six months. The third and final phase will be a repeat of all previously taken measures, except analysis of my DNA, which will not need to be repeated. Some of the tests will be repeated both after ~ 10 weeks of training and again after the entire training program. These repeat tests will include blood pressure, strength, power, muscle volume and body composition. Other tests will be repeated only after the entire training program.

I understand that the blood draw will require providing about 2 to 3 tablespoons of blood. I understand that there is a risk of bruising, pain and, in rare cases, infection or fainting as a result of blood sampling. However, these risks to me will be minimized by allowing only qualified people to draw my blood. A portion of this blood sample will be sent to the University of Pittsburgh to analyze my DNA. I understand that the remainder will be stored at the University of Maryland for later analysis of my blood sugar, the hormone that regulates my blood sugar (insulin), blood fats, and other blood proteins. I understand that a portion of this sample may also be used for potential future studies, but only as such studies examine strength, body composition (i.e., fat, muscle & bone), metabolism of blood sugar, and blood pressure. I understand that I may contact the principal investigator at any future point in time to request that any stored blood sample be destroyed immediately.

I understand that while I am lying on a padded table, my leg muscle and fat mass will be measured by computed tomography (CT). The CT scan will be performed at the Washington Adventist Hospital. My percent body fat and bone mineral density measurements will be performed at the United States Department of Agriculture in Beltsville, Maryland by dual-energy x-ray absorptiometry (DXA). This will require my lying still on a padded exam table wearing metal-free clothing for about 10 minutes at a time, totaling less than 30 total minutes for the entire procedure.

I understand that there will be a total radiation dose of approximately 1 Rem to the whole body (effective dose equivalent) from each CT scan. This amount is well below the maximal annual radiation dose (5 Rems) allowed for exposure in the workplace. The body composition and bone density testing completed by DXA involves a small radiation exposure. The radiation exposure I will receive from DXA is equal to an exposure of less than 50 millirems to the whole body. Naturally occurring radiation (cosmic radiation, radon, etc.) produces whole body radiation of about 300 millirems per year. Therefore, the total dose of radiation exposure due to the DXA measurement is minimal and the combined dose of DXA and CT is considered low. The major risk from high radiation exposure is passing on damaged genes (genetic mutations) to offspring. Consequently, this risk is typically of less concern to those who are beyond childbearing age.

I understand that strength and power assessments will be performed on machines that measure how much force and how fast I can exert force through a typical range of knee extension motion. Strength testing will also be performed on the same exercise machines used for training by measuring the maximal amount of force that I can move through the full range of an exercise. During each strength training session I will be asked to exercise on machines which offer resistance against extending and flexing my arms, legs, and trunk region for approximately 40 minutes or less a day, three times a week for up to six months. I understand that I may experience some temporary muscle soreness as a result of the testing sessions. There is also a risk of muscle or skeletal injury from strength and power testing, as well as from strength training. The investigators of this study will use procedures designed to minimize this risk.

I understand that I will be asked to complete some tasks to measure my ability to carry out normal daily activities. These tasks include rising from a chair, short brisk walks and climbing a flight of stairs. Any risk of injury during the completion of these tasks will be minimized by having all sessions supervised by an exercise physiologist qualified to direct this type of testing and wearing a safety harness during the short brisk walks and climbing a flight of stairs.

I understand that it is also possible that heart or blood vessel problems could arise during my participation in the testing or training involved in this study. Although unusual, it is possible that these problems could lead to a heart attack or even death. Therefore, prior evaluation and permission from my physician will be required to participate in this study. I also understand that it is possible that these risks will not be eliminated completely, even with a medical evaluation prior to participation in the study. However, we believe the risk of harm from study participation is small and that the benefits of the study will likely outweigh any probable risks.

I understand that all information collected in this study is confidential, and that my name will not be identified at any time to anyone other than the investigators of the study.

I understand that this study is not designed to help me personally, but may help the investigators better understand who is likely to be most and least susceptible to losing strength, power, and muscle mass with advanced age and who is most and least likely to benefit from strength training.

I understand that it is my decision and my decision alone whether or not I consent to participate in this study. I understand that I am free to ask questions about this study before I

decide whether or not to consent to participate in it. I understand that if I consent to participate in the study I am free to withdraw from participation at any time without penalty or coercion, or without any requirement that I provide an explanation to anyone of my decision to withdraw.

For my participation in the study I will receive information after the study is completed about my blood pressure, blood test results, bone mineral density, body composition, and functional ability, free of charge. However, I understand that I will not receive any financial compensation in exchange for my participation in this study.

In the event of physical injury resulting from participation in this study, upon my consent, emergency treatment will be available at the medical center of Washington Adventist Hospital with the understanding that any injury that requires medical attention becomes my financial responsibility. I understand that the University of Maryland at College Park will not provide any medical or hospitalization insurance coverage for participants in this research study, nor will they provide compensation for any injury sustained as a result of this research study, except as required by law.

I understand that if I am injured while participating in this research project as a result of the negligence of a United States Government employee who is involved in this research project, I may be able to be compensated for my injury in accordance with the requirements of the Federal Tort Claims Act. If I am a federal employee acting within the scope of my employment, I may be entitled to benefits in accordance with the Federal Employees Compensation Act.

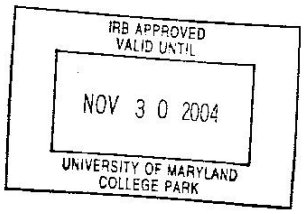
I understand that I can discuss this research study at any time with the principal investigator, Dr. Ben Hurley at (301) 405-2486 or with the study coordinator, Matt Delmonico, at (301) 405-2569.

I have read and understand the above information and have been given an adequate opportunity to ask the investigators any questions I have about the study. My questions, if any, have been answered by the investigators to my satisfaction. By my signature I am indicating my decision to consent to participate voluntarily in this study.

Principal investigator: Ben Hurley, Ph.D., Dept of Kinesiology, HLHP Building, University of Maryland, College Park, MD 20742-2611, Ph: (301) 405-2486.

Printed Name of Subject_____

Signature of Subject_____ Date_____



Detailed Telephone Interview Form

Name of Interviewer:_____ Eligible to Participate: ___Yes ___No
Date of Interview: _____ _____Need More Information or Review

University of Maryland at College Park
Department of Kinesiology

THE GUSTO STUDY
Data Sheet for Detailed Subject Telephone Interview

AGE: _____

50 – 64 years _____
65 or older _____

o **Brief Explanation of Study**
o **Permission to Conduct Interview?** _____Yes _____No

Comment:_____

o **Contact Information**

Name: Mr. Mrs._____
Address:_____
_____
Phone #:(W)_____(H)_____
E-Mail:_____
Best Way and Time to Contact:_____

- **Time Commitment** – Available
  ____Yes ____No Wants to be contacted after _____(Date) Comment:_____
  _____

- **Proximity to UMD Campus**
  Length of commute: _____ miles or _____ minutes
  Within reasonable commute_____ Willing to make unreasonable commute_____
  Too far to commute_____

- **Age**
  Age: _____ yrsDate of Birth: _____/_____/_____
  MM DD YY
  Approximate Height: _____Approximate Weight: _____

- **Racial Identification:**
  ___ American Indian or Alaskan Native
  ___ Asian or Pacific Islander
  ___ Black, not of Hispanic origin
  ___ Hispanic
  ___ White, not of Hispanic origin
  ___ Other/Unknown

- **Smoking**
  Always Non-Smoker_____ Non-Smoker for _____ Smoker_____

- **Communication Log**
  _____
  _____
  _____
  _____
  _____

- **Physical Activity**

1. Do you do any walking/jogging? _____

Hours per week? _____

Times per week?_____

Speed/Pace?_____

Hills? _____

Do you perspire? _____

2. What household jobs do you do? Gardening, housework, yardwork etc. _____

_____

_____

Hours per week? _____

Times per week?_____

Do you perspire? _____

3. Do you do any recreational activities? Sports, fishing, golfing, yoga, pilates, exercise classes etc.

_____

Hours per week? _____

Times per week?_____

Do you perspire? _____

4. What is your profession? _____

Please describe a typical day at work. _____

_____

_____

How much time each day do you spend walking around?_____

5. Do you lift any heavy objects regularly?_____

6. Is there any aspect of your physical activity that is very inconsistent or sporadic?_____

_____

Relatively Sedentary?

_____Yes _____No

Cardiovascular/Respiratory Conditions

____No ____Yes (Record on Medical History/Treatment Form)

Comments:_____

_____

- **Heart Problems:**

  Did your doctor ever tell you that you had a heart problem? ___Yes ___No

  If yes, what was the date of onset? _____

  What did the doctor call it? (Angina, Heart Failure, Heart attack, Rhythm disturbances, heart murmurs, enlarged heart, diseases of heart valves, others).

  _____

  _____

- **Osteoarthritis/Degenerative Arthritis**

  ___No ___Yes

  If yes, how long and what was the severity_____

  _____

- **High Blood Pressure**

No_____

Yes_____ Controlled (Record High BP and Treatment on Medical History/Treatment Form)

Yes_____ Uncontrolled

Comments:_____

_____

- **Lower Back Pain**

  ___No ___Yes

  If yes, how severe?_____

- **Frailty**

  No Incidents_____

  Fracture as Adult?_____ Describe:_____

  _____

  > 2 Falls in One Year?_____ Describe:_____

  _____

  Comments:_____

  _____

- **Diabetes**

_____No

_____Yes – Type II (Non-Insulin Dependent)

(Record Type II Diabetes and Treatment on Medical History/Treatment Form)

_____Yes – Type I – (Insulin Dependent – not qualified for the GUSTO study)

Comments:_____

_____

- **Orthopedic Conditions**

_____No

_____Yes (Record on Medical History/Treatment Form)

Comments:_____

_____

- **Stroke/Paralytic conditions**

_____Yes ____No. (If yes ask subject if there is any residual weakness of any extremity)

- **Surgical History**

___No ___Yes
If yes, what type (surgeries of the joints, heart surgeries, angioplasty, bypass surgery, Pacemakers)_____
When_____

- **Other Medical Conditions**

_____No
_____Yes (Record on Medical History/Treatment Form)
Comments:_____
_____

- **Information on where to send Physician Consent Form**

Name of Physician: _____
Specialty of Physician:_____
Have you seen your physician within the past 12 months? ____Yes ____No
Phone Number:_____
Fax Number: _____
Address (if phone and fax unknown):_____
_____
_____
(Please explain to the subject that he/she is unlikely to get med clearance if they have not seen their doc within the past 12 months and request them to go to the physician. If willing, request them to let us know after they meet their doctor and fax the med clearance form to physician AFTER they go to their doctor)

- **Summary**

Interviewer Signature: _____

Questions/ Comments:_____
_____
_____

Reviewer Initials: _____

_____Qualifies _____Need More Information
_____Needs Dr. Hurley's Review _____ Disqualified

Questions/ Comments:_____
_____

Medical Clearance

Medical Clearance to Participate in Research Project

It is my understanding that _____ (name of the volunteer), a patient under my care, has volunteered to participate in the study entitled, ***"Do Genes Influence Responses to Strength Training?"*** The volunteer must have the approval of her or his physician to participate in this study.

Exclusionary criteria for eligibility are listed below. If you believe that your patient named above has any of the medical conditions indicated below, please place a check in front of the condition(s) indicated:

____ Severe cardiovascular disease, such as ____unstable angina, ____uncontrollable hypertension, ____uncontrolled dysrhythmias, ____severe stenotic or regurgitant valvular disease, ____hypertrophic cardiomyopathy, and ____symptomatic peripheral arterial disease
____ Severe COPD or other signs of significant pulmonary dysfunction
____ Intracranial aneurysm
____ Musculoskeletal diseases that cause severe joint pain at rest or upon exertion
____ Diseases that promote muscle protein breakdown
____ Joint, vascular, abdominal or thoracic surgery in the past year
____ History of bone fragility fractures
____ Having any condition that is likely to be aggravated by muscular exertion
____ Being unable to engage safely in mild to moderate exercise, such as independently walking up at least one flight of stairs or walking two blocks on level ground

Although we are unaware of any cardiac complications that have resulted from strength testing or strength training, there is only a limited amount of data available in people over the age of 75. There is evidence of non-fatal subarachnoid hemorrhage in patients with pre-existing intracranial aneurysms and aortic dissection in predisposed patients, associated with strength training. For this reason, any patient who has known, suspected, or at high risk for intracranial aneurysms, aortic dissection, connective tissue disease or uncontrolled hypertension should not participate in this study.

Please check one of the following:
____ Clearance granted
____ Clearance not granted
____ Please send me the following information about the study:

Volunteers in this study will participate in resistance exercise under the supervision of exercise specialists trained specifically for this study under the direction of the Principal Investigator, Ben Hurley Ph.D., Professor, Department of Kinesiology, College of Health and Human Performance, University of Maryland, College Park, Maryland 20742 (email: benhur@umail.umd.edu; tele: 301-405-2486). Please fax signed form: (301) 405-5578.

Physician's signature:_____ Date:_____

Medical History Form

Name:_____ **Sex**____ **Initials:** ___ ___

Name of Interviewer: _____ **Date:** _____

Emergency contact name, address, phone_____

_____

Have you ever been a patient at Washington Adventist Hospital? _____Yes _____No ____not sure

MEDICAL HISTORY FOR GUSTO STUDY

DIRECTIONS:

Read the following questions out loud to each prospective volunteer and check "yes" or "no". Any answers that require qualification should be written in the space below the question or on the back of the sheet.

YES NO

SECTION *A*

Musculoskeletal system:

Have you ever been told by your doctor that you have any of the following?

a. Osteoarthritis or degenerative arthritis ___ ___

b. Rheumatoid arthritis ___ ___

c. Unknown or other type of arthritis (eg: Ankylosing Spondylitis) ____ ___

d. Osteoporosis ___ ___

e. Any other disease of joint or muscle: ____ ___

Comments:_____

_____

SECTION *B*

Cardiovascular system:

1. Has any family member had a heart attack prior to the age of 55? ___ ___

   If so, please describe the relationship:

	YES	NO
2. Have you ever had frequent cramping in your legs?	___	___
If yes, is it a current problem?	___	___
3. Have you ever had pain or cramping in your legs while walking?	___	___
If yes, is it a current problem?	___	___
If yes, is this pain relieved by rest or by discontinuing your walk?	___	___
4. Have you ever been told that you have high blood pressure?	___	___

If yes,

a. What was the date of diagnosis? _____

b. Were you given any medications? ___ ___

(Please list the medications with dose on the last page)

c. How long have you been on the medications? _____ ___ ___

d. Has there been a recent change in the medications and if so, when? _____

5. Did a doctor ever tell you that you had a heart problem? ___ ___

If yes,

a. What was the date of onset?

b. What did the doctor call it? (eg: Angina, Heart Failure, Heart Attack, Rhythm disturbances, heart murmurs, enlarged heart, diseases of heart valves, others). *Please circle relevant one(s). If others, please ask subject to explain.*

c. Were you given any medications? *(Please list the medications with dose on the last page)*

d. Was Echocardiography ever done? ___ ___

6. Have you ever had any chest pain or discomfort other than breast pain (in women)? or pain and discomfort due to a respiratory or digestive problem? ___ ___

If yes,

a. What was the month and year of the first occurrence? _____

b. What was the month and year of the most recent occurrence? _____

c. What was the frequency of occurrence? (eg: once a month, once a week, once a year etc.)

_____

d. How would you describe the pain or discomfort? (Eg: Pressure, Burning,

Squeezing, Piercing, Stabbing, Shooting or Sticking) *Circle appropriate one or if different, please describe*_____

How many minutes did it last?_____

e. Does the pain or discomfort move? If yes, to where?

f. Does the pain or discomfort tend to occur:

After meals-	____	____
At night-	____	____
When Exercising-	____	____
When walking in cold windy weather-	____	____
When upset, excited or nervous-	____	____
Other-		

g. Is this pain relieved by

A change in posture-	____	____
Rest-	____	____
Physical activity-	____	____
Bicarbonate of soda, Tums or antacids-	____	____
Prescribed medications-	____	____
Other-		

h. Did you ever consult a doctor for this pain or discomfort? ____ ____

If yes,

Do you know the diagnosis?_____

Were you given any medications and if so was there a recent change in the medication (within past one month)? (*Please list on last page, if yes*) _____ _____

7. Do you have any history of high cholesterol in your blood as evident by previous blood lipid tests? ____ ____

Comments:_____

_____

SECTION *C* **YES NO**

Respiratory System:

1. Have you ever had persistent cough with sputum production for almost all days for 3 months for two consecutive years? ____ ____

   If yes,

   a. How long did it last?

   b. Did your doctor prescribe any medications and has there been any recent change in the medication:

(*Please list on last page, if any*)

2. Have you ever had attacks of wheezing? ____ ____

   If yes,

   a. Was it seasonal/ periodic? ____ ____

   b. Have you ever-required hospitalization to abort an acute attack? ____ ____

Comments:_____

_____

SECTION *D*

Endocrine system:

Has your doctor ever told you that you have any of the following?

a. Thyroid problems? ____ ____

b. Adrenal problems? ____ ____

c. Diabetes mellitus? ____ ____

   If yes, which type?

Date of onset-_____

Were you on any medication, diet control ____ ____

SECTION *E* **YES NO**

Reproductive system:

Menstrual History

a. Have you attained menopause? ____ ____

If so,

Are you on Hormone Replacement Therapy? ____ ____

If yes, how long have you been on hormone replacement therapy?_____

Comments:_____

_____

SECTION *F* **YES NO**

Neurological system:

1. Do you have any problems with your memory? If yes,
   a. When answering the telephone, do you recall what you were doing before it rang? ____ ____
   b. If someone calls you, can you give the directions to your house? ____ ____
   c. Can you keep appointments without a reminder? ____ ____
   d. Can you remember what clothes you wore yesterday? ____ ____

   If the subject answers "no" to any of the above questions

   Do a Mini Mental Status Examination of the subject.
2. Any problems with vision other than corrective lens changes? ____ ____

   If yes, which of the following conditions- Blindness, Temporary loss of vision, Double vision, Glaucoma, Cataract, Macular degeneration or others.

	YES	NO
3. Ringing in your ears?	____	____
4. Vertigo (a feeling of spinning, or unsteadiness)	____	____
5. Fainting Spells (black outs)?	____	____
6. Seizure or convulsions?	____	____
7. Migraine or severe headaches?	____	____
8. Paralysis of arm or leg?	____	____
9. A head injury with loss of consciousness?	____	____
10. Pain, numbness or tingling in your arm or hand?	____	____
11. Pain in your lower back?	____	____
12. Kidney stones?	____	____
13. Ruptured vertebral disc in neck or back?	____	____
14. Have you had pain in any part of body (including headache) while exercising?	____	____
15. Numbness or pain in your legs?	____	____
16. Have you been told that you have a peripheral neuropathy?	____	____
17. Tremors?	____	____
18. Problems with walking?	____	____
a. Do you fall frequently?	____	____
b. Is your walking problem related to pain, weakness or loss of balance?	____	____
19. Stroke?	____	____
20. Epilepsy?	____	____
21. Operations on skull or brain?	____	____
22. Multiple sclerosis?	____	____
23. Meningitis or Brain fever?	____	____
24. Parkinson's disease	____	____

25. Any history of neurological consultation? ____ ____

Comments:_____

_____

SECTION *H* **YES** **NO**

Hematology/Immunology/Oncology :

1. Have you ever been told by your physician that you had a problem with anemia or any disease of the red blood cells or the white blood cells? ____ ____
2. Any family history of this problem? ____ ____
3. Do you have any history of bleeding disorders? ____ ____
4. Have you ever been diagnosed as having cancer? ____ ____

   If yes, which organ, date of onset? _____
5. Were you given any medications, radiation or undergone any surgery? ____ ____

Comments:_____

_____

SECTION *I*

Surgical History:

Have you undergone any surgeries? (Please include abdominal surgery) ____ ____

If yes,

a. Where and for what purpose? _____
b. Date of Surgery? _____
c. Length of stay in hospital _____
d. Any complications of Surgery? _____

Comments:_____

_____

Has a doctor ever told that you have been suffering from

a) Cystic medial degeneration _____ _____

b) Any Connective tissue disorder? _____ _____

Has any of your family member had an intracranial aneurysm or bleeding? _____ _____

Have you ever been diagnosed with an abdominal aneurysm? _____ _____

History of severe pain in the abdomen? _____ _____

If yes, Please specify_____

Any history of severe headache? _____ _____

If Yes,

What was the date of onset?_____

Was it associated with neurological signs like blurred vision, nausea/vomiting, seizures, drowsiness,memory impairment,sensory or motor loss(weakness)? _____ _____

Was it a new or different type of headache other than tension, migraine etc? _____ _____

Was it the worst ever experienced? _____ _____

Did it occur after exertion, coughing or straining? _____ _____

SECTION *J*

Do you have any other health problems not covered in this questionnaire? ____ ____

If yes, please do specify.

Comments:_____

_____

Physical Activity Questionnaire

Subject Name:_____ Initials: _ _ _ #: _ _ _ _ _

GUSTO

PHYSICAL ACTIVITY SCALE

(PASE)

INSTRUCTIONS:

Please complete this questionnaire by either circling the correct response or filling in the blank. Here is an example:

During the past 7 days, how often have you seen the sun?

(0) NEVER (1) SELDOM (1-2 DAYS) (2) SOMETIMES (3-4 DAYS) (3) OFTEN (5-7 DAYS)

Answer all items as accurately as possible. All information is strictly confidential.

Initials: _ _ _ #: _ _ _ _ _

LEISURE TIME ACTIVITY

1. Over the past 7 days how often did you participate in sitting activities such as reading, watching TV or doing handcrafts?

(0) NEVER	(1) SELDOM	(2) SOMETIMES	(3) OFTEN
↓	(1-2 DAYS)	(3-4 DAYS)	(5-7 DAYS)
GO TO Q #2	↓	↓	↓

1a. What were these activities?

_____

1b. On average, how many hours per day did you engage in these sitting activities?

(1) LESS THAN 1 HOUR (2) 1 BUT LESS THAN 2 HOURS

(3) 2-4 HOURS (4) MORE THAN 4 HOURS

2. Over the past 7 days, how often did you take a walk outside your home or yard for any reason? For example, for fun or exercise, walking to work, walking the dog, etc?

(0) NEVER	(1) SELDOM	(2) SOMETIMES	(3) OFTEN
↓	(1-2 DAYS)	(3-4 DAYS)	(5-7 DAYS)
GO TO Q #3	↓	↓	↓

2a. On average, how many hours per day did you spend walking?

(1) LESS THAN 1 HOUR (2) 1 BUT LESS THAN 2 HOURS

(3) 2-4 HOURS (4) MORE THAN 4 HOURS

Initials: __ __ __ #: __ __ __ __ __

3. Over the past 7 days, how often did you engage in light sport or recreational activities such as bowling, golf with a cart, shuffleboard, fishing from a boat or pier or other similar activities? (Do not include walking.)

(0) NEVER	(1) SELDOM	(2) SOMETIMES	(3) OFTEN
↓	(1-2 DAYS)	(3-4 DAYS)	(5-7 DAYS)
GO TO Q #4	↓	↓	↓

3a. What were these activities?

_____

3b. On average, how many hours per day did you engage in these light sport or recreational activities?

(1) LESS THAN 1 HOUR (2) 1 BUT LESS THAN 2 HOURS

(3) 2-4 HOURS (4) MORE THAN 4 HOURS

4. Over the past 7 days how often did you engage in moderate sport and recreational activities such as doubles tennis, ballroom dancing, hunting, ice skating, golf without a cart, softball or other similar activities? (Do not include walking.)

(0) NEVER	(1) SELDOM	(2) SOMETIMES	(3) OFTEN
↓	(1-2 DAYS)	(3-4 DAYS)	(5-7 DAYS)
GO TO Q #5	↓	↓	↓

4a. What were these activities?

_____

4b. On average, how many hours per day did you engage in these moderate sport and recreational activities?

(1) LESS THAN 1 HOUR (2) 1 BUT LESS THAN 2 HOURS

(3) 2-4 HOURS (4) MORE THAN 4 HOURS

Initials: ___ ___ ___ #: ___ ___ ___ ___ ___

5. Over the past 7 days, how often did you engage in strenuous sport and recreational activities such as jogging, swimming, cycling, singles tennis, aerobic dance, skiing (downhill or cross-country) or other similar activities?

(0) NEVER	(1) SELDOM	(2) SOMETIMES	(3) OFTEN
↓	(1-2 DAYS)	(3-4 DAYS)	(5-7 DAYS)
GO TO Q #6	↓	↓	↓

5a. What were these activities?

_____

5b. On average, how many hours per day did you engage in these strenuous sport and recreational activities?

(1) LESS THAN 1 HOUR (2) 1 BUT LESS THAN 2 HOURS

(3) 2-4 HOURS (4) MORE THAN 4 HOURS

6. Over the past 7 days, how often did you do any exercises specifically to increase muscle strength and endurance, such as lifting weights or pushups, etc?

(0) NEVER	(1) SELDOM	(2) SOMETIMES	(3) OFTEN
↓	(1-2 DAYS)	(3-4 DAYS)	(5-7 DAYS)
GO TO Q #7	↓	↓	↓

6a. What were these activities?

_____

6b. On average, how many hours per day did you engage in exercises to increase muscle strength and endurance?

(1) LESS THAN 1 HOUR (2) 1 BUT LESS THAN 2 HOURS

(3) 2-4 HOURS (4) MORE THAN 4 HOURS

Initials: ___ #: _____

HOUSEHOLD ACTIVITY

7. During the past 7 days, have you done any light housework, such as dusting or washing dishes?

   (1) NO (2) YES

8. During the past 7 days, have you done any heavy housework or chores, such as vacuuming, scrubbing floors, washing windows, or carrying wood?

   (1) NO (2) YES

9. During the past 7 days, did you engage in any of the following activities?

   Please answer YES or NO for each item.

		NO	YES
a.	Home repairs like painting, wallpapering, electrical work, etc	1	2
b.	Lawn work or yard care, including snow or leaf removal, wood chopping, etc.	1	2
c.	Outdoor gardening	1	2
d.	Caring for an other person, such as children, dependent spouse, or an other adult	1	2

Initials: __ __ __ #: __ __ __ __ __

WORK-RELATED ACTIVITY

10. During the past 7 days, did you work for pay or as a volunteer?

(1) NO (2) YES
↓

10a. How many hours per week did you work for pay and/or as a volunteer?
_____HOURS

10b. Which of the following categories best describes the amount of physical activity required on your job and/or volunteer work?

(1) Mainly sitting with slight arm movements. (**Examples**: office worker, watchmaker, seated assembly line worker, bus driver, etc.)

(2) Sitting or standing with some walking. (**Examples**: cashier, general office worker, light tool and machinery worker.)

(3) Walking, with some handling of materials generally weighing less 50 pounds. (**Examples**: mailman, waiter/waitress, construction worker, heavy tool and machinery worker.)

(4) Walking and heavy manual work often requiring handling of materials weighing over 50 pounds. (**Examples**: lumberjack, stone mason, farm or general laborer.)

Data Entry Date: _____ Time: _____ GUSTO Team Member Initials: __ __ __
Verification Date: _____ Time: _____GUSTO Team Member Initials: __ __ __

DXA Record

DEXA Body Scan – USDA / University of Maryland
Conway/Hurley/Kostek

Date:_____ Time:_____am/pm

Name:_____ Gender: M / F

Date of Birth:_____

Height:_____ inches _____ cm

Weight:_____ lbs. _____ kg

Subject number:_____

Dominant leg: R / L

Time and composition of last meal (or snack):

_____
_____
_____
_____

Comments:_____
_____

Initials of examiner and DXA technician:_____

CT Appointment Request

The GUSTO Study

"**G**enes **U**nderlying **S**trength **T**raining adaptations in **O**lder adults"

UNIVERSITY OF MARYLAND

College Park

To: Washington Adventist Hospital, Centralized Records & Admitting

Fax #: (301) 891-6149

From: Ben Hurley, Ph.D., Professor, Department of Kinesiology

Fax #: (301) 405-5578 Phone #: (301) 405-2569

RE: Scheduling of patients for CT muscle mass study

Patient Name _____

Previously a patient at Washington Adventist Hospital: ___Yes ___No

Date/Time for CT scan _____ DOB: _____ Age _____ Sex ___

CT scanner: ___Old scanner ___Newer scanner ___Either

Address _____ Phone # _____

_____

_____

Diabetes: __Yes __No If yes, type 1 or type 2? _____ Meds: _____

Scan type: Extremity (bilateral thigh) Contrast: **NO**

Emergency Contact (relationship) _____ Phone # _____

1 RM Data Collection Form

University of Maryland / National Institute on Aging
GUSTO

Symptom-limited Baseline Knee Extension 1-RM

Arms across chest	_____
Seat Belt	_____
Remember to breathe	_____

CHECK EACH LINE BEFORE TEST

Examiners Name_____
Name_____ Date_____
Time _____ Location_____
Body weight_____ Age_____ Predicted 1-RM_____

Seat_____ Leg_____ Blood Pressure_____ ***Right leg / Left leg***

	Resistance	**P/D scale**	**RPE scale**
Rest	_____	_____	_____
Set 1	___0___	_____	_____
Set 2	_____	_____	_____
Set 3	_____	_____	_____
Set 4	_____	_____	_____
Set 5	_____	_____	_____
Set 6	_____	_____	_____
Set 7	_____	_____	_____
Set 8	_____	_____	_____
Set 9	_____	_____	_____
Set 10	_____	_____	_____
Set 11	_____	_____	_____
Set 12	_____	_____	_____

Most severe P/D: _____ Subject's initials: _____

Post BP_____ 3 min. post BP_____ **Valid** **Invalid**

If invalid, please explain: _____
_____
Notes: _____
_____
_____
_____

Muscle Power Testing Form

Subject Initials: _ _ _ **Subject #:** _ _ _ _ _ _

GUSTO STUDY

Name _____ Date _____
Tester _____ Time _____

Post Unilateral Training: Power Test #1

Resting BP: ___/___mmHg

Seat Position:____ 1-RM R:_____ Dominant Leg: R L Order of Testing: _R _L
1-RM L :_____
30% I-RM R____Practice P/D:_____ 30% I-RM L____ Practice P/D:_____

% 1-RM	R Resistance	Test #	P/D & Location (0-6)	Immed dissip (Y/N)	L Resistance	Test #	P/D & Location (0-6)	Immed dissip (Y/N)	File Name Initials number P1 %1-RM.txt
50									_____ _
50									_____1P506
50									070scan.txt
60									_____ _
60									_____1P506
60									070graf.txt
70									
70									
70									

Immediate BP: ___/___mmHg Constant Reminders: Back against seat
Look straight ahead
3 min BP: ___/___mmHg Breathe Normally

General Comments:_____
_____

Test Comment

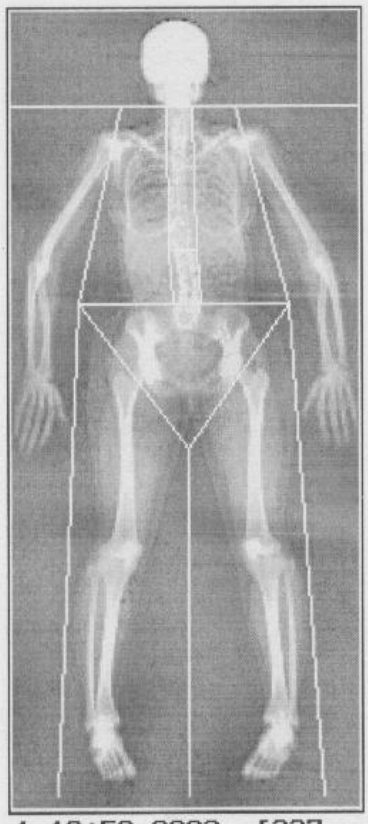
_____
_____
_____
_____

Data Entry Date: _____ Time: _____GUSTO Team Member Initials: _ _ _

Verification Date: _____ Time: _____GUSTO Team Member Initials: _ _ _

DXA Result Example

HOLOGIC



oMay 1 10:50 2003 [327 x 150]
Hologic QDR-4500A (S/N 45816)
Whole Body Fan Beam V8.26a:3*

A11220209 Fri Nov 22 11:34 2002
Name:
Comment: GUSTO post unilateral
I.D.: GUSTO Sex: F
S.S.#: - - Ethnic: W
ZIP Code: Height:5'10"
Operator: MJD Weight: 133
BirthDate: Age: 61
Physician: GUSTO
Image not for diagnostic use
TBAR1790 - 1
F.S. 68.00% 0(10.00)%
Head assumes 17.0% brain fat
LBM 73.2% water

Region	Fat (grams)	Lean+BMC (grams)	% Fat (%)
L Arm	1082.4	2034.7	34.7
R Arm	1104.2	2059.6	34.9
Trunk	6946.6	21128.9	24.7
L Leg	4457.0	6865.2	39.4
R Leg	4287.2	6747.0	38.9
SubTot	17877.4	38835.4	31.5
Head	808.2	3267.2	19.8
TOTAL	18685.6	42102.6	30.7

HOLOGIC

Training Log

Unilateral Strength Training

Subject's Name: _____ Seat position _____ 1 RM value ___ Leg ___

BP Questions:
1) Ever been told high Blood Pressure? -If yes, taken medication today and yesterday?
2) Heavy meal in past 90 minutes?
3) Had coffee/tea in past 30 minutes?
4) Smoked in past 30 minutes?
5) Any type of exercise in past 30 minutes?

Training Session #	FAM I	FAM II	1	2	3	4	5	6
Date								
Pre-Ex .BP (mm Hg)								
5 RM*Resistance (lbs)								
Peak Ex.BP (mm Hg)								
Post Ex.BP (mm Hg)								
Weight (lbs)								

*= Weight adjusted as needed to maintain 5 RM

Training Session #	10	11	12	13	14	15	16	17	18	19	20
Date											
Pre-Ex .BP (mm Hg)											
5 RM*Resistance (lbs)											
Peak Ex.BP (mm Hg)											
Post Ex.BP (mm Hg)											
Weight (lbs)											

*= Weight adjusted as needed to maintain 5 RM

Training Session #	21	22	23	24	25	26	27	28	29	30	31
Date											
Pre-Ex .BP (mm Hg)											
5 RM*Resistance (lbs)											
Peak Ex.BP (mm Hg)											
Post Ex.BP (mm Hg)											
Weight (lbs)											

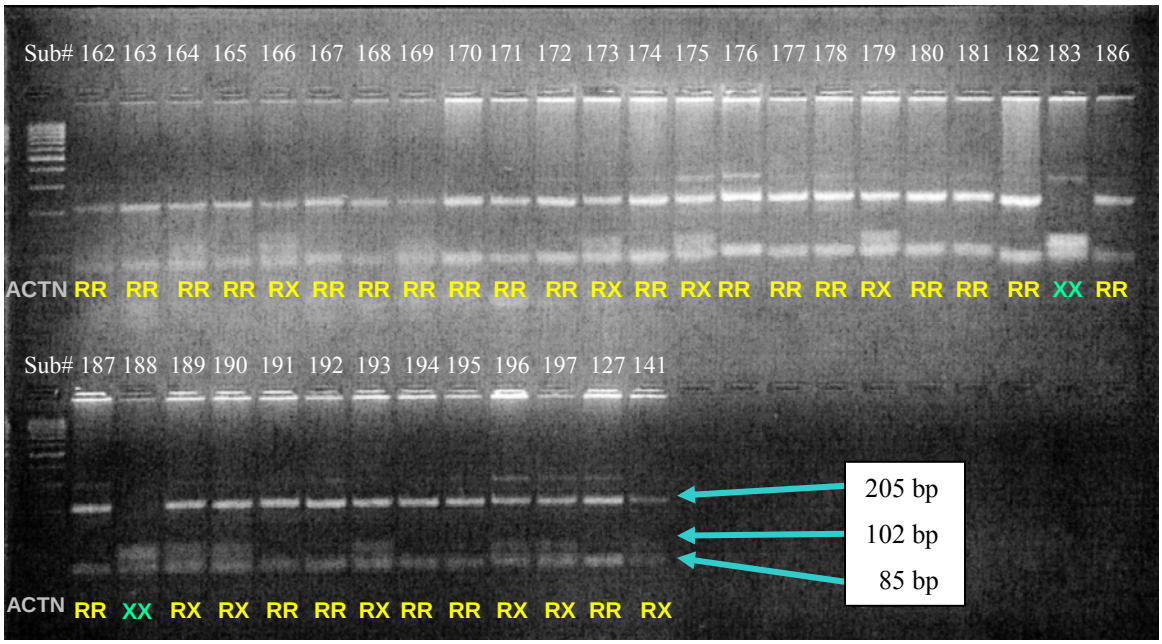
*= Weight adjusted as needed to maintain 5 RM

Training

- 5 reps @ 50% of 1 RM resistance- 30 sec rest
- 5 reps @ 5 RM resistance- 1.5 min rest
- ~5reps @ 5 RM resistance, then lower weight just enough to do 1-3 reps, repeat process until 10 total reps -2.5 min rest.
- ~5reps @ 5 RM resistance, then lower weight just enough to do 1-3 reps, repeat process until 15 total reps -3 min rest.
- ~5reps @ 5 RM resistance, then lower weight just enough to do 1-3 reps, repeat process until 20 total reps

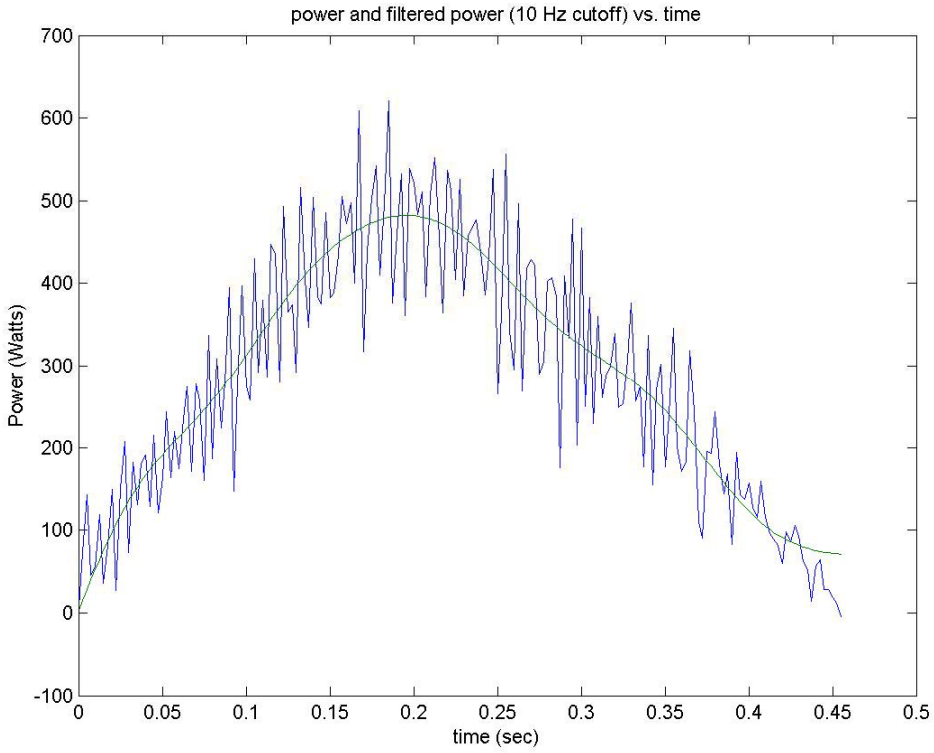
APPENDIX C

Representation of RFLP ACTN3 Genotyping Gels

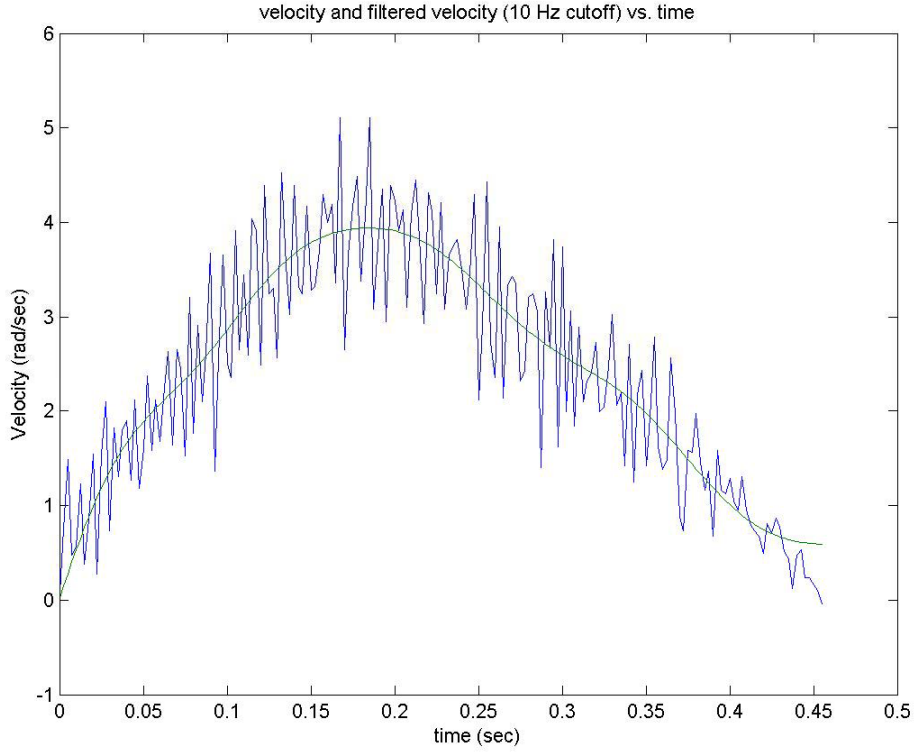


APPENDIX D

Raw and Filtered Power Data



Raw and Filtered Movement Velocity Data



APPENDIX E: RAW DATA

ID Number	Sex	ACTN	Age	Height		Pre fat mass	After fat mass	Pre FFM	After FFM	Pre weight	After weight	Pre body fat %	After body fat %	Pre BMI	After BMI	1RM Pre	1RM After
			yr	cm	grams	grams	grams	grams	grams	kg	kg			kg/m^2	kg/m^2	kg	kg
CON 024	F	RR	74	163.0	24679.8	25773.0	39729.0	40422.0	68.75	68.73	37.5	35.9	25.87	25.87	13.27	21.60
CON 023	F	RX	67	163.0	31064.1	29112.6	42428.0	43572.0	80.27	81.78	35.6	38.7	30.21	30.78	10.42	16.39
CON 005	M	RR	72	180.0	.	22447.0	53101.0	.	78.60	77.94	28.8	.	24.26	24.06	27.84	34.09
CON 011	M	RR	66	178.0	35439.5	34722.7	59901.0	59283.0	98.99	99.78	34.8	35.8	31.24	31.49	25.76	43.46
CON 004	M	RX	70	178.0	31004.1	32201.9	52805.0	55512.0	90.39	89.70	35.9	34.3	28.53	28.31	29.93	40.34
CON 010	M	RR	74	178.0	.	.	.	.	83.74	83.18	.	.	26.43	26.25	26.80	33.05
CON 016	F	RR	65	152.0	29941.5	32341.7	37477.0	36597.0	68.83	74.52	43.4	43.5	29.79	32.25	13.68	16.39
CON 021	F	RX	71	174.0	32052.5	34706.5	45077.0	46748.0	80.53	80.90	42.9	39.8	26.60	26.72	17.43	25.76
CON 007	M	RX	69	168.0	15981.7	16317.5	53298.0	54195.0	71.67	71.57	22.8	22.3	25.39	25.36	27.43	38.26
CON 002	M	RX	72	170.0	15287.5	14672.2	48398.0	48573.0	65.33	66.39	22.1	23.4	22.61	22.97	28.89	37.22
CON 001	M	RR	69	163.0	27683.4	.	47710.0	.	93.21	.	40.6	.	35.08	.	32.01	.
CON 020	F	RR	72	157.0	27729.3	28322.8	36378.0	36370.0	66.34	67.76	41.8	41.8	26.91	27.49	18.47	24.72
CON 003	M	RR	67	173.0	24697.7	26436.6	52948.0	53638.0	82.05	82.36	32.1	30.1	27.42	27.52	37.22	44.50
CON 022	F	RX	70	150.0	29584.4	27377.6	35942.0	35605.0	66.93	63.52	43.1	44.2	29.75	28.23	15.35	16.39
CON 009	M	RR	73	173.0	25240.4	26099.4	54462.0	54989.0	83.86	83.92	31.1	30.1	28.02	28.04	32.01	39.30
CON 014	F	RX	67	165.0	32224.8	32849.0	42311.0	42372.0	75.12	75.69	43.4	42.9	27.59	27.80	17.43	22.64
HUR 014	M	RR	60	182.8	37340.0	.	75606.0	.	112.27	.	33.3	.	33.60	.	40.95	.
HUR 015	F	RR	78	168.5	41978.0	40472.1	45664.3	46447.1	87.64	86.92	47.9	46.6	30.87	30.61	17.84	25.75
HUR 017	M	XX	80	160.5	14556.1	15087.8	51831.3	49790.2	66.39	64.88	21.9	23.3	25.77	25.19	20.54	28.04
HUR 018	M	RR	77	168.6	22331.2	21944.7	56365.1	57662.4	78.70	79.61	28.4	27.6	27.68	28.01	30.96	37.20
HUR 022	M	RR	70	178.9	17122.2	16860.8	56900.1	57877.8	74.02	74.74	23.1	22.6	23.13	23.35	33.87	42.83
HUR 023	F	RR	61	165.1	22166.1	22483.7	40395.7	40976.7	62.56	63.46	35.4	35.4	22.95	23.28	18.88	22.63
HUR 025	F	RX	57	169.6	37612.7	42014.4	52940.7	51198.5	90.55	93.21	41.5	45.1	31.48	32.41	13.05	24.08
HUR 027	F	RR	52	161.6	47347.2	.	54034.5	.	101.38	.	46.7	.	38.82	.	27.21	34.50
HUR 028	F	RR	64	160.0	25492.8	22774.8	38212.7	43174.6	63.71	65.95	40.0	34.5	24.88	25.76	15.31	22.17
HUR 029	M	RR	51	170.1	19632.7	.	54611.6	.	74.24	.	26.4	.	25.65	.	.	.
HUR 030	F	RR	57	162.6	18755.6	17515.1	41604.8	42425.3	60.36	59.94	31.1	29.2	22.84	22.68	18.04	23.88
HUR 031	F	XX	60	165.0	39983.8	41709.8	48257.0	48078.8	88.24	89.79	45.3	46.5	32.41	32.98	15.75	22.63
HUR 032	M	RX	54	168.6	34423.9	32962.8	61266.3	62716.4	95.69	95.68	36.0	34.5	33.66	33.66	34.70	41.37
HUR 033	F	RR	62	178.0	17389.4	18685.6	43149.4	42102.6	60.54	60.79	28.7	30.7	19.11	19.19	23.04	.
HUR 034	F	XX	65	172.7	37378.5	34991.7	53634.5	53730.4	91.01	88.72	41.1	39.4	30.52	29.75	22.63	28.87

ID Number	70% Untrained Leg PP Pre	70% Untrained Leg PP After	70% Untrained Leg PV Pre	70% Untrained Leg PV After	Abs PP Untrained Leg Pre	Abs PP Untrained Leg After	Abs PV Untrained Leg Pre	Abs PV Untrained Leg After	Muscle Volume Untrained Leg Pre
	watts	watts	rad/sec	rad/sec	watts	watts	rad/sec	rad/sec	cm^3
CON 024	.	.	.	.	.	.	.	.	1223.24
CON 023	.	.	.	.	.	.	.	.	870.30
CON 005	.	.	.	.	.	.	.	.	1796.30
CON 011	.	.	.	.	.	.	.	.	1987.08
CON 004	.	.	.	.	.	.	.	.	1803.30
CON 010	.	.	.	.	.	.	.	.	1662.89
CON 016	.	.	.	.	.	.	.	.	1131.00
CON 021	.	.	.	.	.	.	.	.	1223.55
CON 007	.	.	.	.	.	.	.	.	1683.02
CON 002	.	.	.	.	.	.	.	.	1504.33
CON 001	.	.	.	.	.	.	.	.	1768.00
CON 020	.	.	.	.	.	.	.	.	1133.83
CON 003	.	.	.	.	.	.	.	.	1785.40
CON 022	.	.	.	.	.	.	.	.	1089.60
CON 009	.	.	.	.	.	.	.	.	1725.90
CON 014	.	.	.	.	.	.	.	.	1118.42
HUR 014	.	.	.	.	.	.	.	.	.
HUR 015	.	.	.	.	.	.	.	.	1097.24
HUR 017	.	.	.	.	.	.	.	.	1300.02
HUR 018	.	.	.	.	.	.	.	.	1585.25
HUR 022	.	.	.	.	.	.	.	.	1473.05
HUR 023	.	.	.	.	.	.	.	.	1092.76
HUR 025	.	.	.	.	.	.	.	.	1183.84
HUR 027	.	.	.	.	.	.	.	.	1490.29
HUR 028	175.15	190.18	4.1	4.7	175.15	190.18	4.1	4.7	699.95
HUR 029	.	.	.	.	.	.	.	.	.
HUR 030	200.63	184.29	4.1	3.7	197.44	184.29	3.9	3.7	1095.26
HUR 031	.	.	.	.	.	.	.	.	1024.82
HUR 032	485.96	.	3.8	.	591.24	618.94	6.5	6.8	1788.61
HUR 033	253.81	.	3.8	.	253.81	.	3.8	.	1312.27
HUR 034	254.50	.	3.2	.	254.50	.	3.2	.	1556.40

ID Number	70% PP Pre	70% PP After	70% PV Pre	70% PV After	Abs PP Pre	Abs PP After	Abs PV Pre	Abs PV After	Muscle Volume Pre	Muscle Volume After	1RM Untrained Leg Pre	1RM Untrained Leg After
	watts	watts	rad/sec	rad/sec	watts	watts	rad/sec	rad/sec	cm^3	cm^3	kg	kg
CON 024	.	.	.	.	.	.	.	.	1178.50	1295.65	15.34	16.38
CON 023	.	.	.	.	.	.	.	.	920.00	1036.00	6.03	8.96
CON 005	.	.	.	.	.	.	.	.	1718.60	.	28.87	29.91
CON 011	.	.	.	.	.	.	.	.	1966.12	2085.55	25.75	36.16
CON 004	.	.	.	.	.	.	.	.	1769.80	2055.00	29.29	35.12
CON 010	.	.	.	.	.	.	.	.	1696.22	1916.47	21.58	22.63
CON 016	.	.	.	.	.	.	.	.	1090.20	1252.50	14.50	14.92
CON 021	.	.	.	.	.	.	.	.	1258.60	1373.90	17.42	19.50
CON 007	.	.	.	.	.	.	.	.	1614.96	1858.90	31.58	37.20
CON 002	.	.	.	.	.	.	.	.	1527.98	1691.55	26.79	27.83
CON 001	.	.	.	.	.	.	.	.	.	.	29.91	.
CON 020	.	.	.	.	.	.	.	.	1137.50	1257.88	16.38	19.50
CON 003	.	.	.	.	.	.	.	.	1815.40	2000.33	39.29	40.33
CON 022	.	.	.	.	.	.	.	.	935.70	1132.32	19.50	21.58
CON 009	.	.	.	.	.	.	.	.	1893.26	2040.87	27.83	29.91
CON 014	.	.	.	.	.	.	.	.	1217.20	1272.21	16.38	17.42
HUR 014	.	.	.	.	.	.	.	.	.	.	39.70	.
HUR 015	.	.	.	.	.	.	.	.	1188.24	1281.61	15.96	16.59
HUR 017	.	.	.	.	.	.	.	.	1321.77	1432.60	9.54	16.59
HUR 018	.	.	.	.	.	.	.	.	1531.46	1640.99	26.79	30.96
HUR 022	.	.	.	.	.	.	.	.	1729.19	1859.00	14.30	15.54
HUR 023	.	.	.	.	.	.	.	.	1081.50	1183.62	18.88	19.29
HUR 025	.	.	.	.	.	.	.	.	979.83	1139.65	18.88	24.08
HUR 027	.	.	.	.	.	.	.	.	1441.70	1524.58	24.29	25.12
HUR 028	173.74	179.94	4.4	3.1	173.74	232.55	3.9	4.6	758.44	846.04	10.40	9.67
HUR 029	.	.	.	.	.	.	.	.	.	.	.	.
HUR 030	213.23	.	3.9	.	209.60	246.60	3.3	3.9	1265.30	1303.08	15.54	15.96
HUR 031	.	.	.	.	.	.	.	.	1203.36	1296.60	11.38	14.71
HUR 032	486.26	.	3.8	.	579.37	676.67	5.9	6.4	1839.69	1997.04	32.00	37.20
HUR 033	234.43	.	3.8	.	234.43	.	3.8	.	1245.38	.	22.83	.
HUR 034	238.19	.	2.9	.	238.19	.	2.9	.	1566.18	1705.31	22.00	23.67

ID Number	Muscle Volume Untrained Leg After cm^3	Diuretic Usage 1 = yes	ACE Usage 1 = yes	HRT Usage 1 = yes	Anti-inflammatory Drug Usage 1 = yes
CON 024	1226.63	.	.	.	.
CON 023	948.10	2	2	2	2
CON 005	1890.00	1	2	.	2
CON 011	1974.01	2	2	.	2
CON 004	1894.00	2	2	.	2
CON 010	1635.64	2	2	.	2
CON 016	1189.30	.	.	.	.
CON 021	1203.41	2	2	2	2
CON 007	1794.10	2	2	.	2
CON 002	1564.94	2	2	.	2
CON 001	.	2	2	.	2
CON 020	1150.10	2	2	2	2
CON 003	1798.63	2	2	.	2
CON 022	1127.39	.	.	.	.
CON 009	1749.48	2	2	.	2
CON 014	1136.21	2	2	2	1
HUR 014	.	2	2	.	2
HUR 015	1100.21	2	2	2	2
HUR 017	1223.33	2	2	.	2
HUR 018	1578.20	2	2	.	2
HUR 022	1501.06	2	2	.	2
HUR 023	1161.69	2	2	2	2
HUR 025	1208.92	2	2	1	2
HUR 027	1526.51	2	2	1	2
HUR 028	782.06	2	2	2	2
HUR 029	.	2	2	.	2
HUR 030	1094.93	2	1	2	2
HUR 031	1010.66	2	2	2	2
HUR 032	1781.29	2	2	.	2
HUR 033	1314.69	2	2	2	2
HUR 034	1548.20	2	2	1	2

ID Number	Sex	ACTN	Age	Height	Pre fat mass	After fat mass	Pre FFM	After FFM	Pre weight	After weight	Pre body fat %	After body fat %	Pre BMI	After BMI	1RM Pre	1RM After
HUR 036	M	RR	75	167.6	22301.2	23338.5	65136.1	64311.5	87.44	87.65	25.5	26.6	31.13	31.20	21.79	27.83
HUR 038	M	RX	61	164.9	13539.7	14039.5	50103.2	50077.1	63.64	64.12	21.3	21.9	23.41	23.58	21.17	37.20
HUR 039	M	RX	77	179.5	32204.5	32267.8	64732.6	67135.8	96.94	99.40	33.2	32.5	30.09	30.85	29.91	33.25
HUR 041	M	XX	63	163.7	22697.8	21844.1	48925.3	48522.5	71.62	70.37	31.7	31.0	26.73	26.26	19.92	28.46
HUR 042	M	RX	52	154.8	21635.1	.	41178.5	.	62.81	.	34.4	.	26.21	.	15.34	.
HUR 047	M	RX	54	179.6	29267.4	31350.0	63989.0	64174.0	93.26	95.52	31.4	32.8	28.91	29.61	42.41	52.82
HUR 048	F	XX	53	168.3	30944.7	29947.5	44628.3	45767.2	75.57	75.71	40.9	39.6	26.68	26.73	18.43	27.16
HUR 049	F	RX	77	162.6	43610.0	43278.1	43836.3	46081.4	87.45	89.36	49.9	48.4	33.09	33.82	16.35	16.35
HUR 050	M	RX	70	184.0	28547.8	27818.2	.	.	90.21	91.42	31.6	30.4	26.65	27.00	39.70	42.62
HUR 052	F	RX	78	158.0	56761.1	.	54889.0	.	111.88	.	50.7	.	44.82	.	21.17	26.79
HUR 053	F	RR	67	162.0	42347.2	41951.3	50077.4	.	94.42	94.77	44.9	44.3	35.98	36.11	22.42	25.12
HUR 055	F	XX	61	164.7	26346.8	23586.0	40047.6	42024.7	66.39	65.61	39.7	35.9	24.48	24.19	23.21	30.90
HUR 057	M	RR	60	177.8	26478.1	.	65308.9	.	90.45	.	29.3	.	28.61	.	34.08	.
HUR 058	F	RX	60	164.1	26407.5	.	.	.	69.30	.	38.1	.	25.74	.	22.63	.
HUR 059	F	RX	78	145.4	19500.4	19184.1	33904.5	31937.3	53.40	51.62	36.5	37.2	25.26	24.41	9.69	9.54
HUR 060	F	RX	76	159.8	23289.0	25274.0	44671.1	44117.1	67.96	69.39	34.3	36.4	26.61	27.17	15.52	21.55
HUR 061	F	RR	66	161.5	42159.3	46713.6	58914.3	58521.8	101.07	105.24	41.7	44.4	38.75	40.35	10.94	17.39
HUR 062	M	RX	69	172.7	24209.0	22753.7	55830.3	57064.7	80.04	79.82	30.2	28.5	26.84	26.76	34.02	42.33
HUR 063	M	RX	66	171.2	23390.6	21712.3	51426.4	53300.6	74.82	75.01	31.3	28.9	25.53	25.59	24.66	30.90
HUR 065	M	XX	65	178.0	29752.7	29680.3	67797.9	.	97.44	97.94	30.5	30.3	30.75	30.91	30.96	35.12
HUR 066	F	XX	71	160.0	28725.3	28009.8	38384.5	39580.3	67.11	67.59	42.8	41.4	26.21	26.40	13.23	16.97
HUR 068	M	RR	66	178.2	21256.6	20428.7	57791.8	58585.8	79.05	79.01	26.9	25.9	24.89	24.88	28.41	34.02
HUR 069	F	RR	61	169.1	40693.7	.	51567.2	.	92.26	.	44.1	.	32.26	.	18.67	.
HUR 071	M	RR	75	172.3	29124.0	28415.5	57950.5	.	86.89	87.91	33.5	32.3	29.27	29.61	32.00	35.12
HUR 072	F	RX	67	156.3	28998.4	.	41047.3	.	70.05	.	41.4	.	28.67	.	7.20	.
HUR 075	M	RX	71	172.1	25298.8	23839.7	63335.0	61812.5	88.63	85.65	28.5	27.8	29.93	28.92	18.43	30.90
HUR 076	F	RR	58	160.6	21492.2	21873.5	39591.4	38563.2	61.08	60.44	35.2	36.2	23.68	23.43	17.39	19.47
HUR 077	F	RR	70	156.4	26416.8	24636.4	42959.2	41577.8	69.38	66.21	38.1	37.2	28.36	27.07	13.65	18.84
HUR 078	M	XX	71	168.9	17639.0	16042.0	57583.8	57897.8	75.22	73.94	23.4	21.7	26.37	25.92	26.74	39.63
HUR 079	M	RX	71	176.5	29124.5	34278.9	64636.0	64948.7	93.76	99.23	31.1	34.5	30.10	31.85	37.14	45.45
HUR 080	M	RR	81	171.0	13913.2	13036.0	47245.3	46919.4	61.16	59.96	22.7	21.7	20.92	20.50	14.48	19.88
HUR 081	F	RX	83	143.7	19215.4	20499.0	38602.9	39290.1	57.82	59.79	33.2	34.3	28.00	28.95	9.67	11.36
HUR 084	F	XX	80	151.4	18054.7	18042.2	37503.9	36669.3	55.56	54.71	32.5	33.0	24.24	23.87	12.19	15.31

ID Number	70% PP Pre	70% PP After	70% PV Pre	70% PV After	Abs PP Pre	Abs PP After	Abs PV Pre	Abs PV After	Muscle Volume Pre	Muscle Volume After	1RM Untrained Leg Pre	1RM Untrained Leg After
HUR 036	255.70	.	2.9	.	255.70	.	2.9	.	.	.	19.92	21.79
HUR 038	296.70	.	3.5	.	296.70	.	3.5	.	1347.38	1469.19	23.04	35.12
HUR 039	326.72	.	3.1	.	326.72	.	3.1	.	1976.79	2053.46	27.21	28.25
HUR 041	330.94	.	4.4	.	330.94	.	4.4	.	1425.93	1480.35	17.42	19.50
HUR 042	234.28	.	4.0	.	234.28	.	4.0	.	.	.	12.21	.
HUR 047	625.47	.	5.4	.	623.15	680.06	4.3	5.0	2349.34	2605.08	37.20	46.58
HUR 048	266.78	258.07	4.5	3.3	275.56	282.92	4.1	4.1	1026.55	1134.08	19.50	20.13
HUR 049	144.43	158.56	2.6	3.1	144.42	158.56	2.6	3.1	1125.47	1128.07	15.34	15.34
HUR 050	.	.	.	.	.	.	.	.	.	.	38.87	40.33
HUR 052	229.32	230.18	3.7	3.2	237.85	284.87	4.3	4.9	.	.	20.54	22.63
HUR 053	.	.	.	.	.	.	.	.	1525.53	1659.37	24.08	29.08
HUR 055	317.51	311.99	4.8	3.5	317.51	360.43	4.8	5.2	1286.09	1427.21	19.88	.
HUR 057	476.62	.	5.1	.	476.62	.	5.1	.	1810.62	.	32.00	.
HUR 058	.	.	.	.	.	.	.	.	1152.08	.	22.63	.
HUR 059	84.51	127.59	2.5	3.3	84.51	127.59	2.5	3.3	.	.	9.10	6.90
HUR 060	176.86	218.89	3.5	3.2	176.86	210.92	3.5	4.1	963.42	1122.08	3.83	3.10
HUR 061	243.19	333.11	5.4	6.3	243.19	333.11	5.4	6.3	1352.01	1425.04	10.42	14.30
HUR 062	467.61	.	5.0	.	467.61	490.21	5.0	5.3	1731.26	1959.02	38.45	41.37
HUR 063	354.32	355.08	4.9	4.2	383.12	374.05	5.9	6.0	1403.88	1501.43	25.75	25.75
HUR 065	394.12	349.46	4.8	3.8	.	.	.	.	.	.	27.62	27.83
HUR 066	186.20	241.17	4.1	4.4	186.20	231.65	4.1	4.9	754.57	805.09	11.17	.
HUR 068	261.06	383.61	3.5	4.2	208.49	383.58	2.5	4.2	1630.64	1738.86	19.26	24.66
HUR 069	.	.	.	.	.	.	.	.	1323.89	.	17.00	.
HUR 071	156.36	.	3.6	.	350.83	402.44	5.0	5.6	1652.87	1801.06	23.88	24.71
HUR 072	.	.	.	.	.	.	.	.	1010.71	.	8.37	.
HUR 075	378.89	516.09	6.0	5.6	378.89	467.85	6.0	7.2	1432.84	1589.90	18.46	27.83
HUR 076	202.13	237.81	3.5	4.0	224.76	277.23	4.7	5.5	790.02	963.68	16.38	13.46
HUR 077	145.68	205.74	3.4	3.6	156.14	223.59	3.4	4.3	1085.48	1147.77	11.38	14.30
HUR 078	401.37	394.51	4.8	3.5	393.47	411.80	4.1	4.3	1638.03	1709.28	26.79	32.00
HUR 079	416.21	453.64	4.8	5.1	416.21	495.52	4.8	5.1	1885.21	1896.17	37.20	38.24
HUR 080	133.37	245.54	2.8	3.9	124.61	250.67	2.6	4.4	1185.80	1229.72	13.88	15.54
HUR 081	100.60	124.00	2.6	3.3	76.05	124.00	1.9	3.3	789.50	852.31	8.22	8.22
HUR 084	129.17	164.54	3.2	3.5	129.17	175.11	3.2	4.2	754.03	881.17	3.82	.

ID Number	70% Untrained Leg PP Pre	70% Untrained Leg PP After	70% Untrained Leg PV Pre	70% Untrained Leg PV After	Abs PP Untrained Leg Pre	Abs PP Untrained Leg After	Abs PV Untrained Leg Pre	Abs PV Untrained Leg After	Muscle Volume Untrained Leg Pre
HUR 036	227.62	.	2.9	.	227.62	.	2.9	.	.
HUR 038	161.92	.	3.8	.	161.92	.	3.8	.	1427.99
HUR 039	297.34	.	3.0	.	297.34	.	3.0	.	1887.32
HUR 041	298.67	.	4.4	.	298.67	.	4.4	.	1369.61
HUR 042	247.18	.	4.6	.	247.18	.	4.6	.	.
HUR 047	567.18	.	5.7	.	567.18	.	5.7	.	2047.54
HUR 048	286.51	244.33	4.9	4.0	286.51	244.33	4.9	4.0	986.24
HUR 049	189.96	174.99	3.8	3.4	189.96	174.99	3.8	3.4	1016.64
HUR 050	.	.	.	.	.	.	.	.	.
HUR 052	242.40	274.94	3.7	3.2	292.60	273.70	5.9	5.2	.
HUR 053	.	.	.	.	.	.	.	.	1490.47
HUR 055	283.59	171.88	4.7	2.3	283.59	238.81	4.7	4.1	1139.21
HUR 057	466.60	.	5.2	.	466.60	.	5.2	.	1809.79
HUR 058	.	.	.	.	.	.	.	.	1175.04
HUR 059	64.26	90.77	2.1	2.7	64.25	90.77	2.1	2.7	.
HUR 060	46.84	.	2.6	.	46.84	46.83	2.6	2.7	.
HUR 061	221.15	275.30	5.3	5.5	221.15	275.30	5.3	5.5	1218.60
HUR 062	434.67	.	4.4	.	434.67	506.48	4.4	4.9	1650.70
HUR 063	324.84	324.54	4.5	4.4	349.78	373.48	6.0	6.2	1365.89
HUR 065	297.50	268.53	4.0	3.5	297.49	268.53	4.0	3.5	.
HUR 066	172.44	.	4.1	.	.	.	.	.	.
HUR 068	201.15	.	3.4	.	194.17	318.95	2.9	4.7	1523.69
HUR 069	.	.	.	.	.	.	.	.	1238.54
HUR 071	297.62	258.75	4.4	3.7	298.60	236.47	5.4	4.3	1602.07
HUR 072	.	.	.	.	.	.	.	.	1012.27
HUR 075	365.76	436.17	6.1	6.1	365.76	415.77	6.1	6.7	1461.55
HUR 076	200.95	150.68	3.8	3.1	223.99	186.57	5.1	4.6	967.07
HUR 077	118.17	153.94	3.0	3.5	133.00	159.93	2.8	3.5	975.61
HUR 078	324.08	304.01	4.6	3.0	321.84	375.41	3.7	4.2	1599.31
HUR 079	449.32	.	4.7	.	449.32	516.96	4.7	5.3	1894.34
HUR 080	104.59	164.67	2.5	3.1	102.39	164.66	2.0	3.1	1142.33
HUR 081	92.61	119.33	2.9	3.9	92.61	119.33	2.9	3.9	903.83
HUR 084	.	.	3.7	.	84.16	82.06	3.7	3.9	736.80

ID Number	Muscle Volume Untrained Leg After	Diuretic Usage	ACE Usage	HRT Usage	Anti-inflammatory Drug Usage
HUR 036	.	1	2	.	2
HUR 038	1417.28	2	2	.	2
HUR 039	1882.06	1	2	.	2
HUR 041	1381.55	2	2	.	2
HUR 042	.	2	2	1	2
HUR 047	2095.16	2	2	.	2
HUR 048	963.08	2	2	2	2
HUR 049	1036.54	2	2	2	2
HUR 050	.	2	2	.	1
HUR 052	.	2	2	2	2
HUR 053	1546.51	2	2	2	2
HUR 055	1091.69	2	2	2	2
HUR 057	.	2	2	.	2
HUR 058	.	2	2	2	2
HUR 059	.	1	2	2	2
HUR 060	.	2	2	2	2
HUR 061	1292.68	2	2	2	2
HUR 062	1678.13	2	2	.	2
HUR 063	1435.83	2	2	.	2
HUR 065	.	2	2	.	2
HUR 066	.	2	2	2	2
HUR 068	1476.85	2	2	.	2
HUR 069	.	2	1	1	2
HUR 071	1565.27	2	2	.	2
HUR 072	.	2	2	2	2
HUR 075	1422.52	2	2	.	2
HUR 076	919.38	2	2	2	2
HUR 077	965.93	1	2	2	2
HUR 078	1560.93	1	2	.	2
HUR 079	2035.03	2	1	.	2
HUR 080	1087.42	2	2	.	2
HUR 081	906.17	1	2	1	2
HUR 084	723.36	2	2	2	2

ID Number	Sex	ACTN	Age	Height	Pre fat mass	After fat mass	Pre FFM	After FFM	Pre weight	After weight	Pre body fat %	After body fat %	Pre BMI	After BMI	1RM Pre	1RM After
HUR 085	M	RR	71	190.4	33496.6	34465.7	81388.7	80452.7	114.89	114.92	29.2	30.0	31.69	31.70	32.00	38.24
HUR 086	F	XX	78	163.5	33700.0	.	42480.7	.	76.18	.	44.2	.	28.50	.	10.42	.
HUR 087	M	RR	62	170.8	19482.9	22278.2	65519.6	66980.9	85.25	89.26	22.9	25.0	29.14	30.60	46.49	54.81
HUR 088	F	RX	73	161.5	30076.1	.	44790.1	.	74.87	.	40.2	.	28.70	.	16.79	.
HUR 091	F	RR	60	154.9	27092.3	27226.7	37890.4	38210.3	64.98	65.44	41.7	41.6	27.07	27.26	13.85	16.97
HUR 092	M	XX	65	178.7	17934.4	19568.4	59311.2	59198.5	77.25	78.77	23.2	24.8	24.19	24.67	25.50	34.02
HUR 093	F	RR	65	162.1	34871.1	37318.7	43864.9	42358.7	78.74	79.68	44.3	46.8	29.96	30.32	16.35	22.59
HUR 094	F	RX	65	154.7	32213.6	33547.6	40979.0	39387.9	73.19	72.94	44.0	46.0	30.58	30.48	20.30	20.51
HUR 096	M	RX	70	175.5	32571.5	.	69758.7	.	102.33	.	31.8	.	33.22	.	29.91	32.00
HUR 097	F	RR	85	155.6	24450.6	26692.8	42539.2	42014.6	66.99	68.71	36.5	38.8	27.67	28.38	16.35	19.05
HUR 098	M	XX	71	174.1	27517.3	29933.7	60127.3	57247.9	87.64	87.18	31.4	34.3	28.92	28.76	27.78	34.64
HUR 099	M	XX	69	178.5	24762.6	.	64123.8	.	88.89	.	27.9	.	27.90	.	41.30	51.69
HUR100	M	RR	73	175.3	26786.2	.	57087.7	.	83.87	.	31.9	.	27.31	.	27.37	31.52
HUR 101	F	RR	63	157.5	37921.9	.	49321.4	.	87.35	.	43.4	.	35.22	.	18.88	.
HUR 102	F	RX	80	154.9	20435.4	.	29957.9	.	50.55	.	40.4	.	21.06	.	9.10	.
HUR 103	F	RX	65	160.0	31967.0	.	40625.5	.	72.59	.	44.0	.	28.35	.	14.09	.
HUR 104	F	RR	66	167.6	37158.2	.	49045.5	.	86.20	.	43.1	.	30.67	.	22.63	.
HUR 105	F	RX	65	170.2	25519.0	23718.9	35587.1	37492.1	61.11	61.21	41.8	38.7	21.10	21.14	11.78	18.64
HUR 107	F	XX	79	156.3	17784.6	.	33522.0	.	51.28	.	34.7	.	20.99	.	14.30	.
HUR 108	M	RX	59	182.2	35914.8	34733.2	55218.2	59089.3	91.13	93.82	39.4	37.0	27.45	28.26	40.26	42.75
HUR 109	F	XX	62	154.9	26957.2	25587.5	40281.4	41915.9	67.24	67.50	40.1	37.9	28.01	28.12	24.66	27.57
HUR 110	F	RX	70	158.5	32734.0	29854.8	41586.3	42972.1	74.32	72.83	44.0	41.0	29.58	28.99	10.53	17.39
HUR 113	M	RX	67	167.6	.	18221.8	.	60513.5	.	78.74	.	23.1	.	28.02	18.43	28.41
HUR 114	F	RR	70	157.4	24540.8	23474.9	40458.4	41045.6	65.00	64.52	37.8	36.4	26.24	26.04	13.05	19.92
HUR 115	M	RX	60	175.3	16017.9	17623.6	62648.2	59658.9	78.67	77.28	20.4	22.8	25.61	25.16	19.47	25.91
HUR 116	F	RX	56	149.9	14114.5	.	34836.2	.	48.95	.	28.8	.	21.80	.	8.81	.
HUR 117	M	RX	65	166.6	10991.9	11959.2	52397.3	53477.9	63.39	65.44	17.3	18.3	22.83	23.56	26.33	30.90
HUR 118	F	XX	60	170.2	28979.1	29708.0	44219.0	44432.4	73.20	74.14	39.6	40.1	25.27	25.59	12.19	22.59
HUR 120	M	RX	53	190.5	34663.8	.	83707.7	.	118.37	.	29.3	.	32.62	.	49.28	.
HUR 122	M	RX	56	182.9	25118.0	25740.4	56552.4	56004.5	81.67	81.74	30.8	31.5	24.42	24.44	26.74	42.33
HUR 123	F	RR	82	158.1	19599.5	20411.6	38477.2	37708.4	58.08	58.12	33.7	35.1	23.23	23.25	13.23	14.06
HUR 124	F	XX	66	165.1	22039.6	19659.8	43282.8	42626.6	65.32	62.29	33.7	31.6	23.96	22.85	22.59	25.08
HUR 126	F	RX	76	156.2	31331.3	31194.3	39120.2	39275.8	70.45	70.47	44.5	44.3	28.87	28.88	11.15	13.23

ID Number	70% PP Pre	70% PP After	70% PV Pre	70% PV After	Abs PP Pre	Abs PP After	Abs PV Pre	Abs PV After	Muscle Volume Pre	Muscle Volume After	1RM Untrained Leg Pre	1RM Untrained Leg After
HUR 085	379.53	364.86	4.2	3.5	353.49	400.87	5.2	5.1	1968.10	2158.39	35.33	39.29
HUR 086	116.99	.	3.3	.	116.99	.	3.3	.	914.37	.	9.98	.
HUR 087	472.60	593.27	3.8	4.1	513.08	635.53	4.8	5.7	1813.64	2133.39	41.30	46.70
HUR 088	.	.	.	.	.	.	.	.	1105.67	.	14.92	.
HUR 091	239.29	227.42	4.9	4.4	245.30	247.27	5.5	5.4	900.88	995.60	11.15	14.06
HUR 092	407.13	387.32	5.8	4.2	409.36	397.10	5.0	4.8	1625.35	1795.35	21.55	23.62
HUR 093	182.69	167.74	3.7	2.7	151.32	209.54	2.8	3.6	974.09	1057.72	16.97	18.84
HUR 094	247.26	209.27	3.9	3.4	256.32	265.04	4.9	5.2	1067.88	1214.72	19.26	18.43
HUR 096	494.87	.	5.6	.	465.10	.	6.8	.	.	.	32.00	.
HUR 097	133.66	153.63	2.7	2.9	151.27	182.12	3.3	4.0	959.31	1002.85	17.42	16.38
HUR 098	335.22	334.13	4.3	3.8	329.48	326.20	4.8	5.0	1650.67	1785.50	27.83	29.29
HUR 099	394.19	454.27	3.4	3.3	422.55	486.33	4.3	4.9	1834.53	2139.09	40.54	42.20
HUR100	293.16	335.31	3.8	4.1	322.36	371.11	4.8	5.7	1476.77	1576.57	27.83	28.87
HUR 101	240.01	.	4.2	.	261.81	.	5.6	.	1022.31	.	14.30	.
HUR 102	99.95	.	3.0	.	110.55	.	3.8	.	645.95	.	5.73	.
HUR 103	196.10	.	4.2	.	217.60	.	5.4	.	959.34	.	13.46	.
HUR 104	297.92	.	4.6	.	321.93	.	6.1	.	1314.13	.	13.25	.
HUR 105	187.94	254.24	4.4	4.2	187.93	263.42	3.9	5.1	903.23	951.98	.	.
HUR 107	147.09	.	3.1	.	172.13	.	4.4	.	832.57	.	13.05	.
HUR 108	378.40	466.56	3.7	4.3	473.42	534.56	6.1	6.6	1604.73	1736.85	32.21	34.08
HUR 109	207.43	285.34	3.2	4.1	228.80	291.66	3.2	4.4	1163.01	1251.37	22.21	21.58
HUR 110	170.16	191.34	4.2	3.8	170.16	208.04	4.2	4.6	1109.80	1148.80	11.17	15.75
HUR 113	308.68	360.08	5.2	4.4	308.68	356.17	5.2	5.7	1682.50	1862.99	30.28	26.33
HUR 114	103.40	129.45	2.5	2.7	103.40	141.64	2.5	3.3	900.33	1063.76	11.80	12.21
HUR 115	482.99	448.26	5.7	4.3	475.50	527.89	7.3	7.8	1673.82	1880.10	27.16	29.86
HUR 116	140.87	.	4.1	.	165.85	.	5.5	.	.	.	8.81	.
HUR 117	326.87	328.92	4.5	4.3	352.80	323.75	6.0	6.0	1290.43	1363.92	19.68	18.43
HUR 118	265.61	249.08	5.6	4.0	259.82	265.80	6.5	6.5	1125.61	1224.78	11.15	19.47
HUR 120	702.48	.	5.2	.	677.72	.	6.6	.	2230.20	.	49.70	.
HUR 122	384.78	370.83	4.0	3.2	411.90	450.64	5.7	6.4	1664.85	1794.47	34.02	35.47
HUR 123	186.11	200.31	4.3	3.5	193.35	226.68	5.2	5.9	977.95	984.72	12.81	10.94
HUR 124	280.91	290.33	4.3	4.3	318.61	325.33	6.0	6.5	1244.93	1365.60	23.62	24.46
HUR 126	158.02	157.15	4.0	3.6	164.39	169.50	4.4	4.4	884.06	942.64	13.23	13.23

ID Number	70% Untrained Leg PP Pre	70% Untrained Leg PP After	70% Untrained Leg PV Pre	70% Untrained Leg PV After	Abs PP Untrained Leg Pre	Abs PP Untrained Leg After	Abs PV Untrained Leg Pre	Abs PV Untrained Leg After	Muscle Volume Untrained Leg Pre
HUR 085	435.85	451.93	4.5	4.2	435.85	448.75	4.5	4.6	2006.86
HUR 086	127.21	.	3.3	.	127.21	.	3.3	.	868.87
HUR 087	517.15	561.63	4.5	4.4	517.15	616.81	4.5	5.4	2011.20
HUR 088	.	.	.	.	.	.	.	.	1084.38
HUR 091	220.30	219.24	5.1	4.7	221.96	209.46	5.6	5.3	907.93
HUR 092	379.06	349.83	5.9	4.7	379.06	351.12	5.9	5.4	1644.50
HUR 093	.	.	.	.	184.84	171.79	3.5	3.2	965.05
HUR 094	260.63	211.81	4.3	3.5	269.73	250.72	5.4	5.1	1080.98
HUR 096	505.31	.	6.5	.	450.85	.	6.5	.	.
HUR 097	146.17	179.24	3.0	3.6	166.85	189.58	4.1	4.6	958.75
HUR 098	359.33	336.88	4.7	4.4	331.51	301.35	5.7	5.2	1623.93
HUR 099	388.79	414.03	3.6	3.7	416.61	434.53	5.1	5.3	1864.84
HUR100	309.34	334.72	4.1	4.5	330.33	345.57	5.6	6.0	1487.40
HUR 101	219.24	.	4.5	.	231.27	.	5.6	.	1014.27
HUR 102	72.03	.	2.9	.	80.47	.	3.6	.	532.47
HUR 103	164.08	.	3.5	.	181.13	.	4.6	.	887.00
HUR 104	217.27	.	4.7	.	211.80	.	5.6	.	1183.74
HUR 105	.	.	.	.	.	.	.	.	795.42
HUR 107	130.90	.	3.3	.	143.46	.	4.2	.	792.94
HUR 108	366.18	388.04	4.2	4.5	401.28	410.36	6.0	6.1	1466.45
HUR 109	208.75	250.00	3.6	4.1	223.66	256.20	4.5	5.1	1199.18
HUR 110	201.26	110.40	4.8	4.2	.	.	.	.	1092.50
HUR 113	304.34	323.02	3.8	4.5	300.44	317.10	4.7	5.1	1553.32
HUR 114	83.54	108.78	2.8	2.9	133.05	129.25	3.8	4.0	819.66
HUR 115	500.56	393.14	6.1	4.8	489.16	466.35	7.7	7.8	1664.80
HUR 116	151.23	.	4.4	.	144.04	.	5.0	.	.
HUR 117	213.21	228.43	3.6	3.8	248.91	224.27	5.1	4.7	1121.04
HUR 118	264.23	281.19	5.9	4.8	255.99	272.36	6.7	7.0	1147.21
HUR 120	720.08	.	5.3	.	677.72	.	7.1	.	2370.03
HUR 122	383.50	357.69	4.0	3.7	391.66	375.08	5.6	5.5	1576.48
HUR 123	188.79	180.42	4.2	3.7	199.13	193.87	4.7	4.9	927.19
HUR 124	286.10	315.93	4.5	4.8	303.90	317.91	5.7	5.7	1254.24
HUR 126	197.43	168.41	4.7	4.2	207.68	179.96	5.3	5.2	926.25

ID Number	Muscle Volume Untrained Leg After	Diuretic Usage	ACE Usage	HRT Usage	Anti-inflammatory Drug Usage
HUR 085	2069.05	2	1	.	2
HUR 086	.	2	2	2	2
HUR 087	1981.38	2	2	.	2
HUR 088	.	2	2	2	2
HUR 091	894.34	1	1	2	2
HUR 092	1591.36	2	1	.	2
HUR 093	957.53	2	2	1	2
HUR 094	1037.13	2	2	1	2
HUR 096	.	1	2	.	2
HUR 097	998.50	2	2	1	2
HUR 098	1601.09	1	2	.	2
HUR 099	1845.04	1	2	.	2
HUR100	1523.17	2	1	.	2
HUR 101	.	2	2	2	2
HUR 102	.	2	2	2	2
HUR 103	.	2	2	2	2
HUR 104	.	2	2	1	2
HUR 105	866.93	2	2	2	2
HUR 107	.	2	2	2	2
HUR 108	1484.18	2	2	.	2
HUR 109	1216.83	2	2	1	2
HUR 110	1123.80	2	2	2	2
HUR 113	1518.39	1	2	.	2
HUR 114	854.46	2	2	2	2
HUR 115	1647.67	2	2	.	2
HUR 116	.	2	2	2	2
HUR 117	1113.20	2	1	.	2
HUR 118	1149.15	2	2	1	2
HUR 120	.	2	2	.	2
HUR 122	1640.25	2	2	.	2
HUR 123	944.96	2	2	2	2
HUR 124	1242.56	1	2	2	2
HUR 126	985.08	2	2	2	2

ID Number	Sex	ACTN	Age	Height	Pre fat mass	After fat mass	Pre FFM	After FFM	Pre weight	After weight	Pre body fat %	After body fat %	Pre BMI	After BMI	1RM Pre	1RM After
HUR 128	F	RX	52	157.5	12202.1	11840.6	38277.7	36847.7	50.48	48.69	24.2	24.3	20.35	19.63	17.39	18.84
HUR 129	F	XX	52	160.0	33381.6	32728.1	48395.8	49084.6	82.32	81.81	40.6	40.0	32.15	31.95	20.13	28.46
HUR 131	F	RX	64	160.0	21228.3	21206.9	40591.3	39973.8	61.82	61.18	34.3	34.7	24.14	23.89	12.61	13.44
HUR 134	F	RR	52	165.1	43299.7	.	60699.9	.	103.68	.	41.8	.	38.04	.	28.46	.
HUR 135	M	RX	64	177.8	24239.6	23103.0	52392.1	53894.9	76.63	77.00	31.6	30.0	24.24	24.36	29.86	38.38
HUR 139	M	RR	51	180.3	19582.0	19821.8	71832.5	71387.4	91.41	91.21	21.4	21.7	28.11	28.04	45.87	53.77
HUR 140	F	RX	57	157.5	44401.3	.	45888.7	.	90.29	.	49.2	.	36.41	.	15.34	.
HUR 142	F	RX	62	163.8	29833.8	.	44550.7	.	74.38	.	40.1	.	27.71	.	15.54	.
HUR 147	F	RX	54	162.6	28229.6	.	35012.1	.	63.24	.	44.6	.	23.93	.	13.25	.
HUR 151	F	RR	50	162.6	23061.6	22845.9	38237.7	38638.2	61.65	.	37.4	.	23.33	.	17.63	20.54
HUR 152	F	RR	60	172.7	44117.7	.	51145.0	.	95.26	.	46.3	.	31.93	.	16.38	.
HUR 155	F	RR	65	172.7	35556.0	33519.5	58614.3	60691.6	94.17	94.21	37.8	35.6	31.57	31.58	15.93	18.43
HUR 156	M	RX	61	177.8	37702.1	37730.3	73329.1	73812.4	111.03	111.54	34.0	33.8	35.12	35.28	44.62	64.16
HUR 157	F	RR	51	170.2	20469.9	.	48231.0	.	68.70	.	29.8	.	23.72	.	22.21	.
HUR 168	M	RR	67	168.8	20586.8	21438.1	58846.8	58676.4	79.43	80.11	25.9	26.8	27.88	28.12	29.65	32.98
HUR 169	F	RR	64	157.5	20871.7	20471.5	35652.4	33981.7	56.52	54.45	36.9	37.6	22.79	21.96	10.74	15.31
HUR 172	M	RR	56	172.7	21650.5	21299.3	60955.4	60651.6	82.61	81.95	26.2	26.0	27.69	27.47	35.06	42.33
HUR 174	M	RR	74	183.7	19046.4	18523.4	65591.9	66169.2	84.64	84.69	22.5	21.9	25.08	25.10	35.06	46.49
HUR 175	M	RX	51	170.1	36392.2	34770.8	65444.5	67957.9	101.84	102.73	35.7	33.8	35.20	35.50	30.90	40.26
HUR 177	F	RR	51	167.6	23774.5	22669.2	43658.6	44068.5	67.43	66.74	35.3	34.0	24.01	23.76	21.13	27.78
HUR 179	M	RX	59	181.0	31619.1	29220.9	62401.5	64051.9	94.02	93.27	33.6	31.3	28.70	28.47	40.33	45.53
HUR 180	F	RR	53	176.7	22286.7	.	43759.1	.	66.05	.	33.7	.	21.15	.	21.58	23.25
HUR 182	M	RR	52	175.3	23356.6	22145.4	58342.6	60104.3	81.70	82.25	28.6	26.9	26.59	26.77	46.91	57.93
HUR 183	F	XX	57	162.5	34377.9	33100.7	48321.1	49420.1	82.70	82.52	41.6	40.1	31.32	31.25	26.79	26.79
HUR 186	M	RR	50	168.6	17891.0	.	58951.3	.	76.84	.	23.3	.	27.03	.	43.87	.
HUR 187	F	RR	59	158.3	44629.9	41872.1	53518.6	55044.1	98.15	97.75	45.5	42.8	39.17	39.01	22.63	24.71
HUR 188	M	XX	50	175.7	40341.1	40167.6	78859.4	79181.3	118.84	119.35	33.9	33.7	38.50	38.66	50.74	64.28
HUR 191	F	RR	80	155.1	18483.3	.	34903.2	.	53.30	.	34.7	.	22.16	.	10.42	16.38
HUR 193	M	RX	50	185.5	21194.1	.	67001.1	.	88.20	.	24.0	.	25.63	.	49.07	.
HUR 197	M	RX	61	164.7	39221.6	.	66187.8	.	105.41	.	37.2	.	38.86	.	29.91	.
HUR 198	M	XX	50	176.2	30933.2	30129.3	73627.3	70027.5	104.56	100.16	29.6	30.1	33.68	32.26	33.04	37.20
HUR 199	F	RR	54	152.4	52784.3	.	57747.5	.	110.53	.	47.8	.	47.59	.	21.58	.
HUR 200	M	XX	57	180.3	16458.8	.	63836.7	.	80.30	.	20.5	.	24.69	.	40.33	.

ID Number	70% PP Pre	70% PP After	70% PV Pre	70% PV After	Abs PP Pre	Abs PP After	Abs PV Pre	Abs PV After	Muscle Volume Pre	Muscle Volume After	1RM Untrained Leg Pre	1RM Untrained Leg After
HUR 128	214.32	266.78	3.7	4.3	235.29	266.61	4.9	5.5	1083.79	1147.61	13.85	14.69
HUR 129	351.71	373.73	5.4	4.6	309.33	384.35	6.1	7.0	1399.52	.	20.13	21.58
HUR 131	182.25	207.02	3.9	3.6	201.35	225.02	5.1	5.8	808.59	952.63	.	9.23
HUR 134	416.66	.	5.1	.	421.77	.	6.4	.	1536.08	.	19.50	.
HUR 135	329.43	360.57	3.9	3.4	381.81	401.01	5.1	6.2	1352.60	1493.66	29.86	34.64
HUR 139	552.93	609.93	4.4	4.3	589.33	599.31	5.3	5.4	2165.35	2283.57	41.30	38.18
HUR 140	178.25	.	3.6	.	203.09	.	4.8	.	1042.44	.	15.34	.
HUR 142	216.50	.	4.2	.	211.25	.	5.0	.	1204.78	.	15.54	.
HUR 147	143.67	.	4.0	.	158.03	.	4.8	.	.	.	.	.
HUR 151	171.03	192.89	3.4	3.4	187.56	205.98	4.0	4.3	1073.13	1048.02	16.38	15.34
HUR 152	233.62	.	4.6	.	207.62	.	5.0	.	1301.13	.	8.96	.
HUR 155	196.80	311.84	4.0	4.1	205.11	296.67	4.5	5.0	.	.	27.16	26.74
HUR 156	708.27	624.46	5.7	3.9	651.76	748.62	6.1	6.9	2366.45	2619.89	36.72	58.97
HUR 157	234.46	.	3.7	.	247.52	.	4.9	.	1346.31	.	20.54	.
HUR 168	323.58	324.23	3.9	3.5	382.26	398.08	4.9	5.3	1540.69	1620.50	26.74	26.74
HUR 169	146.90	148.65	3.7	3.8	147.56	177.90	4.4	5.1	924.92	935.19	10.40	12.19
HUR 172	512.49	534.70	5.1	4.5	527.02	508.26	6.1	5.8	1928.83	2073.63	28.82	34.02
HUR 174	436.28	459.64	4.5	3.4	436.25	512.77	4.5	4.8	1744.85	1925.93	35.06	41.30
HUR 175	588.45	.	6.4	.	546.35	572.55	7.8	8.9	1862.48	2128.00	25.70	28.20
HUR 177	216.89	248.60	3.5	3.1	240.00	333.40	4.6	5.8	.	.	21.96	26.74
HUR 179	513.66	524.57	4.6	4.2	513.66	542.35	6.3	6.6	1944.20	.	33.45	37.20
HUR 180	237.62	276.50	3.8	4.4	268.83	279.61	5.1	5.4	1275.33	.	18.88	19.50
HUR 182	512.21	612.69	4.0	4.0	522.96	636.02	4.7	5.7	2035.15	2224.04	47.53	51.69
HUR 183	378.31	350.02	5.2	4.4	400.70	366.60	6.5	5.9	1375.95	1586.02	26.17	26.79
HUR 186	574.66	.	4.7	.	619.60	.	6.6	.	.	.	44.49	.
HUR 187	291.66	346.40	4.8	4.6	308.06	369.40	5.4	5.8	1389.78	1512.27	17.42	22.63
HUR 188	634.97	610.90	4.6	3.6	634.78	643.10	6.2	6.1	2224.28	2478.82	47.62	52.82
HUR 191	144.44	155.30	3.3	2.9	150.35	168.60	3.7	4.2	913.85	969.54	11.17	15.34
HUR 193	558.05	.	4.2	.	599.00	.	5.8	.	2139.10	.	40.33	.
HUR 197	423.34	.	4.7	.	433.24	.	6.2	.	1737.55	.	34.08	.
HUR 198	417.65	359.20	4.5	3.6	425.05	457.70	6.0	6.4	2036.36	2188.71	29.91	34.08
HUR 199	274.50	.	4.2	.	293.35	.	5.4	.	1572.06	.	22.63	.
HUR 200	564.80	.	4.7	.	592.80	.	6.6	.	2050.11	.	41.37	.

ID Number	70% Untrained Leg PP Pre	70% Untrained Leg PP After	70% Untrained Leg PV Pre	70% Untrained Leg PV After	Abs PP Untrained Leg Pre	Abs PP Untrained Leg After	Abs PV Untrained Leg Pre	Abs PV Untrained Leg After	Muscle Volume Untrained Leg Pre
HUR 128	230.66	211.58	4.5	4.6	247.22	210.52	5.8	5.4	985.89
HUR 129	334.88	354.10	5.3	6.0	315.37	339.96	6.3	7.0	1356.40
HUR 131	146.47	146.85	3.9	3.6	161.52	164.43	4.8	4.9	809.83
HUR 134	360.86	.	5.7	.	349.42	.	6.8	.	1397.12
HUR 135	361.78	398.48	4.3	4.5	383.69	429.01	5.3	6.1	1435.20
HUR 139	563.08	604.14	5.1	5.9	556.23	587.37	6.6	7.2	2154.39
HUR 140	149.97	.	3.2	.	165.76	.	4.3	.	1034.19
HUR 142	198.08	.	4.1	.	180.21	.	4.7	.	1025.34
HUR 147	136.78	.	3.0	.	159.15	.	4.4	.	.
HUR 151	160.33	168.70	3.3	3.5	162.59	169.60	4.2	4.3	1107.41
HUR 152	.	.	.	.	.	.	.	.	.
HUR 155	297.24	233.17	4.1	4.0	317.30	228.14	5.4	4.9	.
HUR 156	714.52	721.91	7.0	5.0	.	.	.	.	2377.61
HUR 157	247.40	.	4.4	.	249.59	.	5.2	.	.
HUR 168	307.56	317.38	4.4	4.5	318.69	337.75	5.7	5.9	1480.23
HUR 169	136.02	148.65	3.7	3.8	138.37	139.60	4.1	4.0	862.25
HUR 172	580.26	549.61	6.9	5.7	581.73	526.67	7.9	7.0	1837.19
HUR 174	395.83	414.52	4.5	3.9	395.83	403.02	4.5	4.3	1874.68
HUR 175	.	.	.	.	.	.	9.0	8.1	1796.95
HUR 177	252.62	.	4.2	.	265.76	.	5.4	.	.
HUR 179	538.40	478.40	5.7	4.6	521.94	493.25	6.5	6.1	.
HUR 180	233.72	224.78	4.1	4.0	258.72	243.91	5.3	5.2	.
HUR 182	559.39	559.78	4.5	4.1	.	.	.	.	1939.51
HUR 183	357.25	389.38	5.0	5.8	377.70	369.30	6.4	6.2	1436.78
HUR 186	598.93	.	4.9	.	626.94	.	7.1	.	.
HUR 187	259.95	274.90	4.9	5.2	285.75	324.90	6.2	6.7	1275.79
HUR 188	629.14	633.80	4.8	4.5	603.38	577.50	6.2	6.2	2161.44
HUR 191	134.33	157.50	3.4	3.1	126.29	160.10	3.4	3.9	916.78
HUR 193	496.15	.	4.4	.	535.75	.	6.2	.	2051.41
HUR 197	387.25	.	4.2	.	400.17	.	5.9	.	.
HUR 198	344.25	307.30	4.2	3.2	344.60	354.80	5.4	5.3	2051.98
HUR 199	251.35	.	4.0	.	263.85	.	5.4	.	.
HUR 200	489.00	.	4.4	.	505.60	.	6.3	.	.

ID Number	Muscle Volume Untrained Leg After	Diuretic Usage	ACE Usage	HRT Usage	Anti-inflammatory Drug Usage
HUR 128	988.24	2	2	1	2
HUR 129	.	2	2	2	2
HUR 131	816.88	2	2	2	2
HUR 134	.	2	2	1	2
HUR 135	1394.07	2	2	.	2
HUR 139	2133.82	2	2	.	2
HUR 140	.	2	2	2	2
HUR 142	1023.66	2	1	2	2
HUR 147	.	2	2	2	2
HUR 151	1032.30	2	2	2	2
HUR 152	.	2	2	2	2
HUR 155	.	2	2	2	2
HUR 156	2392.46	2	2	.	2
HUR 157	.	2	1	2	2
HUR 168	1506.31	2	1	.	2
HUR 169	871.01	1	2	2	2
HUR 172	1841.92	2	2	.	2
HUR 174	1883.24	2	2	.	2
HUR 175	1803.03	2	2	.	2
HUR 177	.	2	2	2	2
HUR 179	.	2	2	.	2
HUR 180	.	2	2	1	2
HUR 182	1937.14	2	2	.	2
HUR 183	1455.23	2	2	2	2
HUR 186	.	2	2	.	2
HUR 187	1309.10	2	2	2	2
HUR 188	2189.29	2	2	.	2
HUR 191	942.89	2	2	2	2
HUR 193	.	2	2	.	2
HUR 197	.	1	1	.	2
HUR 198	2038.10	2	1	.	2
HUR 199	.	2	2	2	2
HUR 200	.	2	2	.	2

ID Number	Sex	ACTN	Age	Height	Pre fat mass	After fat mass	Pre FFM	After FFM	Pre weight	After weight	Pre body fat %	After body fat %	Pre BMI	After BMI	1RM Pre	1RM After
HUR 203	F	RX	54	168.5	16094.1	15848.7	39446.7	40021.8	55.54	55.87	29.0	28.4	19.56	19.68	14.71	25.33
HUR 204	F	RR	50	155.9	55684.6	56804.3	52259.3	51058.2	107.94	107.86	51.6	52.7	44.41	44.38	21.58	29.91
HUR 206	M	RR	61	179.2	20129.0	20569.6	66760.7	65943.9	86.89	86.51	23.2	23.8	27.06	26.94	43.45	52.41
HUR 207	F	XX	54	162.5	16274.5	.	34415.8	.	50.69	.	32.1	.	19.20	.	9.98	.
HUR 208	M	RX	54	185.1	24255.4	23536.2	68730.6	69911.4	92.99	93.45	26.1	25.2	27.14	27.27	52.82	58.86
HUR 209	M	XX	68	182.2	33497.1	31932.1	69769.5	69024.0	103.27	100.96	32.4	31.6	31.11	30.41	35.12	41.79
HUR 210	F	RX	66	160.1	44261.4	45391.2	48503.4	50560.2	92.76	95.95	47.7	47.3	36.19	37.43	13.67	17.84
HUR 212	M	RR	56	168.7	23194.9	21922.3	61194.8	62504.3	84.39	84.43	27.5	26.0	29.65	29.67	37.20	49.70
HUR 213	F	XX	75	159.9	23603.4	21742.2	39594.0	39026.3	63.20	60.77	37.3	35.8	24.72	23.77	14.71	22.63
HUR 215	F	RX	57	165.6	26900.0	26922.9	42929.1	43900.2	69.83	70.82	38.5	38.0	25.46	25.83	23.04	27.42
HUR 216	M	RX	57	170.9	29432.4	28956.9	60017.1	61451.6	89.45	90.41	32.9	32.0	30.63	30.95	26.17	40.33
HUR 218	F	XX	63	158.9	39324.7	.	48566.3	.	87.89	.	44.7	.	34.81	.	13.25	.
HUR 220	F	RR	57	161.2	24813.1	24614.4	36879.3	37363.2	61.69	61.98	40.2	39.7	23.74	23.85	16.38	18.46
HUR 221	F	RX	79	168.2	29816.3	.	42853.6	.	72.67	.	41.0	.	25.69	.	11.59	.
HUR 222	F	XX	61	165.5	38944.0	.	47205.8	.	86.15	.	45.2	.	31.45	.	12.63	.
HUR 223	F	RR	55	162.8	24775.0	.	39002.0	.	63.78	.	38.8	.	24.06	.	16.38	.
HUR 224	M	RX	56	176.1	.	.	.	.	99.70	.	.	.	32.15	.	36.58	.
HUR 225	F	XX	59	157.4	22110.6	.	45269.1	.	67.38	.	32.8	.	27.20	.	19.50	.
HUR 226	M	RR	67	170.9	41740.6	.	66074.9	.	107.82	.	38.7	.	36.91	.	25.33	.
HUR 227	M	RX	71	165.9	21478.9	.	58946.4	.	80.43	.	26.7	.	29.22	.	29.29	.
HUR 234	M	XX	79	171.0	.	.	.	.	.	.	.	.	.	.	25.96	.

ID Number	70% PP Pre	70% PP After	70% PV Pre	70% PV After	Abs PP Pre	Abs PP After	Abs PV Pre	Abs PV After	Muscle Volume Pre	Muscle Volume After	1RM Untrained Leg Pre	1RM Untrained Leg After
HUR 203	246.75	245.90	4.6	3.7	249.85	277.40	4.6	5.3	1127.55	1247.40	14.71	17.84
HUR 204	296.70	253.90	4.3	3.1	308.18	266.20	5.1	4.7	1244.56	1389.37	20.54	23.67
HUR 206	389.85	550.70	3.6	4.1	466.45	632.30	4.8	5.9	2069.87	2152.22	37.20	34.70
HUR 207	178.50	.	4.2	.	197.65	.	5.4	.	.	.	.	.
HUR 208	907.50	757.80	5.1	4.3	912.30	809.40	7.0	6.8	2208.23	2415.24	59.49	64.28
HUR 209	441.49	489.00	4.2	4.1	477.74	501.50	5.2	5.7	2076.84	2129.36	40.74	45.53
HUR 210	213.70	227.60	4.4	4.3	233.00	244.70	5.6	6.0	1105.77	1214.56	16.79	19.71
HUR 212	630.35	546.20	5.6	3.9	672.75	676.90	7.9	7.8	1914.51	2159.93	39.29	40.33
HUR 213	277.10	277.10	4.7	4.7	277.10	297.40	4.7	5.4	1095.38	1165.86	15.75	18.04
HUR 215	274.85	255.80	3.8	3.2	280.15	295.40	4.4	4.5	1216.86	1290.08	22.63	22.63
HUR 216	427.05	485.70	5.1	4.1	427.05	504.40	5.1	6.0	1851.78	2006.70	28.25	35.12
HUR 218	196.90	.	4.1	.	201.00	.	5.0	.	.	.	11.80	.
HUR 220	186.80	213.80	3.5	4.0	212.10	215.40	4.7	4.0	983.40	1085.10	16.38	15.34
HUR 221	123.05	.	3.0	.	162.40	.	4.3	.	.	.	9.98	.
HUR 222	220.20	.	4.7	.	223.85	.	5.6	.	.	.	11.59	.
HUR 223	194.90	.	3.7	.	238.50	.	5.1	.	.	.	14.30	.
HUR 224	688.10	.	6.4	.	644.40	.	8.1	.	.	.	36.16	.
HUR 225	176.55	.	3.7	.	196.95	.	4.9	.	.	.	16.79	.
HUR 226	298.10	.	4.2	.	319.95	.	5.4	.	.	.	24.08	.
HUR 227	326.90	.	3.9	.	358.45	.	5.5	.	.	.	32.00	.
HUR 234	299.40	.	4.1	.	315.90	.	5.4	.	.	.	25.12	.

ID Number	70% Untrained Leg PP Pre	70% Untrained Leg PP After	70% Untrained Leg PV Pre	70% Untrained Leg PV After	Abs PP Untrained Leg Pre	Abs PP Untrained Leg After	Abs PV Untrained Leg Pre	Abs PV Untrained Leg After	Muscle Volume Untrained Leg Pre
HUR 203	235.11	241.10	4.4	4.1	235.50	257.40	5.2	5.2	1108.50
HUR 204	252.90	272.10	4.3	4.0	252.90	258.80	4.3	4.3	1228.95
HUR 206	346.05	389.20	3.4	3.9	429.85	455.60	5.6	6.0	1811.37
HUR 207	182.85	.	4.3	.	.	.	.	.	.
HUR 208	640.70	594.10	4.4	3.9	682.50	633.10	6.4	4.7	2556.46
HUR 209	490.84	520.00	4.4	4.4	490.84	520.60	4.4	4.8	2153.00
HUR 210	271.15	257.90	5.0	4.6	276.05	274.10	5.6	5.7	1151.57
HUR 212	558.30	521.10	4.9	4.8	583.75	555.80	7.1	6.8	1795.76
HUR 213	238.00	202.60	4.5	3.5	238.00	222.60	4.5	4.2	1019.77
HUR 215	247.10	269.70	3.9	3.7	259.20	254.70	5.2	4.6	1156.52
HUR 216	419.30	425.90	4.9	4.1	408.70	441.60	5.5	6.0	1812.26
HUR 218	180.75	.	4.0	.	173.55	.	4.6	.	.
HUR 220	219.95	200.80	4.1	3.9	233.50	209.90	4.3	4.4	971.60
HUR 221	124.25	.	3.6	.	134.25	.	4.4	.	.
HUR 222	181.70	.	4.3	.	196.10	.	5.4	.	.
HUR 223	168.95	.	3.7	.	200.35	.	4.9	.	.
HUR 224	624.30	.	5.8	.	610.80	.	7.7	.	.
HUR 225	201.40	.	4.2	.	205.90	.	5.3	.	.
HUR 226	301.30	.	4.3	.	296.50	.	5.1	.	.
HUR 227	354.05	.	4.1	.	384.25	.	5.7	.	.
HUR 234	.	.	.	.	.	.	.	.	.

ID Number	Muscle Volume Untrained Leg After	Diuretic Usage	ACE Usage	HRT Usage	Anti-inflammatory Drug Usage
HUR 203	1095.60	2	2	1	2
HUR 204	1245.01	2	2	2	2
HUR 206	1802.95	2	2	.	2
HUR 207	.	2	2	2	2
HUR 208	2485.65	2	2	.	2
HUR 209	2059.61	2	2	.	2
HUR 210	1193.79	2	2	2	2
HUR 212	1765.31	1	2	.	2
HUR 213	1004.67	1	2	2	2
HUR 215	1164.64	2	2	2	2
HUR 216	1802.16	2	2	.	2
HUR 218	.	2	2	2	2
HUR 220	977.10	2	2	2	2
HUR 221	.	2	2	2	2
HUR 222	.	2	2	2	2
HUR 223	.	2	2	1	2
HUR 224	.	2	1	.	2
HUR 225	.	2	2	2	2
HUR 226	.	1	1	.	2
HUR 227	.	1	1	.	2
HUR 234	.	1	1	.	2

APPENDIX F: LITERATURE REVIE

Aging and Sarcopenia

The Effects of Aging on the Components of Sarcopenia

The Effects of Strength Training as an Intervention on the Components of Sarcopenia

Variability in Muscle Size and Function in Response to Aging and Strength Training

Heritability of the Components of Sarcopenia

Candidate Genes for the Components of Sarcopenia

ACTN-3 and the *ACTN3* R577X Polymorphism

APPENDIX F: LITERATURE REVIEW

The following review of literature provides background information on sarcopenia, the use of strength training (ST) as an intervention for sarcopenia, and the role of genetics in influencing ST adaptations. This review will focus on the following topics: 1) aging and sarcopenia, 2) the effects of aging on the components of sarcopenia, 3) the effects of strength training as an intervention on the components of sarcopenia, 4) variability in muscle size and function in response to aging and strength training, 5) heritability of the components of sarcopenia, 6) candidate genes for the components of sarcopenia, 7) ACTN-3 and the *ACTN3* R577X polymorphism.

Aging and Sarcopenia

Sarcopenia is defined as the loss of muscle mass with aging, which subsequently affects performance and muscle function (146). Sarcopenia has also been expanded to include other components including strength, muscle quality, and power (101, 107), but the primary measures of loss of muscle function are muscle strength and mass. No sole factor has been identified that explains the aging-related loss of muscle size or function, as sarcopenia is also considered to be a multifactorial condition that occurs naturally, to some extent, with aging. However, there is significant inter-individual variability in sarcopenia and the factors that influence sarcopenia. Some of the major factors appear to contribute to sarcopenia are decreases in alpha motor neurons, motor units, protein synthesis, myosin heavy chain (MHC) expression, and an rise in catabolic stimuli such as cytokines (e.g. TNF-alpha) (28, 110, 160).

For example, the loss of muscle neurons that is known to decline with age seems to have a greater affect on fast motor units (24, 38, 40, 145), which are associated with

the aging-related loss in muscle strength. However, more recent data indicate that the motor neuron loss with aging is not as considerable as previous reports suggested (123). The accompanying increase in motor unit size that is observed with senescence can be ascribed to this disproportionate loss of fast motor units, which are reinervated by slow motor units (40). Despite the loss of fast motor units with aging, Urbanchek et al. (185) reported that deinervated muscle fibers account for only ~ 11% of the force difference in skeletal muscle between young and older adult rats.

In addition to the loss of fast motor units, muscle contractile protein synthesis rate is reduced with aging (7, 126). Balagopal et al. (7) reported that whole body muscle protein (i.e. myosin heavy chain proteins (MHC)) synthesis was ~ 50% lower in the elderly than in the young, but whole body non-muscle protein synthesis did not exhibit this relationship. Follow-up data from this group (8), indicated that mixed muscle protein synthesis and gene transcript levels of MHC-IIa and MHC-IIx were found to be lower with increasing age, but MHC-I synthesis was not different among age groups. Furthermore, age-related decline in MHC-IIa and MHC-IIx transcript levels were not reversed with ST, whereas exercise results in a higher synthesis rate of MHC-I isoform transcripts. These data confirm earlier work by Welle et al. (193) who measured total and fractional protein synthesis in healthy, moderately active young and older men, and found that the fractional rate of myofibrillar protein synthesis was 28% slower in the older men than in the younger men. Total myofibrillar protein synthesis via measurement of creatinine excretion was estimated to be 44% slower in the older subjects. Additionally, whole body protein synthesis was lower in the older than the younger group, even after correcting for total FFM. However, not all investigations agree with

this finding. Morais et al. (122) reported that after correction for FFM, whole body protein turnover is not decreased in the elderly. Despite some conflicting reports, the majority of the published data indicate several different interrelated factors that explain the aging-related loss of muscle mass and function, which has been observed in a host of investigations.

Earlier reports on sarcopenia by Young et al. (200) found that quadriceps CSA was 23% and 33% smaller in elderly men and women, respectively, than in younger subjects. These data are supported by the later work of Hakkinen and Hakkinen (67) who found a 27% lower mid-thigh CSA in older women when compared to younger women. However, these data may have underestimated the actual extent of sarcopenia due to the increase of connective tissue and fat infiltration into the muscle tissue that earlier muscle CSA measurement techniques could not detect. More recently, cross-sectional data reported by Janssen et al. (85) measured muscle mass of 468 subjects from 18 – 88 years of age and found a decrease in muscle mass starting at ~ age 60, amounting to 1.9 and 1.1 kg per decade in men and women, respectively. The loss of muscle mass was greater in the lower extremities. The initial amount of muscle mass and the rate of muscle loss with aging determine the progression of sarcopenia (110).

Sarcopenia also has significant consequences on functional ability, injury risk, and mortality (5, 10, 138, 142). Data from both cross-sectional and longitudinal investigations indicate that muscle function decreases with advancing age (54, 104, 105, 115). This decline in muscle function is due to a host of factors, including a decrease or unfavorable change in muscle volume, strength, contractile protein gene expression, metabolic properties, motor unit innervation, and loss of type II muscle fibers (107).

The sequela of sarcopenia range from decreases in functional ability to increased mortality risk. A number of investigations have demonstrated a relationship between diminished muscle strength and increased mortality rate (58, 99, 143). Although reports vary, muscle mass declines with aging occur at a rate of ~ 1% - 2% per year after age 50 (75, 157). However, this decrease in muscle mass often goes unnoticed because of a concomitant increase in fat mass, which results in relative constancy in body weight. Muscle volume and strength reach a peak between 40 and 50 yrs of age and remain relatively stable until the sixth decade. Beginning at ~ age 60, muscle strength will begin to decline at approximately 12 – 14% per decade and muscle mass will decrease at ~ 6% per decade (105). This is equivalent to a loss of muscle function of ~ 40% by the eighth decade of life and often leads to disability and morbidity and possibly even mortality (116, 118). Data from the New Mexico Elder Health Survey (14) found that up to 25% of persons under age 70 were sarcopenic as measured by muscle mass index (muscle mass (kg)/height) and defined as being more than two SD below the mean of the young referent population. In addition, 30% of women and 50% of men over age 80 in that cohort were sarcopenic. Moreover, more recent data using DXA to quantify appendicular skeletal muscle mass in ~ 200 women aged 64 – 93 and ~ 140 men aged 64 – 92 yr found that the overall prevalence of sarcopenia was ~ 23% in women and ~ 27% in men and up to 45% in those over age 80 (79).

Furthermore, it has been reported that adjusted arm muscle area is a better predictor of mortality than BMI, which is often used as a predictor of mortality in the older adults (118). Recent data from the Baltimore Longitudinal Study on Aging (BLSA)

show that hand grip strength, independent of physical activity or muscle mass, is also a predictor of mortality (116).

The Effects of Aging on the Components of Sarcopenia

Declines in muscle mass with age is strongly correlated with strength, and the losses associated with aging (55, 144). However, depending on the measurement method used, muscle mass has been shown to decline at a slower rate with aging than muscle strength (113). Although various measurement techniques have been used to estimate losses in muscle mass with age (e.g. ultra-sound, computed tomography scans (CT), magnetic resonance imaging (MRI), ^{40}K counting, creatinine excretion, dual-energy x-ray absorptiometry (DXA), and hydrodensitometry), little information is available from direct measurement of muscle mass. Metter et al. (116) measured total creatinine excretion to estimate FFM in a BLSA cohort of ~ 950 men and found that FFM loss of ~ 33% occurs during the adult age span. The post-mortem examination of cadavers allows a more direct measurement of muscle mass that overcomes certain ethical and logistical problems. For example, Lexell et al. (103) employed a whole muscle post-mortem examination to quantify size of whole muscle, number of fibers, and fiber size to measure total age-related changes in muscle. In this study, autopsied cross-sections of whole vastus lateralis muscle from 43 previously healthy men between the ages of 15 and 83 years were examined. The results showed that sarcopenia begins around 25 years of age and accelerates thereafter. Furthermore, this muscle mass decline is caused mainly by a decrease in fiber number, with no preferential loss of any fiber type, and to a lesser degree by a loss of type II fiber size. These data are supported by later work by Overend et al. (132) who found from computed tomography (CT) scans of the thigh muscles of

young and older men that comparisons of relative leg muscle strength in these subjects may be misleading due to the decrease in muscle tissue associated with aging. The authors stressed that appropriate measurement of muscle size and CSA need to be performed prior to making such comparisons. More recently, Trappe et al. (182) found that in men and women each of the four muscles of the quadriceps atrophy similarly with aging, exhibiting a CSA that is ~ 27% lower in elderly subjects than in the younger subjects as measured by CT.

Aging-related declines in muscle strength and power are related to changes in the number of motor units, altered muscle pennation angle, increases in connective tissue and fat infiltration, fiber type grouping, loss of type II fibers, and decreased expression of myosin heavy chain (MHC) proteins (7, 89, 94, 103). These age associated reductions have been demonstrated by both cross-sectional and longitudinal studies, which have shown that there is a considerable loss of muscle strength beginning after the 50s for men, and somewhat earlier for women (104, 105). However, investigations that examine aging effects often employ cross-sectional designs. These studies have limitations when trying to establish cause and effect, due to confounders such as diet, physical activity, or generational differences when comparing subjects of different ages/generations, and these confounders persist to some extent even when using longitudinal data to assess age-related changes. Despite these methodological constraints, cross-sectional studies can provide some important contributions to the literature, especially when combined with other studies using large sample sizes.

Kallman et al. (87) reported cross-sectional data from the Baltimore Longitudinal Study on Aging (BLSA), which measured grip strength in 847 men aged 20 – 89 years,

and found that muscle strength is highest in the 30s and subsequently declines after age 40 in curvilinear fashion. After the 80s, strength declines by ~ 37%. On the other hand, longitudinal analysis of the data showed that ~ 15% of the subjects over age 60 yrs demonstrated no strength decline during an ~ 9 year follow-up suggesting that there is significant inter-individual variability in strength losses. This was followed up by another report from the BLSA, which found that concentric, eccentric, and isometric knee and elbow flexor and extensor strength declines with aging when ~ 650 men and women aged 20 – 93 years were examined (104). In addition, Era et al. (42) reported the maximal isometric strength of five muscle groups in three groups of men in their 30s, 50s, and 70s. The results showed significant age-related differences between age groups in isometric handgrip, elbow flexion, knee extension, trunk extension and flexion strength that was similar to the BLSA results mentioned above by Kallman et al. (87). Both studies examined strength differences over a similar portion of the adult age range. Arm flexor and extensor data show that the declines in arm strength with aging are similar to the loss of leg strength, but start later. Another earlier cross-sectional study by Frontera et al. (55), measured isokinetic strength of the elbow and knee extensors and flexors in 200 healthy, 45 – 78 yr old men and women to examine the relationship between muscle strength, age, and body composition. Peak torque about the knee was measured at 60 and 240 degrees/s and at 60 and 180 degrees/s for the elbow. Strength in all muscle groups in men and women at both testing speeds was significantly lower (15.5 – 26.7%) in the 65 – 78 year old age group than in the 45 – 54 year old group. However, when strength was adjusted for FFM, age-associated differences among age groups were not significant in all muscle groups except the knee extensors, when tested at the high velocity (240

degrees/s). These data support the hypothesis that age-related declines in muscle mass are at least partially responsible for decreases in strength. This conclusion confirms an earlier report by Borges (19) who tested ~ 140 healthy men and women aged from 20 – 70 years. Maximum isometric and isokinetic knee extension and flexion muscle torque was measured at slow, medium, and faster velocities (12, 90 and 150 degrees/sec). Both isokinetic and isometric torque was lower with advancing age in both sexes. Isokinetic torque decreased significantly between 20 and 30 years of age in men and between 40 and 50 years of age in women. A significant decrease was also found between the ages of 60 and 70 years in both sexes. Maximum isometric torque showed a significant decrease between 60 and 70 years in men and women. Significant correlations were observed between peak torque and body mass, height, and body surface area.

Cross-sectional data at the muscle fiber level provide support for these results. For example, Frontera et al. (57) reported a 35% reduction in type II muscle fiber force production in older men (~ 75 yrs) than in younger men. This corresponds to other cross-sectional data (178) showing 25 - 40% less power in single fibers in older women than young women, old men, and young men. This investigation showed that older women demonstrate attenuated force production in single skeletal muscle fibers.

These data suggest that the decline in whole muscle strength is at least partially caused by the decrease in the force generating capacity of individual muscle fibers. However, if elderly subjects are unable to maximally activate existing motor units, then limited force production of muscle fibers may be a limiting factor. Maximal voluntary contraction with twitch interpolation provides evidence that older subjects can fully and maximally contract their musculature (33, 78, 90), although some report less than full

activation (as low as 69%) of the musculature in older adults (169). On the other hand, a recent report suggests that with sufficient attempts, elderly men can fully activate their elbow flexors and extensors, as well as younger men, even if an impairment previously existed (84). This highlights a design flaw in many previous studies that measured muscle strength without providing an adequate familiarization period prior to strength testing.

Longitudinal studies are not as common as cross-sectional investigations due to logistical difficulties and expense. Furthermore, although longitudinal studies are also subject to other problems such as loss to follow-up and observations that are not often equally spaced, they are a preferable design for assessing the effects of aging. Typically, longitudinal studies on sarcopenia report a more rapid rate of decline in strength than do cross sectional studies. For instance, a study by Bassey and Harries (11) reported that in men and women > 65 years old, the rate of decline in strength with aging was ~ 2% per year. However, a four-year follow-up on 620 survivors showed that grip strength had declined by 12% in men and 19% in women, and these losses were significantly related to age (11). A significant decline was also found in physical activity and functional capacity. These findings are supported by data reported by Sowers et al. (168) who found that in 712 younger African-American and Caucasian women aged 34 – 58 years, almost 9% of women had at least a 6% loss (> 2.5 kg) of lean mass over a three-year observation period. This loss of muscle mass was associated with a greater decrease in physical functioning as determined by slower walking velocity and decreased leg strength. Additionally, another longitudinal study by Aniansson et al. (4) found that over a seven-year period, between the age of 70 and 75, there was a significant decline in knee

extensor, elbow extensor and flexor strength in both sexes, but a smaller decrease in isometric than in isokinetic strength. Isokinetic muscle strength in the knee-extensors and flexors was higher in men with a higher level of physical activity than in those with a lower activity level. Seven-year follow-up results showed a body mass decrease of 6% and a quadriceps muscle strength decrease of 10% - 22% over this period (3). There was also a reduction in fast-twitch fiber area in the quadriceps during this time span. Seven-year follow-up data from this cohort found that in these active elderly men between 76 and 80 yr of age, isokinetic strength for 30 degrees/s decreased significantly at a rate of 2 – 3% per year (2). There was also a significant increase in both type I and type II fiber areas, and this was interpreted as a compensatory adaptation for the loss of motor units with aging (2).

These findings are supported by Rantanen et al. (139), who examined aging-related changes in maximal isometric strength, over a five-year span in ~ 100 men and ~ 185 women aged 75 years at baseline. Results showed that there was substantial inter-individual variability in the % change in strength over ~ 5 years ranging from a 4% increase in knee extension strength in men and women to a 16% decrease in grip strength in women. Reduced grip strength was more extensive in women than men, and the more active men maintained their trunk extension strength better than the sedentary men. In women who decreased their activity levels, the rate of decline in grip and elbow flexion strength was 32% and 27% respectively, which was greater than other similarly aged subjects who either remained sedentary or who were more active. The more active women retained their knee extension strength at a higher level than the other groups. Those who died before follow-up tests exhibited poorer strength test results at baseline,

indicating that low muscle strength might be a predictor of mortality. Conclusions from these results also indicate that participation in everyday physical tasks (i.e. household work, walking, and gardening), which are also the most common physically demanding activities of older people, may be essential for maintaining strength at a sufficient level for functional abilities. These conclusions are supported by other recent findings that examined muscle strength thresholds that are associated with compromised performance on ambulatory tasks. For example, cross-sectional data from the BLSA (96) indicated that gait time decreases linearly with increasing knee extensor peak torque, then plateaus at higher strength levels (> 130 N m for normal gait, and > 190 N m for faster gait). More recently, another study found that subjects with isometric leg extension peak torque to body weight ratio < 3.0 N m/kg are at a substantial risk for impaired function chair rise, gait speed, and stair ascent and descent tasks (136).

The above findings by Rantanen et al. (139) concur with more recent findings by Frontera et al. (54) who examined age-associated changes in skeletal muscle mass and function over 12 year span. Twelve healthy, older (~ 65 yrs), sedentary men were examined at two time points. Isokinetic muscle strength of the knee and elbow extensors and flexors showed declines from 20% to 30% at slow and fast velocities. CT scans also showed an ~ 16% loss in the cross-sectional area (CSA) of the quadriceps. Linear regression results showed that strength at baseline and changes in CSA over time were independent predictors of strength after 12 years. Additionally, vastus lateralis muscle biopsies showed a 30% reduction type I fiber percentage, but no change in mean area in either fiber type. The conclusions of this investigation were that a loss in muscle CSA is a major contributor to the decrease in muscle strength with advancing age and, together

with muscle strength at baseline, accounts for ~ 90% of the variability in strength during the 12-year period. This data is supported by other recent data that showed a smaller mid-thigh cross-sectional area and greater fat infiltration in the muscle are associated with lower strength (128) and functional ability in older men and women (191).

Muscle quality (MQ) sometimes referred to as specific tension or strength per unit of muscle, also appears to be influenced by age. MQ considers neuromuscular factors and is a precise estimate of skeletal muscle function as opposed to overall FFM. MQ declines both at the whole muscle (105) and single muscle fiber level (57). Early studies were conflicting, as Young et al. (200) reported no difference in MQ of the knee extensors of older women compared to younger controls when strength was measured isometrically. In men, Young et al. (201) reported that, in contrast to the findings in women, older men showed a 19% lower MQ than younger men. Lynch et al. (105) reported a difference in MQ in the leg musculature between young and older adults, and that arm muscle quality decreased to a similar extent in men compared to women. However, leg MQ declined approximately 20% more than arm MQ with increasing age in women. Furthermore, Frontera et al. (57) studied single muscle fibers in younger and older men and women and found a difference in muscle fiber quality in men, with fibers from young men having greater capacity for force than fibers from older men. More recently, cross-sectional data by Newman et al. (128) found that upper and lower extremity MQ decreased as age increased in a large cohort of ~ 2600 men and women between the ages of 70 – 79. Therefore, the data show that MQ decreases with age, but the magnitude of this decline seems to depend on sex and the muscle group studied.

Muscle power (i.e. the rate of performing mechanical work) accounts for a greater amount of the variance in physical performance than strength in older adults (16, 50) and deteriorates at a faster rate than strength with advanced age (10, 114, 164). Although the literature is not as extensive for the examination of muscle power losses with aging when compared to strength, recent studies have focused on the changes in muscle power with aging and with exercise training. This lack of data on muscle power and the elderly is partially attributable to the difficulty in safely and accurately measuring power (41). The use of isokinetic dynamometers allow for power to be measured in a single muscle group based on peak torque, but this measurement does not consider the power needed to accomplish daily tasks at various external resistances and overcome speed (107). Furthermore, another major drawback of using isokinetic testing for muscle power assessment is that it doesn't allow for the measurement of velocity, as velocity is pre-determined by the tester and the device, instead of the subject being tested. Finally, the allowable speed of movement for isokinetic devices is limited and may not reflect the optimal speed of movement obtained during unloaded movements in humans (107).

In addition, elevated antagonist muscle activity in the elderly may limit the full movement efficiency depending on the type of muscle contraction and the movement velocity. Earlier measurement of power employed vertical jumping from a force platform (45, 62), which functioned similar to a scale, whereby muscle power is the product of force (after subtraction of body weight from the vertical component of the ground reaction force) and the movement velocity. However, the subject must move his/her body mass, which likely represents a higher than optimal external load for peak power production based on the force-velocity curve (107). Furthermore, this type of

measurement may not be safe for older subjects. To address the safety concerns associated with power testing using a force platform, Bassey and Short (12) invented an apparatus that measured average leg extensor power from force against a pedal that accelerates a flywheel of known inertia. However, older subjects were still required to use a higher percentage of their maximal power capacity because of the fixed inertia characteristic of the apparatus (107), but this problem has been since corrected by the development of a variable inertia testing apparatus (134). More recently, Delmonico et al. (37) reported the measurement of peak power during a single trial, rather than average power throughout the range of movement in a trial. A single maximal knee extension repetition was performed in older adults by using a machine equipped with load cell force transducers and position sensors to detect rotary motion at the joint. Peak power is calculated by filtering power data points during a single knee extension trial with a 10^{th} order Butterworth filter.

Izquierdo et al. (83) determined the optimal loads for maximal power production and found that peak power is maximized at 30 – 45% of peak strength for the upper extremity and at 60-70% for the lower extremity in middle aged and older adults. Furthermore, the results confirm previous data that shows that peak power decreases with increasing age to a greater extent than strength. This work is supported by more recent data reported by Macaluso and De Vito (106) who found that maximum peak (average) power is obtained at ~ 60% of maximum isometric strength in both young and older women, and this peak power is 61% lower in the older women. They also reported that power is influenced to a greater extent with aging than isometric strength. In contrast to these findings, Cuoco et al. (34) reported that lower external loads (~ 40% of leg press 1

RM) explained more of the variability in normal gait speed in the elderly than did power at higher external loads (~ 70% of 1 RM). Habitual gait speed is known to be a predictor of future disability, thus the authors suggest that lower external resistances should be used when evaluating peak power in older adults (34).

Previous cross sectional data suggest that the decline in peak muscle power with age is associated with muscle structure and function, tendon characteristics, and sarcopenia in specific muscle groups (151). In that investigation, 169 women and 89 men between 18 and 88 years were studied, and muscle force and power were assessed by jumping mechanography. These healthy subjects showed a difference of > 50% between the ages of 20 and 80 without a reduction in muscle cross sectional area suggesting that power declines might be a central role in the aging process. In addition, because muscle power may be a better predictor than strength in predicting impaired functional ability in the elderly (16, 50), determining the age-related causes of decreased muscular power provides important and relevant information to the understanding of sarcopenia. Bassey et al. (10) examined leg extensor power in elderly (~ 88 yrs old) patients in a chronic care facility using a custom built rig that measured maximal power output over < 1 s of a single extension of one leg. Functional ability was measured by timing a standard chair rise, four-stair climb, and a ~ 6 m walk. Leg extensor power was significantly correlated with all functional ability measures, but the functional ability measures were not correlated with each other except for chair rise time and gait speed. In addition, women had significantly lower leg extensor power than men, but their power scores accounted for 86% of the variance in walking speed, which was higher than in men. These data agree with recent findings that average leg extension power is a key factor that helps

explain the increased prevalence of mobility impairments in the elderly (138). More recent cross-sectional and longitudinal data from the BLSA (114) show age-associated reductions in power and isometric strength in the upper extremities in men and women over an average ~ 10 year period. Peak arm power was measured in 10 - 15 sec periods of maximal arm cranking using a bicycle which was converted and functioned as a drive shaft to power a generator. Strength and power declined beginning by age 40 in both women and men, but power declines were ~ 10% greater than strength losses in men, while no significant declines were found in women. The differences between the changes in power and strength with age in men support the hypothesis that there are variables other than strength, such as movement velocity, that influence power reductions. Suzuki et al. (170) found that ankle flexor and extensor muscle power together with self-reported measures of health and physical functioning were essential components of functional mobility in community dwelling older women. This finding confirmed an earlier study by Skelton et al. (164) who found that between the ages of 65 and 89 years, power declines at a rate of ~ 3 – 4% per year, which is higher than the rate of isometric strength loss (~ 1 – 2% per year). Runge et al. (151) also reported that there is a significant decrease in muscle power between the ages of 20 and 80 years, without a decline in muscle CSA. Most recently, Petrella et al. (135) examined age and gender differences in knee extensor strength and power in young (~ 26 yr old) and older (~ 63 yr old) men and women. The results showed that there were significant strength differences between the young and older subjects, and there was also a significant difference between age groups in knee extension power when normalized for thigh muscle mass. In addition, older adults had a significant decrease in peak velocity over 10 repetitions of knee extension

exercise, indicating that attenuation of velocity in older adults may likely be a contributing factor for decreases in power. This decrease in velocity may also contribute to increased risk of falls and mobility loss in the elderly.

The mechanisms that cause a more rapid decrease in power than strength with aging are not yet fully understood. However, because power is the product of force and velocity, variables that influence either of these two factors will have affect peak power (107). Thus, many of the aforementioned mechanisms that influence muscle strength decline with aging are likely to also be at least partially responsible for the decreases in power with advancing age. Additionally, specific changes that might influence muscle contraction speed will have a more significant impact on peak power than on strength. For example, with aging there is a preferential loss of type II skeletal muscle fiber number and size. Additionally, older skeletal muscle has been shown to be more likely to express more than one MHC isoform than the skeletal muscle of young subjects (91). Animal studies report that type II skeletal muscle fibers are capable of a four-fold greater power and force output and a faster shortening speed than type I fibers (107). The loss of type II fiber size leads to the decreased expression of fast MHC isoforms, which would likely have a significant impact on power output (71), and supports the evidence of change from fast to slow motor units with aging (189).

Other potential mechanisms have also been identified, which include decreased tendon stiffness with aging (107) and neural influences, which include dopaminergic neuron loss in the substantia nigra. This could result in a decrease in coordination, movement speed, and power. Furthermore, decreases in the sliding speed of actin on myosin with aging may play an important role in the observed power decline with

advancing age. For example, Hook et al. (74) reported an 18 – 25% age-associated reduction in the speed of actin filaments on myosin from 62 single fibers. The mechanisms underlying the aging-related slowing of motility speed remain unknown, but it hypothesized that posttranslational modifications of myosin by oxidative stress, glycosylation, or variations in muscle protein expression might explain this decrease.

The Effects of Strength Training as an Intervention on the Components of Sarcopenia

As a result of the increased prevalence of sarcopenia, the total health care costs and detrimental physical consequences that follow, it is imperative from a public health perspective to find a safe and effective method to increase muscle strength and mass in the elderly. For this reason, interventions designed for the prevention and treatment of sarcopenia should positively affect muscle mass, strength, and power without adverse side effects. A recent report indicates that the administration of growth hormone, one of the more commonly recommended interventions for sarcopenia, should not be used for this purpose due to its untoward side effects and questionable efficacy (18). Therefore, ST should be the intervention of choice for sarcopenia due to the substantial evidence for its efficacy within a very short time frame and safety (47, 77, 148). Numerous investigations have shown the efficacy of ST to increase muscle mass and strength in older adults ranging from 50 – 98 years of age (23, 47, 56, 81, 93). Additionally, the muscle adaptations in the elderly with ST have been shown to improve functional abilities (43).

Earlier work by Frontera et al. (56) found that ST in older men leads to increased strength of the quadriceps with an increase in muscle fiber size. Since this data was published, numerous other investigations have been done (64, 68, 72, 81, 102, 162, 171,

176, 180) showing that muscle strength increases ~ 20 to 40% in response to ST in the elderly. This large range is at least partially due to study design differences. Problems arise when attempting to make comparisons between different ST studies, especially with different outcomes. First, studies vary greatly with regard to muscle group studied (e.g. upper body vs. lower body) as well as the volume (i.e. repetitions x sets) and intensity (% of strength) used as an intervention. Furthermore, between-study comparisons are also problematic due to differences in the session frequency and duration of training interventions. Some report that improvements can be seen in as few as one session per week (171), while others used as many as seven sessions per week (159). The duration of ST interventions also vary considerably, with some lasting as little as four weeks (159) to almost two years (112), but most last between 8 – 12 weeks (107). Perhaps most importantly, the problem with comparing studies on the effects of ST interventions in older adults is the differences in subjects among the various studies. These variations include sex differences between groups, with some studies examining one sex, while other studies include both men and women (107). The ages of the study subjects can also vary significantly, with older subjects included ranging from those in their 50s to their 90s. In addition, subjects vary based on medical condition, medications, previous exercise experience, socioeconomic status, racial and genetic backgrounds.

Although the majority of studies indicate that there is little age difference in muscle strength response to ST (86, 107), Lemmer et al. (102) reported an ~ 34% increase in strength in 20 – 30 year old men and women, which was significantly greater than the ~ 28% increase observed in 65 – 75 old subjects. However, in that study muscle volume increases with ST did not exhibit these age differences. These data suggest that

in response to ST, skeletal muscle adaptations in older adults are comparable the changes in younger adults.

There are three general phases that occur in both young and older subjects that are responsible for strength increase during a ST program. First, during approximately the first two weeks of a ST program, there is a strong learning effect that improves the subject's ability to perform the ST exercise. This phase of neurological adaptation results in improved coordination and rapid strength gains, especially if the strength training modality involves a high level of skill (107). This effect can often be attenuated by familiarization sessions, which can prevent observed strength gains from being inflated, especially in older adults. The next phase, which occurs at weeks ~ 3 – 7, involves increases in muscle strength without a concomitant increase in muscle mass. This improvement in strength is ascribed to continuing neural adaptations including increased activation of the agonist muscle group (i.e. increase motor unit (MU) recruitment and better coordinated MU firing), improved involvement of synergistic muscles, decreased antagonist muscle activation, and increased central nervous system (CNS) drive (152). Finally, the third phase of ST adaptations that occur at ~ 6 weeks and later results in increased strength along with a matching increase in muscle size.

Muscle mass generally increases with ST in older adults, but this increase is dependent on the measurement tool used, the type of training program, and the age and sex of the subjects. The increase in muscle mass increase is quite variable ranging from little or no change to a ~ 23% increase with an average increase of ~ 8% (47, 48, 56, 64). For example, Tracy et al. (176) measured quadriceps muscle volume using MRI at baseline and after nine weeks of ST in 65 – 75 year old men and women. The results

showed that there was ~ 12% increase in muscle volume. Earlier data by Frontera et al. (56) reported an ~ 9% increase in the CSA of the knee extensors in a group of 60 – 72 yr old men who underwent a 12 week ST program, as measured by CT imaging.

Muscle volume or cross-sectional area in current studies is usually measured by CT imaging or MRI. Changes in muscle volume or CSA allows for the measurement of a specific muscle being trained and can differentiate between the various tissue components (i.e. muscle bone, and adipose tissue). Some investigators have measured muscle volume rather than CSA to examine the changes in muscle size with ST (80, 93, 124). Studies that report muscle volume changes with ST often report similar or greater increases than CSA, leading some to suggest that muscle volume, which is a more direct measure of the overall muscle mass of the trained musculature, might be a more valid measurement option for detecting changes in muscle size with ST (177). Despite the improved accuracy of the measurement of muscle size by these imaging techniques when compared to other methods (e.g. anthropometric methods), they are not capable of detecting changes in the individual muscle fibers.

Several training studies have been done in older adults to examine the muscle function changes that occur at the muscle fiber level. Data show that type I and type II muscle fibers in older adults maintain the ability to undergo hypertrophy with ST (30, 56, 68, 137), but some investigations found that there was only slight or no change in fiber areas (64, 76). Changes in fiber size with ST are typically at least 10%, which is typically greater than at the level of a whole muscle group. This is partly because MRI and CT assessment of whole muscles or muscle groups also measure other tissues (e.g. connective tissue), which are not apt to experience the same magnitude of change as

muscle tissue. In addition, several studies have found evidence for MHC II subtype transformations with ST in older adults, with MHC IIb changing to IIab to IIa, which is a similar response that occurs in younger adults (69, 71, 158). However, one investigation reported an increase in MHC I expression with ST (195), which could be attributed to a lower intensity training protocol in that investigation. It has been suggested that this lower intensity training program was not enough of a stimulus to recruit the fast MUs necessary for optimal increases MHC II expression. At the muscle fiber level, Trappe et al. (179, 181) found that in older men and women, skeletal muscle fibers increase in size, strength, and power with 12 weeks of ST. Other investigations report increases in protein synthesis in older adults with ST along with improvement in strength (73, 193, 199). Hasten et al. (73) found that at baseline older men and women have a lower MHC and mixed vastus lateralis muscle protein synthesis rate than younger adults. In addition, baseline actin protein synthesis rates were similar between the two age groups. A bout of ST increased mixed muscle and MHC protein synthesis rates in both age groups indicating that contractile protein synthesis in response to an acute ST session is not impaired in older adults when adjusted for FFM.

Muscle quality (i.e. strength per unit of muscle mass) has been shown to improve with ST in older adults (81, 176, 194). For example, Tracy et al. (176) reported a 14% and 16% increase in MQ in the quadriceps in response to a nine-week ST program for older men and women, respectively. More recently, Welle et al. (194) examined the arm and thigh muscles of older women (62 – 72 yrs) and reported that although aging might impair the hypertrophic response to ST, aging does not impair increases in MQ. In that

study, older women increased their knee extensor MQ by ~ 32% which was similar to the ~ 38% change observed in younger women (194).

As mentioned earlier, muscle power has been shown to account for a greater percentage of the variance in functional abilities than strength in the elderly (16, 50). Furthermore, muscle power deteriorates at a faster rate than strength with advancing age (10, 114, 164). For these reasons, recent studies of ST in the elderly have focused on the effect of ST on muscle power (15, 37, 41, 46, 49, 68, 86).

A randomized study by Earles et al. (41) compared the effects of a high-velocity ST program combined with moderate non-resistive exercise to an intervention of walking on leg press and knee extension peak power in men and women over the age of 70. Power improved significantly in the high-velocity ST group only for leg press (22%) and knee extension (increases of 50%, 77%, and 141% when power was tested at external resistances of 50%, 60%, and 70% of body weight, respectively). However, these improvements in power did not lead to improvements in functional abilities, although their cohort was considered high functioning at baseline. A more recent randomized study by Fielding et al. (49) examined 30 older women with mild functional limitations and compared the changes in skeletal muscle power between 16 weeks of high-velocity ST and a more traditional, low-velocity ST intervention. The results indicate that although leg press and knee extensor 1 RM strength increased similarly in both groups with ST, leg press peak power increased significantly more in a high-velocity group (97%) than in a low-velocity group (45%). The conclusion was that higher-velocity training programs might be more efficacious for increasing peak power in older individuals with functional impairments. However, it is still not well established whether

a high velocity training program is well tolerated by older subjects (44), especially subjects who are frail and could benefit the most from increased muscle power. Most studies that examined peak power used lower-velocity ST protocols that have extensive track records for being generally safe for older subjects (48, 86, 166). In these investigations, muscle power increased significantly with ST, ranging from ~ 18 – 28%, although the increases in strength were greater due to specificity of training.

In an earlier investigation, Fiatarone et al. (48) conducted a randomized, placebo-controlled trial comparing ST, multinutrient supplementation, both interventions, and neither in 100 frail nursing home residents over a 10-week period. Power, as measured by stair-climbing performance improved in the exercise group compared with the non-exerciser group (28.4% vs. 3.6%). These data indicated that there is a relationship between power adaptations to ST and functional ability. That study was followed by a report by Skelton et al. (166), who found that in 20 relatively healthy, independent elderly (76 to 93 years) women, knee extension power increased by 18% (as measured by the Nottingham Power Rig developed by Bassey and Short (12)) when adjusted for body weight. More recent data reported by De Vito et al. (36) examined the effects of a 12 week of a low-intensity general conditioning program on maximal power in 20 elderly women (~ 63 yrs) randomized to a training or control group. Peak power was determined at baseline and after the training regimen via vertical jump on a force platform. Peak power increased significantly in the training group, but did not change in the control group. The authors suggested that this increase in power could be due to improvements in neuromuscular activation. Additionally, Jozsi et al. (86) reported that with ST in men and women age 56 – 66 years, there was an increase in knee extensor and arm flexor

power with ST of 30% and 18%, respectively. These increases in peak power were independent of age or sex and occurred at 40% and 60% of 1 RM, and were similar to the changes observed in younger subjects. Izquierdo et al. (82) also reported that 16 weeks of ST resulted in large gains in strength and power load characteristics of the upper and lower extremity musculature, but the pattern of strength and power development seemed to differ between the upper and lower extremities in middle aged and older men. These studies, when taken together, suggest that both traditional and higher-velocity ST interventions are capable of increasing muscle power in older adults.

As mentioned earlier, one of the problems with muscle power testing is the difficulty in safely and accurately measuring power (107). Previous investigations (41, 49, 82, 86) reported peak power as the highest average power obtained during multiple trials of a power test, as opposed to the highest power value attained during a single trial. The highest peak power (i.e., the highest combination of force and velocity that occurs simultaneously during a single trial) might be a more accurate measure of the explosive capacity of the trained musculature than average (area under curve) power of a single trial. This is because average power includes two phases of movement that represent reduced power. The first is at the beginning of the movement when one is trying to overcome inertial forces and the other is near the end of the movement when co-contraction of the antagonist muscle group produces a reduced force and velocity. Although some previous investigations did exclude data from the first and last 5% of the range of movement in the power tests (16, 49, 50), these studies still used the average power for a given trial, and reported it as peak power.

Furthermore, these earlier reports (41, 49, 82, 86) on the effects of strength training (ST) on muscle power also did not report how the training affected power per unit of the muscle involvement (muscle power quality, MPQ), or peak movement velocity (PV), the latter possibly being an important component of power and possibly functional abilities in the elderly. The expression of peak power and PV normalized for muscle volume allows better understanding of potential mechanisms (e.g., hypertrophy and neuromuscular adaptations) for training-induced adaptations. It is also important when comparing groups who possess different amounts of muscle mass, such as men compared to women. Most recently, Delmonico et al. (37) reported the effects of a 10-wk, moderate velocity ST intervention on peak knee extensor power in relatively healthy older men (n = 30) and women (n = 32). Results showed that peak power (PP) increased significantly in both men and women at the same absolute (same absolute resistance before and after ST) and relative (70% of 1 RM at baseline and 70% of the improved 1 RM after ST) external loads. In addition, men and women both increased their absolute peak movement velocity with ST, and there was a significant 9% training-induced increase in MPQ in women, but no change in men. This latter finding indicates that women may not rely on muscle hypertrophy as much as men to improve muscle function with training. This could possibly be due to some type of neuromuscular adaptation that compensates for the reduced capacity of women to undergo muscle hypertrophy with ST compared to men, resulting in a compensatory increase in power per unit of muscle. Support of a sex difference in MPQ comes from work by Trappe et al. (179, 181) who found that the response of skeletal muscle fibers to ST on peak power normalized for cell size and unloaded shortening velocity differ with the same training stimulus between men

and women. However, no change in muscle fiber unloaded shortening velocity or normalized peak power was found in older women, indicating a sex difference in response to ST, although the cause for this difference is unclear.

Muscle power is a more complex phenotype than strength, thus there may be more interrelated factors that influence peak power changes with ST than are responsible for muscle strength changes alone. First, there are possible preferential increases in type II fibers leading to overall increases in muscle mass, which in turn leads to enhanced force production and muscle fiber shortening (49). Previous data has shown that adaptations to single MUs can help increase contraction speed with ST (187). Changes in MU function consist of earlier activation, shorter interspike intervals, and increased maximal firing rate (187). In addition, neural adaptations, including increased activation of the agonist muscle groups, decreased co-activation of the antagonist muscle groups, improved coordination and activation of synergistic muscles, and increased neural drive from the CNS, might lead to improvement in power with ST (107). Nevertheless, it may be problematic to directly examine these potential neurological components during power testing using electrophysiological methods because there are a host of physiological, mechanical, and electrical changes that happen during the contraction that might impact the correlation between signal amplitude and muscular force (107). Finally, tendon stiffness may be affected by ST, which may affect power changes. Maganaris et al. (109) used an *in vivo* method for assessing tendon stiffness in older adults, and found that patellar tendons stiffened structurally and materially by ~ 65% in response to a 14-week ST intervention. The rate of muscle torque production also increased by ~ 27%, indicating that there is a faster contractile force transmission to the skeleton. These data

provide support for several mechanisms that might play a role in the changes in power with ST. However, there appears to be a great deal of inter-individual variability in the rate of decline in muscle mass and muscle function with aging (111).

Variability in Muscle Size and Function in Response to Aging and Strength Training

Muscle mass, strength, and power responses to ST vary substantially among individuals. In a previous investigation from our lab, after only nine weeks of a highly standardized quadriceps strength training program in a healthy and homogeneous group of 65 to 75 year old men and women, there were observed knee extension strength gains that ranged from 5 to 86 pounds (80). Others have also observed large variations in strength and muscle mass changes with ST (26). They reported one repetition maximum (1 RM) strength increases that ranged from 1 to 50 kg after 20 weeks of ST. The standard deviations of the changes were larger than the mean changes and the coefficients of variation (CV) were > 100 %. In addition, muscle power changes with ST also are quite variable, as data from our lab indicates that changes with ST of the knee extensors for men and women in peak power range from – 19 to 126 W at the same absolute resistance, and peak movement velocity changes ranging from -1.1 to 2.7 rad/sec at the same absolute resistance (37). These data indicate that there are large inter-individual variations in strength changes even in response to very short term, highly standardized strength training interventions. Studies here have also reported increases in quadriceps muscle volume with ST that range from 19 to 344 cm, further demonstrating the wide variation of inter-individual changes in muscle mass from ST (80). These large inter-individual differences among older men and women are consistent with the possibility that genetic factors are involved in determining muscle strength, muscle mass, and

muscle power responses to strength training. This large inter-individual variability and the fact that twin studies show that a major portion of the variance in strength and muscle mass can be accounted for by heredity, suggest that heredity and specific gene polymorphisms may explain a large portion of inter-individual differences in responses to ST.

Heritability of the Components of Sarcopenia

The estimation of heritability of a specific trait is commonly estimated by the study twins and families. The most common analysis of heritability is phenotype measurement between and among sets of monozygotic and dizygotic twins. If a trait is completely determined by genetics, there would be correlation of 1.00 between sets of monozygotic twins, but a correlation of only 0.50 between dizygotic twins because dizygotic twins only share ~ 50% of their genetic makeup. However, skeletal muscle phenotypes are also influenced by many other factors beyond genetics, which can have an effect on the heritability estimate. Factors such as shared/non-shared environmental factors, additive/dominant genetic effects, and measurement error can influence these heritability estimates (22).

Evidence from heritability studies suggest that many skeletal muscle-related phenotypes, including strength, fat-free mass (FFM), and skeletal muscle fiber composition are at least partially explained by genetic factors. Twin studies indicate that strength has a moderate to high heritability, with different studies reporting a range of 30 – 80% depending on the population studied. For example, Frederiksen (52) reported that in 1,757 Danish twin pairs aged 45 - 96 years, that handgrip strength heritability is 52% and is as high as 62% when examining only healthy twin pairs from the cohort. Grip

strength has been shown to correlate strongly with other muscle groups with respect to strength and power. Men and women were used in this analysis and age was stratified into quartiles in the model. Results further indicated that a large portion of the variance is explained by additive genetic effects and non-shared environmental factors. In addition, there was no significant influence of age or sex in this analysis, indicating that these variables were not confounders or effect modifiers in this study. This heritability estimate is higher than previous data from postmenopausal female twins (6) that indicate a heritability estimate of 30%. Moreover, because of the evidence for heritability of grip strength, and because grip strength has been previously shown to be predictor of overall muscle function (140, 141) and subsequent disability (142), measurement of grip strength in future investigations on sarcopenia is justifiable. Other data on strength in older male twins indicated that a heritability of 65% at baseline, but when shared environmental factors were included in the model, this estimate dropped to 35% (29). A 10-year follow up indicated a heritability estimate of only 22% (29). More recently, Tiainen et al. (174) indicated that handgrip and knee extension strength share a common genetic component, accounting for 14% of the variance in older female twins. Furthermore, additive genetic effects accounted for 46% of the variance in knee extension strength.

Although there is currently not enough data to conclusively state what the heritability is for the loss of muscle power with aging, recent evidence suggests that knee extensor strength and power share a common genetic component (174). Data from the Finnish Twin Study on Aging, examined the genetic component of maximal voluntary knee extension power and strength in 101 monozygotic (MZ) and 116 dizygotic (DZ) female twin pairs aged 63 – 76 yr (175). Results indicate that a common genetic factor

accounted for 32% of the total variance in leg extensor power and only 4% of the variance in power is attributable to non-shared environmental factors. Additional evidence from twin studies on younger subjects indicate that the heritability of muscle power is 0.84 from a 5s Wingate cycle test (27). Many more studies will need to be done in order to more accurately determine the heritability of the explosive type of skeletal muscle power and the heritability of its decline with aging.

Muscle mass has also been investigated with regard to heritability using family and twin studies and it has been shown that estimates range from 50 – 80%. Data from an inbred founder population (Hutterites) with detailed family pedigree records indicates that FFM is highly heritable ($h^2 = 0.76$) (1). In addition, Arden (6) indicated that in postmenopausal women, FFM has a heritability estimate of 56% when height and weight are covaried. This is somewhat lower than what Seeman et al. (156) reported in younger female twins, who found that FFM is ~ 80% due to genetic factors. This corresponds to data that shows FFM is the phenotype that is most similar between girls and their parents when compared to % fat, total body mass, and BMI (183). In addition, the estimation of FFM values has been shown to correlate more strongly among relative than among unrelated individuals (20). More recent twin data confirm these estimates, finding a heritability estimate of 77% for FFM in both men and women (70). Again, age and sex do not appear to be significant covariates of within pair differences. With regard to skeletal muscle fiber composition, earlier heritability estimates suggest that muscle fiber type composition is over 90% genetically determined (92), but later studies indicate it is only around 45% (161). Furthermore, skeletal muscle enzyme activity also seems to be somewhat heritable, with estimates of 25 – 50% when adjusted for age and sex (21). In

order to more fully understand the specific contribution of specific gene variants toward explaining muscle phenotypes, an additional approach is to identify biologically plausible genes and conduct a candidate gene association study.

Candidate Genes for the Components of Sarcopenia

There have been relatively few candidate genes that have been consistently associated with skeletal muscle phenotypes and human performance. The angiotensin-converting enzyme gene (*ACE*) seems to be the most promising candidate gene to explain individual variation in skeletal muscle phenotypes. *ACE* is the most studied gene with regard to exercise related phenotypes, and has also been widely studied with respect to other pathophysiologic phenotypes, including CHF, essential hypertension, diabetic kidney disease, and CHD (13). Within the *ACE* gene, there have been several polymorphisms discovered with the insertion/deletion (I/D) polymorphism, a 287 bp insertion or deletion of an Alu element in intron 7 being the most widely studied polymorphism in this gene. The *ACE* I/D polymorphism has been shown to perhaps explain ~ 50% of the variance in ACE levels (13). The D allele has been associated with higher ACE levels in a dose-dependent manner, with the D homozygotes having the highest ACE levels, followed by I/D genotype, with the I homozygotes displaying the lowest levels of ACE activity. This has been consistently shown despite the fact that this polymorphism is not found in a coding region of the gene. The I/D polymorphism is very common in the Caucasian population, with genotype frequencies of 25%, 50%, and 25% for the I/I, I/D, and D/D genotypes respectively. The allele frequencies from the limited African-American data suggest that the D allele is substantially higher in this population with a frequency of approximately 70% (9).

Data from numerous cross-sectional investigations show that there is some evidence that *ACE* plays a significant role in various phenotypes, including skeletal muscle. Aerobic testing data has found that in post menopausal women, I homozygotes carriers have a greater increase in the a-vO_2 difference during maximal exercise testing (66). The a-vO2 difference might be considered more of an intermediate phenotype than VO_2 max and also a better indication of skeletal muscle metabolism. Myerson et al. (125) examined the distribution of the I/D polymorphism in elite (mostly Caucasian) track athletes and found that there was a significantly higher I allele frequency in endurance athletes. This corresponds to previous data (59) that also found a significantly higher frequency of the I allele among elite Australian rowers who were aerobically trained. Nazarov et al. (127) also reported that there is a higher proportion of Russian track & field athletes and swimmers who engage in events of greater than one minute who also have the I allele. Furthermore, Woods et al. (196) reported that there is a higher frequency of the D allele among sprint swimmers when compared to swimmers who compete in longer duration events. Despite these compelling data, not all reports agree. At the skeletal muscle fiber level Zhang et al. (203) reports that muscle fiber area is associated with *ACE* I/D genotype in a dose-dependent manner (DD > ID > II). Thomis et al. (173) found no association at baseline between this polymorphism and muscle torque, strength, or cross-sectional area in 33 pairs of Caucasian twins. Folland et al. (51) also reported no association between the *ACE* I/D genotypes and muscle strength at baseline in young sedentary males. Although these studies are not all in agreement and these study designs (cross-sectional) do not allow causal inference. Taken together,

however, they do suggest that there may be an underlying mechanism for the *ACE* I/D polymorphism and an effect on performance.

In addition to the numerous cross-sectional studies that have been reported with regard to the *ACE* I/D polymorphism, training studies provide additional information on the potential effects of the *ACE* I/D polymorphism and allow for insight as to whether or not there is a gene-exercise interaction. The data regarding aerobic exercise training and the association between the I/D polymorphism and various skeletal muscle phenotypes have been inconsistent. Montgomery et al. (121) reported that arm endurance is more improved in I homozygotes when compared to D allele carriers. Moreover, the delta efficiency ratio (work performed divided by work expended), a strong indicator of skeletal muscle efficiency, has been found to increase only in I homozygotes. Montgomery et al. (120) also noted that after 10 wks of aerobic exercise training, that I homozygotes show a greater anabolic response to training, showing increases in fat mass and fat-free mass compared to the other genotypes. This might represent greater metabolic efficiency of substrate use as perfusion of skeletal muscle and other oxidative-favoring changes in skeletal muscle have been shown to occur with decreased ACE levels. These data are in contrast to the findings of Um et al. (184) who found that there was no association between the *ACE* I/D genotype and BMI among Korean women. However, this was not a training intervention study. In addition, Folland et al. (51) found that there was a greater increase in strength among D allele carriers with ST, and this again followed a dose-dependent pattern (DD > ID > II). Not all studies agree with these findings, as Thomis et al. (173) found no association between the I/D polymorphism and muscle cross-sectional area, strength, or torque among genotype groups. In fact, a trend

toward increase flexion torque was noted among I homozygotes, which was not expected based on previous findings. Furthermore, Sonna et al. (167) found that in US army recruits that there was no association between vigorous exercise training-related phenotypes and the *ACE* I/D polymorphism. However, it should be pointed out that the training regimen was mixed (endurance/strength) and the measures of muscle strength were questionable as their efficacy to measure peak strength. Taken together, these training data do suggest that there may be a gene-exercise interaction with respect to the *ACE* I/D polymorphism.

In addition to *ACE* being a promising candidate gene for explaining the inter individual variability of skeletal muscle phenotypes, there are other candidate genes that have demonstrated a consistent relationship for predicting phenotypic variation. First, the vitamin D receptor (VDR) gene is a potential candidate for skeletal muscle phenotypes, including gene-exercise interactions. Although a great deal research has been done examining the association between *VDR* polymorphism and bone mineral density, there recently have been reports linking certain polymorphisms of the *VDR* gene with muscle strength and sarcopenia (65, 150). In elderly women, a significant difference in quadriceps strength was observed between the *bb* and *BB* genotype of the *VDR* BsmI polymorphism (60). Other investigations have found an association between FFM and the FokI polymorphism of VDR (150), while others found no association between this polymorphism and muscle strength in older adults (188). Although many more studies need to be done, the majority of the evidence suggests that *VDR* gene polymorphisms play a role in the determining the training response to ST with regard to various skeletal muscle phenotypes.

Another potential candidate gene is the insulin-like growth factor-2 gene (*IGF2*), as IGF II has been shown to have proliferative effects in adult skeletal muscle and is one of the major hormones for fetal growth. The ApaI polymorphism has been recently studied with regard to its effects on strength and muscle mass, and has shown mixed results. In an investigation by Sayer et al. (154) that examined 693 British men and women, the ApaI genotype was found to be a significant predictor of adult grip strength in men after adjustment for age and height, but these associations were not seen in women. However, the ApaI polymorphism does not appear to explain the association between size at birth and future grip strength. This data is complemented by recent longitudinal data by Schrager et al. (155) who reported lower isokinetic arm strength in men who are A homozygotes at the ApaI polymorphism when compared to the G/G group. Women who were A homozygotes have less total body FFM when compared to G/G women, and have lower isokinetic arm and leg strength at baseline, and at age 35 for each phenotype. These differences between the genotype groups are maintained at age 65 and across the adult age span. These results support the hypothesis that ApaI polymorphism may influence developing muscle and may affect muscle mass and muscle function in later life.

In addition, there are other candidate genes that have been suggested as candidates for explaining phenotypic variation in skeletal muscle, but have not been studied as extensively. Ciliary neurotrophic factor (*CNTF)* appears to be another candidate gene that could potentially have an effect on peak muscular power with aging as CNTF has trophic effects on muscle tissue by functioning as a maintenance and repair factor for adult motor neurons (95, 149). A single nucleotide polymorphism (SNP) at this

locus results in a G-to-A transition, which produces a new splice acceptor site and the results in an atypical protein (172). A recent investigation that examined the association between peak torque, muscle quality, and this SNP showed that heterozygotes had significantly greater knee extensor and flexor peak torques during isokinetic testing at higher velocities (3.14 rad/sec) than G homozygotes (149). It has been shown that there is a strong correlation between isokinetic strength at high velocities and knee extensor power (88), which suggests that this polymorphism may also influence peak power.

Tumor necrosis factor-alpha (*TNF*), also known as *CACHECTIN, DIF, TNFA,* and *TNFSF2* seems to also be an interesting candidate gene with regard to its potential role for influencing muscle phenotypes. TNF-α, a cytokine, is reported to be involved in numerous biological processes including cell proliferation, differentiation, and mediating muscle wasting (97). TNF-α has also been associated with a variety of diseases, including autoimmune diseases, insulin resistance, and cancer. Mouse data indicate that TNF-α is involved in the recovery of muscle function after traumatic muscle injury, as mice that are TNF-a deficient exhibit strength deficits twice that of wild-type mice following freeze injury to skeletal muscle (192). However, with ST in elderly subjects, both TNF-α mRNA and protein levels were decreased, indicating attenuation of age-related muscle wasting (63). This data is confirmed by more recent evidence in very elderly subjects, who experienced low-grade inactivation of the TNF-α system following ST (25). There are SNPs that have been identified at the *TNF* locus that may be worthy of investigation, such as the G-308A SNP in the promoter region that have been reported to influence the expression of TNF-α (153).

These candidate genes have been identified as being at least partial contributors to the inter-individual variation observed in skeletal muscle phenotypes. While the influence of various polymorphisms at multiple gene loci has been examined, many more studies are needed to identify the genetic basis for the variability of complex phenotypes such as skeletal muscle. Identification of the specific gene variations, gene x gene interactions, and haplotypes that influence this variability is important for clinical applications for eventually allowing for individualized exercise prescriptions based on a genetic predisposition for sarcopenia. Recent attention has focused on the alpha-actinin-3 (*ACTN3*) gene, which has been called the "gene for speed" by some (108). A more thorough examination of the influence of this gene may give insight regarding these inter-individual variations in response to ST.

ACTN-3 and the *ACTN3* R577X Polymorphism

Alpha-Actinins (ACTNs) are cellular proteins that are encoded by the spectrin superfamily genes that are distinguished by their ability to bind actin (39). ACTN isoforms have been observed over a broad variety of taxa, which include protists, invertebrates, birds, and mammals. As a result of both gene duplication and alternative splicing during the course of evolution, substantial functional variety has resulted with regard to the ACTN family (108). Antiparallel ACTN dimers have actin cross-linking activity and bind with actin, as well as preserve a spatial association among myofilaments (131). The binding ability of ACTNs to actin is due to the presence of two N terminal calponin-homology domains in the ACTN protein. The existence of calcium-sensitive EF (elongation factor) hands at the C-terminus of the ACTN allows for the release of actin from ACTN. ACTN proteins are present in both non-muscle and muscle tissues,

with its purpose in skeletal and cardiac muscle being the primary constituent of the Z-disks of the sarcomere, forming a lattice arrangement anchoring together the actin (thin) filaments and helps to stabilize the muscle contractile structure. Additionally, four different isoforms of the ACTN protein have been identified (39). Of these, ACTN-2 and ACTN-3 are present in striated muscle, with the latter being present only in skeletal muscle (17).

Evidence suggests that ACTNs are essential proteins with regard to maintenance of muscle structure, contraction, and connection of the sarcomere to the plasma membrane. In addition, ACTNs may also play a critical role in intracellular signaling between the sarcomere and metabolic pathways with regard to skeletal muscle metabolism (108).

A host of proteins have been shown to interact and bind with ACTNs, although most of the evidence is from ACTN-2 data. However, due to the high sequence similarity between the two isoforms, it is suggested that similar interactions exist for ACTN-3, as well. It appears that ACTNs bind high affinity to each other, via interactions involving their spectrin-like repeats (SLRs, 1-4) that form homo- and heterodimers. Formation of dimers allows for a long molecule that has an actin binding domain (ABD) at the end that allows for cross-linking of actin, and it permits the C-terminal region of one of the ACTN molecules near the N-terminal ABD of the other molecule, facilitating interactions of the two areas (108). These appear to be similar in affinity and stability that implies functional resemblance between the two dimers.

Another category of proteins that bind to ACTNs include structural proteins of the muscle contraction apparatus. The most highly studied binding partner of these proteins

is actin. In addition, ACTNs also bind with myotilin, an actin cross-linking protein, as well as with titin, nebulin, and CapZ, a filament capping protein. ACTNs are also involved in two of the protein structures that attach the sarcomere to the plasma membrane, via interactions with dystrophin and integrin (108).

In addition to the structural and contractile relationships between ACTNs and various striated muscle proteins, ACTNs also interact with a host of signaling proteins as well as with membrane receptors and ion channel proteins. Furthermore, ACTNs have been reported to interact with calsarcin proteins, which are found at the Z-line and bind to calcineurin (53). Calcineurin, a signaling protein, is postulated to play an important role in hypertrophy and fiber type determination. Interaction between ACTNs and metabolic enzymes also has been reported, but the meaning of these interactions is unknown (61). However, the presence of metabolic enzymes (e.g. F-1,6-BP) at the Z disk held by ACTNs might add to the local accessibility of necessary metabolites for production of energy (108).

Earlier data suggested that a deficiency of ACTN-3 expression is linked to merosin-positive congenital muscular dystrophy (CMD) (130). Evidence from muscle biopsies indicated that ~ 25% of subjects with merosin-positive CMD were ACTN-3 deficient, but it was not clear from this data whether or not ACTN-3 deficiency was due to a mutation(s) in ACTN-3 or is a secondary marker. Later biopsy data (186) from subjects with various forms of MD showed that subjects from the same families and with the identical disease were discordant for ACTN-3 deficiency, and it was concluded that ACTN-3 deficiency is only a secondary effect in the various forms of MD. Thus, a

deficiency of ACTN-3 doesn't seem to lead to a disease phenotype, as the ACTN-2 isoform may help compensate, but this compensation may not be complete.

ACTN-2 expression occurs in all skeletal muscle fiber types, but ACTN-3 expression is restricted to type 2 fibers (131). *ACTN3* is located on chromosome 11 (11q13-q14), spans ~17 kbp, and contains 21 exons. A previous investigation identified a single nucleotide polymorphism (SNP) along exon 16 of the *ACTN3* gene when investigating congenital muscular dystrophy and a complete absence of ACTN-3. This SNP results from a C to T transition at position 1,747 that results in a change in the 577 residue from arginine to a premature stop codon (R577X) (131). Homozygosity of R577X results in an absence of ACTN-3 expression, although the individuals affected typically appear phenotypically normal. Investigations of various populations estimate that approximately 19% of Caucasians are ACTN-3 deficient, indicating that this SNP is non-pathogenic and in humans is likely redundant (119).

The absence of ACTN-3 due the R577X SNP has raised questions regarding the subtle potential effects on athletic performance. Since ACTN-2 and ACTN-3 are roughly 90% similar and ACTN-2 entirely overlaps ACTN-3, some have speculated that due a functional redundancy, no observable changes in athletic performance would likely occur in the ACTN-3 deficient individuals as ACTN-2 would have a compensatory effect (119). Nonetheless, ACTN-2 and ACTN-3 are differentially expressed indicating that *ACTN3* continues to be highly conserved in the genome (119). In this regard, recent cross-sectional data suggests that a deficiency of ACTN-3 is associated with an enhancement of athletic performance. Zantoneli, et al. (202) reported that when vastus lateralus muscle biopsies from elite marathon runners were examined for muscle fiber

type ratios and ACTN isoforms, one out the six had a complete deficiency of ACTN-3. This deficiency was not related to a lack of type II fibers suggesting that ACTN-3 is redundant and may actually impede endurance performance, although no information was provided by the authors if this was a statistically significant finding and what the potential mechanism for increased performance is. In support of this data, Yang (198) genotyped 429 unrelated elite Caucasian athletes (men and women), as defined by competition at the international level. Control subjects (n = 436) were also genotyped. A subset of the cohort (n = 107) was created and represented athletes who competed in power-related events such as sprinting, as well as a subset of 194 endurance athletes to make the groups homogenous. Chi-square analyses revealed that the power athletes had a significantly lower frequency of the X homozygotes when compared to controls and a higher R homozygote frequency. In addition, there was a difference between the power and endurance athletes with respect to the X homozygote frequency, which explained why the athlete vs. non-athlete analyses showed no difference in genotype/allele frequencies. The case-control design of the Yang study (198), has limitations particularly when assessing gene-exercise interactions, because all subjects were grouped by event type or athlete/non-athlete and no measures were made to quantify performance or changes in performance. However, this data was recently confirmed by a recent report that examined the R577X polymorphism in elite Finnish sprint (n = 89) and endurance (n = 52) athletes (129). The results show that the frequency of the XX genotype is significantly higher and the RR genotype is lower in these endurance athletes. In addition, none of the sprinters were X homozygotes, which supports the hypothesis that this polymorphism confers an athletic performance advantage.

More recently, the first intervention study was done to assess the effects of the R577X polymorphism on changes in muscle strength with ST (31). In that investigation, 602 young adults (247 men & 355 women) of diverse racial backgrounds were tested at baseline for maximal voluntary isometric contraction (MVC) and 1 RM strength of the elbow flexors at baseline and after ~ 12 weeks of ST with the non-dominant arm. Magnetic resonance imaging (MRI) was done on each subject's arm to determine the baseline cross-sectional area (CSA) and change in the CSA with ST. Analyses of covariance (ANCOVAs) within each sex by *ACTN3* R577X genotype found that there were no differences in men by genotype group for baseline MVC, 1 RM, or CSA. In addition, there were no changes with ST by genotype group for these muscle function measures. In women, there was significantly greater (~ 13%) baseline MVC in the RX group than the XX group, but no difference in baseline 1 RM. Furthermore, the data showed that there was a significantly greater increase in 1 RM strength in the XX group than in the RR group, and there is evidence of a dose-response relationship based on the number of X alleles present. Additionally, the data indicate that the *ACTN3* R577X polymorphism explains ~ 2% of the variance in baseline MVC and change in 1 RM strength in women. One possible explanation for these unexpected results given by the authors was that there were lower initial values in the XX group and thus there was a greater potential for increase with ST. Another explanation given was that there is less stability and greater disruption of the Z-disk in X homozygotes, which makes the muscle more easily stimulated with eccentric contractions to form new sarcomeres, leading to greater strength increases. This explanation is not supported by follow-up data from this same cohort (32), which showed that there was no influence of *ACTN3* R577X genotype

on plasma creatine kinase (CK) or myoglobin (Mb) with eccentric exercise. These data refute the explanation that structural differences between ACTN-3 deficient muscle and normal muscle influence muscle damage with eccentric exercise. Finally, the sex differences in baseline MVC and 1 RM strength response by *ACTN3* genotype were explained by the fact that women have lower baseline values and their percent increase was greater than in men, making the detection of differences by genotype easier. Furthermore, the hypothesis that steroid hormone differences might be at least partially responsible for the sex differences observed by *ACTN3* genotype, as steroid hormones, might mask the subtle effect of the *ACTN3* R577X polymorphism on skeletal muscle function measures. However, there were limitations to this investigation. First, the measurement of biceps CSA did not employ the use of bony landmarks for MRI scanning, rather soft tissue landmarks were used, which are subject to testing error and can actually change with ST. Furthermore, the use of 1 RM and MVC may not be the most appropriate tests to determine the true influence of the *ACTN3* R577X polymorphism on muscle function. A test that employs faster speed of contraction and peak power would likely be a better measurement to examine the effect of this polymorphism on muscle performance.

In summary, sarcopenia is associated with loss of functional abilities, and increases in morbidity and mortality rates in the elderly (140, 141). Studies indicate that the approximate age-associated decline in strength is 20 – 40% when young subjects are compared to those in their 70s or beyond (98, 200). The actual decline in the entire population may even be greater than the decline indicated by various investigations, because older individuals may not be adequately represented in these studies due to the

presence of disease (160). Men have a greater absolute decrease in strength than women, but initial values are higher in men (19, 35, 190). As a result, men retain a higher absolute amount of muscle strength than women, even after aging-related losses. Starting with a lower absolute value combined with the fact that their life expectancy is greater, women are considered to be more susceptible to sarcopenia and long-term disability than men (100). Furthermore, strength tends to peak in the 30s, then remains stable until the 50s, then declines at a rate of ~ 10 – 15% per decade (55, 98, 104). This reduction is at least partially due to a decline in force production by muscle fibers. The decrease in power observed in older adults with aging is typically greater than the declines in strength and may be an independent predictor of mortality (117). However, data indicate that thigh muscle composition, strength, and body fat mass are important contributors to peak power production in the lower limbs in older adults (163). This decline in peak power appears to be a better predictor of impaired functional capacity than strength (165) and is influenced by other factors besides loss of muscle mass. There are numerous adaptations that influence the muscle adaptations to ST, and many of these adaptations that improve muscle size and strength are known to affect muscle power. However, some of the specific mechanisms that lead to increases in muscle power with ST are still unclear. However, interventions specifically designed to optimally improve muscle power have not been established and their safety often questionable. Studies that examined the effect of ST on muscle power in older adults often show inconsistent results. These discrepancies are likely to be at least partially due to inter-individual variability in the rate of decline in muscle mass and muscle function with aging, and variation in response to ST (111). Some of this inter-individual is likely due to genetic factors as twin and

family studies indicate. In addition, several candidate genes have been identified that are hypothesized to explain part of the inter-individual differences observed in skeletal muscle phenotypes. The *ACTN3* R577X polymorphism is functional and has been shown to be a strong candidate gene to explain inter-individual differences in skeletal muscle phenotypes, especially muscle power. This is based on its pattern of expression in type II skeletal muscle fibers, which are known to be specific for the generation high movement velocities and greater force production than type I muscle fibers. However, many more studies will need to be done in order to fully understand the contribution of this polymorphism to the variability of skeletal muscle phenotypes.

REFERENCES

1. **Abney M, McPeek MS and Ober C**. Broad and narrow heritabilities of quantitative traits in a founder population. *Am J Hum Genet* 68: 1302-1307, 2001.
2. **Aniansson A, Grimby G and Hedberg M**. Compensatory muscle fiber hypertrophy in elderly men. *J Appl Physiol* 73: 812-816, 1992.
3. **Aniansson A, Hedberg M, Henning GB and Grimby G**. Muscle morphology, enzymatic activity, and muscle strength in elderly men: a follow-up study. *Muscle Nerve* 9: 585-591, 1986.
4. **Aniansson A, Sperling L, Rundgren A and Lehnberg E**. Muscle function in 75-year-old men and women. A longitudinal study. *Scand J Rehabil Med Suppl* 9: 92-102, 1983.
5. **Aniansson A, Zetterberg C, Hedberg M and Henriksson KG**. Impaired muscle function with aging. A background factor in the incidence of fractures of the proximal end of the femur. *Clin Orthop Relat Res* 193-201, 1984.
6. **Arden NK and Spector TD**. Genetic influences on muscle strength, lean body mass, and bone mineral density: A twin study. *J Bone Miner Res* 12: 2076-2081, 1997.
7. **Balagopal P, Rooyackers OE, Adey DB, Ades PA and Nair KS**. Effects of aging on in vivo synthesis of skeletal muscle myosin heavy-chain and sarcoplasmic protein in humans. *Am J Physiol* 273: E790-E800, 1997.
8. **Balagopal P, Schimke JC, Ades P, Adey D and Nair KS**. Age effect on transcript levels and synthesis rate of muscle MHC and response to resistance exercise. *Am J Physiol Endocrinol Metab* 280: E203-E208, 2001.

9. **Barley J, Blackwood A, Carter ND, Crews DE, Cruickshank JK, Jeffery S, Ogunlesi AO and Sagnella GA**. Angiotensin converting enzyme insertion/deletion polymorphism: association with ethnic origin. *J Hypertens* 12: 955-957, 1994.
10. **Bassey EJ, Fiatarone MA, O'Niell EF, Kelly M, Evans WJ and Lipsitz LA**. Leg extensor power and functional performance in very old men and women. *Clin Sci* 82: 321-327, 1992.
11. **Bassey EJ and Harries UJ**. Normal values for handgrip strength in 920 men and women aged over 65 years, and longitudinal changes over 4 years in 620 survivors. *Clin Sci (Lond)* 84: 331-337, 1993.
12. **Bassey EJ and Short AH**. A new method for measuring power output in a single leg extension: feasibility, reliability and validity. *Eur J Appl Physiol* 60: 385-390, 1990.
13. **Baudin B**. New aspects on angiotensin-converting enzyme: from gene to disease. *Clin Chem Lab Med* 40: 256-265, 2002.
14. **Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, Garry PJ and Lindeman RD**. Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol* 147: 755-763, 1998.
15. **Bean JF, Herman S, Kiely DK, Frey IC, Leveille SG, Fielding RA and Frontera WR**. Increased Velocity Exercise Specific to Task (InVEST) training: a pilot study exploring effects on leg power, balance, and mobility in community-dwelling older women. *J Am Geriatr Soc* 52: 799-804, 2004.

16. **Bean JF, Kiely DK, Herman S, Leveille SG, Mizer K, Frontera WR and Fielding RA**. The relationship between leg power and physical performance in mobility-limited older people. *J Am Geriatr Soc* 50: 461-467, 2002.

17. **Beggs AH, Byers TJ, Knoll JHM, Boyce FM, Bruns GAP and Kunkel LM**. Cloning and Characterization of 2 Human Skeletal-Muscle Alpha-Actinin Genes Located on Chromosome-1 and Chromosome-11. *J Biol Chem* 267: 9281-9288, 1992.

18. **Blackman MB, Sorkin JD, Munzer T, Bellantoni MF, Busby-Whitehead J, Stevens TE, Jayme J, O'Connor KG, Christmas C, Tobin JD, Stewart KJ, Cottrell E, St Clair C, Pabst KM and Harman SM**. Growth hormone and sex steroid administration in healthy aged women and men - A randomized controlled trial. *JAMA* 288: 2282-2292, 2002.

19. **Borges O**. Isometric and isokinetic knee extension and flexion torque in men and women aged 20-70. *Scand J Rehabil Med* 21: 45-53, 1989.

20. **Bouchard C, Perusse L, Leblanc C, Tremblay A and Theriault G**. Inheritance of the amount and distribution of human body fat. *Int J Obes* 12: 205-215, 1988.

21. **Bouchard C, Simoneau JA, Lortie G, Boulay MR, Marcotte M and Thibault MC**. Genetic effects in human skeletal muscle fiber type distribution and enzyme activities. *Can J Physiol Pharmacol* 64: 1245-1251, 1986.

22. **Bouchard C, Malina RM and Pérusse L**. *Genetics of Fitness and Physical Performance*. Champaign, IL: Human Kinetics, 1997, p. 230.

23. **Brown AB, McCartney N and Sale DG**. Positive adaptations to weight-lifting training in the elderly. *J Appl Physiol* 69: 1725-1733, 1990.

24. **Brown WF**. A method for estimating the number of motor units in thenar muscles and the changes in motor unit count with ageing. *J Neurol Neurosurg Psychiatry* 35: 845-852, 1972.

25. **Bruunsgaard H, Bjerregaard E, Schroll M and Pedersen BK**. Muscle strength after resistance training is inversely correlated with baseline levels of soluble tumor necrosis factor receptors in the oldest old. *J Am Geriatr Soc* 52: 237-241, 2004.

26. **Buchner DM, Cress ME, de Lateur BJ and Wagner EH.** Variability in the effect of strength training on skeletal muscle strength in older adults. *Facts and Research in Gerontology* 7, 143-153. 1993.

27. **Calvo M, Rodas G, Vallejo M, Estruch A, Arcas A, Javierre C, Viscor G and Ventura JL**. Heritability of explosive power and anaerobic capacity in humans. *Eur J Appl Physiol* 86: 218-225, 2002.

28. **Campbell WW, Crim MC, Dallal GE, Young VR and Evans WJ**. Increased protein requirements in elderly people: new data and retrospective reassessments. *Am J Clin Nutr* 60: 501-509, 1994.

29. **Carmelli D and Reed T**. Stability and change in genetic and environmental influences on hand-grip strength in older male twins. *J Appl Physiol* 89: 1879-1883, 2000.

30. **Charette SL, McEvoy L, Pyka G, Snow-Harter C, Guido D, Wiswell RA and Marcus R**. Muscle hypertrophy response to resistance training in older women. *J Appl Physiol* 70: 1912-1916, 1991.

31. **Clarkson PM, Devaney JM, Gordish-Dressman H, Thompson PD, Hubal MJ, Urso M, Price TB, Angelopoulos TJ, Gordon PM, Moyna NM, Pescatello LS, Visich PS, Zoeller RF, Seip RL and Hoffman EP**. ACTN3 genotype is associated with increases in muscle strength in response to resistance training in women. *J Appl Physiol* 99: 154-163, 2005.

32. **Clarkson PM, Hoffman EP, Zambraski E, Gordish-Dressman H, Kearns A, Hubal M, Harmon B and Devaney JM**. ACTN3 and MLCK genotype associations with exertional muscle damage. *J Appl Physiol* 99: 564-569, 2005.

33. **Connelly DM, Rice CL, Roos MR and Vandervoort AA**. Motor unit firing rates and contractile properties in tibialis anterior of young and old men. *J Appl Physiol* 87: 843-852, 1999.

34. **Cuoco A, Callahan DM, Sayers S, Frontera WR, Bean J and Fielding RA**. Impact of muscle power and force on gait speed in disabled older men and women. *J Gerontol A Biol Sci Med Sci* 59: 1200-1206, 2004.

35. **Danneskiold-Samsoe B, Kofod V, Munter J, Grimby G, Schnohr P and Jensen G**. Muscle strength and functional capacity in 78-81-year-old men and women. *Eur J Appl Physiol Occup Physiol* 52: 310-314, 1984.

36. **De Vito G, Bernardi M, Forte R, Pulejo C and Figura F**. Effects of a low-intensity conditioning programme on VO2max and maximal instantaneous peak power in elderly women. *Eur J Appl Physiol Occup Physiol* 80: 227-232, 1999.

37. **Delmonico MJ, Kostek MC, Doldo NA, Hand BD, Bailey JA, Rabon-Stith KM, Conway JM, Carignan CR and Hurley BF**. Effects of Moderate Velocity

Strength Training on Peak Muscle Power and Movement Velocity: Do Women Respond Differently than Men? *J Appl Physiol*, In Press, 2005.

38. **Desypris G and Parry DJ**. Relative efficacy of slow and fast alpha-motoneurons to reinnervate mouse soleus muscle. *Am J Physiol* 258: C62-C70, 1990.
39. **Dixson JD, Forstner MRJ and Garcia DM**. The alpha-actinin gene family: A revised classification. *J Mol Evol* 56: 1-10, 2003.
40. **Doherty TJ, Vandervoort AA, Taylor AW and Brown WF**. Effects of motor unit losses on strength in older men and women. *J Appl Physiol* 74: 868-874, 1993.
41. **Earles DR, Judge JO and Gunnarsson OT**. Velocity training induces power-specific adaptations in highly functioning older adults. *Arch Phys Med Rehabil* 82: 872-878, 2000.
42. **Era P, Lyyra AL, Viitasalo JT and Heikkinen E**. Determinants of isometric muscle strength in men of different ages. *Eur J Appl Physiol Occup Physiol* 64: 84-91, 1992.
43. **Evans WJ**. Exercise strategies should be designed to increase muscle power. *J Gerontol A Biol Sci Med Sci* 55: M309-M310, 2000.
44. **Evans WJ**. High-velocity resistance training for increasing peak muscle power in elderly women. *Clin J Sport Med* 13: 66, 2003.
45. **Ferretti G, Narici MV, Binzoni T, Gariod L, Le Bas JF, Reutenauer H and Cerretelli P.** Determinants of peak muscle power: effects of age and physical conditioning. *Eur J Appl Physiol* 68, 111-115. 1994.

46. **Ferri A, Scaglioni G, Pousson M, Capodaglio P, Van Hoecke J and Narici MV**. Strength and power changes of the human plantar flexors and knee extensors in response to resistance training in old age. *Acta Physiol Scand* 177: 69-78, 2003.

47. **Fiatarone MA, Marks EC, Ryan ND, Meredith CN, Lipsitz LA and Evans WJ**. High-intensity strength training in nonagenarians. Effects on skeletal muscle. *JAMA* 263: 3029-3034, 1990.

48. **Fiatarone MA, O'Neill EF, Ryan ND, Clements KM, Solares GR, Nelson ME, Roberts SB, Kehayias JJ, Lipsitz LA and Evans WJ**. Exercise training and nutritional supplementation for physical frailty in very elderly people. *N Engl J Med* 330: 1769-1775, 1994.

49. **Fielding RA, LeBrasseur NK, Cuoco A, Bean J, Mizer K and Fiatarone Singh MA**. High-velocity resistance training increases skeletal muscle peak power in older women. *J Am Geriatr Soc* 50: 655-662, 2002.

50. **Foldvari M, Clark M, Laviolette LC, Bernstein MA, Kaliton D, Castaneda C, Pu CT, Hausdorff JM, Fielding RA and Fiatarone MA**. Association of muscle power with functional status in community-dwelling elderly women. *Journal of Gerontology: Medical Sciences* 55A: M192-M199, 2000.

51. **Folland J, Leach B, Little T, Hawker K, Myerson S, Montgomery H and Jones D**. Angiotensin-converting enzyme genotype affects the response of human skeletal muscle to functional overload. *Exp Physiol* 85: 575-579, 2000.

52. **Frederiksen H, Gaist D, Petersen HC, Hjelmborg J, McGue M, Vaupel JW and Christensen K**. Hand grip strength: a phenotype suitable for identifying

genetic variants affecting mid- and late-life physical functioning. *Genet Epidemiol* 23: 110-122, 2002.

53. **Frey N and Olson EN**. Calsarcin-3, a novel skeletal muscle-specific member of the calsarcin family, interacts with multiple Z-disc proteins. *J Biol Chem* 277: 13998-14004, 2002.

54. **Frontera WR, Hughes VA, Fielding RA, Fiatarone MA, Evans WJ and Roubenoff R**. Aging of skeletal muscle: a 12-yr longitudinal study. *J Appl Physiol* 88: 1321-1326, 2000.

55. **Frontera WR, Hughes VA, Lutz KJ and Evans WJ**. A cross-sectional study of muscle strength and mass in 45- to 78-yr-old men and women. *J Appl Physiol* 71: 644-650, 1991.

56. **Frontera WR, Meredith CN, O'Reilly KP, Knuttgen HG and Evans WJ**. Strength conditioning in older men: skeletal muscle hypertrophy and improved function. *J Appl Physiol* 64: 1038-1044, 1988.

57. **Frontera WR, Suh D, Krivickas LS, Hughes VA, Goldstein R and Roubenoff R**. Skeletal muscle fiber quality in older men and women. *Am J Physiol Cell Physiol* 279: C611-C618, 2000.

58. **Fujita Y, Nakamura Y, Hiraoka J, Kobayashi K, Sakata K, Nagai M and Yanagawa H**. Physical-strength tests and mortality among visitors to health-promotion centers in Japan. *J Clin Epidemiol* 48: 1349-1359, 1995.

59. **Gayagay G, Yu B, Hambly B, Boston T, Hahn A, Celermajer DS and Trent RJ**. Elite endurance athletes and the ACE I allele--the role of genes in athletic performance. *Hum Genet* 103: 48-50, 1998.

60. **Geusens P, Vandevyver C, Vanhoof J, Cassiman JJ, Boonen S and Raus J**. Quadriceps and grip strength are related to vitamin D receptor genotype in elderly nonobese women. *J Bone Miner Res* 12: 2082-2088, 1997.

61. **Gizak A, Rakus D and Dzugaj A**. Immunohistochemical localization of human fructose-1,6-bisphosphatase in subcellular structures of myocytes. *Histol Histopathol* 18: 135-142, 2003.

62. **Grassi B, Cerretelli P, Narici MV and Marconi C**. Peak anaerobic power in master athletes. *Eur J Appl Physiol Occup Physiol* 62: 394-399, 1991.

63. **Greiwe JS, Cheng B, Rubin DC, Yarasheski KE and Semenkovich CF**. Resistance exercise decreases skeletal muscle tumor necrosis factor alpha in frail elderly humans. *FASEB J* 15: 475-482, 2001.

64. **Grimby G, Aniansson A, Hedberg M, Henning GB, Grangard U and Kvist H**. Training can improve muscle strength and endurance in 78- to 84-yr-old men. *J Appl Physiol* 73: 2517-2523, 1992.

65. **Grundberg E, Brandstrom H, Ribom EL, Ljunggren O, Mallmin H and Kindmark A**. Genetic variation in the human vitamin D receptor is associated with muscle strength, fat mass and body weight in Swedish women. *Eur J Endocrinol* 150: 323-328, 2004.

66. **Hagberg JM, Ferrell RE, McCole SD, Wilund KR and Moore GE**. VO2 max is associated with ACE genotype in postmenopausal women. *J Appl Physiol* 85: 1842-1846, 1998.

67. **Hakkinen K and Hakkinen A**. Muscle cross-sectional area, force production and relaxation characteristics in women at different ages. *Eur J Appl Physiol Occup Physiol* 62: 410-414, 1991.

68. **Hakkinen K, Kraemer WJ, Newton RU and Alen M**. Changes in electromyographic activity, muscle fibre and force production characteristics during heavy resistance/power strength training in middle-aged and older men and women. *Acta Physiol Scand* 171: 51-62, 2001.

69. **Hakkinen K, Newton RU, Gordon SE, McCormick M, Volek JS, Nindl BC, Gotshalk LA, Campbell WW, Evans WJ, Hakkinen A, Humphries BJ and Kraemer WJ**. Changes in muscle morphology, electromyographic activity, and force production characteristics during progressive strength training in young and older men. *J Gerontol A Biol Sci Med Sci* 53: B415-B423, 1998.

70. **Hanisch D, Dittmar M, Hohler T and Alt KW**. Contribution of genetic and environmental factors to variation in body compartments--a twin study in adults. *Anthropol Anz* 62: 51-60, 2004.

71. **Harridge SD, Bottinelli R, Canepari M, Pellegrino M, Reggiani C, Esbjornsson M, Balsom PD and Saltin B**. Sprint training, in vitro and in vivo muscle function, and myosin heavy chain expression. *J Appl Physiol* 84: 442-449, 1998.

72. **Harridge SD, Kryger A and Stensgaard A**. Knee extensor strength, activation, and size in very elderly people following strength training. *Muscle Nerve* 22: 831-839, 1999.

73. **Hasten DL, Pak-Loduca J, Obert KA and Yarasheski KE**. Resistance exercise acutely increases MHC and mixed muscle protein synthesis rates in 78-84 and 23-32 yr olds. *Am J Physiol Endocrinol Metab* 278: E620-E626, 2000.

74. **Hook P, Sriramoju V and Larsson L**. Effects of aging on actin sliding speed on myosin from single skeletal muscle cells of mice, rats, and humans. *Am J Physiol Cell Physiol* 280: C782-C788, 2001.

75. **Hughes VA, Frontera WR, Roubenoff R, Evans WJ and Singh MA**. Longitudinal changes in body composition in older men and women: role of body weight change and physical activity. *Am J Clin Nutr* 76: 473-481, 2002.

76. **Hunter SK, Thompson MW, Ruell PA, Harmer AR, Thom JM, Gwinn TH and Adams RD**. Human skeletal sarcoplasmic reticulum Ca2+ uptake and muscle function with aging and strength training. *J Appl Physiol* 86: 1858-1865, 1999.

77. **Hurley BF and Roth SM**. Strength Training in the Elderly, Effects on Risk Factors for Age-Related Diseases. *Sports Med* 30: 249-268, 2000.

78. **Hurley MV, Rees J and Newham DJ**. Quadriceps function, proprioceptive acuity and functional performance in healthy young, middle-aged and elderly subjects. *Age Ageing* 27: 55-62, 1998.

79. **Iannuzzi-Sucich M, Prestwood KM and Kenny AM**. Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women. *J Gerontol A Biol Sci Med Sci* 57: M772-M777, 2002.

80. **Ivey FM, Roth SM, Ferrell RE, Tracy BL, Lemmer JT, Hurlbut DE, Martel GF, Siegel EL, Fozard JL, Metter EJ, Fleg JL and Hurley BF**. Effects of age,

gender, and myostatin genotype on the hypertrophic response to heavy resistance strength training. *J Gerontol A Biol Sci Med Sci* 55: M641-M648, 2000.

81. **Ivey FM, Tracy BL, Lemmer JT, NessAiver M, Metter EJ, Fozard JL and Hurley BF**. Effects of strength training and detraining on muscle quality: Age and gender comparisons. *J Gerontol A Biol Sci Med Sci* 55: B152-B157, 2000.
82. **Izquierdo M, Häkkinen K, Ibanez J, Garrues M, Antón A, Zúniga A, Larrión JL and Gorostiaga EM**. Effects of strength training on muscle power and serum hormones in middle-aged and older men. *J Appl Physiol* 90: 1497-1507, 2001.
83. **Izquierdo M, Ibanez J, Gorostiaga E, Garrues M, Zuniga A, Anton A, Larrion JL and Hakkinen K**. Maximal strength and power characteristics in isometric and dynamic actions of the upper and lower extremities in middle-aged and older men. *Acta Physiol Scand* 167: 57-68, 1999.
84. **Jakobi JM and Rice CL**. Voluntary muscle activation varies with age and muscle group. *J Appl Physiol* 93: 457-462, 2002.
85. **Janssen I, Heymsfield SB, Wang ZM and Ross R**. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. *J Appl Physiol* 89: 81-88, 2000.
86. **Jozsi AC, Campbell WW, Joseph L, Davey SL and Evans WJ**. Changes in power with resistance training in older and younger men and women. *J Gerontol A Biol Sci Med Sci* 54: M591-M596, 1999.

87. **Kallman DA, Plato CC and Tobin JD**. The role of muscle loss in the age-related decline of grip strength: cross-sectional and longitudinal perspectives. *J Gerontol* 45: M82-M88, 1990.

88. **Kannus P and Järvinen M**. Maximal peak torque as a predictor of peak angular impulse and average power of thigh muscles - An isometric and isokinetic study. *Int J Sports Med* 11: 146-149, 1990.

89. **Kent-Braun JA, Ng AV and Young K**. Skeletal muscle contractile and noncontractile components in young and older women and men. *J Appl Physiol* 88: 662-668, 2000.

90. **Klein CS, Rice CL and Marsh GD**. Normalized force, activation, and coactivation in the arm muscles of young and old men. *J Appl Physiol* 91: 1341-1349, 2001.

91. **Klitgaard H, Mantoni M, Schiaffino S, Ausoni S, Gorza L, Laurent-Winter C, Schnohr P and Saltin B**. Function, morphology and protein expression of ageing skeletal muscle: a cross-sectional study of elderly men with different training backgrounds. *Acta Physiol Scand* 140: 41-54, 1990.

92. **Komi PV, Viitasalo JH, Havu M, Thorstensson A, Sjodin B and Karlsson J**. Skeletal muscle fibres and muscle enzyme activities in monozygous and dizygous twins of both sexes. *Acta Physiol Scand* 100: 385-392, 1977.

93. **Kostek MC, Delmonico MJ, Reichel JB, Roth SM, Douglass L, Ferrell RE and Hurley BF**. Muscle strength response to strength training is influenced by insulin-like growth factor 1 genotype in older adults. *J Appl Physiol* 98: 2147-2154, 2005.

94. **Kubo K, Kanehisa H, Azuma K, Ishizu M, Kuno SY, Okada M and Fukunaga T**. Muscle architectural characteristics in young and elderly men and women. *Int J Sports Med* 24: 125-130, 2003.

95. **Kuzis K and Eckenstein FP**. Ciliary neurotrophic factor as a motor neuron trophic factor. *Perspect Dev Neurobiol* 4: 65-74, 1996.

96. **Kwon IS, Oldaker S, Schrager M, Talbot LA, Fozard JL and Metter EJ**. Relationship between muscle strength and the time taken to complete a standardized walk-turn-walk test. *J Gerontol A Biol Sci Med Sci* 56: B398-B404, 2001.

97. **Langen RC, Van Der Velden JL, Schols AM, Kelders MC, Wouters EF and Janssen-Heininger YM**. Tumor necrosis factor-alpha inhibits myogenic differentiation through MyoD protein destabilization. *FASEB J* 18: 227-237, 2004.

98. **Larsson L, Grimby G and Karlsson J**. Muscle strength and speed of movement in relation to age and muscle morphology. *J Appl Physiol* 46: 451-456, 1979.

99. **Laukkanen P, Heikkinen E and Kauppinen M**. Muscle strength and mobility as predictors of survival in 75-84-year-old people. *Age Ageing* 24: 468-473, 1995.

100. **Launer LJ, Harris T, Rumpel C and Madans J**. Body mass index, weight change, and risk of mobility disability in middle-aged and older women. The epidemiologic follow-up study of NHANES I. *JAMA* 271: 1093-1098, 1994.

101. **Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, Corsi AM, Rantanen T, Guralnik JM and Ferrucci L**. Age-associated changes

in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol* 95: 1851-1860, 2003.

102. **Lemmer JT, Hurlbut DE, Martel GF, Tracy BL, Ivey FM, Metter EJ, Fozard JL, Fleg JL and Hurley BF**. Age and gender responses to strength training and detraining. *Medicine and Science in Sports and Exercise* 32: 1505-1512, 2000.
103. **Lexell J, Taylor CC and Sjostrom M**. What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. *J Neurol Sci* 84: 275-294, 1988.
104. **Lindle RS, Metter EJ, Lynch NA, Fleg JL, Fozard JL, Tobin J, Roy TA and Hurley BF**. Age and gender comparisons of muscle strength in 654 women and men aged 20-93 yr. *J Appl Physiol* 83: 1581-1587, 1997.
105. **Lynch NA, Metter EJ, Lindle RS, Fozard JL, Tobin JD, Roy TA, Fleg JL and Hurley BF**. Muscle quality. I. Age-associated differences between arm and leg muscle groups. *J Appl Physiol* 86: 188-194, 1999.
106. **Macaluso A and De Vito G**. Comparison between young and older women in explosive power output and its determinants during a single leg-press action after optimisation of load. *Eur J Appl Physiol* 90: 458-463, 2003.
107. **Macaluso A and De Vito G**. Muscle strength, power and adaptations to resistance training in older people. *Eur J Appl Physiol* 91: 450-472, 2004.
108. **MacArthur DG and North KN**. A gene for speed? The evolution and function of alpha-actinin-3. *Bioessays* 26: 786-795, 2004.

109. **Maganaris CN, Narici MV and Reeves ND**. In vivo human tendon mechanical properties: effect of resistance training in old age. *J Musculoskelet Neuronal Interact* 4: 204-208, 2004.

110. **Marcell TJ**. Sarcopenia: causes, consequences, and preventions. *J Gerontol A Biol Sci Med Sci* 58: M911-M916, 2003.

111. **Martin JC, Farrar RP, Wagner BM and Spirduso WW**. Maximal power across the lifespan. *J Gerontol A Biol Sci Med Sci* 55: M311-M316, 2000.

112. **McCartney N, Hicks AL, Martin J and Webber CE**. A longitudinal trial of weight training in the elderly: continued improvements in year 2. *J Gerontol A Biol Sci Med Sci* 51: B425-B433, 1996.

113. **Melton LJ, III, Khosla S, Crowson CS, O'Connor MK, O'Fallon WM and Riggs BL**. Epidemiology of sarcopenia. *J Am Geriatr Soc* 48: 625-630, 2000.

114. **Metter EJ, Conwit R, Tobin J and Fozard JL**. Age-associated loss of power and strength in the upper extremities in women and men. *J Gerontol A Biol Sci Med Sci* 52: B267-B276, 1997.

115. **Metter EJ, Lynch N, Conwit R, Lindle R, Tobin J and Hurley B**. Muscle quality and age: cross-sectional and longitudinal comparisons. *J Gerontol A Biol Sci Med Sci* 54: B207-B218, 1999.

116. **Metter EJ, Talbot LA, Schrager M and Conwit R**. Skeletal muscle strength as a predictor of all-cause mortality in healthy men. *J Gerontol A Biol Sci Med Sci* 57: B359-B365, 2002.

117. **Metter EJ, Talbot LA, Schrager M and Conwit RA**. Arm-cranking muscle power and arm isometric muscle strength are independent predictors of all-cause mortality in men. *J Appl Physiol* 96: 814-821, 2004.

118. **Miller MD, Crotty M, Giles LC, Bannerman E, Whitehead C, Cobiac L, Daniels LA and Andrews G**. Corrected arm muscle area: an independent predictor of long-term mortality in community-dwelling older adults? *J Am Geriatr Soc* 50: 1272-1277, 2002.

119. **Mills MA, Yang N, Weinberger RP, Vander Woude DL, Beggs AH, Easteal S and North KN**. Differential expression of the actin-binding proteins, α-actinin-2 and -3, in different species: implications for the evolution of functional redundancy. *Hum Mol Genet* 10: 1335-1346, 2001.

120. **Montgomery H, Clarkson P, Barnard M, Bell J, Brynes A, Dollery C, Hajnal J, Hemingway H, Mercer D, Jarman P, Marshall R, Prasad K, Rayson M, Saeed N, Talmud P, Thomas L, Jubb M, World M and Humphries S**. Angiotensin-converting-enzyme gene insertion/deletion polymorphism and response to physical training. *Lancet* 353: 541-545, 1999.

121. **Montgomery HE, Marshall R, Hemingway H, Myerson S, Clarkson P, Dollery C, Hayward M, Holliman DE, Jubb M, World M, Thomas EL, Brynes AE, Saeed N, Barnard M, Bell JD, Prasad K, Rayson M, Talmud PJ and Humphries SE**. Human gene for physical performance. *Nature* 393: 221-222, 1998.

122. **Morais JA, Gougeon R, Pencharz PB, Jones PJ, Ross R and Marliss EB**. Whole-body protein turnover in the healthy elderly. *Am J Clin Nutr* 66: 880-889, 1997.

123. **Morrison JH and Hof PR**. Life and death of neurons in the aging brain. *Science* 278: 412-419, 1997.

124. **Morse CI, Thom JM, Mian OS, Muirhead A, Birch KM and Narici MV**. Muscle strength, volume and activation following 12-month resistance training in 70-year-old males. *Eur J Appl Physiol* 2005.

125. **Myerson S, Hemingway H, Budget R, Martin J, Humphries S and Montgomery H**. Human angiotensin I-converting enzyme gene and endurance performance. *J Appl Physiol* 87: 1313-1316, 1999.

126. **Nair KS**. Muscle protein turnover: methodological issues and the effect of aging. *J Gerontol A Biol Sci Med Sci* 50 Spec No: 107-112, 1995.

127. **Nazarov IB, Woods DR, Montgomery HE, Shneider OV, Kazakov VI, Tomilin NV and Rogozkin VA**. The angiotensin converting enzyme I/D polymorphism in Russian athletes. *Eur J Hum Genet* 9: 797-801, 2001.

128. **Newman AB, Haggerty CL, Goodpaster B, Harris T, Kritchevsky S, Nevitt M, Miles TP and Visser M**. Strength and muscle quality in a well-functioning cohort of older adults: The health, aging and body composition study. *J Am Geriatr Soc* 51: 323-330, 2003.

129. **Niemi AK and Majamaa K**. Mitochondrial DNA and ACTN3 genotypes in Finnish elite endurance and sprint athletes. *Eur J Hum Genet* 13: 965-969, 2005.

130. **North KN and Beggs AH**. Deficiency of a skeletal muscle isoform of alpha-actinin (alpha-actinin-3) in merosin-positive congenital muscular dystrophy. *Neuromuscular Disord* 6: 229-235, 1996.

131. **North KN, Yang N, Wattanasirichaigoon D, Mills M, Easteal S and Beggs AH**. A common nonsense mutation results in alpha-actinin-3 deficiency in the general population. *Nat Genet* 21: 353-354, 1999.

132. **Overend TJ, Cunningham DA, Paterson DH and Lefcoe MS**. Thigh composition in young and elderly men determined by computed tomography. *Clin Physiol* 12: 629-640, 1992.

133. **Pearson D**. The national strength and conditioning association basic guidelines for the resistance training of athletes. *Strength Cond J* 22(6), 14-27. 2005.

134. **Pearson SJ, Harridge SD, Grieve DW, Young A and Woledge RC**. A variable inertial system for measuring the contractile properties of human muscle. *Med Sci Sports Exerc* 33: 2072-2076, 2001.

135. **Petrella JK, Kim JS, Tuggle SC, Hall SR and Bamman MM**. Age differences in knee extension power, contractile velocity, and fatigability. *J Appl Physiol* 98: 211-220, 2005.

136. **Ploutz-Snyder LL, Manini T, Ploutz-Snyder RJ and Wolf DA**. Functionally relevant thresholds of quadriceps femoris strength. *J Gerontol A Biol Sci Med Sci* 57: B144-B152, 2002.

137. **Pyka G, Lindenberger E, Charette S and Marcus R**. Muscle strength and fiber adaptations to a year-long resistance training program in elderly men and women. *J Gerontol* 49: M22-M27, 1994.

138. **Rantanen T and Avela J**. Leg extension power and walking speed in very old people living independently. *J Gerontol A Biol Sci Med Sci* 52A: M225-M231, 1997.

139. **Rantanen T, Era P and Heikkinen E**. Physical activity and the changes in maximal isometric strength in men and women from the age of 75 to 80 years. *J Am Geriatr Soc* 45: 1439-1445, 1997.

140. **Rantanen T, Guralnik JM, Ferrucci L, Leveille S and Fried LP**. Coimpairments: Strength and balance as predictors of severe walking disability. *J Gerontol A Biol Sci Med Sci* 54: M172-M176, 1999.

141. **Rantanen T, Guralnik JM, Foley D, Masaki K, Leveille S, Curb JD and White L**. Midlife hand grip strength as a predictor of old age disability. *JAMA* 281: 558-560, 1999.

142. **Rantanen T, Guralnik JM, Sakari-Rantala R, Leveille S, Simonsick EM, Ling S and Fried LP**. Disability, physical activity, and muscle strength in older women: the Women's Health and Aging Study. *Arch Phys Med Rehabil* 80: 130-135, 1999.

143. **Rantanen T, Harris T, Leveille SG, Visser M, Foley D, Masaki K and Guralnik JM**. Muscle strength and body mass index as long-term predictors of mortality in initially healthy men. *J Gerontol A Biol Sci Med Sci* 55: M168-M173, 2000.

144. **Reed RL, Pearlmutter L, Yochum K, Meredith KE and Mooradian AD**. The relationship between muscle mass and muscle strength in the elderly. *J Am Geriatr Soc* 39: 555-561, 1991.

145. **Roos MR, Rice CL and Vandervoort AA**. Age-related changes in motor unit function. *Muscle Nerve* 20: 679-690, 1997.

146. **Rosenberg I**. Epidemiologic and methodologic problems in determining nutritional status of older persons - Proceedings of a held in Albuquerque, New Mexico, October 19-21, 1988 - Summary Comments. *Am J Clin Nutr* 50, 1231-1233. 1989.

147. **Ross R, Rissanen J, Pedwell H, Clifford J and Shragge P**. Influence of diet and exercise on skeletal muscle and visceral adipose tissue in men. *J Appl Physiol* 81: 2445-2455, 1996.

148. **Roth SM, Ferrell RE and Hurley BF.** Strength training for the prevention and treatment of sarcopenia. *J Nutr Health Aging* 4, 143-55, 2000.

149. **Roth SM, Schrager MA, Ferrell RE, Riechman SE, Metter EJ, Lynch NA, Lindle RS and Hurley BF**. CNTF genotype is associated with muscular strength and quality in humans across the adult age span. *J Appl Physiol* 90: 1205-1210, 2001.

150. **Roth SM, Zmuda JM, Cauley JA, Shea PR and Ferrell RE**. Vitamin D receptor genotype is associated with fat-free mass and sarcopenia in elderly men. *J Gerontol A Biol Sci Med Sci* 59: 10-15, 2004.

151. **Runge M, Rittweger J, Russo CR, Schiessl H and Felsenberg D**. Is muscle power output a key factor in the age-related decline in physical performance? A comparison of muscle cross section, chair-rising test and jumping power. *Clin Physiol Funct Imaging* 24: 335-340, 2004.

152. **Sale DG**. Neural adaptation to resistance training. *Med Sci Sports Exerc* 20: S135-S145, 1988.

153. **Sallakci N, Akcurin G, Koksoy S, Kardelen F, Uguz A, Coskun M, Ertug H and Yegin O**. TNF-alpha G-308A polymorphism is associated with rheumatic fever and correlates with increased TNF-alpha production. *J Autoimmun* 2005.

154. **Sayer AA, Syddall H, O'Dell SD, Chen X, Briggs PJ, Briggs R, Day INM and Cooper C**. Polymorphism of the IGF2 gene, birth weight and grip strength in adult men. *Age Ageing* 31: 468-470, 2002.

155. **Schrager MA, Roth SM, Ferrell RE, Metter EJ, Russek-Cohen E, Lynch NA, Lindle RS and Hurley BF**. Insulin-like growth factor-2 genotype, fat-free mass, and muscle performance across the adult life span. *J Appl Physiol* 97: 2176-2183, 2004.

156. **Seeman E, Hopper JL, Young NR, Formica C, Goss P and Tsalamandris C**. Do genetic factors explain associations between muscle strength, lean mass, and bone density? A twin study. *Am J Physiol* 270: E320-E327, 1996.

157. **Sehl ME and Yates FE**. Kinetics of human aging: I. Rates of senescence between ages 30 and 70 years in healthy people. *J Gerontol A Biol Sci Med Sci* 56: B198-B208, 2001.

158. **Sharman MJ, Newton RU, Triplett-McBride T, McGuigan MR, McBride JM, Hakkinen A, Hakkinen K and Kraemer WJ**. Changes in myosin heavy chain composition with heavy resistance training in 60- to 75-year-old men and women. *Eur J Appl Physiol* 84: 127-132, 2001.

159. **Sherrington C and Lord SR**. Home exercise to improve strength and walking velocity after hip fracture: a randomized controlled trial. *Arch Phys Med Rehabil* 78: 208-212, 1997.

160. **Short KR and Nair KS**. Mechanisms of sarcopenia of aging. *J Endocrinol Invest* 22: 95-105, 1999.

161. **Simoneau JA and Bouchard C**. Genetic determinism of fiber type proportion in human skeletal muscle. *FASEB J* 9: 1091-1095, 1995.

162. **Singh MA, Ding W, Manfredi TJ, Solares GS, O'Neill EF, Clements KM, Ryan ND, Kehayias JJ, Fielding RA and Evans WJ**. Insulin-like growth factor I in skeletal muscle after weight-lifting exercise in frail elders. *Am J Physiol* 277: E135-E143, 1999.

163. **Sipila S, Koskinen SO, Taaffe DR, Takala TE, Cheng S, Rantanen T, Toivanen J and Suominen H**. Determinants of lower-body muscle power in early postmenopausal women. *J Am Geriatr Soc* 52: 939-944, 2004.

164. **Skelton DA, Greig CA, Davies JM and Young A**. Strength, power and related functional ability of healthy people aged 65-89 years. *Age Ageing* 23: 371-377, 1994.

165. **Skelton DA, Kennedy J and Rutherford OM**. Explosive power and asymmetry in leg muscle function in frequent fallers and non-fallers aged over 65. *Age Ageing* 31: 119-125, 2002.

166. **Skelton DA, Young A, Greig CA and Malbut KE**. Effects of resistance training on strength, power, and selected functional abilities of women aged 75 and older. *J Am Geriatr Soc* 43: 1081-1087, 1995.

167. **Sonna LA, Sharp MA, Knapik JJ, Cullivan M, Angel KC, Patton JF and Lilly CM**. Angiotensin-converting enzyme genotype and physical performance during US Army basic training. *J Appl Physiol* 91: 1355-1363, 2001.

168. **Sowers MR, Crutchfield M, Richards K, Wilkin MK, Furniss A, Jannausch M, Zhang D and Gross M**. Sarcopenia is related to physical functioning and leg strength in middle-aged women. *J Gerontol A Biol Sci Med Sci* 60: 486-490, 2005.

169. **Stackhouse SK, Dean JC, Lee SC and Binder-MacLeod SA**. Measurement of central activation failure of the quadriceps femoris in healthy adults. *Muscle Nerve* 23: 1706-1712, 2000.

170. **Suzuki T, Bean JF and Fielding RA**. Muscle power of the ankle flexors predicts functional performance in community-dwelling older women. *J Am Geriatr Soc* 49: 1161-1167, 2001.

171. **Taaffe DR, Duret C, Wheeler S and Marcus R**. Once-weekly resistance exercise improves muscle strength and neuromuscular performance in older adults. *J Am Geriatr Soc* 47: 1208-1214, 1999.

172. **Takahashi R, Yokoji H, Misawa H, Hayashi M, Hu J and Deguchi T**. A null mutation in the human CNTF gene is not causally related to neurological diseases. *Nat Genet* 7: 79-84, 1994.

173. **Thomis MA, Huygens W, Heuninckx S, Chagnon M, Maes HH, Claessens AL, Vlietinck R, Bouchard C and Beunen GP**. Exploration of myostatin polymorphisms and the angiotensin-converting enzyme insertion/deletion

genotype in responses of human muscle to strength training. *Eur J Appl Physiol* 92: 267-274, 2004.

174. **Tiainen K, Sipilä S, Alen M, Heikkinen E, Kaprio J, Koskenvuo M, Tolvanen A, Pajala S and Rantanen T**. Heritability of maximal isometric muscle strength in older female twins. *J Appl Physiol* 96: 173-180, 2004.

175. **Tiainen K, Sipila S, Alen M, Heikkinen E, Kaprio J, Koskenvuo M, Tolvanen A, Pajala S and Rantanen T**. Shared genetic and environmental effects on strength and power in older female twins. *Med Sci Sports Exerc* 37: 72-78, 2005.

176. **Tracy BL, Ivey FM, Hurlbut D, Martel GF, Lemmer JT, Siegel EL, Metter EJ, Fozard JL, Fleg JL and Hurley BF**. Muscle quality. II. Effects of strength training in 65- to 75-yr-old men and women. *J Appl Physiol* 86: 195-201, 1999.

177. **Tracy BL, Ivey FM, Metter EJ, Fleg JL, Siegel EL and Hurley BF**. A more efficient magnetic resonance imaging-based strategy for measuring quadriceps muscle volume. *Med Sci Sport Exer* 35: 425-433, 2003.

178. **Trappe S, Gallagher P, Harber M, Carrithers J, Fluckey J and Trappe T**. Single muscle fibre contractile properties in young and old men and women. *J Physiol* 552: 47-58, 2003.

179. **Trappe S, Godard M, Gallagher P, Carroll C, Rowden G and Porter D**. Resistance training improves single muscle fiber contractile function in older women. *Am J Physiol Cell Physiol* 281: C398-C406, 2001.

180. **Trappe S, Williamson D and Godard M**. Maintenance of whole muscle strength and size following resistance training in older men. *J Gerontol A Biol Sci Med Sci* 57: B138-B143, 2002.

181. **Trappe S, Williamson D, Godard M, Porter D, Rowden G and Costill D**. Effect of resistance training on single muscle fiber contractile function in older men. *J Appl Physiol* 89: 143-152, 2000.

182. **Trappe TA, Lindquist DM and Carrithers JA**. Muscle-specific atrophy of the quadriceps femoris with aging. *J Appl Physiol* 90: 2070-2074, 2001.

183. **Treuth MS, Butte NF, Ellis KJ, Martin LJ and Comuzzie AG**. Familial resemblance of body composition in prepubertal girls and their biological parents. *Am J Clin Nutr* 74: 529-533, 2001.

184. **Um JY, Mun KS, An NH, Kim PG, Kim SD, Song YS, Lee KN, Lee KM, Wi DH, You YO and Kim HM**. Polymorphism of angiotensin-converting enzyme gene and BMI in obese Korean women. *Clin Chim Acta* 328: 173-178, 2003.

185. **Urbanchek MG, Picken EB, Kalliainen LK and Kuzon WM, Jr.** Specific force deficit in skeletal muscles of old rats is partially explained by the existence of denervated muscle fibers. *J Gerontol A Biol Sci Med Sci* 56: B191-B197, 2001.

186. **Vainzof M, Costa CS, Marie SK, Moreira ES, Reed U, PassosBueno MR, Beggs AH and Zatz M**. Deficiency of alpha-actinin-3 (ACTN3) occurs in different forms of muscular dystrophy. *Neuropediatrics* 28: 223-228, 1997.

187. **Van Cutsem M, Duchateau J and Hainaut K**. Changes in single motor unit behaviour contribute to the increase in contraction speed after dynamic training in humans. *J Physiol-London* 513: 295-305, 1998.

188. **Van P, I, Goemaere S, De Bacquer D, De Paepe A and Kaufman M**. Vitamin D receptor gene allelic variants, bone density, and bone turnover in community-dwelling men. *Bone* 31: 631-637, 2002.

189. **Vandervoort AA**. Aging of the human neuromuscular system. *Muscle Nerve* 25: 17-25, 2002.

190. **Vandervoort AA and McComas AJ**. Contractile changes in opposing muscles of the human ankle joint with aging. *J Appl Physiol* 61: 361-367, 1986.

191. **Visser M, Kritchevsky SB, Goodpaster BH, Newman AB, Nevitt M, Stamm E and Harris TB**. Leg muscle mass and composition in relation to lower extremity performance in men and women aged 70 to 79: the health, aging and body composition study. *J Am Geriatr Soc* 50: 897-904, 2002.

192. **Warren GL, Hulderman T, Jensen N, McKinstry M, Mishra M, Luster MI and Simeonova PP**. Physiological role of tumor necrosis factor alpha in traumatic muscle injury. *FASEB J* 16: 1630-1632, 2002.

193. **Welle S, Thornton C, Jozefowicz R and Statt M**. Myofibrillar protein synthesis in young and old men. *Am J Physiol* 264: E693-E698, 1993.

194. **Welle S, Totterman S and Thornton C**. Effect of age on muscle hypertrophy induced by resistance training. *J Gerontol A Biol Sci Med Sci* 51: M270-M275, 1996.

195. **Williamson DL, Godard MP, Porter DA, Costill DL and Trappe SW**. Progressive resistance training reduces myosin heavy chain coexpression in single muscle fibers from older men. *J Appl Physiol* 88: 627-633, 2000.

196. **Woods D, Hickman M, Jamshidi Y, Brull D, Vassiliou V, Jones A, Humphries S and Montgomery H**. Elite swimmers and the D allele of the ACE I/D polymorphism. *Hum Genet* 108: 230-232, 2001.

197. **Yang N.** (Personal communication, 2005).

198. **Yang N, MacArthur DG, Gulbin JP, Hahn AG, Beggs AH, Easteal S and North K**. ACTN3 genotype is associated with human elite athletic performance. *Am J Hum Genet* 73: 627-631, 2003.

199. **Yarasheski KE, Zachwieja JJ, Campbell JA and Bier DM**. Effect of growth hormone and resistance exercise on muscle growth and strength in older men. *Am J Physiol* 268: E268-E276, 1995.

200. **Young A, Stokes M and Crowe M**. Size and strength of the quadriceps muscles of old and young women. *Eur J Clin Invest* 14: 282-287, 1984.

201. **Young A, Stokes M and Crowe M**. The size and strength of the quadriceps muscles of old and young men. *Clin Physiol* 5: 145-154, 1985.

202. **Zanoteli E, Lotuffo RM, Oliveira ASB, Beggs AH, Canovas M, Zatz M and Vainof M**. Deficiency of muscle alpha-actinin-3 is compatible with high muscle performance. *J Mol Neurosci* 20: 39-42, 2003.

203. **Zhang B, Tanaka H, Shono N, Miura S, Kiyonaga A, Shindo M and Saku K**. The I allele of the angiotensin-converting enzyme gene is associated with an increased percentage of slow-twitch type I fibers in human skeletal muscle. *Clin Genet* 63: 139-144, 2003.