A Genotype-Phenotype Model for Predicting Resistance Training Effects on Leg Press Performance

Authors
Tao Mei[1], Yanchun Li[1], Xiaoxia Li[2], Xiaolin Yang[1], Liang Li[3], Xu Yan[4], Zi-hong He[5]

Affiliations
1 China Institute of Sport and Health Science, Beijing Sport University, Beijing, China
2 Department of Teaching Affairs, Shandong Sport University, Jinan, China
3 Academy of Sports, Sultan Idris Education University, Tanjung Malim, Malaysia
4 Institute for Health and Sport, Victoria University, Melbourne, Australia
5 Exercise Biology Research Center, China Institute of Sport Science, Beijing, China

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70469 Stuttgart, Germany

Correspondence
Dr. Zi-hong He
China Institute of Sport Science
Biology Center
100061 Beijing
China
zihonghe@163.com

ABSTRACT

This study develops a comprehensive genotype-phenotype model for predicting the effects of resistance training on leg press performance. A cohort of physically inactive adults (N = 193) underwent 12 weeks of resistance training, and measurements of maximum isokinetic leg press peak force, muscle mass, and thickness were taken before and after the intervention. Whole-genome genotyping was performed, and genome-wide association analysis identified 85 novel SNPs significantly associated with changes in leg press strength after training. A prediction model was constructed using stepwise linear regression, incorporating seven lead SNPs that explained 40.4 % of the training effect variance. The polygenic score showed a significant positive correlation with changes in leg press strength. By integrating genomic markers and phenotypic indicators, the comprehensive prediction model explained 75.4 % of the variance in the training effect. Additionally, five SNPs were found to potentially impact muscle contraction, metabolism, growth, and development through their association with REACTOME pathways. Individual responses to resistance training varied, with changes in leg press strength ranging from −55.83 % to 151.20 %. The study highlights the importance of genetic factors in predicting training outcomes and provides insights into the potential biological functions underlying resistance training effects. The comprehensive model offers valuable guidance for personalized fitness programs based on individual genetic profiles and phenotypic characteristics.

Introduction

In sedentary adults, skeletal muscle mass typically decreases by 3 %–8 % every decade [1], accompanied by varying degrees of muscle strength decline [2]. Low muscle mass and strength are known risk factors for all-cause mortality, either independently or combined [3, 4]. Strength training is the preferred approach for improving muscle mass and strength [5]. However, individual differences in training effects exist, at least partially due to differences in subject backgrounds, which results in different responses of the body to similar stimuli [6]. These individual differences in training effects are the basis for the development of personalized fitness guidance programs, which have gained increasing attention in sports science in recent years. Isokinetic muscle strength testing is widely recognized as the “gold standard” for evaluating muscle strength [7]. Isokinetic muscle strength can also be used to evaluate ankle joint status in chronic ankle instability (CAI) [8] and anterior cruciate ligament (ACL) reconstruction status [9] in sports injuries. The ratio of isokinetic quadriceps to hamstring muscle strength can predict

the occurrence of hamstring muscle injury [10, 11]. If the eccentric strength of hamstring muscles is weaker, especially when the angular velocity is lower than 60 °/s, hamstring muscle injury is likely to occur [12]. This study focuses on changes in isokinetic leg press muscle strength, which can be improved by long-term resistance training, and is associated with relatively few reports on individual differences in isokinetic muscle strength.

Individual differences in muscle strength training effects are determined by a combination of innate genetic factors and environmental factors. Previous studies have demonstrated that genetic factors alone, or its interaction with training, significantly influence individual differences in response to exercise training [13, 14]. Candidate gene studies have revealed that the *ACTN3* gene can explain 2.1 % of strength training effects [15], while the single nucleotide polymorphism (SNP) rs3136617 and rs2296135 of the *IL15RA* gene accounts for 3.5 % and 7.1 % of the variation in lean body weight training effects from regression models, respectively [16]. Additionally, the response of different *ACE* genotypes in muscle strength after training varies [17]. Meta-analysis reveals that the six candidate genes (ACE, ACTN3, AKT1, COX4I1, mTOR, and VEGF-A) collectively account for 72 % of the variation in the muscular strength phenotype as assessed based on 1RM evaluation [18]. However, training effects are complex traits determined by multiple genetic markers [19], and the candidate gene approach is unlikely to be sufficient for developing personalized exercise fitness programs.

Genome-wide association study (GWAS) is a method for identifying genetic markers and polymorphisms in the entire genome of multiple individuals. By obtaining genotypes and conducting statistical analysis at the population level, the most likely genetic markers that determine a trait can be identified [20, 21]. The polygenic score (PGS) is a weighted sum of the effects of effective alleles associated with a specific trait, including behaviors, characteristics, or diseases [22]. It can be used to estimate an individual's risk of developing a certain phenotype or trait [23]. Since training effects are influenced by both genetic and environmental factors, a training effect prediction model that combines genetic markers and phenotypic indicators can provide the most comprehensive explanation for individual differences.

In this study, we utilized GWAS methods to screen for genetic markers, mainly SNPs, related to the strength training effects of isokinetic leg press strength in a Chinese cohort. We constructed a genomic prediction model, based on the identified genetic markers and then combined phenotype indicators, to establish a comprehensive genomic-phenotypic model for predicting resistance training effects. Additionally, we conducted bioinformatics analysis on the lead SNPs to gain insights into the possible mechanisms by which they affect training effects. Our findings provide operational approaches for developing precision fitness guidance programs and they serve as a basis for further research.

Materials and Methods

Participants

The study was conducted on a Chinese strength training cohort. The inclusion criteria for research subjects were as follows: (1) Participants had no prior experience with resistance training and were classified as non-regular exercisers [24, 25] using the Global Physical Activity Questionnaire (GPAQ) [26]; (2) Participants with no risk of resistance training-related injuries as determined by the Physical Activity Readiness Questionnaire (PAR-Q); (3) Participants had no adverse dietary habits and maintained a regular diet during the intervention period, as determined by the Chinese Resident Nutrition and Health Survey Food Frequency Questionnaire. Exclusion criteria for participants: (1) Participants who were unable to complete the intervention due to injuries, illnesses, or other reasons. (2) Participants with incomplete data collection. (3) Participants who were not of Chinese Han ethnicity. All subjects voluntarily participated and completed informed consent forms. A total of 193 participants of Chinese Han ethnicity were included in the study, comprising 95 males (with an average age of 20 ± 1 years, height of 177.8 ± 5.8 cm, and weight of 71.3 ± 12.4 kg) and 98 females (with an average age of 20 ± 3 years, height of 164.7 ± 5.9 cm, and weight of 56.5 ± 9.2 kg). The study was approved by the Ethics Committee of Sports Science Experiments at Beijing Sport University (Ethics Approval Number: 2019191H).

Procedures

Subjects who met the inclusion criteria were enrolled in a 12-week resistance training program. Prior to the intervention, detailed instructions were provided to familiarize the subjects with the standardized movement patterns and ensure their comprehension of the exercises. Throughout the intervention, close monitoring of training loads was implemented to ensure adherence to the prescribed training volume and adherence to the standardized movements. Phenotypic measurements and DNA samples were collected both before and after the 12-week intervention to facilitate subsequent analysis in the predictive models, with a 72-hour gap between the testing and training sessions.

Resistance training program

The resistance training program involved the use of a Smith machine for intervention, in which back squats and bench presses were performed with a load equivalent to 70 % of the one-repetition maximum (1RM). Subjects completed 5 sets of 10 repetitions with a 2-minute rest between sets, twice a week, for a period of 12 weeks. To accommodate changes in strength growth, a 1RM test was conducted every 4 weeks to determine a new training load [27]. During the intervention process, participants' training loads were monitored, and they were required to complete the entire training volume. If a participant was unable to complete the training independently, minimal assistance was provided to ensure that the training stimulus on the body remained consistent after completing the same training content.

One repetition maximum

Participants begin with a warm-up activity, which involves performing back squats/bench presses at 40 % of their subjective 1RM perception. After warming up, the weight is increased by 15–20 kg on top of the warm-up load, and they complete 3–5 back squats/bench presses. A rest period of 2–4 minutes follows, after which the weight is increased again by 15–20 kg (for back squats) or 5–10 kg (for bench presses), and they complete 2–3 back squats/bench presses. A further rest period of 2–4 minutes is taken, and the pre-

vious step is repeated. If the participant successfully completes the lift, continue to increase the load; if they fail, reduce the load by 5–10 kg (for back squats) or 2.5–5 kg (for bench presses) until they can complete 1RM with proper technique. The determination should be made within five attempts for both back squats and bench presses 1RM.

Muscle mass

The GE Lunar iDXA dual-energy X-ray bone densitometer (GE Healthcare, USA) was utilized to measure muscle mass. Before testing, it was ensured that the subject had not undergone a barium meal examination, radioactive isotope injection, or injection or oral contrast agent for CT and MRI examination within the last 7 days. The subject was required to fast for a minimum of two hours, remove any clothing that could affect the test results, and lie flat on the instrument table. The subject's basic information was entered into enCORE (2011), and the scanning frame was set to scan layer by layer from head to foot to obtain muscle mass measurements.

Muscle thickness

GE portable color ultrasound diagnostic system LOGIQ e (GE Healthcare, USA) was used to measure the thickness of the rectus femoris, rectus femoris-vastus intermedius, and pectoralis major muscles according GE LOGIQ user manual [28]. To measure the thickness of the rectus femoris muscle, the marker was placed at the midpoint of the line connecting the anterior superior iliac spine to the upper edge of the patella. The subject lay supine with both legs naturally relaxed and at shoulder width. For the thickness of pectoralis major muscle, the marker was placed at the midpoint of the line connecting the anterior axillary line to the nipple in males and at one-third the distance from the anterior axillary line in females. The instrument was calibrated before the test and subject information was entered. Muscle thickness was measured on both sides using a 12 MHz linear array ultrasound probe perpendicular to the direction of the muscle fibers. Three measurements for each side were recorded and averaged.

Isokinetic leg press maximum peak force

The isokinetic leg press maximum strength of the lower limbs was measured using the ISOMED isokinetic dynamometer (ISOMED 2000, Germany) [29]. The testing procedure was as follows: (1) Prior to commencing the test, the equipment was calibrated by the testing personnel. (2) Participants engaged in a warm-up session on-site, which included a 200-meter slow run, 2 sets of 10 repetitions of bodyweight squats, and 2 sets of 10 repetitions of lunge squats. (3) Participants were secured to the ISOMED, with the pelvis and back snug against the seatback, and a strap was used to fasten the waist. The soles of the participants' feet were positioned firmly on the footplate component. During leg press, the reference range of motion for the knee and hip joints was set at 90° to 130°, and the speed of the leg press was set at 10 cm/s. (4) Once the participants are securely fastened to the ISOMED, they execute 3–5 movements mirroring the speed and range of motion of the formal test. This acclimatizes them to the movement velocity and range. Afterward, they embark on a submaximal warm-up involving 3–5 incremental loads, spanning from 20 % to 80 % of their perceived maximum intensity during exercise (e. g. 25 %, 50 %, 75 %). Subsequent to this warm-up phase, participants are required to perform at least one maximal intensity exercise. (5) Throughout the testing procedure, participants were instructed to exert maximum force with both legs. Each participant completed three leg press tests. The peak force (PF) during the concentric phase of the leg press was used for subsequent analysis.

Chip-based whole genome genotyping and quality control

Venous blood (5 mL) was collected from each participant for DNA extraction, using a magnetic bead-based genomic DNA extraction kit (Tiangen, China). The DNA concentration and purity were determined using a Nanodrop 2000 (Thermo Fisher Scientific, USA), while DNA integrity was assessed through agarose gel electrophoresis. For optimal quality, the DNA concentration should exceed 100 ng/μl, the OD260/280 ratio of the sample should be higher than 1.8, and agarose gel electrophoresis should show a clear main band without signs of degradation. DNA samples that passed the quality control stage were genotyped using an Infinium chip (CGA-24v1–0) (Illumina, USA). The genotyping results were analyzed using GenomeStudio 2.0 (Illumina, USA), and the data were formatted. Pre-imputation genotypes were quality-controlled, and the quality control and imputation methods were consistent with previous studies [30, 31]. The genotype data were imputed using Eagle/Minimac4 with default parameters (chunk size of 10 Mb and step size of 3 Mb) against the 1000 Genomes Project Phase 3 v5 reference haplotypes. The imputed chip data were quality-controlled using plink1.9 software based on quality control standards [32], which included the following exclusion criteria: 1) minimum allele frequency less than 5 % (MAF < 0.05); 2) not in Hardy-Weinberg equilibrium ($p < 1 \times 10^{-5}$); 3) SNPs with more than 10 % missing genotypes (mind 0.01); and 4) individuals with more than 10 % missing genotypes (geno 0.01). After genotype imputation, 4,110,727 SNPs were retained. Subsequent GWAS analysis was conducted using the quality-controlled SNPs.

Statistical analysis

Data entry, processing, and statistical analyses were performed using Excel 2016 and SPSS 19.0. Descriptive statistics are presented as mean ± standard deviation (Mean ± SD). The normal distribution of the data was assessed using the K-S test. The training effect was represented as the percentage (ΔPF) change in isokinetic leg press maximum strength before and after the intervention. The quartile method was employed to classify subjects' responses to the training effect. Negative-responders were defined as those with a ΔPF ≤ 0 %, low responders as those with 0 < ΔPF ≤ 25 %, medium responders as those with 25 % < ΔPF ≤ 50 %, and high responders as those with ΔPF > 50 %.The overall training effect was assessed using a paired-sample t-test with a significance level of $P < 0.05$. Principal component analysis (PCA) was used for population stratification quality control.

Plink 1.9 software was used for genome-wide association analysis, with the initial value of isokinetic leg press maximum strength, sex, age, and the first 10 principal components of PCA analysis as covariates. The significance level was defined as $p < 1 \times 10^{-5}$. The genome-wide significance was $p < 5 \times 10^{-8}$.

The genomic inflation factor (λ) was calculated for GWAS association results to evaluate bias and the influence of population stratification [33]. GWAS Manhattan plots were drawn using the R package CMplot. Lead SNPs were selected using FUMA [34].

The weighted PGSs were calculated using the PRSice average method [35]:

$$\mathrm{PGS} = \sum_i \frac{SNP_i \times beta_i}{n}$$

(*n* represents the number of effective alleles, *i* represents the number of selected lead SNPs, and *beta* represents the beta value obtained from GWAS.)

Linear regression was used to establish the relationship between the training effect on isokinetic leg press maximum strength and PGS. The GWAS-selected lead SNPs were used as independent variables (x) to establish the genomic prediction model. The training effect prediction model was established using stepwise regression with the GWAS-selected lead SNPs and phenotype indicators (sex, age, initial isokinetic leg press maximum strength, muscle mass, and muscle thickness) as independent variables (x).

The selected genetic markers were subjected to bioinformatics analysis using SNPnexus [36] and REACTOME [37] databases.

Results

Individual variability in leg press response to resistance training

Following the 12-week strength training intervention, isokinetic leg press maximum strength of the subjects significantly increased (ΔPF = 15.39 %, p = 1.55E-4) (▶ **Fig. 1a**). The range of individual differences in strength improvement varied from −55.83 % to 151.20 % (▶ **Fig. 1b**). The histogram reveals a positively skewed distribution, characterized by a longer tail on the right side. Among the subjects, 35.4 % had ΔPF values of ≤ 0 %, 33.3 % had ΔPF between 0 % and 25 %, 19.3 % had ΔPF between 25 % and 50 %, and 12.0 % had ΔPF values > 50 % (▶ **Fig. 1c**).

Genome-wide association analysis

Eighty-five SNPs exhibited significant associations with the change in isokinetic leg press maximum strength after 12 weeks of resistance training ($p < 1 \times 10^{-5}$) (▶ **Fig. 2**,▶ **Table 1**). The inflation coefficient λ was calculated to be 1.014 (▶ **Fig. 3**), indicating that the p-value was not influenced by population stratification and there was no false positive. Among these SNPs, 14 were identified as lead SNPs ($p < 1 \times 10^{-5}$), with nine SNPs reaching genome-wide significance ($p < 5 \times 10^{-8}$) (▶ **Table 1**).

Correlation analysis between PGS and isokinetic leg press maximum strength

There was a significant positive correlation between ΔPF and PGS (r = 0.68, p < 0.01). The regression equation is Y = 0.09*X + 1.02, with an X-axis intercept of −11.89 and a Y-axis intercept of 1.02. The PGS score for negative-responders is less than 1.02; for low-responders it is 1.02 < PGS ≤ 3.17; for middle-responders it is 3.17 < PGS ≤ 5.31, and for high-responders it is PGS > 5.31 (▶ **Fig. 4**).

Models for predicting the effectiveness of isokinetic leg press maximum strength training

Seven SNPs (rs1419957, rs2619732, rs8010482, rs73044028, rs12480160, rs12326802, rs61973994) out of the 14 lead SNPs were incorporated in the genomic prediction model (model $R^2 = 0.404$) (▶ **Table 2**). By incorporating PGS and phenotypic indicators, the comprehensive model included the PGS, initial values of isokinetic peak force, and sex, which accounted for 75.4 % of the variation in training effect (i. e. the model R^2, which is the sum of the coefficients' R^2) (▶ **Table 3**). The PGS could explain 49.9 % of the variance in leg press response ($R^2 = 0.499$), and the second highest predictor was the initial values of isokinetic peak force, which could explain 22.9 % of the variance in leg press response ($R^2 = 0.229$).

Biological functional analysis

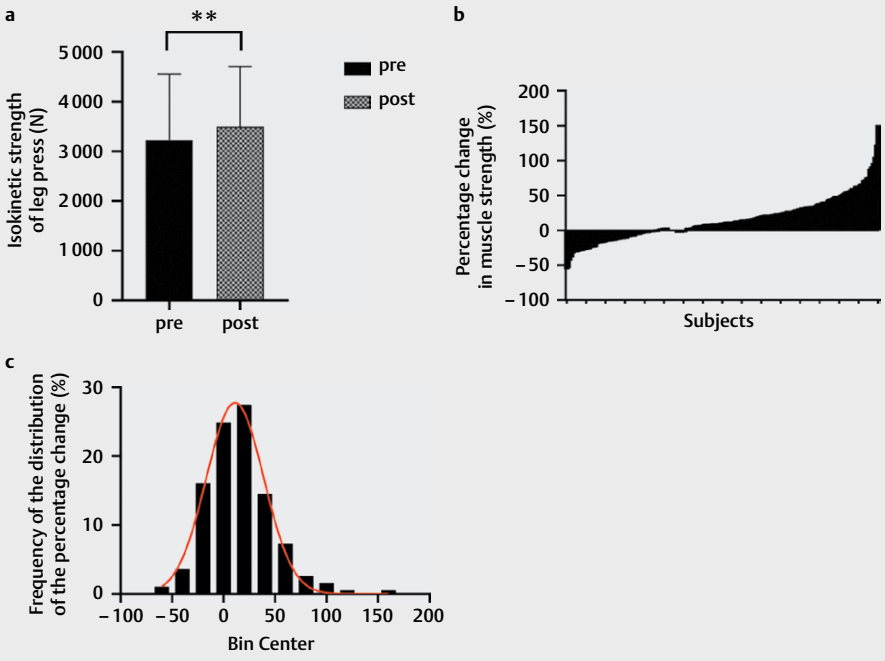
The results of gene ontology analysis (GO) showed that SNPs associated with maximal isokinetic leg press training response were mainly enriched in 20 biological processes, including inorganic ion transmembrane transport, epithelial structure maintenance, and organ or tissue-specific immune response. Additionally, they were enriched in seven molecular functions, including sodium channel regulator activity, inorganic molecular entity transmembrane transporter activity, and carbohydrate binding, as well as seven cellular components, including transmembrane transporter complex, intercalated disc, and RNA polymerase II transcription regulator complex (▶ **Fig. 5**).

The lead SNPs were analyzed by SNPnexus for REACTOME pathway analysis. Five SNPs (rs3774611, rs9812977, rs2869782, rs8010482, rs61973994) may play a role in REACTOME pathways related to muscle contraction, metabolism, and growth and development (▶ **Table 4**).

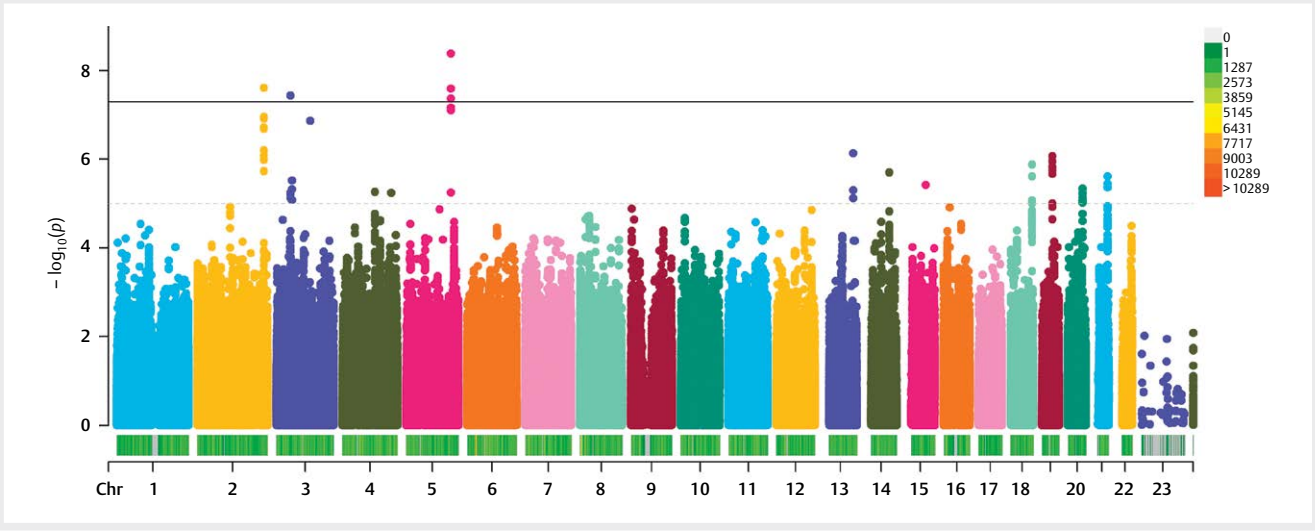
Discussion

This is the first study at the whole-genome level to require genetic markers with resistance training response of leg press. Fourteen lead SNPs were identified, with a PGS greater than 5.31 were classified as high responders. Furtherly, combing genetic and phenotypic variables, a comprehensive predictive model was established, which explain 75.4 % of the variance. Bioinformatics analysis revealed that the lead SNPs might play a role in REACTOME pathways related to muscle contraction, metabolism, and growth and development.

Evaluating isokinetic muscle strength is important in assessing the effectiveness of strength training and sports injury rehabilitation for athletes, and improving isokinetic muscle strength is beneficial for maintaining muscle strength and improving posture balance [38]. A 12-week progressive resistance training program was found to improve the isokinetic peak contraction force of knee joint muscles in postmenopausal women [39], and a 12-week dynamic resistance training program had a significant effect on improving the peak isokinetic hip/leg extension muscle force in elderly men with osteoporosis [40]. In our study, 12 weeks of resistance training significantly improved the isokinetic leg press maximum strength (with an average increase of 15.39 %), while there exist individual differences in sensitivity to the training program, resulting



▶ **Fig. 1** Individual variations in the training effect on isokinetic leg press maximum strength. (A: Change in isokinetic leg press maximum strength pre- and post-intervention; B: Individual variations in the training effect on maximal isokinetic leg press strength; C: Distribution of individual variations in the training effect on isokinetic leg press maximum strength).**indicated $p<0.01$ for the paired samples t-test.



▶ **Fig. 2** Manhattan plot of GWAS analysis of the training effect on isokinetic leg press maximum strength. The x-axis represents chromosomes, which are distinguished by different colors. The y-axis represents -log10 (P), and the color of the legend represents the number of SNPs on each chromosome. The dashed line indicates a significance level of $p<1\times10^{-5}$, and the solid line indicates a significance level of $p<5\times10^{-8}$.

in varying training effects among subjects. Although strength-related indicators such as biceps curls, leg extension, and shoulder press 1RM increased significantly ($P=0.001$) after 12 weeks of progressive resistance training intervention from a previous study, there were differences in response rates, with 11.7 %, 5.9 %, and 29.4 % of subjects showing ineffective responses, respectively [41]. After 12 weeks of progressive resistance training targeting the elbow flexor muscles, the subjects' range of isometric strength in their arms showed a significant difference, ranging from a decrease of 32 % to an increase of 149 % (−15.9 to 52.6 kg) [42]. The intervention approach used in this study adhered to the commonly practiced load and frequency of strength training, which has been proven highly effective in enhancing 1RM muscle strength [43]. However, concerning isokinetic strength changes, resistance training

▶ **Table 1** GWAS analysis of the training effect on isokinetic leg press maximum strength.

rsID*	CHR	Position	REF Allele	ALT Allele (IUPAC)	Minor Allele	MAF	Beta	GWAS_P	Function	Overlapped Gene	Nearest Upstream Gene	Nearest Downstream Gene
rs2619732	5	153877722	T	G	G	0.08	37.79	4.15E-09	None	None	CTB-158E9.2	CIR1P1
rs283442	5	153881665	T	C	C	0.07	37.79	4.15E-09	None	None	CTB-158E9.2	CIR1P1
rs283443	5	153881676	A	G	G	0.08	37.79	4.15E-09	None	None	CTB-158E9.2	CIR1P1
rs283445	5	153882962	T	A	A	0.06	37.79	4.15E-09	None	None	CTB-158E9.2	CIR1P1
rs1419957	2	230029563	G	A	A	0.26	20.46	2.45E-08	non-coding intronic,intronic	PID1	None	None
rs3101863	5	153862679	A	C	C	0.06	34.52	2.56E-08	None	None	HAND1	CTB-158E9.1
rs9812977	3	48720303	G	A	A	0.09	37.38	3.67E-08	5upstream,intronic,5utr	NCKIPSD	None	None
rs176104	5	153865158	A	G	G	0.07	34.14	4.27E-08	non-coding intronic	CTB-158E9.1	None	None
rs442533	5	153867280	G	A	A	0.08	34.14	4.27E-08	None	None	CTB-158E9.1	CTB-158E9.2
rs17116169	5	153837482	G	A	A	0.05	34.12	6.82E-08	3utr,3downstream	SAP30L	None	None
rs111287651	5	153843293	T	M	A	0.05	33.16	7.93E-08	None	None	SAP30L	HAND1
rs72795453	5	153844742	C	T	T	0.05	33.16	7.93E-08	None	None	SAP30L	HAND1
rs72795454	5	153850486	A	T	T	0.06	33.16	7.93E-08	None	None	SAP30L	HAND1
rs1419956	2	230029360	G	A	A	0.29	19.28	1.12E-07	non-coding intronic,intronic	PID1	None	None
rs17676310	2	230030367	T	M	C	0.12	19.38	1.23E-07	non-coding intronic,intronic	PID1	None	None
rs9973574	2	230031411	T	C	C	0.26	19.38	1.23E-07	non-coding intronic,intronic	PID1	None	None
rs2869782	3	117084425	T	M	T	0.26	27.11	1.36E-07	intronic	LSAMP	None	None
rs11900642	2	230028108	A	G	G	0.26	18.94	1.92E-07	non-coding intronic,intronic	PID1	None	None
rs10171031	2	230031029	C	W	A	0.25	18.94	2.10E-07	non-coding intronic,intronic	PID1	None	None
rs62190426	2	230033010	A	G	G	0.12	18.59	6.33E-07	non-coding intronic,intronic	PID1	None	None
rs61973994	13	101762201	C	T	T	0.18	17.15	7.26E-07	intronic	NALCN	None	None
rs145706639	2	230031680	GGAAGG	-	-	0.25	18.44	8.38E-07	non-coding intronic,intronic	PID1	None	None
rs73044028	19	35657612	G	A	A	0.12	16.7	8.62E-07	3utr,non-coding intronic,intronic	FXYD5	None	None
rs11900497	2	230027887	A	G	G	0.26	18.11	1.03E-06	non-coding intronic,intronic	PID1	None	None
rs73044024	19	35657334	A	G	G	0.12	16.56	1.13E-06	non-coding intronic,3utr,intronic	FXYD5	None	None
rs12326802	18	73657606	A	G	A	0.33	19.69	1.31E-06	None	None	RP11–173L6.1	RP11–357H3.1
rs2073948	19	35651806	A	T	T	0.09	16.77	1.49E-06	non-coding intronic,intronic,3downstream	FXYD5	None	None
rs150686717	19	35655985	T	-	-	0.12	16.34	1.54E-06	non-coding intronic,intronic	FXYD5	None	None
rs56058408	19	35655990	G	H	T	0.12	16.34	1.54E-06	non-coding intronic,intronic	FXYD5	None	None
rs73044014	19	35653275	C	T	T	0.12	17.13	1.79E-06	non-coding intronic,5upstream,intronic	FXYD5	None	None
rs12470314	2	230035585	C	T	T	0.12	18.35	1.85E-06	non-coding intronic,intronic	PID1	None	None
rs8010482	14	81815011	C	W	C	0.30	14.54	1.98E-06	intronic	STON2	None	None

▶ **Table 1** GWAS analysis of the training effect on isokinetic leg press maximum strength.

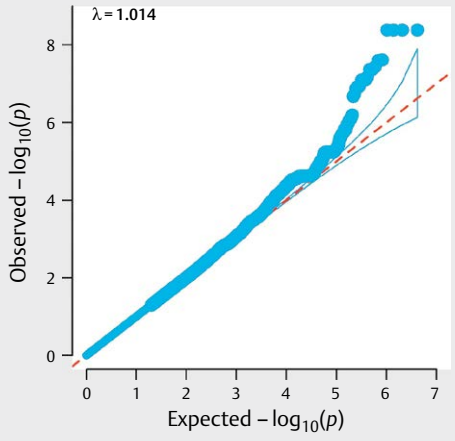
rsID*	CHR	Position	REF Allele	ALT Allele (IUPAC)	Minor Allele	MAF	Beta	GWAS_P	Function	Overlapped Gene	Nearest Upstream Gene	Nearest Downstream Gene
rs73044015	19	35653348	T	A	A	0.09	16.09	2.16E-06	non-coding intronic,5upstream,intronic	FXYD5	None	None
rs9945171	18	73690476	T	C	C	0.09	22.92	2.44E-06	None	None	RP11–173L6.1	RP11–357H3.1
rs691587	21	43776179	G	W	G	0.20	−14.15	2.45E-06	None	None	TFF2	TFF1
rs3774611	3	53840665	G	A	A	0.39	−12.75	3.04E-06	intronic	CACNA1D	None	None
rs172825	21	43773253	C	R	C	0.15	−13.96	3.58E-06	None	None	TFF2	TFF1
rs12442146	15	70446518	G	H	T	0.25	17.9	3.79E-06	None	None	TLE3	RNU6–745P
rs225338	21	43772432	A	S	A	0.15	−13.74	4.35E-06	None	None	TFF2	TFF1
rs225339	21	43772438	G	H	G	0.15	−13.74	4.35E-06	None	None	TFF2	TFF1
rs12480160	20	49990155	A	G	G	0.12	17.7	4.64E-06	None	None	AL035457.1	AL079339.1
rs2359132	3	53836937	A	G	G	0.21	−12.48	4.80E-06	intronic	CACNA1D	None	None
rs78781545	13	101762277	T	C	C	0.05	16.52	5.05E-06	intronic	NALCN	None	None
rs75318253	4	112680279	A	G	G	0.06	−24.05	5.47E-06	None	None	RP11–255I10.2	RP11–269F21.1
rs79268297	4	112680281	G	T	T	0.06	−24.05	5.47E-06	None	None	RP11–255I10.2	RP11–269F21.1
rs283444	5	153882472	C	T	T	0.11	25.4	5.61E-06	None	None	CTB-158E9.2	CIR1P1
rs112928349	3	48714335	G	C	C	0.14	28.73	5.71E-06	intronic,non-coding intronic	NCKIPSD	None	None
rs12107252	3	48691316	T	C	C	0.21	28.73	5.71E-06	coding nonsyn	CELSR3	None	None
rs12107418	3	48689787	A	G	G	0.20	28.73	5.71E-06	intronic	CELSR3	None	None
rs12715429	3	48709246	G	W	T	0.14	28.73	5.71E-06	3downstream,intronic	NCKIPSD	None	None
rs13070798	3	48705934	T	C	C	0.14	28.73	5.71E-06	intronic	NCKIPSD	None	None
rs13324119	3	48710606	G	C	C	0.13	28.73	5.71E-06	3downstream,intronic	NCKIPSD	None	None
rs144754472	3	48710301	-	AAC	AAC	0.14	28.73	5.71E-06	3downstream,intronic	NCKIPSD	None	None
rs2286651	3	48694147	G	A	A	0.10	28.73	5.71E-06	coding syn	CELSR3	None	None
rs2286652	3	48689192	G	A	A	0.10	28.73	5.71E-06	intronic	CELSR3	None	None
rs2302295	3	48690110	T	C	C	0.14	28.73	5.71E-06	intronic	CELSR3	None	None
rs28452701	3	48708575	C	T	T	0.13	28.73	5.71E-06	intronic	NCKIPSD	None	None
rs34051806	3	48713669	AT	-	-	0.13	28.73	5.71E-06	non-coding intronic,intronic	NCKIPSD	None	None
rs3733086	3	48699519	C	T	T	0.10	28.73	5.71E-06	coding syn	CELSR3	None	None
rs3821875	3	48697654	C	R	G	0.10	28.73	5.71E-06	coding nonsyn|nonsyn	CELSR3	None	None
rs6768448	3	48714165	A	G	G	0.20	28.73	5.71E-06	non-coding intronic,intronic	NCKIPSD	None	None
rs71074265	3	48702890	CT	-	-	0.10	28.73	5.71E-06	intronic	NCKIPSD	None	None
rs9809222	3	48714411	C	T	T	0.20	28.73	5.71E-06	3downstream,non-coding intronic,intronic	NCKIPSD	None	None

▶ **Table 1** GWAS analysis of the training effect on isokinetic leg press maximum strength.

rsID*	CHR	Position	REF Allele	ALT Allele (IUPAC)	Minor Allele	MAF	Beta	GWAS_P	Function	Overlapped Gene	Nearest Upstream Gene	Nearest Downstream Gene
rs9811318	3	48702606	A	G	G	0.20	28.73	5.71E-06	intronic	NCKIPSD	None	None
rs9858236	3	48709529	G	A	A	0.13	28.73	5.71E-06	3downstream,intronic	NCKIPSD	None	None
rs9873726	3	48712367	C	T	T	0.20	28.73	5.71E-06	non-coding intronic,intronic	NCKIPSD	None	None
rs9877501	3	48718390	C	K	G	0.20	28.73	5.71E-06	5upstream,intronic,3downstream	NCKIPSD	None	None
rs9877794	3	48718388	G	C	C	0.19	28.73	5.71E-06	3downstream,5upstream,intronic	NCKIPSD	None	None
rs730741	4	168610140	T	C	C	0.49	15.8	5.74E-06	None	None	RN7SKP188	RP11–521F1.1
rs742992	20	49988935	G	A	A	0.10	17.62	5.92E-06	None	None	AL035457.1	AL079339.1
rs9812200	3	48695667	G	A	A	0.21	28.56	6.12E-06	intronic	CELSR3	None	None
rs9836462	3	48712791	A	G	G	0.21	28.56	6.12E-06	non-coding intronic,intronic	NCKIPSD	None	None
rs9841602	3	48713570	A	G	G	0.21	28.56	6.12E-06	non-coding intronic,intronic	NCKIPSD	None	None
rs1033597	20	49980774	A	T	T	0.08	18.98	7.40E-06	None	None	AL035457.1	AL079339.1
rs13353481	3	48709463	C	R	G	0.13	28.53	7.40E-06	3downstream,intronic	NCKIPSD	None	None
rs79076253	13	101762151	C	T	T	0.05	16.6	7.50E-06	intronic	NALCN	None	None
rs893365	3	53841146	C	T	T	0.40	−12.08	8.31E-06	intronic	CACNA1D	None	None
rs113945797	18	73688365	A	T	T	0.04	21.8	8.41E-06	None	None	RP11–173L6.1	RP11–357H3.1
rs12480218	20	49990445	G	T	T	0.09	17.45	8.73E-06	None	None	AL035457.1	AL079339.1
rs1039718	18	73681247	G	A	A	0.22	23.34	9.30E-06	None	None	RP11–173L6.1	RP11–357H3.1
rs28578250	18	73680467	C	T	T	0.22	23.34	9.30E-06	None	None	RP11–173L6.1	RP11–357H3.1
rs28612749	18	73680476	C	K	T	0.22	23.34	9.30E-06	None	None	RP11–173L6.1	RP11–357H3.1
rs111397679	20	49981156	G	T	T	0.10	17.86	9.65E-06	None	None	AL035457.1	AL079339.1
rs56050577	19	35660138	G	T	T	0.09	15.35	9.89E-06	non-coding intronic,intronic	FXYD5	None	None
rs140487242	18	73668588	ATACAC	-	-	0.03	22.51	9.98E-06	None	None	RP11–173L6.1	RP11–357H3.1

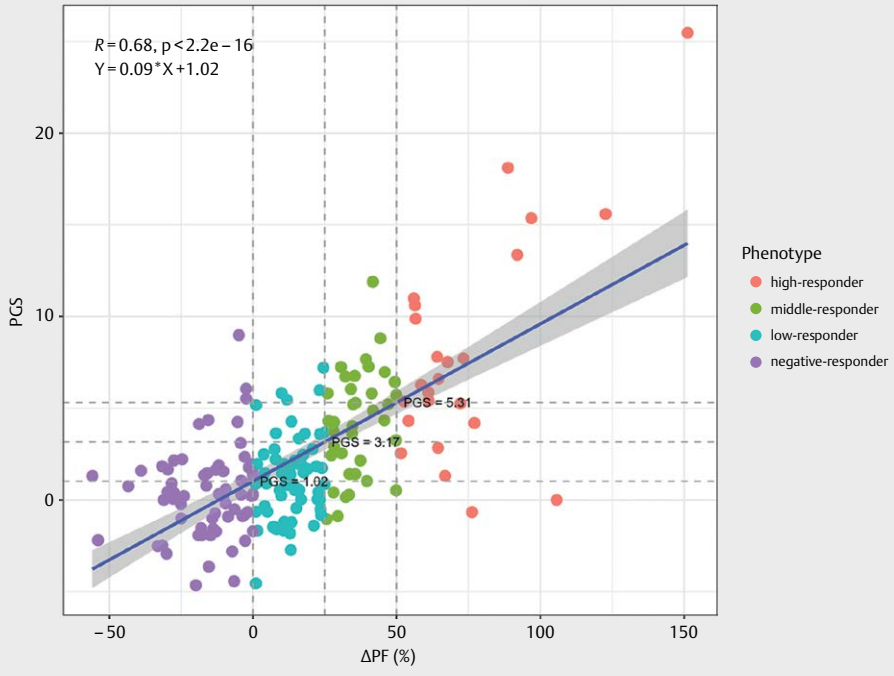
*in the rsID column, lead SNPs are in bold.

exhibits significant variability in improving isokinetic strength (▶ **Fig. 1b** shows that around one-third of participants experienced a decrease in isokinetic strength post-training). Similar findings were observed in other studies, where roughly one-third of participants either showed a decline or no change in isokinetic (60 °/sec) and isometric leg extensor strength after a 12-week resistance training program. Conversely, another third of participants displayed a slight increase in both isokinetic and isometric strength, while the remaining third experienced a noteworthy improvement in both types of strength [44]. These results imply that a reduction in isokinetic strength after resistance training is not uncommon in long-term studies and may be linked to individual differences, physiological responses, or other factors. It is noteworthy that despite meticulous control over the intervention and testing processes, this study observed highly overlapping error bars (▶ **Fig. 1a**). Similar observations were made in other studies, exemplified by a 16-week resistance training intervention involving 113 participants, showing a 14 ± 12 % increase in 1RM after 8 weeks and a 31 ± 23 % increase after 16 weeks. This overlapping trend is considered a reasonable outcome in studies with larger participant sizes, indicating genuine individual variations in the effects of training.



▶ **Fig. 3** Quantile-Quantile (QQ) plot and genomic inflation factor λ.λ ≈ 1, the curve lifts up at the back end, indicating that the p-values are not due to population stratification, and there is no false positive.

Individual differences in training effects are influenced by both innate genetic factors and environmental factors. It is widely accepted that the individual factors affecting training effects under the same program mainly come from innate genetic factors (genomics) and postnatal physical characteristic factors (phenotypes) [45]. Among the phenotype factors, multiple indicators such as age, sex, BMI, and muscle mass can affect the training effects of resistance training. Age and sex can influence the response of specific muscle fiber types to resistance training. Studies have shown a significant increase in the percentage of type I fibers (40 ~ 51 %; $p < 0.05$) after resistance training in young women, but not in young men or elderly people [46]. Additionally, after 12 weeks of progressive resistance training, the 1RM of the bench press increased significantly in male and female subjects, but the degree of improvement was different, with 14 % and 23 %, respectively, indicating sex differences [47]. Muscle mass is the foundation of muscle strength and therefore may also be a factor affecting training effects. As for



▶ **Fig. 4** Relationship between the training effect on isokinetic leg press maximum strength (ΔPF) and PGS. The slope of the equation is 0.09, the X-axis intercept is −11.89, and the Y-axis intercept is 1.02.

▶ **Table 2** Models for predicting the training effect on isokinetic leg press maximum strength based on SNPs.

coefficient	Unstandardized Coefficients		Standardized Coefficients	Sig.	R^2	Adjusted R^2
	B	Std. Error	BETA			
(constant)	−9.239	3.149		0.004		
rs1419957	14.308	3.741	0.261	0	0.14	0.134
rs2619732	26.172	7.288	0.244	0	0.085	0.08
rs8010482	8.641	3.264	0.179	0.009	0.057	0.053
rs73044028	8.249	3.479	0.168	0.019	0.041	0.037
rs12480160	10.751	4.126	0.175	0.01	0.03	0.026
rs12326802	10.452	4.162	0.168	0.013	0.027	0.023
rs61973994	8.123	3.463	0.155	0.02	0.024	0.02

▶ **Table 3** Comprehensive models for predicting the training effect on isokinetic leg press maximum strength based on PGS and phenotypic indicators.

coefficient	Unstandardized Coefficients		Standardized Coefficients	Sig.	R^2	Adjusted R^2
	B	Std. Error	BETA			
(constant)	40.608	3.128		0		
PGS	5.206	0.283	0.699	0	0.499	0.497
isokinetic maximum flexor strength	−0.014	0.001	−0.58	0	0.229	0.228
SEX	11.996	2.674	0.192	0	0.026	0.025

genetic factors, the heritability of muscle strength and power is about 52 % [48]. Candidate gene studies have identified four genes with seven SNPs (*ACE* rs4646994/rs1799752/rs4340/rs13447447, *ACTN3* rs1815739, *IL15RA* rs2296135, *PPARA* rs4253778) that are related to resistance training effects [49]. There may be more genetic markers determining training effects, but currently, there is a lack of GWAS studies at the genomic level.

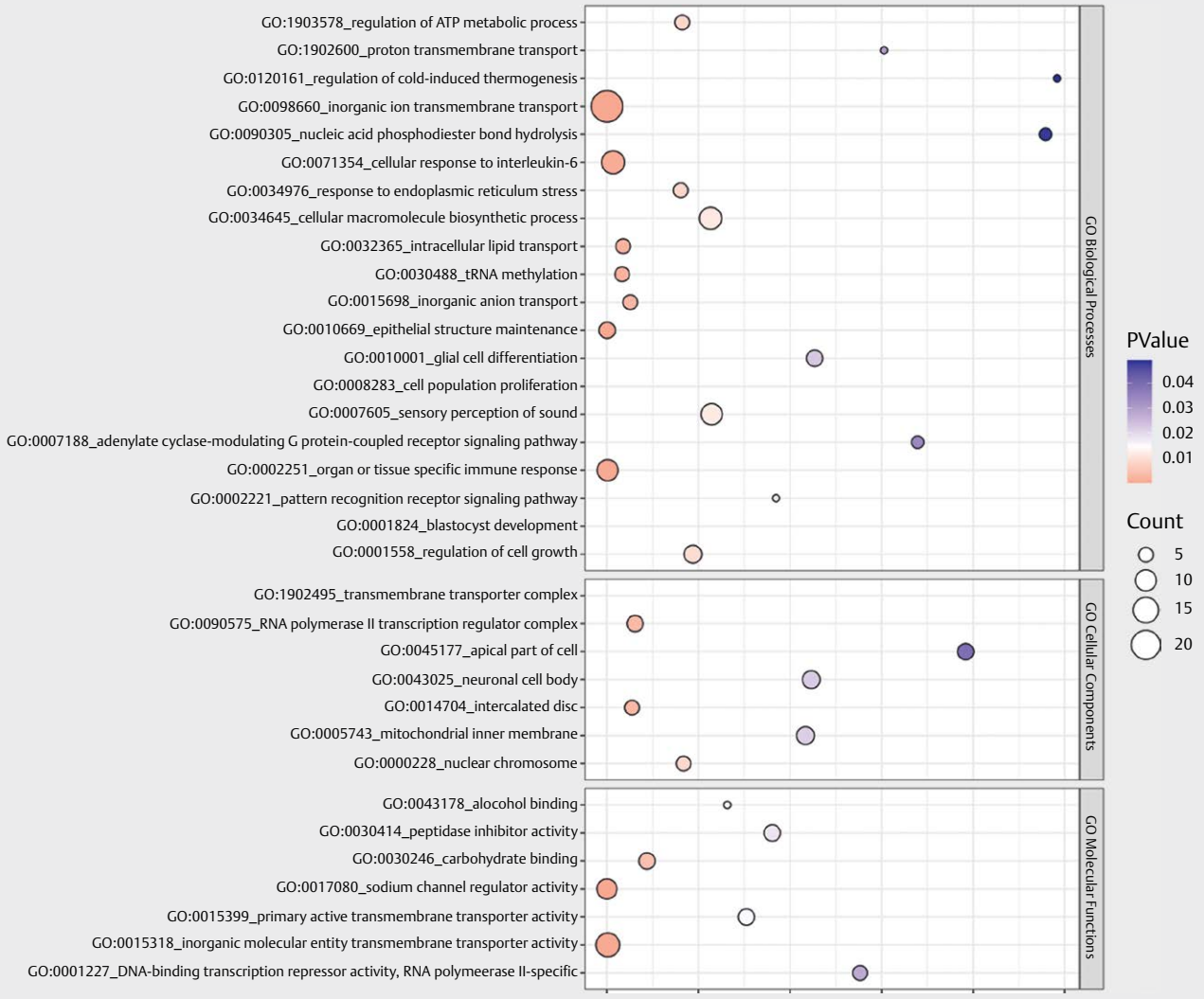
In this study, we utilized GWAS analysis to identify 85 SNPs that exhibited a significant association ($p < 1 \times 10^{-5}$) with the percentage change in isokinetic leg press maximum strength after 12 weeks of resistance training. Among these SNPs, 9 (rs2619732, rs283442, rs283443, rs283445, rs1419957, rs3101863, rs9812977, rs176104, and rs442533) reached genome-wide significance ($p < 5 \times 10^{-8}$). Fourteen SNPs (rs2619732, rs1419957, rs9812977, rs2869782, rs61973994, rs73044028, rs12326802, rs8010482, rs691587, rs3774611, rs12442146, rs12480160, rs79268297, and rs730741) were identified as lead SNPs, which are the most strongly associated SNPs with the phenotype of interest during genetic association analysis [34].

Of these SNPs, 10 (rs2619732, rs283442, rs283443, rs283445, rs176104, rs442533, rs12326802, rs12480160, rs79268297, and rs730741) were found to be located near pseudogenes, lincRNAs, and miRNAs. Pseudogenes, lincRNAs, and miRNAs are three types of non-coding RNA in the genome [50, 51]. Pseudogenes are thought to be products of gene duplication and rearrangement, possessing DNA sequences and structures similar to normal genes but lacking the regulatory elements and coding regions required by normal genes. They may play a role in regulating gene expression or become toxic genes that affect normal gene expression [52]. LincRNAs are non-coding RNAs longer than 200 nt and are usually located between two genes in the genome. They do not participate in protein synthesis but regulate gene expression, chromatin modification, histone modification, and RNA processing [53]. MiRNAs are non-coding RNAs approximately 20–24 nucleotides long that can bind to the 3' untranslated region (3'UTR) of target genes, inducing their degradation or inhibiting their translation. LincRNAs and miRNAs have been shown to play important roles in regulating gene expression, cell proliferation, apoptosis, differentiation, immune response, and many diseases such as tumors, cardiovascular diseases, and neuromuscular diseases [54, 55]. However, their mechanisms in skeletal muscle growth, development, and function require further exploration.

In this study, the other SNPs discovered were primarily located in non-coding regions of genes. These regions, which include promoter regions, enhancer regions, and transcription factor binding sites, can regulate gene transcription and translation [56]. SNPs located in these regions may affect transcription factor binding, promoter methylation status, or recruitment of RNA polymerase, which can influence gene expression and function [57]. Moreover, these SNPs play a critical role in disease susceptibility, drug response, and training sensitivity, as evidenced in this study.

One of the identified SNPs, rs1419957, is located in the intron of the Phosphotyrosine Interaction Domain Containing 1 (PID1) gene, which is involved in energy metabolism in skeletal muscle and adipose tissue. PID1, showing significant upregulation in abdominal adipose tissue of obese individuals, is associated with glucose uptake pathways and insulin resistance in both adipose and muscle tissues [58].

Another SNP discovered, rs3101863, is an intergenic variation located between the Heart And Neural Crest Derivatives Expressed 1 (HAND1) and CTB-158E9.1 genes. The protein encoded by the HAND1 gene comprises a basic helix-loop-helix (bHLH) domain, facilitating its interaction with target genes and regulation of cardiac developmental processes [59]. CTB-158E9.1 is a long intergenic non-coding RNA (lincRNA), and at present, there is no research linking either of these genes to muscle strength. Rs9812977 is lo-



▶ **Fig. 5** GO analysis enriched terms. This figure illustrates the results of the Gene Ontology (GO) analysis, including biological processes, cellular components, and molecular functions. The size of the bubbles represents the number of genes enriched in the corresponding GO terms, while the color of the bubbles indicates the magnitude of the enrichment p-values, transitioning from blue to red as the p-values decrease.

cated at the 5'UTR region of the NCK interacting protein with SH3 domain (*NCKIPSD*) gene on chromosome 3. The NCKIPSD gene is involved in signal transduction and contributes to the assembly of myofibrils into sarcomeres, as well as the formation of stress fibers. Furthermore, this protein plays a crucial role in the development and maintenance of dendritic spines, while also exerting regulatory control over synaptic activity in neurons [60, 61]. REACTOME pathway analysis shows that rs9812977 affects the RHO GTPases Activate WASPs and WAVEs signaling pathway. Rs2869782 is situated within the intron of the LSAMP gene. Additionally, the protein encoded by this gene has been identified as a potential tumor suppressor. Nevertheless, there is currently no available research elucidating its direct impact on skeletal muscle. *LSAMP* is one of the target genes of miR-206, a skeletal muscle-specific miRNA that promotes the transformation of type II fast glycolytic fibers into type I slow oxidative fibers [62]. REACTOME pathway analysis suggests that rs2869782 affects the metabolism of the proteins pathway (i. e. post-translational modification: synthesis of GPI-anchored proteins). Rs61973994 is situated within the intron of the NALCN gene, which encodes for the NALCN ion channel, also known as the sodium leak channel. In recent years, many studies have reported that NALCN plays an important role in many other basic physiological processes, such as motor function, pain sensitivity, and circadian rhythms [63]. Given the important role of NALCN in congenital motor neuron development, it is speculated that rs61973994 may be related to this gene's effect on the isokinetic leg press maximum strength during steady-state cycling. REACTOME pathway analysis suggests that rs61973994 affects the Transport of small molecules (Stimuli-sensing channels) pathway. Rs73044028 is located at the 3' UTR region of the FXYD5 gene on chromosome 19.

The FXYD family is a recently discovered group of small-molecule single-pass transmembrane proteins that have ion channel or

▶ **Table 4** Biological pathway analysis of SNPs related to the training effect of maximal isokinetic leg press strength.

Pathway ID	Description	Parent(s)	p-Value	Genes Involved	Variation IDs
R-HSA-5576893	Phase 2 – plateau phase	Muscle contraction	0.0117	CACNA1D	rs3774611
R-HSA-400042	Adrenaline,noradrenaline inhibits insulin secretion	Metabolism	0.0131	CACNA1D	rs3774611
R-HSA-5663213	RHO GTPases Activate WASPs and WAVEs	Signal Transduction	0.0164	NCKIPSD	rs9812977
R-HSA-419037	NCAM1 interactions	Developmental Biology	0.0196	CACNA1D	rs3774611
R-HSA-5576892	Phase 0 – rapid depolarisation	Muscle contraction	0.0196	CACNA1D	rs3774611
R-HSA-375165	NCAM signaling for neurite out-growth	Developmental Biology	0.0293	CACNA1D	rs3774611
R-HSA-422356	Regulation of insulin secretion	Metabolism	0.0358	CACNA1D	rs3774611
R-HSA-163125	Post-translational modification: synthesis of GPI-anchored proteins	Metabolism of proteins	0.0417	LSAMP	rs2869782
R-HSA-8856825	Cargo recognition for clathrin-mediated endocytosis	Vesicle-mediated transport	0.0485	STON2	rs8010482
R-HSA-163685	Integration of energy metabolism	Metabolism	0.0490	CACNA1D	rs3774611
R-HSA-2672351	Stimuli-sensing channels	Transport of small molecules	0.0490	NALCN	rs61973994

ion channel regulatory functions, and are closely associated with the structure and function of Na,K-ATPase. The FXYD family comprises a group of small-molecule single-pass transmembrane proteins, including FXYD1–7 in mammals. These proteins are known for their involvement in ion channel regulation and their close association with the structure and function of Na,K-ATPase. Among them, FXYD1, also referred to as phospholemman, and FXYD5, known as dysadherin, are the predominant FXYD proteins found in skeletal muscle [64]. Studies have demonstrated that participation in high-intensity interval training (HIIT) results in a reduction in FXYD5 levels and an elevation in the relative distribution of glycosylated NKAβ1 within type IIa muscle fibers. Additionally, a negative correlation has been observed between the abundance of FXYD5 in type IIa muscle fibers and maximal oxygen consumption [65]. Rs8010482 is located at an intron of the STON2 gene on chromosome 12. The STON2 gene encodes a membrane protein that regulates endocytic complexes. This protein interacts with synaptotagmin 1, which is required for neurotransmitter release, and is involved in synaptic vesicle recycling. Multi-tissue eQTL analysis shows that rs8010482 has the strongest normalized effect size (NES = 0.152, $P = 9.1 \times 10^{-7}$) on STON2 expression in skeletal muscle (▶ **Fig. 5**). REACTOME pathway analysis suggests that rs8010482 affects the vesicle-mediated transport signaling pathway. Rs691587 is located between the *TFF2* and *TFF1* genes, which belong to the trefoil factor (TFF) family. TFF1 was first identified in the MCF-7 breast cancer cell line, and its full gene sequence was subsequently cloned [66]. Since then, numerous studies have found abnormal expression of TFF family proteins (mainly TFF1 and TFF3) in various solid tumors [67–69]. Research has shown that *TFF2* is associated with energy metabolism and can regulate skeletal muscle mass. *TFF2* KO mice had reduced gastrocnemius muscle mass but an increased percentage of gastrocnemius muscle mass (because of simultaneous weight loss). Tff2 KO mice exhibited increased mitochondrial energy production and improved energy utilization in skeletal muscle, resulting in higher energy expenditure.[70]. Rs3774611 is located at the intron of the alpha1 D subunit of the calcium voltage-gated channel (CACNA1D) gene. The *CACNA1D* gene mediates the entry of calcium ions into excitable cells and is involved in various calcium-dependent processes, including muscle contraction, hormone or neurotransmitter release, and gene expression. REACTOME pathway analysis showed that this SNP may affect muscle contraction (Phase 0 – rapid depolarization, Phase 2 – plateau phase), metabolic pathways (adrenaline, noradrenaline inhibits insulin secretion, regulation of insulin secretion, integration of energy metabolism), and growth and development (NCAM1 interactions, NCAM signaling for neurite outgrowth). Rs12442146 is located between the *RNU6–745P* and *TLE3* genes. The upstream gene is a pseudogene, which is studied to a lesser extent. The downstream gene encodes a protein that is involved in the regulation of skeletal muscle growth and development. ChIP assays have revealed that TLE3 disrupts the binding of MyoD to the promoter region of myogenin, indicating that TLE3 functions in the maintenance of skeletal muscle homeostasis by suppressing the differentiation of satellite cells through inhibiting the transcriptional activity of MyoD [71].

In the model predicting training effects on muscle strength from isokinetic leg press using the lead SNPs as independent variables, seven SNPs (rs1419957, rs2619732, rs8010482, rs73044028, rs12480160, rs12326802, rs61973994) were included, and the model's explanatory power for the training effect was 40.4 % (coefficient of determination $R^2 = 0.404$). When phenotype indicators including sex, age, the initial value of isokinetic leg press strength, muscle mass, and muscle thickness, were added as independent variables along with the PGS, the coefficient of determination for the training effect prediction model increased to 75.4 %. PGS emerged as a predictive factor with high explanatory power for training effects. A genetic risk score known as PGS is calculated based on the genetic information of multiple SNPs to predict an individual's risk of developing a particular disease or exhibiting a specific trait. PGS can assess an individual's genetic risk more accurate-

ly and provide personalized exercise training recommendations than single SNPs. Currently, PGS is mainly used in precision medicine to predict complex diseases [72, 73], and it is rarely used to evaluate sports performance or training effects. In this current study, the PGS constructed by lead SNPs was positively correlated with isokinetic leg press strength ($r = 0.68$, $p < 0.01$), suggesting that PGS can distinguish different responders to strength training. Those who are identified as negative-responders need to analyze possible reasons and adjust their training programs. In the predictive model established in this study, the combined explanatory power of multiple genetic markers (PGS) for the effectiveness of maximum muscle strength training in isokinetic leg press is 49.9 %, indicating that genetic factors and phenotype factors (initial value, sex, combined 25.5 %) are equally important in determining maximum muscle strength in isokinetic leg press. In the comprehensive model for predicting the resistance training effect, the initial value of isokinetic leg press strength was included as phenotype indicator, with coefficients of determination of 22.9 %. These results suggest that the initial value has a greater impact on the training effect, and individuals with lower initial values are more likely to achieve higher improvements. Kassiano et al. compared changes in lower limb muscle strength after 12 weeks of resistance training in subjects with different levels of muscle strength, and they found that the maximal muscle strength of leg extension changed more in subjects with lower baseline values than those with higher baseline values [ESdiff = −0.45 (95 %CI: −0.86, −0.04), P = 0.030] [74]. Subjects with different initial values achieved varying training effects on leg muscles, single-leg press, and maximal isometric torque in knee extension after strength training, with improvements of 3.3 ± 3.3 %, 42 ± 17 %, and 8 ± 10 %, respectively, indicating individual differences [75]. After combined training (resistance training + aerobic training), well-trained individuals (with high initial values) showed negative effects on the maximum weight of leg press and squat (effect size of −0.35, $p < 0.01$) when compared to resistance training alone, but there was no negative effect in individuals with moderate training levels (−0.20, $p = 0.08$) or those who were untrained (with low initial values) (effect size of 0.03, $p = 0.87$). These findings suggest that the training effect of different protocols is also related to the initial value [76]. Sex is considered one of the predictive factors influencing the training effects of isokinetic leg press muscle strength. Multiple studies have consistently demonstrated that the capacity for strength adaptation is not influenced by one's sex. Research conducted revealed that following an 8-week resistance training program, both female and male participants exhibited comparable improvements in isokinetic and isometric peak torque [77]. Another study revealed that although males demonstrated higher peak torque values for elbow flexors compared to females before and after the intervention, no significant gender difference was observed in terms of changes in strength [78]. Indeed, in this study, despite including sex as a variable in the predictive model, it was found that sex accounted for only 2.6 % of the variation in the training effects of isokinetic leg press muscle strength. This further supports the notion that the benefits of resistance training in enhancing muscle strength are not heavily reliant on an individual's sex.

Contributor's Statement

None

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Conflict of Interest

The authors declare that they have no conflict of interest.

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