A Whole Genome Scanning for QTL affecting Leg Weakness and Its Related Traits in a White Duroc × Erhualian Resource Population

Dissertation

to obtain the Ph. D. degree

in the Faculty of Agricultural Sciences,

Georg-August-University Göttingen, Germany

Presented by

Yuanmei Guo

Born in Jiangxi/P. R. China

Göttingen, December 2008

D7

1. Name of referee: Prof. Dr. Dr. Bertram Brenig

2. Name of co-referee: Prof. Dr. Henner Simianer

Date of dissertation: 11th December, 2008

To my deeply beloved family

Table of Contents

Parts of this dissertation have been published

1. ***Guo Y. -M.***, Lee G. J., Archibald A. L., Haley C. S. (2008) Quantitative trait loci for production traits in pigs: a combined analysis of two Meishan × Large White populations. *Animal Genetics* 39(5): 486-95.

2. ***Guo Y. -M.***, Mao H. -R., Ren J., Yan X. -M., Duan Y. -Y., Yang G. -C., Ren D. -R., Zhang Z. -Y., Yang B., Ouyang J., Brenig B., Haley C. S., Huang L. -S. (2009) A linkage map of the porcine genome from a large scale White Duroc × Erhualian resource population and evaluation of factors affecting recombination rates. *Animal Genetics* 40(1): 47-52.

3. Mao H. -R.*, ***Guo Y. -M.****, Yang G. -C., Yang B., Ren J., Liu S. -F., Ai H. -S., Ma J. -W., Brenig B., Huang L. -S. (2008) A Genome-wide scan for quantitative trait loci affecting limb bone lengths and areal bone mineral density of the distal femur in a large White Duroc × Erhualian F_2 population. *BMC Genetics* 9: 63.

4. ***Guo Y. -M.***, Ai H. -S., Ren J., Wang G. -J., Wen Y., Mao H. -R., Lan L. -T., Ma J. -W., Brenig B., Rothschild M. F., Haley C. S., Huang L. -S. (2009) A whole genome scanning for quantitative trait loci for leg weakness and its related traits in a large F_2 intercross population between White Duroc and Erhualian. *Journal of Animal Science* (Accepted).

Abstract

A linkage map comprising 194 microsatellite markers across the pig genome was constructed with a large scale White Duroc × Erhualian resource population. The marker order on this linkage map was consistent with the USDA-MARC reference map except for 2 markers on pig chromosome (SSC) 3, 2 markers on SSC13 and 2 markers on the X chromosome. The length of the sex-average map (2,344.7 cM) was nearly the same as those of the USDA-MARC and the NIAI maps. A highly significant heterogeneity in recombination rates between sexes was observed. The female autosomes had higher average recombination rates than the male autosomes except for SSC1 and SSC13. However, recombination rates in the pseudoautosomal region were greater in males than in females. These observations are consistent with the previous reports. The recombination events on each paternal and maternal chromosome of F_2 animals were also inferred by SimWalk2. Recombination rates were not significantly affected by the age (in the unit of day) and the parity of F_1 animals. However, the recombination rates on the paternal chromosomes were affected by the mating season of F_1 animals. This could represent an effect of environmental temperature on spermatogenesis.

To detect quantitative trait loci (QTL) for leg weakness in pigs, a total of 1,484 F_2 pigs were recorded for their leg scores (at 76 d and 213 d) and gait scores (at 153 d and 223 d) in the White Duroc × Erhualian resource population. Moreover, the lengths of the limb bones, the areal mineral density of the femoral bone (aBMD) and the length and the weight of the *biceps brachii* muscle were recorded after these F_2 animals were harvested at 240 d. A whole genome scan was performed with 194 microsatellite markers in the resource population to identify QTL for these traits. A total of 79 QTL were detected, including 35 at the 1% genome-wide significant level and 9 at the 5% genome-wide significant level. Seventy-two of the 79 QTL showed significant additive effects and 20 of the 79 QTL had significant dominance effects.

At least two QTL were detected for each trait except for the leg score at 76 d, for which no QTL was identified. Some of QTL for leg scores, gait scores and lime bone lengths confirmed previous findings. Eighteen QTL for the weight and the length of the *biceps brachii* muscle and two QTL for the aBMD were detected in present study. To our knowledge, this was the first report about QTL for the three traits in pigs. Two chromosome regions each on SSC4 and SSC7 showed significant and multiple associations with leg weakness and the growth of the *biceps brachii* muscle and the lime bones, which are worthwhile for further investigation.

Combined analysis of data from two or more resource populations can improve the power and accuracy of QTL mapping and allow some cross-validation of results. In this study, we performed a genome-wide scan using combined data from two F_2 populations derived from a cross between Large White and Chinese Meishan pigs. A total of 739 pigs were included in the analysis. In total 187 markers were genotyped in the two populations, including 115 markers genotyped in both populations, and these markers covered 2,282 cM of the pig genome with an average of 13.58 cM between adjacent markers. Seven traits (teat number, birth weight, weaning weight, test-end weight, fat depth at shoulder, fat depth at mid back and fat depth at loin) were analyzed for both individual populations and the combined population. There were 9 (2, 10), 1 (4, 4) and 14 (5, 18) QTL that achieved 1% genome-wide, 5% genome-wide and suggestive significance levels, respectively, in population 1 (population 2, combined population). Additive effects of QTL detected in the two populations at all significance levels were largely consistent suggesting that the QTL represent real genetic effects, but this was not the case for dominance or imprinting effects. There were also a number of significant interactions between detected QTL effects and population.

Abbreviations

aBMD	areal bone mineral density
AIL	advanced intercross lines
BMD	bone mineral density
C_a	additive coefficient
C_d	dominance coefficient
$CI_{0.95}$	95% confidence interval
cM	Centimorgan
DXA	dual energy X-ray absorptiometry
FGS	gait score of front legs
FLS	front leg score
IGF2	insulin-like growth factor 2
LOD	likelihood of odds
LR	likelihood ratio
MARC	Meat Animal Research Center
ML	maximum likelihood
NIAI	National Institute of Animal Industry of Japan
PiGMaP	European Pig Gene Mapping Project Consortium
PRKAG3	protein kinase AMP-activated gamma 3
QTL	quantitative trait locus
RFLP	restriction fragment length polymorphism
RGS	gait score of rear legs
RLS	rear leg score
SAS	Statistics Analysis System
SNP	single nucleotide polymorphism
SSC	*Sus scrofa* chromosome
USDA	United States Department of Agriculture

1

General Introduction

1.1 Introduction

Pork is the most popular meat in the world, and occupies 43% of red meat market in the world (Rothschild and Ruvinsky, 1998). As an animal domesticated over 7,000 years ago and a kind of very important agricultural livestock, pigs have undergone artificial selections in the history. In recent decades, the artificial selections imposed on pigs became more intensive, and some economical traits of the pig, such as average daily gain (ADG) and backfat thickness, have got a substantial improvement. However, artificial selections for production traits have adverse effects on leg structures, and poor leg structures cause leg weakness (Lee *et al*., 2003). Leg weakness or leg soundness disorder becomes more popular and has resulted in huge economical loss in the pig industry (Rothschild and Christian, 1988). Leg weakness can be evaluated with leg scores and gait scores, and is related with the weight and the length of the *biceps brachii* muscle and the length and the mineral density (BMD) of limb bones (Draper *et al*., 1991), but the genetic architecture of leg weakness is still poorly understood.

Combined analysis of data from two or more resource populations can improve the power and accuracy of quantitative trait locus (QTL) mapping and allow some cross-validation of results. But just few joint analyses of specific chromosomes have been reported (Walling *et al.*, 2000; Kim *et al.*, 2005; Pérez-Enciso *et al.*, 2005).

In the present study, a three-generation population was developed by a cross between two White Duroc boars and 19 Erhualian sows at Jiangxi Agricultural University (Ren *et al*., 2006). The lengths of limb bones, the weight and the length of the *biceps brachii* muscle, leg scores and gait scores of the F_2 animals were recorded. A total of 194 microsatellite markers were genotyped and a linkage map was constructed. The effects of some environmental factors including sex and season on

recombination ratios were also investigated. Furthermore, a whole genome scan was performed to identify QTL for leg weakness and its related traits. Finally, to evaluate the merits of the joint data QTL analysis, a genome-wide scan was performed using combined data from two F_2 populations derived from a cross between Large White and Chinese Meishan pigs.

1.2 Linkage maps of pig

Linkage map, also called genetic map, is the fundament of the QTL mapping, and a lot of efforts have been devoted to construct and extend the swine linkage map in the recent decades. Until now, four linkage maps have been reported, and more than 3,000 genetic markers have been assigned on the swine genome. The four genetic maps are the Meat Animal Research Center of United States Department of Agriculture (USDA-MARC) map (Rohrer *et al*., 1994; Rohrer *et al*., 1996), the European Pig Gene Mapping Project consortium (PiGMaP) map (Archibald *et al*., 1992; Archibald *et al*., 1995), the Scandinavian map (Ellegren *et al*., 1994; Marklund *et al*., 1996) and the National Institute of Animal Industry of Japan (NIAI) map (Mikawa *et al*., 1999). On these linkage maps, most of the common markers have the same order except for few closely linked markers having different orders. But the distances between adjacent markers are more variable than the order, which might be caused by the small population size (the number of F_2 animals varying from 94 to 200 in the four reference populations). To improve the swine linkage map, a large scale experimental population with more informative meioses is required (Rohrer *et al*., 1996).

1.2.1 The factors affecting the linkage maps

It has been reported that recombination occurs unevenly across chromosomes, and their occurrences are also influenced by several other factors, such as sex, age of the animal producing the gamete and environmental temperature (Morgan *et al*., 1925; Simchen and Stamberg, 1969).

1.2.1.1 Sex

Sex has remarkably significant effects on recombination frequency in a number of species, such as human, cattle, horse, dog, chicken (Dunn and Bennett, 1967; Callan and Perry, 1977; Andersson and Sandberg, 1984; Broman *et al*., 1998; Groenen *et al*., 1998; Neff *et al*., 1999). The general tendency for recombination is less frequent in the heterogametic sex. Pig is not an exception; the recombination of the female is greater than that of the male in most chromosomal regions (Archibald *et al*., 1995; Marklund *et al*., 1996; Rohrer *et al*., 1996; Mikawa *et al*., 1999).

The average ratios of the recombination rates between females and males were 1.402, 1.545 and 1.303 in the Scandinavian, the NIAI and the PiGMaP maps, respectively. The USDA-MARC map did not consider the different recombination rates between sexes because the population size was too small to get a reliable estimate. On the four reported maps, linkage maps of all chromosomes were longer in females than in males except for few chromosomes. On the NIAI and the PigMap maps, although females had higher recombination rates at both ends of SSC1, they had lower recombination rate in the *SW781-SW974* region, which ultimately caused the male linkage map to be longer than the female (Figure 1). Besides SSC1, the linkage maps of SSC2, SSC9, SSC13 and SSC14 were also longer in males than in females on the PigMap map. On the Scandinavian map, only the linkage map of SSC13 was longer in males than in females.

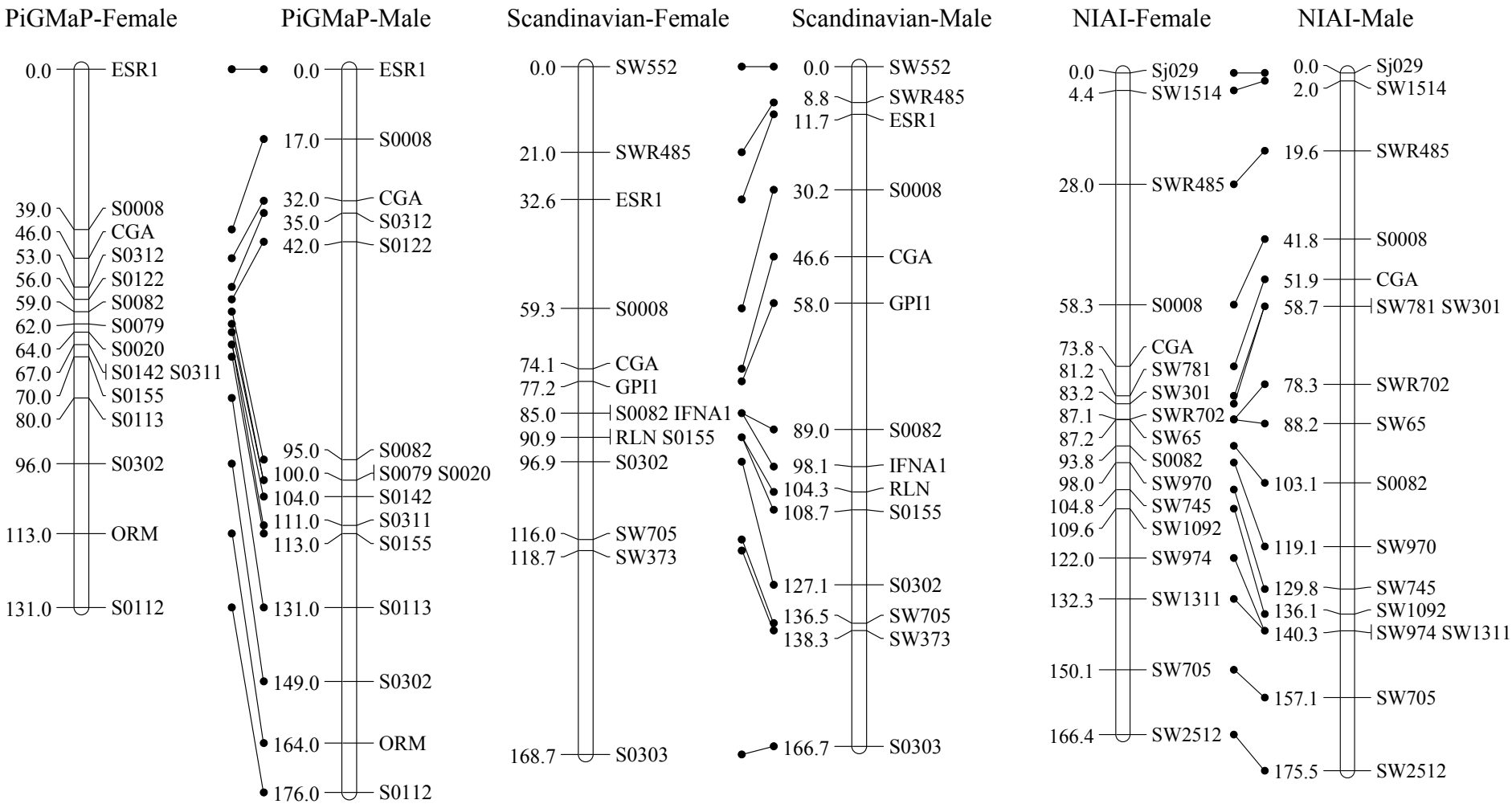

Figure 1 The sex-specific linkage maps of SSC1 from the PiGMaP, the Scandinavian and the NIAI maps.

1.2.1.2 Age of the animal producing the gamete

The age of the animal producing the gamete is another factor affecting the recombination. Bridges reported as early as 1915 that crossing over in *Drosophila* varied with the age of the mother, which was confirmed later (Redfield, 1966). In *C. elegans*, recombination frequency varied with the maternal age (Rose and Baillie 1979). In humans, some studies also indicated that the recombination was related with age (Weitkamp, 1973), but it was not confirmed in other studies (Renwick and Schulze 1965; Weitkamp *et al*., 1973; Lange *et al*., 1975; Elston *et al*., 1976). There was no significant evidence of an age effect in the horse (Andersson and Sandberg, 1984).

1.2.1.3 Environmental temperature

The environmental temperature also has an influence on the recombination rate. In *C. elegans*, recombination frequency was increased two times when the ambient temperature increased from 13.5 °C to 26 °C in some regions on linkage groups *I* and *V* (Rose and Baillie, 1979). Temperature shock treatments at 0 °C and 37 °C usually increased recombination frequency in *Drosophila* (Grushko *et al*., 1991). In *Coprinus lagopus*, both descending and ascending temperature could increase the recombination frequency (Lu, 1974). The increased recombination frequency by low temperature might be attributable to the increased duration of pachytene, because the recombination frequency is a function of the duration of pachytene. The longer the homologous chromosomes are holding together, the higher is the recombination frequency (Lu, 1974).

1.2.1.4 Genes

The recombination rate can be influenced by genetic variation (Simchen and Stamberg, 1969; Maynard Smith, 1978). Domesticated animals are different from

natural populations for having unusually high chiasmata counts (Burt and Bell, 1987). In *C. elegans*, a recessive mutation (rec-1) can expand map distances across the gene cluster and contract map distances near the right end of the chromosome *I* (Zetka and Rose, 1995)

1.2.1.5 Location on the chromosome

Short chromosomal arms have higher recombination rates than long arms, and recombination rates are more frequent in telomeric regions than in pericentric regions (Marklund *et al*., 1996; Rohrer *et al*., 1996).

1.2.2 The length of the swine linkage map

The estimated length of the sex-average linkage map was 2,470 cM on the USDA-MARC map (Rohrer *et al*., 1996), 2,500 cM on the Scandinavian map (Marklund *et al*., 1996), and 2,561.9 cM on the NIAI map (Mikawa *et al*., 1999). Considering that the NIAI map extended the USDA-MARC map about 48.5 cM at the ends of SSC1, SSC5, SSC11 and SSCX, the sizes of these three maps have no significant difference, and 2,500 cM is possible the best estimated length. The PiGMaP map did not cover the whole genome, so the reported 1,800 cM on this map obviously underestimated the length of the sex-average linkage map (Archibald *et al*., 1995). The lengths of male-specific (female-specific) linkage maps were 1,931.3 (2,984) cM, 1,650 (2,150) cM and 1,830 (2,565) cM in NIAI, PiGMaP and Scandinavian maps, respectively (Archibald *et al*., 1995; Marklund *et al*., 1996; Mikawa *et al*., 1999).

1.3 QTL mapping

Mapping of QTL is the first step of positional cloning and position candidate gene approach. Following the first study of QTL mapping in pigs in 1994 (Andersson *et al*., 1994), a number of QTL studies have been carried out (Rothschild *et al*., 1995; Knott *et al*., 1998; Lee *et al*., 2003; Ren *et al*., 2006). So far a total of 1,831 QTL across the pig genome have been recorded in the pig QTL database (PigQTLdb: http://www.animalgenome.org/QTLdb/pig.html). Studies of QTL mapping have contributed to the identification of some economically important genes in pigs, such as the protein kinase AMP-activated gamma 3 gene (*PRKAG3*) (Milan *et al*., 2000) and the insulin-like growth factor 2 gene (*IGF2*) (Van Laere *et al*., 2003).

1.3.1 Resource family

A specific experimental population, namely resource family, is required for QTL mapping. Resource families include backcross populations, F_2 (the second filial generation) populations, advanced intercross lines (AIL) and other complex populations.

1.3.1.1 Backcross population

To produce a backcross population, two parental lines cross each other to produce the first filial generation (F_1), and then F_1 animals mate with the animals from the parental lines to generate the backcross population. In a backcross population, the segregation and recombination events of each backcross animal can be traced only in one gamete (the male or the female F_1 gamete). But in an F_2 population, they can be traced in both gametes (the male and the female F_1 gametes). At the same population size, backcross populations have less statistic power than F_2 populations and are gradually replaced by F_2 populations.

1.3.1.2 F_2 population

The first step to produce an F_2 population is the same as that for the development of a backcross population, but the second step is different. Instead of mating to the paternal lines, F_1 individuals intercross to get F_2 animals. The F_2 population is widely used in QTL mapping now, because they are more powerful than other populations (Knott *et al*., 1998; de Koning *et al*., 2001; Ren *et al*., 2006).

1.3.1.3 Advanced intercross lines

Advanced intercross lines (AIL) are based on F_2 populations. The F_2 population keeps randomly and sequentially intercrossing for *n* generations, resulting in an advanced intercross line (Darvasi and Soller, 1995). Sequentially intercrossing of AIL increases the probability of recombination between loci, so AIL has high resolution of QTL map position. However, construction of AIL is time consuming, especially for livestock with long generation intervals, so AIL populations are not widely engaged in QTL mapping in farm animals. Usually, they are applied in QTL fine mapping in crops or small animals with short generation intervals (Iraqi, 2000; Iraqi *et al*., 2000; Wang *et al*., 2003a; Wang *et al*., 2003b; Balint-Kurti *et al*., 2007).

1.3.1.4 Other complex populations

For the large livestock species, such as dairy cattle, the experimental populations described above are impractical for establishment because of the cost and the time consumption. The natural populations from farms can be applied in QTL mapping in these species with less statistical power. The half-sib design and the grand-daughter design are two mainly methods used in QTL mapping of dairy cattle (Heyen *et al*., 1999; Bennewitz *et al*., 2003; Mariasegaram *et al*., 2007).

1.3.2 Marker selection

A genetic marker is a segment of DNA with an identifiable physical location on a chromosome and tracable inheritance. A genetic marker can be a gene or a fragment of DNA with unknown function, for example an anonymous marker.

1.3.2.1 Classification of genetic markers

There are four kinds of genetic markers: type I, type II, type III and type IV. A type I marker is a segment of a gene; a type II marker is an anonymous sequence, including restriction fragment length polymorphism (RFLP) and microsatellite; a type III marker is a single nucleotide polymorphism (SNP); and a type IV marker is a copy number variation. The type II marker is widely used in QTL mapping because it is more polymorphic than the others. The type III marker is usually applied in the QTL fine mapping for its abundance in the genome.

1.3.2.2 Criterion of maker selection

Marker selection is a key step for QTL mapping. The criteria for the selection of genetic marker are listed below: (1) coverage of the whole swine genome at an interval of 20 to 30 cM; (2) informative in the population; (3) ease to genotype; (4) usage in other studies (Lee *et al*., 2003).

1.3.3 Information content and segregation distortion

Information content and segregation distortion are two factors reflecting the quality of the genotype data. In general, information content is increasing with the increment of the marker's polymorphism, and segregation distortion is decreasing with the enhancement of the accuracy of the marker's genotypes.

1.3.3.1 Information content

Information content indicates how much information that marker can provide at any location on the genome. If the location is full informative for an F_2 animal, then the QTL genotype of the F_2 animal can be known without error. So the additive coefficient (C_a) of the F_2 animal is 1 (when the QTL genotype of this animal is QQ), 0 (Qq or qQ) or -1 (qq), and the dominance coefficient (C_d) is 1 (Qq or qQ) or 0 (QQ or qq). If the location is completely non-informative for an F_2 individual, then all of the probabilities of the QTL genotypes of QQ, Qq, qQ and qq are 0.25, and C_a of the animal is 0 (equal to 0.25 minus 0.25) and C_d is 0.5 (equal to 0.25 plus 0.25). The variance of C_a plus twice the variance of C_d is used to indicate the information content, which varies between 0 and 1.125 (Knott *et al*., 1998).

1.3.3.2 Segregation distortion

There are two kinds of segregation distortion, one is an excess of alleles from either of the original lines and the other is an excess or lack of heterozygotes (Knott *et al*., 1998).

The expected values of C_a and C_d are zero and 0.5 in an F_2 population, respectively. When the alleles from one original line excess those from the other, the population mean of C_a tends to 1 or -1. If the heterozygote is more or less than its expected value, then the population mean of C_d tends to 1 or 0. A *t* test can determine whether a segregation distortion exists at a given location on the genome. The deviations of the population mean of C_a and C_d from their expected values probably arise from the genotypic errors in the data.

1.3.4 QTL analysis method

Two methods are often applied in QTL analyses. One is linear regression and the other is maximum likelihood (ML). The former is easy to extend the linear regression

model and requires few computing time, so it can fix more factors into the model and consider more models (Haley and Knott 1992; Haley *et al*., 1994). The latter uses the full information from the marker-trait distribution, so it is considered more powerful, but it need more computing time (Lander and Botstein, 1989; Jansen and Stam, 1994).

1.3.4.1 Linear regression

The linear regression method has been widely used in QTL mapping (Nii *et al*., 2005; Nii *et al*., 2006; Reiner *et al*., 2007; Edwards *et al*., 2008). This method includes the following four steps.

Firstly, determine the fixed effects and the covariates of the regression models. To enhance the power of the QTL analysis, the fixed effects and covariates should be included into the model to reduce the residual variance.

Secondly, infer the coefficients of the additive, the dominance and/or the imprinting effects at a given point based on the information of flanking markers (Haley and Knott, 1992; Haley *et al*., 1994).

Thirdly, regress these coefficients to the phenotype and estimate the effects of additive, dominance and/or imprinting. Comparing the model with QTL (full model) to the model without QTL (reduce model), if the full model is significantly better than the reduce model, the analysis point probably exists a QTL. In a linkage group, it might be that many test statistics exist that are greater than the threshold value, but only the analysis point with the maximum test statistics is considered as the position of the QTL.

Finally, determine whether the QTL effects exist. It exists if the effect of the QTL is significantly greater than zero. Usually, if the estimate of the effect is more than two times of its standard error, the effect is considered to exist.

1.3.4.2 Maximum likelihood

The maximum likelihood (ML) method had been popular in the QTL mapping in the past (Lander and Botstein, 1989; Jansen and Stam, 1994; Jansen, 1996). But now

it is gradually replaced by the linear regression method.

If there exists a QTL linkage with a marker M (the alternative hypothesis), assuming that the phenotypes of all individuals with QTL genotype Q_k follow a normal distribution with mean of μ_{Qk} and variance of σ^2, then the likelihood for an individual with phenotypic value z and marker genotype M_j at an analysis point is

$$l(z \mid M_j) = \sum_{k=1}^{N} \varphi(z, \mu_{Q_k}, \sigma^2) \Pr(Q_k \mid M_j)$$

where $\varphi(z, \mu_{Q_k}, \sigma^2)$ is the density function for a normal distribution with mean of μ_{Qk} and variance of σ^2, and N is the number of genotype of the QTL. The $\Pr(Q_k|M_j)$ are the probability of Q_k given the marker genotype M_j, and can be calculated provided the genetic map and the genotypes of the markers. The overall likelihood for n F_2 individuals at the analysis point is the product of the individual likelihoods,

$$l(z) = \prod_{i=1}^{n} l(z_i \mid M_i)$$

where n is the number of F_2 individuals, $l(z_i|M_i)$ is the likelihood of the ith individual.

If there doesn't exist a QTL linkage with the markers (the null hypothesis), assuming that the phenotypes of all individuals follow a normal distribution with mean of μ and variance of σ^2, then the likelihood for an individual with phenotypic value z becomes

$$l_N(z \mid M_j) = \varphi(z, \mu, \sigma^2)$$

The overall likelihood for n F_2 individuals is the product of the individual likelihoods,

$$l_N(z) = \prod_{i=1}^{n} l_N(z_i \mid M_i)$$

where n is the number of F_2 individuals, $l_N(z_i|M_i)$ is the likelihood of the ith individual.

After the ML estimation under the null hypothesis and the alternative hypothesis, the likelihood ratio (LR) statistic can be used to test whether a QTL locates at the analysis point. The LR can be obtained from the MLs according to the following

equation,

$$LR = -2\ln\left[\frac{Max\ l_N(z)}{Max\ l(z)}\right]$$

The likelihood ratio follows an approximate chi-square distribution with the degrees of freedom equal to the extra number of parameters fitted in the alternative hypothesis model.

1.3.5 Threshold value

There are a lot of analysis points in the QTL analysis. Each point needs a test, so a large number of tests are performed. Some of them are independent, but the others are not. In order to control false positive results arising from the multiple comparisons, a Bonferroni correction or a permutation approach is often used to adjust the threshold values (Churchill and Doerge, 1994; de Koning *et al*., 2001).

1.3.5.1 Significant level

Four significant levels are widely applied in QTL mapping studies: 5% and 1% chromosome-wide and 5% and 1% genome-wide significant levels. When scanning QTL on a part of the chromosomes, the 5% and 1% chromosome-wide significant levels are often used. While identifying QTL across the whole genome, the 5% and 1% genome-wide significant levels are applied, and the average 5% chromosome-wide threshold is often considered as the suggestive significance level. The 5% and 1% genome-wide threshold values can be obtained directly from genome-wide permutation, and the suggestive threshold value is obtained from the formula: $P_{Genome-wide} = 1-(1-P_{Chromosome-wide})^{1/r}$, where r is the proportion of total genome length attributed to the chromosome (de Koning *et al*., 2001).

1.3.5.2 Bonferroni correction

The Bonferroni correction can be used for multiple dependent tests. Provided that an entire significant level γ is set for the whole experiment with *n* dependent tests, an overall significance level γ requires each individual test based on a significant level of $\alpha = 1-(1-\gamma)^{\frac{1}{n}}$. In QTL analyses, some tests are independent, but the others are not. The number of dependent tests is difficult to obtained, so the Bonferroni correction is not often used in QTL mapping (Lynch and Walsh, 1998).

1.3.5.3 Permutation approach

A more robust method to obtain overall significant threshold value is a permutation approach proposed by Churchill and Doerge (1994). The principle of the method is to generate an empirical distribution of the test statistic under the null hypothesis. Significance thresholds can be determined based on the empirical distribution (Churchill and Doerge, 1994; Doerge and Churchill, 1996). To produce a population under null hypothesis with the original data, the association between the phenotype and the genotype must be removed by randomly reassigning the phenotypic values. Iterating *n* times of the reassignment procedure will generate *n* populations. The values of the test statistic from these populations will give an empirical distribution under the null hypothesis. When *n* is big enough, the empirical distribution of test statistics will be approximate to the true distribution of the test statistic.

1.3.6 95% confidence interval

The location with the maximum value of the test statistic is the point estimate of the QTL position, and the 95% confidence interval ($CI_{0.95}$) is the interval estimate of the QTL position. In QTL mapping, the interval estimate is more important than the

point estimate, because it point out the direction of the study following the QTL study. If the $CI_{0.95}$ is large, a QTL fine mapping is required to narrow it. If it is small enough, the positional cloning or positional candidate gene approach can be followed to dissect the causative gene(s) and mutation(s). There are two ways to construct the $CI_{0.95}$ (Lander and Botstein, 1989; Visscher *et al*., 1996).

1.3.6.1 One-LOD rule

The $CI_{0.95}$ comprises all of locations of which the logarithm of odds (LOD score) are greater than the maximum LOD score minus one. In a large sample, the statistic of likelihood ratio (LR) follows a chi-square distribution. Dropping one LOD score is equal to the LR decrement of 4.61, which corresponds to $P = 0.0318$ for a chi-square distribution with one degree of freedom. So if the degree of freedom of LR statistic is one, one-LOD support interval approximates the $CI_{0.95}$ (Conneally *et al*., 1985; Lander and Botstein, 1989). But in most of QTL mapping studies, the degree of freedom is more than one, so the one-LOD support interval constructs an unconservative confidence interval. Thus, some researchers proposed that a 1.5 or 2-LOD support interval may be a better choice (van Ooijen, 1992; Mangin *et al*., 1994). When the ML method is used to do the QTL analysis, the bootstrap approach is not suitable to set up the $CI_{0.95}$ due to its requirement of computer time, so the one-LOD rule is often used to construct the $CI_{0.95}$ (Lander and Botstein, 1989).

1.3.6.2 Bootstrap approach

The bootstrap approach is one kind of re-sampling method and a very robust and popular procedure for constructing the $CI_{0.95}$ of a QTL position (Visscher *et al*., 1996). Suppose that the original data contain *n* individuals, a bootstrap sample is generated by drawing *n* individuals out of the original data with replacement. So a bootstrap sample contains some of the original values presenting multiple times and some are not present at all. When *N* times of such samples have been drawn, the empirical distribution of the position can be constructed. The $CI_{0.95}$ can easily be determined on

the base of the empirical distribution.

1.3.7 Joint analysis

In most cases, data from different studies were analyzed separately (Andersson *et al*., 1994; Rothschild *et al*., 1995; Knott *et al*., 1998), but in principle, the data can be put together to perform a more powerful combined analysis (Lander and Kruglyak, 1995). Until now, only few combined QTL studies have been reported in farm animals (Walling *et al*., 1998; Walling *et al*., 2000; Bennewitz *et al*., 2003; Lee *et al*., 2003; Kim *et al*., 2005).

1.3.7.1 The advantage and the disadvantage of a joint analysis

A joint analysis can increase the power to detect QTL or confirm the QTL detected only in one population, and improve the accuracy with which QTL parameters are estimated, especially when population sizes were small (Lander and Kruglyak, 1995). Combined analyses also permit testing more highly parameterized or complicated models.

In the other hand, joint analyses also encounter some problems. Different populations will have different founder animals, potentially not from the same breeds, so the QTL genotypes are probably not common in these populations. Furthermore, each population is often reared in a different location, and the traits will be measured with different testing regimes. The genotyped markers are often not the same set across the populations.

Some methods have been proposed to solve these discordant problems among the populations (Walling *et al*., 1998; Walling *et al*., 2000; Bennewitz *et al*., 2003; Lee *et al*., 2003; Kim *et al*., 2005). Firstly, take the population as a fixed effect in the QTL analysis model to correct the environmental effect. Secondly, test the interaction between the QTL and the population. If the interaction is significant, then the QTL probably just exists in a subset of the populations; otherwise the QTL has different

effects in different populations. Thirdly, the phenotypes from each population are separately standardized to a mean of zero and variance of one. The standardization can get rid of the effect of the different testing regimes. Finally, use all of the genotyped markers in the populations; it can make the markers cover the genome as widely as possible.

1.3.7.2 Advance of joint analysis in pigs

Three joint analyses have been reported for specific chromosomes in pigs (Walling *et al*., 2000; Kim *et al*., 2005; Perez-Enciso *et al*., 2005). Walling *et al.* (2000) collected data from almost 3,000 pigs in seven F_2 crosses between Western commercial breeds and either the European wild boar or the Chinese Meishan breed, and scanned chromosome 4 for birth weight, average backfat depth and growth rate from birth to slaughter or end of test. A QTL influencing birth weight found in one population was confirmed by the joint analysis. Kim *et al*. (2005) combined the data from a Berkshire × Yorkshire F_2 population and a Berkshire × Duroc F_2 population, and scanned chromosomes 2, 6, 13 and 18 for 26 traits. The results suggested that the combined analysis using a range of QTL models increased the power of QTL mapping. Pérez-Enciso *et al.* (2005) demonstrated the advantages of a multibreed analysis for analysing the X chromosome with data from five different crosses.

1.3.8 Computer software and program

Ordinary linear regression can be performed with commercial statistic packages, such as Statistics Analysis System (SAS) and Statistical Package for the Social Science (SSPS), but calculation of the coefficients of the additive and the dominance effects in the QTL analysis is required special programs. For ML, it also requires special programs to calculate the probability of each QTL genotype. There are many programs written for QTL analysis. Some of them can be download freely from http://linkage.rockefeller.edu/soft/, such as MAPMAKER/QTL (Lander and

Botstein, 1989) and MAPQTL (van Ooijen and Maliepaard, 1996). And some can be used online without charge, such as QTL Express at http://qtl.cap.ed.ac.uk/ (Seaton *et al*., 2002) and GridQTL at http://www.gridqtl.org.uk/ (Seaton *et al*., 2006).

1.3.8.1 QTL Express

QTL Express is a free online program (http://qtl.cap.ed.ac.uk/), which is widely used in the QTL analysis in pigs (Seaton *et al*., 2002). The statistical approach adopted for QTL analysis in QTL Express is developed by Haley *et al*. (1994). It is a linear regression method as described above. For a cross between outbred lines, it is based on the assumption that the QTL is fixed for alternative alleles in the two founder breeds.

A positive value of the additive effect means that the allele from first line associates with the high numerical value of the trait. Both the dominance and the additive effects are positive or negative, the allele from the first line is dominant; otherwise the allele from second line is dominant. When both the additive and the imprinting effects are positive or negative, the paternal allele expresses; otherwise the maternal allele expresses.

1.4 Leg weakness

Leg weakness is used to describe a poor leg conformation or a clinical condition associated with lameness and stiffness. Leg weakness may occur in any leg at all ages and sexes of pigs. Leg weakness does not affect the daily gain or food conversion efficiency. However, it can restrict the sale and the utility of breeding boars and gilts. Leg weakness increases involuntary culling and results in huge economic loss. It makes 20-50% of otherwise eligible boars completing a performance test to be rejected as breeding animals (Webb *et al*., 1983; Sternbergen, 1989). Genetic

correlations between leg weakness and stayability of breeding sows suggest that a better leg status would decrease involuntary culling (Lopez-Serrano *et al*., 2000).

1.4.1 The factors causing leg weakness

There are many factors resulting in leg weakness in pigs, such as poor leg conformations, bone and joint diseases, nutritional imbalances or deficiencies, hereditary component, space available for exercise and others (Rothschild and Christian, 1988; Lee *et al*., 2003).

1.4.1.1 Poor leg conformation

Leg conformation is definitely the primary determinant of leg weakness. Structures causing leg weakness in pigs include buckling of the knees, bowed legs, splayed legs, uneven toe size, pigeon toes and sickle hocks. A pig with weak legs tends to have straight front and/or rear legs, resulting in an arched back, short strides and unwillingness to move. In comparison, a pig with sound legs usually has a flatter top and higher tail setting.

1.4.1.2 Bone and joint disease

Osteochondrosis, arthritis and osteoporosis are the three most common bone diseases, and also the major underlying causes of leg weakness in pigs (Grondalen, 1974; Hill, 1990a, b; Jorgensen *et al*., 1995; Jørgensen and Andersen, 2000).

Osteochondrosis, also called epiphyseal ischemic necrosis, is relatively common temporary orthopedic disorder, in which the epiphysis (growing end) of a bone dies and then is gradually replaced over a period of years. The immediate cause of bone death is loss of blood supply, so the bone cannot obtain the necessary nutrients for maintaining and endochondral ossification. Osteochondrosis usually occurs in rapidly growing pigs, especially when the growing pigs do not ingest enough of the essential

trace element boron.

Arthritis literally means inflammation of one or more joints. It is a kind of joint disorder characterized by joint stiffness, swelling, redness, and warmth. Arthritis is frequently accompanied by joint pain and limited function of joints, and serious arthritis lead pigs to lose their movement. The causes of arthritis are injury, normal wear and tear, or disease.

Osteoporosis is a silent and painless disease, in which bones lose their normal density and become fragile and more likely to break. Osteoporosis leads to abnormally porous bone that is more compressible like a sponge than dense like a brick. This disorder of the skeleton weakens the bone, leading to an increase of the risk of breaking bones. Fractures, can occur in almost any skeletal bone area, but more often happen in the hip, spine and wrist. Bones that are affected by osteoporosis can fracture with only a minor fall or injury that normally would not cause a bone fracture. The bone mineral density test is the best way to check osteoporosis.

1.4.1.3 Nutritional deficiencies

Normal bones are composed mainly of protein, collagen and calcium. If the intake quantities of these materials are less than the body requires, the bone will be absorbed and osteoporosis will occur. To keep bones strong, the diet must be rich in calcium, protein and vitamin D. Vitamin D significantly improves the absorption of calcium. As mentioned above, the deficiency of the essential trace element boron in rapidly growing pigs will also cause osteochondrosis.

1.4.1.4 Space available for exercise

Appropriate exercise can improve leg soundness of pigs. But the space for pig exercise become limited with the modern confinement rearing systems widely applied in swine industry. The confinement rearing system deprives the possibility for exercise and fuels the prevalence of leg weakness.

1.4.1.5 Genetics

Many reports have supported a hereditary component determining leg weakness, and the heritability of leg weakness is estimated from low to moderate (Reiland *et al*., 1978; Bereskin, 1979; Webb *et al*., 1983; Rothschild and Christian, 1988). A divergent selection experiment for leg weakness also proved that the leg weakness was determined by heredity. After five-generation selection, a line with sound legs and a line with weak legs had been developed (Rothschild and Christian, 1988).

1.4.2 Methods to assess leg weakness

Leg weakness can be assessed in three ways: leg score (LS), gait score (GS) and bone mineral density (BMD).

1.4.2.1 Leg score and gait score

Leg score is used to assess the weakness of the leg conformation and gait score is employed to record the smoothness of the legs' movement. There are two systems to score the leg conformation and the movement as supposed by Rothschild and Christian (1988) and Lee *et al.* (2003), respectively. The first system scores the structure and the movement of the front legs, and the latter assess the structure and the gait of both front legs and rear legs.

Leg score is determined according to the strength of the leg, buckling of the knees, even toe size and the damage and angles of the joints (shoulder angle for front leg and stifle angle for rear leg). Gait score assesses the speed of walking, the ease and the smoothness of leg movement and the steadiness of the body, especially the hindquarters while walking (Rothschild and Christian, 1988; Lee *et al*., 2003). The desirable and undesirable shoulder and stifle angles are shown in Figure 2. The smaller the angles, the more sound the legs are.

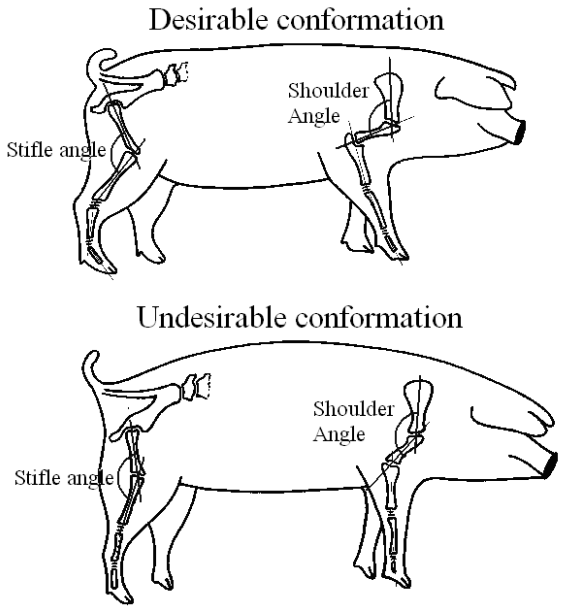

Figure 2 The desirable and the undesirable shoulder and stifle angles in pigs.
(Cited from http://www.thepigsite.cn/pighealth/article/189/leg-weakness with slight modification)

1.4.2.2 Bone mineral density

Bone mineral density is a major determinant of risk for osteoporosis and bone fractures, and BMD screening can be applied in the fracture risk assessment in the pig industry (Dequeker *et al*., 1987; Melton *et al*., 1989; Nielsen *et al*., 2007). With the advance of technologies and the application of new equipments, dual energy X-ray absorptiometry (DXA) can measure BMD accurately, precisely and reliably (Mitchell *et al*., 2000, 2001; Fink *et al*., 2002). Bone mineral density scanning works by measuring the amount of X-rays that are absorbed by the bones. The bone with more mineral density absorbs more X-rays. The two X-ray energies can differentiate the bone density from the soft tissue density, giving a more accurate estimation of BMD.

1.4.3 The known QTL for leg weakness related traits in pigs

To dissect the genes controlling the leg weakness in pigs, genome-wide scanning

for the loci affecting leg weakness and its related traits has been performed. The identified QTL significantly affecting leg weakness and their related traits in different populations are listed in Table 1 (Andersson-Eklund *et al*., 2000; Lee *et al*., 2003).

Table 1 QTL for leg weakness and their related traits in different populations

Trait[a]	Population	Chromosome[b]	Favorable allele
Osteochondrosis	Wild boar×Large White	**SSC5**	Wild boar
Osteochondrosis	Wild boar×Large White	SSC13	Wild boar
Gait score	Large White×Meishan	**SSC1**	Large White
Back legs score	Large White×Meishan	SSC1	Large White
Front feet score	Large White×Meishan	SSC1	Large White
Gait score	Large White×Meishan	SSC2	Meishan
Back legs score	Large White×Meishan	SSC3	Large White
Gait score	Large White×Meishan	SSC4	Large White
Gait score	Large White×Meishan	SSC5	Meishan
Physis score	Large White×Meishan	SSC7	Meishan
Gait score	Large White×Meishan	SSC10	Large White
Front feet score	Large White×Meishan	SSC13	Meishan
Front legs score	Large White×Meishan	SSC13	Large White
Front feet score	Large White×Meishan	SSC14	Meishan
Front legs score	Large White×Meishan	SSC14	Large White
Back legs score	Large White×Meishan	SSC14	Large White
Back feet score	Large White×Meishan	SSC15	Large White

[a]. The QTL for osteochondrosis were reported by Andersson-Eklund *et al.* (2000) and the rest were identified by Lee *et al* (2003); [b]. Bold and regular fonts indicate the QTL reaching 5% genome-wide and suggestive significant level, respectively.

1.5 Limb bones and *biceps brachii* muscle

Limb bones and the *biceps brachii* muscle are related with the function of legs. Moderate lengths of limb bones combined with appropriate body length will improve leg soundness of pigs (Wood, 2001). Pigs from leg soundness lines have shorter and lighter *biceps brachii* muscles than those from leg weakness lines (Draper *et al*., 1991).

1.5.1 Limb bones

The lengths of limb bones are generally regarded as a very important parameter to assess the bone growth in pigs, and the growth of limb bones will affect the leg soundness. Dissection of the genes controlling the growth of limb bones in pigs will shed light on the genetics of the leg weakness in pigs.

1.5.1.1 The relationship between limb bone length and other traits

An individual with long limb bones usually has a tall body height or a tall height at shoulder. Previous studies indicate that the height at shoulder is an important parameter in determining the yield of some carcass characteristics in pigs, such as the yield of ham, loin, picnic shoulder and shoulder butt (Hetzer *et al*., 1950; Hetzer and Miller, 1972). It has been shown that visual selection for moderate length of the leg combined with appropriate body length in boars and gilts can improve structural soundness and decrease the economic loss resulting from structural unsoundness for producers (Wood, 2001).

1.5.1.2 Bone growth

Longitudinal growth of the skeleton occurs through the action of chondrocytes in the proliferative and hypertrophic zones of the growth plate (Karsenty and Wagner,

2002). A long bone, such as the femur (thigh bone), grows in length at both ends in regions called epiphyseal plates (growth plates). Growth occurs when cartilage cells divide and increase in number in these growth plates. When cartilage cells become older, they will change into larger cartilage cells and will be towards the middle of a bone. Finally, these older cartilage cells die and the space they occupied is replaced with bone. Long bone growth comes to an end around the end of puberty, at that time the growth plates of bone are completely ossified.

Bone growth is under the influence of the intake quantity of protein, calcium and vitamin D. Deficiency of these nutriments will impede the growth of bone. Some other growth factors are also required for bone growth (Mitchell *et al*., 2001). Furthermore, bone growth is regulated by growth hormone from the anterior pituitary gland and sex hormones from ovaries or testes.

1.5.1.3 Advance of QTL mapping for limb bone length

To my knowledge, so far, just one QTL study on limb bone length has been reported in pigs. Only one 5% genome-wide QTL and three suggestive QTL for femur dimensions were detected in pigs, which are located on SSC17, SSC2, SSC4 and SSC16, respectively (Andersson-Eklund *et al*., 2000).

1.5.2 *Biceps brachii* muscle

Biceps brachii muscle, as an important movement muscle, affects the front leg soundness. It was reported that both the weight and the length of *biceps brachii* muscle were significantly greater in leg weakness lines than in normal and leg soundness lines (Draper *et al*., 1991). No QTL study of *biceps brachii* muscle has been reported until now.

1.5.2.1 Types of muscle

There are three types of muscle (skeletal, cardiac and smooth muscle) in animals. Skeletal muscle is striated and voluntary; cardiac muscle is striated and involuntary; smooth muscle is non striated and involuntary. Skeletal muscles are attached to the bones through tendons, and their contraction gives rise to the body's movement. *Biceps brachii* muscle is a tubular skeletal muscle located in the front legs, and its weight and length will affect the function of front legs.

1.5.2.2 Relationship between the weight and the length of brachial muscle and leg weakness

Both the weight and length of *biceps brachii* muscle are significantly greater ($P < 0.05$ and $P < 0.01$, respectively) in leg weakness than in normal or leg soundness lines. But the weights and lengths of other brachial muscles show no differences between these lines except for the *tensor fascia antibrachii*, which is significantly longer ($P < 0.01$) in the leg weakness than in normal or soundness lines (Draper *et al*., 1991). *Biceps brachii* muscle is the most important brachial muscle that affects the front leg soundness. With the increase of the weight and length of *biceps brachii* muscle the front legs become weaker.

1.6 References

Andersson-Eklund L., Uhlhorn H., Lundeheim N., Dalin G. and Andersson L. (2000) Mapping quantitative trait loci for principal components of bone measurements and osteochondrosis scores in a wild boar × large white intercross. *Genet Res* **75**, 223-30.

Andersson L., Haley C.S., Ellegren H., Knott S.A., Johansson M., Andersson K.,

Andersson-Eklund L., Edfors-Lilja I., Fredholm M., Hansson I., Håkansson J. and Lundström K. (1994) Genetic mapping of quantitative trait loci for growth and fatness in pigs. *Science* **263**, 1771-4.

Andersson L. and Sandberg K. (1984) Genetic linkage in the horse. II. Distribution of male recombination estimates and the influence of age, breed and sex on recombination frequency. *Genetics* **106**, 109-22.

Archibald A.L., Brown J.F., Haley C.S., Fredholm M., Wintero A.K., Coppieters W., Van de Weghe A., Signer E., Larsen N.J., Nielsen V.H., Johansson M. and Andersson L. (1992) Linkage mapping in the domestic pig (Sus scrofa). *Anim Genet* **23**, 88.

Archibald A.L., Haley C.S., Brown J.F., Couperwhite S., McQueen H.A., Nicholson D., Coppieters W., Van de Weghe A., Stratil A., Winterø A.K., Fredholm M., Larsen N.J., Nielsen V.H., Milan D., Woloszyn N., Robic A., Dalens M., Riquet J., Gellin J., Caritez J.-C., Burgaud G., Ollivier L., Bidanel J.-P., Vaiman M., Renard C., Geldermann H., Davoli R., Ruyter D., Verstege E.J.M., Groenen M.A.M., Davies W., Høyheim B., Keiserud A., Andersson L., Ellegren H., Johansson M., Marklund L., Miller J.R., Anderson Dear D.V., Signer E., Jeffreys A.J., Moran C., Le Tissier P., Muladno, Rothschild M.F., Tuggle C.K., Vaske D., Helm J., Liu H.-C., Rahman A., Yu T.-P., Larson R.G. and Schmitz C.B. (1995) The PiGMaP consortium linkage map of the pig (Sus scrofa). *Mamm Genome* **6**, 157-75.

Balint-Kurti P.J., Zwonitzer J.C., Wisser R.J., Carson M.L., Oropeza-Rosas M.A., Holland J.B. and Szalma S.J. (2007) Precise mapping of quantitative trait loci for resistance to southern leaf blight, caused by Cochliobolus heterostrophus race O, and flowering time using advanced intercross maize lines. *Genetics* **176**, 645-57.

Bennewitz J., Reinsch N., Grohs C., Leveziel H., Malafosse A., Thomsen H., Xu N., Looft C., Kuhn C., Brockmann G.A., Schwerin M., Weimann C., Hiendleder S., Erhardt G., Medjugorac I., Russ I., Forster M., Brenig B., Reinhardt F., Reents R., Averdunk G., Blumel J., Boichard D. and Kalm E. (2003)

Combined analysis of data from two granddaughter designs: A simple strategy for QTL confirmation and increasing experimental power in dairy cattle. *Genet Sel Evol* **35**, 319-38.

Bereskin B. (1979) Genetic aspects of feet and leg soundness in swine. *J Anim Sci* **48**, 1322-28.

Bridges C.B. (1915) A linkage variation in *Drosophila*. *J. Exp. Zool.* **19**, 1-21.

Broman K.W., Murray J.C., Sheffield V.C., White R.L. and Weber J.L. (1998) Comprehensive human genetic maps: individual and sex-specific variation in recombination. *Am J Hum Genet* **63**, 861-9.

Burt A. and Bell G. (1987) Mammalian chiasma frequencies as a test of two theories of recombination. *Nature* **326**, 803-5.

Callan H.G. and Perry P.E. (1977) Recombination in male and female meiocytes contrasted. *Philos Trans R Soc Lond B Biol Sci* **277**, 227-33.

Churchill G.A. and Doerge R.W. (1994) Empirical threshold values for quantitative trait mapping. *Genetics* **138**, 963-71.

Conneally P.M., Edwards J.H., Kidd K.K., Lalouel J.M., Morton N.E., Ott J. and White R. (1985) Report of the Committee on Methods of Linkage Analysis and Reporting. *Cytogenet Cell Genet* **40**, 356-9.

Darvasi A. and Soller M. (1995) Advanced intercross lines, an experimental population for fine genetic mapping. *Genetics* **141**, 1199-207.

de Koning D.J., Harlizius B., Rattink A.P., Groenen M.A., Brascamp E.W. and van Arendonk J.A. (2001) Detection and characterization of quantitative trait loci for meat quality traits in pigs. *J Anim Sci* **79**, 2812-9.

Dequeker J., Nijs J., Verstraeten A., Geusens P. and Gevers G. (1987) Genetic determinants of bone mineral content at the spine and radius: a twin study. *Bone* **8**, 207-9.

Doerge R.W. and Churchill G.A. (1996) Permutation tests for multiple loci affecting a quantitative character. *Genetics* **142**, 285-94.

Draper D.D., Rothschild M.F. and Christian L.L. (1991) Effects of Divergent Selection for Limb Weakness on Bone and Muscle Cross-Sectional Areas in

Duroc Swine. *American Journal of Veterinary Research* **52**, 164-68.

Dunn L.C. and Bennett D. (1967) Sex differences in recombination of linked genes in animals. *Genet Res* **9**, 211-20.

Edwards D.B., Ernst C.W., Tempelman R.J., Rosa G.J., Raney N.E., Hoge M.D. and Bates R.O. (2008) Quantitative trait loci mapping in an F_2 Duroc × Pietrain resource population: I. Growth traits. *J Anim Sci* **86**, 241-53.

Ellegren H., Chowdhary B.P., Johansson M., Marklund L., Fredholm M., Gustavsson I. and Andersson L. (1994) A primary linkage map of the porcine genome reveals a low rate of genetic recombination. *Genetics* **137**, 1089-100.

Elston R.C., Lange E. and Namboodiri K.K. (1976) Age trends in human chiasma frequencies and recombination fractions. II. Method for analyzing recombination fractions and applications to the ABO: nail-patella linkage. *Am J Hum Genet* **28**, 69-76.

Fink C., Cooper H.J., Huebner J.L., Guilak F. and Kraus V.B. (2002) Precision and accuracy of a transportable dual-energy X-ray absorptiometry unit for bone mineral measurements in guinea pigs. *Calcif Tissue Int* **70**, 164-9.

Groenen M.A., Crooijmans R.P., Veenendaal A., Cheng H.H., Siwek M. and van der Poel J.J. (1998) A comprehensive microsatellite linkage map of the chicken genome. *Genomics* **49**, 265-74.

Grondalen T. (1974) Osteochondrosis, arthrosis and leg weakness in pigs. *Nord Vet Med* **26**, 534-7.

Grushko T.A., Korochkina S.E. and Klimenko V.V. (1991) Temperature control of the crossing-over frequency in Drosophila melanogaster. Effect of infra- and super-optimal shock temperatures in early ontogenesis on the recombination frequency. *Genetika* **27**, 1714-21.

Haley C.S. and Knott S.A. (1992) A simple regression method for mapping quantitative trait loci in line crosses using flanking markers. *Heredity* **69**, 315-24.

Haley C.S., Knott S.A. and Elsen J.M. (1994) Mapping quantitative trait loci in crosses between outbred lines using least squares. *Genetics* **136**, 1195-207.

Hetzer H.O., Hankins O.G., King J.X. and Zeller J.H. (1950) Relationship between certain body measurements and carcass characteristics in swine. *J Anim Sci* **9**, 37-47.

Hetzer H.O. and Miller R.H. (1972) Correlated responses of various body measurements in swine selected for high and low fatness. *J Anim Sci* **35**, 743-51.

Heyen D.W., Weller J.I., Ron M., Band M., Beever J.E., Feldmesser E., Da Y., Wiggans G.R., VanRaden P.M. and Lewin H.A. (1999) A genome scan for QTL influencing milk production and health traits in dairy cattle. *Physiol Genomics* **1**, 165-75.

Hill M.A. (1990a) Causes of degenerative joint disease (osteoarthrosis) and dyschondroplasia (osteochondrosis) in pigs. *J Am Vet Med Assoc* **197**, 107-13.

Hill M.A. (1990b) Economic relevance, diagnosis, and countermeasures for degenerative joint disease (osteoarthrosis) and dyschondroplasia (osteochondrosis) in pigs. *J Am Vet Med Assoc* **197**, 254-9.

Iraqi F. (2000) Fine mapping of quantitative trait loci using advanced intercross lines of mice and positional cloning of the corresponding genes. *Exp Lung Res* **26**, 641-9.

Iraqi F., Clapcott S.J., Kumari P., Haley C.S., Kemp S.J. and Teale A.J. (2000) Fine mapping of trypanosomiasis resistance loci in murine advanced intercross lines. *Mamm Genome* **11**, 645-8.

Jørgensen B. and Andersen S. (2000) Genetic parameters for osteochondrosis in Danish Landrace and Yorkshire boars and correlations with leg weakness and production traits. *Animal Science* **71**, 427-34.

Jansen R.C. (1996) A general Monte Carlo method for mapping multiple quantitative trait loci. *Genetics* **142**, 305-11.

Jansen R.C. and Stam P. (1994) High resolution of quantitative traits into multiple loci via interval mapping. *Genetics* **136**, 1447-55.

Jorgensen B., Arnbjerg J. and Aaslyng M. (1995) Pathological and radiological investigations on osteochondrosis in pigs, associated with leg weakness.

Zentralbl Veterinarmed A **42**, 489-504.

Karsenty G. and Wagner E.F. (2002) Reaching a genetic and molecular understanding of skeletal development. *Dev Cell* **2**, 389-406.

Kim J.J., Rothschild M.F., Beever J., Rodriguez-Zas S. and Dekkers J.C. (2005) Joint analysis of two breed cross populations in pigs to improve detection and characterization of quantitative trait loci. *J Anim Sci* **83**, 1229-40.

Knott S.A., Marklund L., Haley C.S., Andersson K., Davies W., Ellegren H., Fredholm M., Hansson I., Hoyheim B., Lundstrom K., Moller M. and Andersson L. (1998) Multiple marker mapping of quantitative trait loci in a cross between outbred wild boar and large white pigs. *Genetics* **149**, 1069-80.

Lander E. and Kruglyak L. (1995) Genetic dissection of complex traits: guidelines for interpreting and reporting linkage results. *Nat Genet* **11**, 241-7.

Lander E.S. and Botstein D. (1989) Mapping mendelian factors underlying quantitative traits using RFLP linkage maps. *Genetics* **121**, 185-99.

Lange K., Page B.M. and Elston R.C. (1975) Age trends in human chiasma frequencies and recombination fractions. I. Chiasma frequencies. *Am J Hum Genet* **27**, 410-8.

Lee G.J., Archibald A.L., Garth G.B., Law A.S., Nicholson D., Barr A. and Haley C.S. (2003) Detection of quantitative trait loci for locomotion and osteochondrosis related traits in Large White × Meishan pigs. *Anim Sci* **76**, 155-65.

Lopez-Serrano M., Reinsch N., Looft H. and Kalm E. (2000) Genetic correlations of growth, backfat thickness and exterior with stayability in Large White and Landrace sows. *Livest Prod Sci* **64**, 121-31.

Lu B.C. (1974) Genetic Recombination in Coprinus. IV. a Kinetic Study of the Temperature Effect on Recombination Frequency. *Genetics* **78**, 661-77.

Lynch M. and Walsh B. (1998) *Genetics and Analysis of Quantitative Traits*. Sinauer Associates, Sunderland, MA.

Mangin B., Goffinet B. and Rebai A. (1994) Constructing confidence intervals for QTL location. *Genetics* **138**, 1301-8.

Mariasegaram M., Robinson N.A. and Goddard M.E. (2007) Empirical evaluation of

selective DNA pooling to map QTL in dairy cattle using a half-sib design by comparison to individual genotyping and interval mapping. *Genet Sel Evol* **39**, 267-83.

Marklund L., Johansson Moller M., Hoyheim B., Davies W., Fredholm M., Juneja R.K., Mariani P., Coppieters W., Ellegren H. and Andersson L. (1996) A comprehensive linkage map of the pig based on a wild pig-Large White intercross. *Anim Genet* **27**, 255-69.

Maynard Smith J. (1978) *The evolution of sex*. Cambridge University Press, Cambridge.

Melton L.J., 3rd, Kan S.H., Frye M.A., Wahner H.W., O'Fallon W.M. and Riggs B.L. (1989) Epidemiology of vertebral fractures in women. *Am J Epidemiol* **129**, 1000-11.

Mikawa S., Akita T., Hisamatsu N., Inage Y., Ito Y., Kobayashi E., Kusumoto H., Matsumoto T., Mikami H., Minezawa M., Miyake M., Shimanuki S., Sugiyama C., Uchida Y., Wada Y., Yanai S. and Yasue H. (1999) A linkage map of 243 DNA markers in an intercross of Göttingen miniature and Meishan pigs. *Anim Genet* **30**, 407-17.

Milan D., Jeon J.T., Looft C., Amarger V., Robic A., Thelander M., Rogel-Gaillard C., Paul S., Iannuccelli N., Rask L., Ronne H., Lundstrom K., Reinsch N., Gellin J., Kalm E., Roy P.L., Chardon P. and Andersson L. (2000) A mutation in PRKAG3 associated with excess glycogen content in pig skeletal muscle. *Science* **288**, 1248-51.

Mitchell A.D., Scholz A.M. and Pursel V.G. (2000) Dual-energy X-ray absorptiometry measurements of the body composition of pigs of 90- to 130-kilograms body weight. *Ann N Y Acad Sci* **904**, 85-93.

Mitchell A.D., Scholz A.M. and Pursel V.G. (2001) Total body and regional measurements of bone mineral content and bone mineral density in pigs by dual energy X-ray absorptiometry. *J Anim Sci* **79**, 2594-604.

Morgan T.H., Bridges C.B. and Sturtevant A.H. (1925) The genetics of drosophila. *Bibliogr. Genet.* **2**, 1-262.

Neff M.W., Broman K.W., Mellersh C.S., Ray K., Acland G.M., Aguirre G.D., Ziegle J.S., Ostrander E.A. and Rine J. (1999) A second-generation genetic linkage map of the domestic dog, *Canis familiaris*. *Genetics* **151**, 803-20.

Nielsen D.H., McEvoy F.J., Madsen M.T., Jensen J.B. and Svalastoga E. (2007) Relationship between bone strength and dual-energy X-ray absorptiometry measurements in pigs. *J Anim Sci* **85**, 667-72.

Nii M., Hayashi T., Mikawa S., Tani F., Niki A., Mori N., Uchida Y., Fujishima-Kanaya N., Komatsu M. and Awata T. (2005) Quantitative trait loci mapping for meat quality and muscle fiber traits in a Japanese wild boar x Large White intercross. *J Anim Sci* **83**, 308-15.

Nii M., Hayashi T., Tani F., Niki A., Mori N., Fujishima-Kanaya N., Komatsu M., Aikawa K., Awata T. and Mikawa S. (2006) Quantitative trait loci mapping for fatty acid composition traits in perirenal and back fat using a Japanese wild boar x Large White intercross. *Anim Genet* **37**, 342-7.

Perez-Enciso M., Mercade A., Bidanel J.P., Geldermann H., Cepica S., Bartenschlager H., Varona L., Milan D. and Folch J.M. (2005) Large-scale, multibreed, multitrait analyses of quantitative trait loci experiments: the case of porcine X chromosome. *J Anim Sci* **83**, 2289-96.

Redfield H. (1966) Delayed mating and the relationship of recombination to maternal age in Drosophila melanogaster. *Genetics* **53**, 593-607.

Reiland S., Ordell N., Lundeheim N. and Olsson S.E. (1978) Heredity of osteochondrosis, body constitution and leg weakness in the pig. A correlative investigation using progeny testing. *Acta Radiol Suppl* **358**, 123-37.

Reiner G., Kliemt D., Willems H., Berge T., Fischer R., Kohler F., Hepp S., Hertrampf B., Daugschies A., Geldermann H., Mackenstedt U. and Zahner H. (2007) Mapping of quantitative trait loci affecting resistance/susceptibility to Sarcocystis miescheriana in swine. *Genomics* **89**, 638-46.

Ren J., Guo Y.M., Ma J.W. and Huang L.S. (2006) Growth and meat quality QTL in pigs with special reference to a very large Erhualian×White Duroc resource population. In: *8th World Congress on Genetics Applied in Livestock*

Production, Brazil.

Renwick J.H. and Schulze J. (1965) Male and female recombination fractions for the *nailpatella*: *ABO* linkage in man. *Ann. Hum. Genet.* **28**, 379-92.

Rohrer G.A., Alexander L.J., Hu Z., Smith T.P., Keele J.W. and Beattie C.W. (1996) A comprehensive map of the porcine genome. *Genome Res* **6**, 371-91.

Rohrer G.A., Alexander L.J., Keele J.W., Smith T.P. and Beattie C.W. (1994) A microsatellite linkage map of the porcine genome. *Genetics* **136**, 231-45.

Rohrer G.A., Thallman R.M., Shackelford S., Wheeler T. and Koohmaraie M. (2006) A genome scan for loci affecting pork quality in a Duroc-Landrace F population. *Anim Genet* **37**, 17-27.

Rose A.M. and Baillie D.L. (1979) The Effect of Temperature and Parental Age on Recombination and Nondisjunction in *Caenorhabditis Elegans*. *Genetics* **92**, 409-18.

Rothschild M.F. and Christian L.L. (1988) Genetic control of front-leg weakness in Duroc swine. I. Direct response to five generations of divergent selection. *Livest Prod Sci* **19**, 459-71.

Rothschild M.F., Liu H.C., Tuggle C.K., Yu T.P. and Wang L. (1995) Analysis of pig chromosome 7 genetic markers for growth and carcass performance traits. *J Anim Breed Genet* **112**, 341-8.

Rothschild M.F. and Ruvinsky A. (1998) *The Genetic of the Pig*. CAB International, Oxon, UK.

Seaton G., Haley C.S., Knott S.A., Kearsey M. and Visscher P.M. (2002) QTL Express: mapping quantitative trait loci in simple and complex pedigrees. *Bioinformatics* **18**, 339-40.

Seaton G., Hernandez J., Grunchec J.A., White I., Allen J., De Koning D.J., Wei W., Berry D., Haley C.S. and Knott S.A. (2006) GridQTL: A Grid Portal for QTL Mapping of Compute Intensive Datasets. *Proceedings of the 8th World Congress on Genetics Applied to Livestock Production, August 13-18, 2006. Belo Horizonte, Brazil.*

Simchen G. and Stamberg J. (1969) Fine and coarse controls of genetic recombination.

Nature **222**, 329-32.

Sternbergen E.J.v. (1989) Description and evaluation of a linear scoring system for exterior traits in pigs. *Livest Prod Sci* **23**, 163-81.

van Ooijen J.W. (1992) Accuracy of mapping quantitative trait loci in autogamous species. *Theor. Appl. Genet.* **84**, 803-11.

van Ooijen J.W. and Maliepaard C. (1996) MapQTL Version 3.0: Software for the Calculation of QTL Positions on Genetic Maps. *Plant Genome IV (Abs.)*, p105.

Visscher P.M., Thompson R. and Haley C.S. (1996) Confidence intervals in QTL mapping by bootstrapping. *Genetics* **143**, 1013-20.

Walling G.A., Archibald A.L., Cattermole J.A., Downing A.C., Finlayson H.A., Nicholson D., Visscher P.M., Walker C.A. and Haley C.S. (1998) Mapping of quantitative trait loci on porcine chromosome 4. *Anim Genet* **29**, 415-24.

Walling G.A., Visscher P.M., Andersson L., Rothschild M.F., Wang L., Moser G., Groenen M.A., Bidanel J.P., Cepica S., Archibald A.L., Geldermann H., de Koning D.J., Milan D. and Haley C.S. (2000) Combined analyses of data from quantitative trait loci mapping studies. Chromosome 4 effects on porcine growth and fatness. *Genetics* **155**, 1369-78.

Wang M., Lemon W.J., Liu G., Wang Y., Iraqi F.A., Malkinson A.M. and You M. (2003a) Fine mapping and identification of candidate pulmonary adenoma susceptibility 1 genes using advanced intercross lines. *Cancer Res* **63**, 3317-24.

Wang X., Le Roy I., Nicodeme E., Li R., Wagner R., Petros C., Churchill G.A., Harris S., Darvasi A., Kirilovsky J., Roubertoux P.L. and Paigen B. (2003b) Using advanced intercross lines for high-resolution mapping of HDL cholesterol quantitative trait loci. *Genome Res* **13**, 1654-64.

Webb A.J., Russell W.S. and Sales D.I. (1983) Genetics of leg weakness in performance-tested boars. *Animal Production* **36**, 117-30.

Weitkamp L.R. (1973) Human autosomal linkage groups. In: *Proceedings of the 4th International Congress on Human Genetics*, pp. 445-60, Exerpta Medica

International Congress Series.

Weitkamp L.R., van Rood J.J., Thorsby E., Bias W., Fotino M., Lawler S.D., Duausset J., Maryr W.R., Bodmer J., Ward F.E., Seignalet J., Payne R., Kissmeyer-Nielsen F., Gatti R.A., Sachs J.A. and Lamm L.U. (1973) The relation of parental sex and age to reombination in the HL-A system. *Hum. Hered.* **23**, 197-205.

Wood C.M. (2001) Don't Ignore Feet and Leg Soundness in Pigs, Livestock Update. *Animal & Poultry Sciences, VA Tech*.

Zetka M.C. and Rose A.M. (1995) Mutant rec-1 eliminates the meiotic pattern of crossing over in Caenorhabditis elegans. *Genetics* **141**, 1339-49.

2

Quantitative trait loci for production traits in pigs:

a combined analysis of two Meishan × Large White populations

Y.-M. Guo[1, 2, 3], G. J. Lee[1], A. L. Archibald[1], C. S. Haley[1]

[1] *Roslin Institute (Edinburgh), Roslin, Midlothian EH25 9PS, UK*

[2] *Key Laboratory for Animal Biotechnology of Jiangxi Province and the Ministry of Agriculture of China, Jiangxi Agricultural University, Nanchang 330045, China*

[3] *Institute of Veterinary Medicine, Georg-August-University of Göttingen, Burckhardtweg 2, 37077 Göttingen, Germany*

Animal Genetics 39(5): 486-495

3

A linkage map of the porcine genome from a large scale White Duroc × Erhualian resource population and evaluation of factors affecting recombination rates

Yuanmei Guo[1,2,3], Huirong Mao[1], Jun Ren[1], Xueming Yan[1], Yanyu Duan[1], Guangcheng Yang[1], Dongren Ren[1], Zhiyan Zhang[1], Bin Yang[1], Jing Ouyang[1], Bertram Brenig[3], Chris Haley[2,4], Lusheng Huang[1†]

[1] *Key Laboratory for Animal Biotechnology of Jiangxi Province and the Ministry of Agriculture of China, Jiangxi Agricultural University, Nanchang 330045, China*

[2] *Roslin Institute and Royal (Dick) School of Veterinary Studies, University of Edinburgh, Roslin BioCentre, Roslin, Midlothian EH25 9PS, UK*

[3] *Institute of Veterinary Medicine, Georg-August-University of Göttingen, Burckhardtweg 2, 37077 Göttingen, Germany*

[4] *MRC Human Genetics Unit, Western General Hospital, Crew Road, Edinburgh, EH4 2XU*

Animal Genetics 40(1): 47-52

4

A whole genome scanning for quantitative trait loci for leg weakness and its related traits in a large F_2 intercross population between White Duroc and Erhualian

Y. M. Guo[*, †, ‡], H. S. Ai[*], J. Ren[*], G. J. Wang[#], Y. Wen[*], H. R. Mao[*], L. T. Lan[*], J. W. Ma[*], B. Brenig[†], M. F. Rothschild[§], C.S. Haley[‡], L. S. Huang[*]

[*] *Key Laboratory for Animal Biotechnology of Jiangxi Province and the Ministry of Agriculture of China, Jiangxi Agricultural University, Nanchang 330045, China*

[†] *Institute of Veterinary Medicine, Georg-August-University of Göttingen, Burckhardtweg 2, 37077 Göttingen, Germany*

[‡] *Roslin Institute and Royal (Dick) School of Veterinary Studies, University of Edinburgh, Roslin BioCentre, Roslin, Midlothian EH25 9PS, UK*

[§] *Department of Animal Science, Center for Integrated Animal Genomics, 2255 Kildee Hall, Iowa State University Ames, Iowa 50011-3150, USA*

[#] *PIC China, Xin'an Mansion, 99 Tian Zhou Road, Shanghai 200233, China*

Accepted by *Journal of Animal Science*

5

A genome-wide scan for quantitative trait loci affecting limb bone lengths and areal bone mineral density of the distal femur in a large White Duroc × Erhualian F_2 population

Huirong Mao[1†], **Yuanmei Guo**[1, 2†], Guangcheng Yang[1], Bin Yang[1], Jun Ren[1], Sanfeng Liu[1], Huashui Ai[1], Junwu Ma[1], Bertram Brenig[2], Lusheng Huang[1*]

[1] *Key Laboratory for Animal Biotechnology of Jiangxi Province and the Ministry of Agriculture of China, Jiangxi Agricultural University, Nanchang 330045, China*

[2] *Institute of Veterinary Medicine, Georg-August-University of Göttingen, Burckhardtweg 2, 37077 Göttingen, Germany*

† These authors have the same contribution to the paper

BMC Genetics 9: 63

Acknowledgements

I sincerely appreciate my dissertation director Prof. Dr. Dr. Bertram Brenig and the two co-directors of the dissertation Prof. Dr. Dr. Chris Haley and Prof. Dr. Dr. Lusheng Huang. Their supervisions and advice in the last four years led me to the success of completion my PhD degree at the Faculty of Agriculture Sciences, Georg-August-University of Göttingen. I am very grateful to Dr. Dirk-Jan de Koning, Dr. Wenhua Wei, Dr. Yinhua Huang, Dr. Monique Germerodt and Mr. Yuyun Xing for their helps when I studied in Roslin Institute and Göttingen. I also want express my appreciation to Dr. Jun Ren for his review of the thesis.

I acknowledge my friends and colleagues at Jiangxi Agricultural University in my home country, Mrs. Jun Gao, Lihua Zhou and Lin Li, and Mr. Nengshui Ding, Huashui Ai, Congyin Chen and Junwu Ma for their encouragements and their helps during the last four years.

I wish to give my sincere gratitude to all the other colleagues in Roslin Institute, Göttingen and Jiangxi Agricultural University whom I didn't listed in detail for their kindly helps in my dissertation.

Finally I would appreciate my family for their endless supports and encouragements. Without their supports and encouragements, I couldn't finish this dissertation.

List of Publications

1. Chen C.-Y., Gilbert C.L., Yang G.-C., **Guo Y.-M.**, Segonds-Pichon A., Ma J.-W., Brenig B., Sargent C., Affara N. and Huang L.-S. (2008) Maternal infanticide in sows: Incidence and behavioural comparisons between savaging and non-savaging sows at parturition. *Appl Animl Behav Sci*. 109: 238-48.

2. Chen R.-R., Day A.E., Ren J., Chen C.-Y., Ai H.-S., Ding N.-S., Ma J.-W., **Guo Y.-M.**, Siggens K.W., Harvey K.M., Evans G.J. and Huang L.-S. (2005) Characterization of three SNPs and localization of the porcine sperm adhesion molecule (SPAM1) gene to chromosome 18 by radiation hybrid mapping. *Anim Genet* **36**, 273-5.

3. Chistiakov D. A., Tsigenopoulos C. S., Lagnel J., **Guo Y.-M.**, Hellemans B., Haley C. S., Volckaert F. A. M. and Kotoulas G. (2008) A combined AFLP and microsatellite linkage map and pilot comparative genomic analysis of European sea bass *Dicentrarchus labrax* L. *Anim Genet* 39(6): 623-34.

5. **Guo Y.-M.**, Lee G. J., Archibald A. L. and Haley C. S. (2008) Quantitative trait loci for production traits in pigs: a combined analysis of two Meishan × Large White populations. *Anim Genet* 39(5): 486-95.

6. **Guo Y. -M.**, Mao H. -R., Ren J., Yan X. -M., Duan Y. -Y., Yang G. -C., Ren D. -R., Zhang Z. -Y., Yang B., Ouyang J., Brenig B., Haley C. S. and Huang L. -S. (2009) A linkage map of the porcine genome from a large scale White Duroc × Erhualian resource population and evaluation of factors affecting recombination rates. *Anim Genet* 40(1): 47-52.

7. Huang L.-S., Ma J.-W., Ren J., Ding N.-S., **Guo Y.-M.**, Ai H.-S., Li L., Zhou L.-H. and Chen C.-Y. (2004) Genetic variations of the porcine PRKAG3 gene in Chinese indigenous pig breeds. *Genet Sel Evol* **36**, 481-6.

8. Lai F.-J., Ren J., Ai H.-S., Ding N.-S., Ma J.-W., Zeng D.-Q., Chen C.-Y., **Guo Y.-M.** and Huang L.-S. (2007) Chinese White Rongchang Pig Does Not Have the Dominant White Allele of KIT but Has the Dominant Black Allele of MC1R. *J Hered* **98**, 84-7.

9. Li S.-J., Ren J., Yang G.-C., **Guo Y.-M.** and Huang L.-S. (2008) Characterization of the porcine Kisspeptins receptor gene and evaluation as candidate for timing of puberty in sows. *J Anim Breed Genet* **125**, 219-27.

10. Mao H.-R.*, **Guo Y.-M.***, Yang G.-C., Yang B., Ren J., Liu S.-F, Ai H.-S, Brenig B. and Huang L.-S. A genome-wide scan for quantitative trait loci affecting limb bone lengths and areal bone mineral density of the distal femur in a White Duroc × Erhualian F_2 population. *BMC Genet*. 2008, 9: 63.

11. Ren D.-R., Ren J., Xing Y.-Y., **Guo Y.-M.**, Wu Y.-B., Yang G.-C., Mao H.-R. and Huang L.-S. (2008) A genome scan for quantitative trait loci affecting male reproductive traits in a White Duroc × Chinese Erhualian resouce population. *J Anim Sci* (Online on July 3, 2008 as doi:10.2527/jas.2008-0923**)**.

12. Ren J., **Guo Y.-M.**, Ma J.-W. and Huang L.-S. (2006) Growth and meat quality QTL in pigs with special reference to a very large Erhualian×White Duroc resource population. In: *8th World Congress on Genetics Applied in Livestock Production*, Brazil.

13. Ren J., Knorr C., **Guo Y.-M.**, Ding N.-S., Ai H.-S., Brenig B. and Huang L.-S. (2004) Characterization of five single nucleotide polymorphisms in the porcine stearoyl-CoA desaturase (SCD) gene. *Anim Genet* **35**, 255-7.

14. Xing Y.-Y., Ren J., Ren D.-R., **Guo Y.-M.**, Wu Y.-B., Yang G.-C., Mao H.-R., Brenig B. and Huang L.-S. Quantitative trait loci for traits related to sperm quality and ejaculation in a White Duroc × Erhualian intercross. *Anim Reprod Sci*. (Online on 8 August 2008, doi: 10.1016/j.anireprosci.2008.08.008).

15. Xu G.-L., Ren J., Ding N.-S., Ai H.-S., **Guo Y.-M.**, Chen C.-Y. and Huang L.-S. (2006) Genetic analysis of the KIT and MC1R genes in Chinese indigenous pigs with belt-like coat color phenotypes. *Anim Genet* **37**, 518-9.

16. Yan X.-M., Ren J., Ai H.-S., Ding N.-S., Gao J., **Guo Y.-M.**, Chen C.-Y., Ma J.-W., Shu Q.-L. and Huang L.-S. (2004) Genetic variations analysis and characterization of the fifth intron of porcine NRAMP1 gene. *Asian Austral J Anim Sci* **17** 1183-87.

17. Yang G.-C., Ren J., **Guo Y.-M.**, Ding N.-S., Chen C.-Y. and Huang L.-S. (2006) Genetic evidence for the origin of an IGF2 quantitative trait nucleotide in Chinese pigs. *Anim Genet* **37**, 179-80.

18. Yang G.-C., Ren J., Li S.-J., Mao H.-R., **Guo Y.-M.**, Zou Z.-Z., Ren D.-R., Ma J.-W. and Huang L.-S. (2008) Genome-wide identification of QTL for age at puberty in gilts using a large intercross F_2 population between White Duroc × Erhualian. *Genet Sel Evol* 40: 529-39.

Curriculum vitae

Surname:	**Yuanmei**
Family name:	**Guo**
Address:	Key Laboratory for Animal Biotechnology of Jiangxi Province and the Ministry of Agriculture of China, Jiangxi Agricultural University (JXAU), Nanchang 330045, China
Tel:	0086-791-3813080, 0086-15879098500
Fax:	0086-791-3900189
E-mail:	gyuanmei@hotmail.com

Personal Data

Date of birth:	August 18, 1974
Place of birth:	Jiangxi, China
Sex:	Male
Marital Status:	Single
Nationality:	Chinese

Education and Professional Experience

July, 2004 - Now	Institute of Veterinary Medicine, University of Göttingen Postgraduate student for Philosophy Doctor Degree Major: Quantitative Genetics and Molecular Biology
January, 2005 – August, 2007	Roslin Institute (Edinburgh), Roslin, Midlothian EH25 9PS, UK Visitor Scholar Major: Quantitative Genetics
September, 2002 – December, 2004	Faculty of Animal Science and Veterinary, JXAU Lecturer Major: Quantitative Genetics
September, 1999 – July, 2002	Faculty of Animal Science and Veterinary, JXAU Postgraduate student for Master of Science degree Major: Quantitative Genetics
September, 1995 – July, 1999	Department of Animal Husbandry and Veterinary, JXAU Undergraduate student for Bachelor of Science degree Major: Animal Husbandry