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From Single Nucleotide Polymorphisms to Phenotypes: Comparative Analysis between Genome Wide Association (GWAS) and Quantitative Trait Loci (QTL) Mapping: A Review Article

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Abstract: This review provided a broad overview of the basic theory, methodology and applications of Genome-Wide Association Studies (GWAS) and Quantitative Trait Loci (QTL) mapping, two cornerstone technologies in plant genetics. This will be combined with an introduction of GWAS and QTL mapping, emphasizing the function of these methods to identify genetic variations underlying plant complex traits. Additionally, we explored the statistical models behind both methods, understanding the science behind regression models, including linear and logistic regression, but also addressing Type I and Type II errors and methods to minimize them, highlighting the keys such as multiple testing correction, replication and functional validation. the review also showed the practical applications of GWAS and QTL mapping in agriculture, crop improvement, livestock breeding and sustainable farming. Examples like flood resistant rice and drought tolerant maize showed the power of these technologies. Finally, the review discussed the challenges and future directions in the agriculture field including the integration of new technologies like CRISPR and high throughput phenotyping.

Keywords: GWAS, QTL, phenotype, complex traits, SNP's, Statistic model.

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Introduction

Genome-Wide Association Studies (GWAS) and Quantitative Trait Loci (QTL) mapping are two of the most powerful genomic tools that have changed plant breeding by allowing us to find the single nucleotide polymorphisms associated with complex traits that complete the phenotype of the organisms. Such of these knowledges consider now essential in modern agriculture applications to understand the genetic makeup of traits like yield, disease resistance, abiotic stress tolerance and nutritional quality. GWAS uses natural genetic variation in diverse populations to find the association between single nucleotide polymorphisms (SNPs) and phenotypic traits, it's very useful in dissecting the genetic basis of complex traits in crops (1). QTL mapping on the

other hand uses controlled crosses and genetic recombination to find the genomic regions that influence quantitative traits, it's the foundation of marker assisted selection (MAS) and precision breeding (2).

Both GWAS and QTL mapping have been tandemly used into plant breeding programs to develop better crop varieties with higher productivity, resilience and nutritional value. For example, GWAS has identified loci for drought tolerance in maize and submergence tolerance in rice, so climate resilient varieties were developed (3,4). QTL mapping has also enabled the introgression of beneficial alleles from wild relatives into cultivated crops, for example, transfer of disease resistance genes from wild tomato species to commercial varieties(2). These have not only improved crop performance but also sustainable agriculture by reducing chemical inputs and increasing resource use efficiency (5).

Despite of their success, there are still challenges in fully utilizing the power of GWAS and QTL mapping. These are the polygenic nature of many traits, understanding genotype by environment interaction and integrating genomic data with emerging technologies like CRISPR/Cas9 gene editing and high throughput phenotyping (6,7). By addressing these challenges GWAS and QTL mapping will continue to be key in addressing global food security and developing next generation crops.

Genome-Wide Association Studies (GWAS)

A Genome-Wide Association Study (GWAS) is a research approach used in genetics to identify associations between genetic variants, typically single nucleotide polymorphisms (SNPs) and specific traits or diseases across the entire genome. By scanning the DNA of large populations number. It's changed the face of genetics by finding thousands of loci for many conditions and giving us insight into the genetic architecture of complex traits(8).

GWAS uses the principle of linkage disequilibrium where genetic variants that are close to each other on a chromosome tend to be inherited together. By comparing the frequency of SNPs between cases (people with a trait or disease) and controls (people without the trait or disease), researchers can identify regions of the genome that might be associated with the trait of interest. The power of GWAS is highly dependent on sample size, bigger is better for detecting true associations and reducing false positives(9).

Since GWAS started, it has found genetic risk factors for many conditions including diabetes, cardiovascular diseases and psychiatric disorders. However, the variants found only explain a small proportion of the heritability, the so called "missing heritability" problem. This has led to ongoing work to improve GWAS methods, incorporate functional genomics data and polygenic risk scores to understand the genetics of complex traits (10).

It is necessary to differentiate between genome-wide selection (GWS) and genome-wide association studies (GWAS) in this idea since they have different uses in genomics. By examining correlations across populations, GWAS finds certain genetic markers (often SNPs) associated with traits, assisting in the discovery of biological processes. GWS, on the other

hand, prioritises useful applications above identifying causative variations by predicting breeding values using all available markers to improve selection efficiency in breeding programmes. GWS seeks to speed up genetic advancement in agriculture, whereas GWAS concentrates on genetic discoveries.

Quantitative Trait Loci (QTL)

QTL analysis is a statistical method to find regions of the genome that are associated with variation in quantitative traits, which are phenotypes that vary continuously and are influenced by many genetic and environmental factors. Mendelian traits are controlled by single genes and have discrete inheritance patterns, whereas quantitative traits like height, weight and susceptibility to complex diseases are polygenic, meaning many genes each with a small effect (11).

QTL mapping involves correlating phenotypic variation in a trait of interest with genetic markers across the genome. This is done in experimental populations, such as crosses between inbred strains of organisms (e.g., plants, animals or model organisms like mice) where the genetic architecture can be controlled and analyzed. By looking at the co-segregation of genetic markers and traits, researchers can find genomic regions that harbour genes for the trait. The resolution of QTL mapping depends on the density of genetic markers and the size of the population studied, more markers and larger population gives higher precision of localization (12).

QTL has been used in agricultural genetics to improve yield, disease resistance and other economically important traits. In medical research QTL has given insights into the genetic basis of complex diseases and traits like blood pressure, cholesterol levels and metabolic disorders. Yet the exact genes that underlie identified QTLs are elusive because the detected QTLs tend to act over broad genomic regions and because of potentially complex gene interactions and regulatory mechanisms (13). Technological advancements in genomics, including high-throughput sequencing and GWAS, have complemented classical QTL mapping, providing higher-resolution visualization of candidate genes and functional variants. QTL data can also be combined with expression profiling and is referred to as eQTL analysis, allowing researchers to establish connections between levels of genetic variation and levels of gene expression to reveal mechanistic bases for phenotypic variation encoded at QTLs(14).

The main difference between GWAS and QTL

Genome Wide Association Surveys (GWAS) and Quantitative Trait Loci (QTL) functions are equally potent inherited approaches used to locate genomic regions related to a trait, yet they differ in their methodologies, uses, and the type of groups they study.

GWAS is applied mainly to human genetics and includes a genome scan of huge, different communities to detect associations among individual nucleotide polymorphisms (SNPs) and other diseases. GWAS confidence in the model of organic biological variation and linkage disequilibrium (LD) in outbred groups, which is well suited to recognizing common discrepancies with small in order to moderate impacts over the complex trait. Nevertheless, GWAS regularly requires very large sample sizes to obtain sufficient statistical

authority and to limit the resolution of LD, which may make it difficult to identify causal discrepancies (8).

Unlike this, QTLs are typically managed in controlled experimental groups, such as crossbreeding between inbred plant, animal, or otherwise model organisms. The QTL map uses heritable recombination during meiosis to locate regions of the genome associated with the Quantitative trait. The present method enables the detection of the same common and uncommon discrepancies, as well as higher resolution when the fine-tuning procedure is performed. Nevertheless, QTL functions are confined to trait and type where control crosse is feasible, and their conclusions may not always be directly applicable to outbred groups such as humans (11).

The essence of trait analysis contains another mandatory disparity. GWAS is commonly used for both binary traits (e.g., disease standing) and quantitative trait, while QTL function is particularly focused on quantitative trait. Moreover, GWAS is more successful in determining common discrepancies, while the QTL map can reveal both common and rare discrepancies, depending on the heritable diversity of the guardian strain used in the cross (13).

In drumhead, they differ in their experimental design, population composition, and intentions during the joint GWAS and QTL map objective to discover the heritable basis of trait. GWAS is well suited to human research and common discrepancies, while QTLs are perfect for controlled experimental settings and can provide understandings of simultaneously common and rare discrepancies.

Models of statistical analysis

At the same time, the Genome-Wide Association Survey (GWAS) and Quantitative Trait Loci (QTL) maps depend on the statistical models to distinguish associations among inherited differences and phenotypic differences. However, the particular model and analytical systems applied in different ways differ due to the specific nature of the analysis group and the objectives of the analysis.

1- GWAS Models

To examining association amongst individual heritable discrepancies (typically SNPs) and trait GWAS, we typically use a linear alternatively logistic arrested development model. For quantitative traits, a linear arrested development model is normally used, where the trait value, Y is modelled as:

$$Y = \mu + \beta X + \epsilon$$

Were μ represents the mean trait value, β is the effect size of the SNP, X and ϵ is the residual error term. For **binary traits** (e.g., disease status), logistic regression is used to model the log-odds of the trait as a function of the SNP:

$$Log\left(\frac{p}{1-P}\right) = \mu + \beta X$$

Where p is the probability of having the trait, and β represents the effect of the SNP on the log-odds scale. To account for population stratification and other confounding factors, GWAS models often include covariates such as principal components or ancestry indicators (15).

2- QTL Mapping Models

On the other hand, the QTL function regularly uses the interval function or the composite time interval function method. The basic interval function model, identical to the Haley-Knott arrested development skeleton, is:

$$Y = \mu + \beta Q + \epsilon$$

Where Y is the trait value, μ is the mean, β is the effect of the QTL Q, and ϵ is the residual error. The QTL effect is inferred based on the probability of the underlying genotype at each genomic position, derived from genetic markers flanking the region. Composite interval mapping extends this by including additional markers as covariates to control for the effects of other QTLs, improving the precision of QTL detection (16).

For more complex traits, assorted models are commonly used in QTL functions for reporting simultaneously fixed impacts (e.g., QTLs) and random effects (e.g., polygenic environment or other ecological elements). The different models may continue to be expressed in the following way.

$$Y = X\beta + Z\pi + \epsilon$$

Where X and Z are design matrices for fixed and random effects, respectively, β represents the fixed effects (e.g., QTLs), π represents the random effects, and ϵ is the residual error (17).

From the previous sections, it appears that the main differences between these two techniques, GWAS frequently incorporate covariates to manage community structure while,assorted models are commonly used in QTL functions.

Increasing the power of the statistical analysis for both approaches

At the same time, techniques have been developed to integrate sophisticated statistical methods like Bayesian and machine learning to enhance the detection and interpretation of biological associations (18,19).

Increasing statistical power in heritable association studies, such as Genome-Wide Association Studies (GWAS) and Quantitative Trait Loci (QTL) functions, will be helpful in determining the real hereditary association in order to minimize Type II error (false negative). A number of elements, including sample size, impact size, heritage architecture, and design evaluation, affect the authority. There are big plans to increase the influence in heritable analysis under the surface.

1. Increase Sample Size

The influence of a larger sample shall be directly proportional to the size of the sample. The increase in the number of individuals involved in the intrigue enhances the ability to detect inherited discrepancies as well as small differences to moderate the consequences of the intrigue. To obtain a larger sample size, cooperative undertakings, such as consortiums and meta-analyses, pool information from several surveys (20). Multi-ethnic communities that include people of a variety of heritable backgrounds can increase the frequency of rare discrepancies and broaden the scope of conclusions, although this should remain reserved to explanations concerning society stratification (21).

2. Optimize Phenotypic Measurement

Precise phenotyping: Clear, uniform assessment of traits decrease random noise and increase signal-to-noises ratio for genetic association signals. Phenotypic precision can be enhanced, for example by high resolution imaging or biochemical assays (22). Endophenotypes: Investigating endophenotypes such as gene expression levels or metabolite concentrations seem to be more proximal and using these can reduce heterogeneity in the sample (23).

3. Improve Genotyping and Sequencing Quality

High-density Genotyping Arrays, which use a wider range of inherited markers and a higher density of inherited markers, enhance the coverage of the genome and increase the probability of capturing causal discrepancies. Whole Genome Sequencing (WGS) Whole Genome Sequencing (WGS) offers comprehensive coverage of ancestral variation, including rare discrepancies and organizational inconsistencies, which may improve the control for association detection (9).

4. Advanced Statistical Methods

In order to expose the population framework, relatedness, and polygenic setting, assorted models integrate random outcomes in order to reduce specious association and increase power (15). Polygenic danger scores (PRS), which aggregate the consequences of the various heritable discrepancies within the individual mark, may have a greater influence on the prediction of complex traits and diseases (22). Bayesian Approaches Bayesian techniques can integrate prior intelligence roundabout inherited architecture, such as influence size distribution, to advance influence for discerning association.

5. Leverage Functional Genomic Data

Integration of functional genomic data, e.g. chromatin accessibility, and epigenetic signatures can predict expected causal divergences and reduce the number of testing responsibilities, thus increasing the authority (14). Gene-based and Pathway Analysis Aggregating signals from genes or other natural nerve pathways can increase influence by uniting testimony from a number of discrepancies (8).

6. Optimize Study Design

Extreme Phenotype sampling, which enriches the investigative society alongside human beings near the extremes of trait dispersion, can increase influence by increasing the difference between categories (24). Family-based design: using a family-based cohort to detect rare discrepancies planned to enrich hereditary discrepancies within the limits of families (25).

7. Replication and Validation

Reproduction in Independent Cohorts: validate discoveries in independent societies ensure robustness and increase certainty of findings, obliquely improving control by reducing false positives (26). Meta-analysis brings together the results of a number of surveys using meta-analysis as an additional powerful sample size and control, particularly in the detection of discrepancies in small data sets (27).

Reducing and testing for Type I and Type II

Reducing and testing for Type I (false positives) and Type II (false negatives) errors is a critical aspect of genetic association studies, including Genome-Wide Association Studies (GWAS) and Quantitative Trait Loci (QTL) mapping. Both types of errors can significantly impact the validity and reproducibility of findings, and various statistical and methodological strategies have been developed to address them.

1- Reducing and Testing for Type I Errors

Type I errors occur when a genuine null proposition is falsely rejected, leading to a false positive association. In order to mitigate this issue, the following approach is normally used.

Multiple Testing Correction

Thousands, if not countless, of statistical trials are performed in GWAS and QTL functions, increasing the probability of false positives. To adjust the importance threshold, strategies similar to Bonferroni correction, false discovery rate (FDR), direct, and substitution testing are used. For instance, the Bonferroni correction divides the relevance tier (e.g., 0.05) by the number of trials, as FDR aims at limiting the proportion of false positives with significant consequences (28).

Genomic Control and Mixed Models:

Community stratification and relatedness may increase trial statistics, mainly due to Type I errors. Genomic control processes adjust trial statistics established on the determined increase factor, while different models integrate random consequences to the explanation of population structure and relatedness, thereby reducing specious association (15, 29).

Replication Studies

A gold standard for valid associations and minimizing false positives is retroflex conclusions in independent cohorts. Consistency throughout the analysis contributes to the conviction of the findings (26).

2- Reducing and Testing for Type II Errors

Type II error occurs when an actual association is wrong, principally negative. Approaches to reducing Type II error coverage.

Increasing Sample Size:

The statistical influence is directly related to the size of the sample. Larger cohorts, especially for discrepancies with small effect sizes, make it more likely to identify real associations. Collaborative initiatives, such as meta-analyses, combine information from different studies to enhance influence(20).

Improving Phenotypic Precision

In order to find true hereditary association, correct and precise measurement of traits reduces noise and increases skill. Phenotypic statistical quality can be improved through the use of standard protocols or advanced imagination strategies (22). For instance, in human height studies, using calibrated stadiometers and standardized measurement protocols reduces environmental and technical variability, thereby improving phenotypic data quality (30). Similarly, in neuroimaging genetics, employing high-resolution MRI with uniform scanning parameters enhances the precision of brain structural measurements, strengthening genotype-phenotype correlations (31). Such methodological rigor, as emphasized by Wray *et al*. (22), is critical for distinguishing true genetic effects from measurement artifacts in genome-wide association studies.

Optimizing Study Design:

In QTL functions, using progressive experimental design, such as high-tech intercrops lines (AIL), otherwise multiparent groups, can increase recombination events and increase function resolution, thus improving the detection of QTLs (32).

Functional Annotation and Prioritization:

Incorporating functional genomic facts, (e.g., articulation QTLs, and chromatin accessibility) may help to identify anticipated causal discrepancies and thus reduce the burden of a large number of tests, thus gaining influence(14).

Testing for Type I and Type II Errors

1- Simulation research emulates the facts below established heritable architecture sanctions experts in order to estimate Type me and Type II error rates for precise techniques and design analysis.
2- Influence analysis can estimate the sample size required for notice association together with the given ramification size and meaning level to avoid Type II errors.
3- The use of unfavourable controls, similar to the test of association with a trait improbable to be affected by genetics, may help to judge the evaluation of the Type myself error.
4- Scholars are capable of determining the balance between Type I and Type II errors, guaranteeing robust and reliable heritage discoveries by combining the above schemes.

Application of GWAS and QTL mapping in agriculture

Genome Wide Association Analysis (GWAS) and Quantitative Trait Loci (QTL) functions have become indispensable tools for agricultural research, enabling the identification of biological divergences associated with economically important traits in crops and animals. These techniques revolutionized animal breeding through supply revelations within the inherited architecture of the trait concerned, facilitate marker-assisted selection (MAS), and advanced the development of improved collection and breeding. Under this heading, I will discuss the practical purposes of GWAS and QTL functions in farming, focusing on their support for crop progression, livestock breeding, and renewable farming techniques.

1- Applications of GWAS in Agriculture

Crop Improvement:

Trait revelation GWAS is familiar with the distinction between hereditary discrepancies associated with output, disease resistance, drought tolerance, and food efficiency in crops such as rice, corn, wheat, and soybean. For instance, GWAS in rice detects loci that are closely related to grain size and quality, facilitating the development of a high yield group (1).

Climate toughness The GWAS has helped identify genes involved in stress tolerance, similar to drought and heat tolerance in corn and wheat, which contributes to the development of climate resilient crops (33). Nutrient enrichment GWAS has been applied to increase the nutritional content of crops, similar to increased iron and zinc stages in wheat and rice in order to overcome micronutrient deficiency (5).

Livestock Breeding:

The GWAS has established a heritable discrepancy associated with milk development, meat quality, and expansion rates for cattle, pigs, and domestic poultry. For example, GWAS in dairy cattle has shown that loci affect milk production and composition (34). GWAS has been applied to identify biological markers for disease resistance in livestock, similar to Mastitis resistance in dairy cattle and PRRS resistance in pigs (35). The procreative trait GWAS has made it easier to identify genes associated with birth rates and generative performance in livestock, improving sex efficiency(36).

2- Applications of QTL Mapping in Agriculture

Crop Improvement:

Marker-Assisted Selection (MAS) QTL function enables the designation of a marker linked to desirable characteristics, such as disease resistance, abiotic stress tolerance, and output component. These markings are used in MAS to accelerate the development of upgraded collections. For instance, the QTL function in tomatoes has a determined place for fruit size and disease resistance, which is important for the evolution of high yielding, disease resistant varieties (2).

The introduction of a beneficial allele from a wild relative within a cultivated crop has been made easier by the QTL function. For instance, the QTL function in rice allowed the transfer of the drought tolerance gene from the wild rice type to the cultivable variety (37). Clarity breeding The QTL function provides the foundations for genomic choice and accuracy breeding, allowing breeders to predict plant performance based on their ancestral makeup (6).

Livestock Breeding

The biological advance QTL function has detected loci associated with development, feed efficiency, and carcase quality in cattle. For instance, the QTL function in hogs has been proven to influence meat quality, similar to marbling and tenderness (38). The QTL function has been applied to identify heritable territories associated with resistance to diseases such as avian influenza in chicken and bovine tuberculosis in cattle (39). The procreative trait QTL function has determined loci correlated with birthrate, litter size, and other generative traits in livestock, promoting engender productivity and productivity(40).

3- Combined Applications of GWAS and QTL Mapping

Genomic Selection

The GWAS and QTL map contribute to the evolution of a genomic choice model employing a genome-wide marker to predict a person's hereditary value. The present strategy has been significantly adopted in agricultural and livestock breeding projects with a view to increasing biological diversity (41).

Functional Genomics

Integration of GWAS and QTL functions into functional genomics, e.g., transcriptomics, and proteomics helps identify campaigner genes and clarify the mechanism underlying the complex trait. For instance, a QTL map combined with gene utterance statistics contains a candidate drought tolerance gene in corn (42).

Breeding for Sustainability

GWAS and QTL functions are used in combination with improved provision efficiency, such as nitrogen utilization efficiency for crops and feedstuffs for animals. Such improvements contribute to long-term livestock production by reducing environmental effects (43).

Real-World Examples

The rice GWAS and QTL functions have a known gene for submergence tolerance (e.g.), enabling the development of flood-resistant rice varieties which benefit countless farmers in flood-prone areas (3).

The QTL function of corn has recognized a location of drought tolerance, a key element in the development of drought-tolerant corn loan blends which increase yield under water-limited conditions (4).

Dairy Cattle GWAS has a closely examined ancestral discrepancy related to milk production and composition, which enables the selection of high-performance dairy cattle together with improved milk quality (44).

Challenges and Future Directions

Complex traits: many agriculturally significant traits are controlled by a number of genes with small effects, large sample sizes, and sophisticated statistical approaches to identify associations. Genotype-environment communication: the performance of hereditary discrepancies can be altered by the environment, requiring multi-environment tests and adaptive breeding strategies. Further accelerate crop and livestock development by integrating emerging tools such as GWAS and QTL functions, CRISPR/Cas9 gene editing, and high-throughput phenotyping. Agronomists and breeders are able to develop a refined collection and breed that can cope with global challenges such as food safety, climate change, and resilience by exploiting the GWAS and QTL functions.

References

1. Huang, X.; Wei, X.; Sang, T.; Zhao, Q.; Feng, Q.; Zhao, Y.; *et al*. (2010). Genome-wide association studies of 14 agronomic traits in rice landraces. *Nature Genetics*, 42(11), 961–967.
2. Tanksley, S. D. (2004). The genetic, developmental, and molecular bases of fruit size and shape variation in tomato. *The Plant Cell*, 16(S1), S181–S189.
3. Xu, K.; Xu, X.; Fukao, T.; Canlas, P.; Maghirang-Rodriguez, R.; Heuer, S.; *et al*. (2006). Sub1A is an ethylene-response-factor-like gene that confers submergence tolerance to rice. *Nature*, 442(7103), 705–708.
4. Messmer, R.; Fracheboud, Y.; Bänziger, M.; Vargas, M.; Stamp, P. and Ribaut, J. M. (2011). Drought stress and tropical maize: QTL-by-environment interactions and stability of QTLs across environments for yield components and secondary traits. *Theoretical and Applied Genetics*, 123(3), 369–382.
5. Varshney, R. K.; Sinha, P.; Singh, V. K.; Kumar, A.; Zhang, Q. and Bennetzen, J. L. (2018). 5Gs for crop genetic improvement. *Current Opinion in Plant Biology*, 45, 226–237.
6. Bernardo, R. (2008). Molecular markers and selection for complex traits in plants: Learning from the last 20 years. *Crop Science*, 48(5), 1649–1664.
7. Wallace, J. G.; Rodgers-Melnick, E. and Buckler, E. S. (2018). On the road to breeding 4.0: Unraveling the good, the bad, and the boring of crop quantitative genomics. *Annual Review of Genetics*, 52, 421–444.
8. Visscher, P. M.; Wray, N. R.; Zhang, Q.; Sklar, P.; McCarthy, M. I.; Brown, M. A. and Yang, J. (2017). 10 Years of GWAS Discovery: Biology, Function, and Translation. *The American Journal of Human Genetics*, 101(1), 5–22.
9. Tam, V.; Patel, N.; Turcotte, M.; Bossé, Y.; Paré, G. and Meyre, D. (2019). Benefits and limitations of genome-wide association studies. *Nature Reviews Genetics*, 20(8), 467–484.
10. Uffelmann, E.; Huang, Q. Q.; Munung, N. S.; de Vries, J.; Okada, Y.; Martin, A. R.; Martin, H. C.; Lappalainen, T. and Posthuma, D. (2021). Genome-wide association studies. *Nature Reviews Methods Primers*, 1(1), 59.
11. Mackay, T. F. C. (2001). Quantitative trait loci in *Drosophila*. *Nature Reviews Genetics*, 2(1), 11–20.
12. Doerge, R. W. (2002). Mapping and analysis of quantitative trait loci in experimental populations. *Nature Reviews Genetics*, 3(1), 43–52.
13. Flint, J. and Mackay, T. F. C. (2009). Genetic architecture of quantitative traits in mice, flies, and humans. *Genome Research*, 19(5), 723–733.
14. **Albert**, F. W. and Kruglyak, L. (2015). The role of regulatory variation in complex traits and disease. *Nature Reviews Genetics*, 16(4), 197–212.
15. Yang, J.; Zaitlen, N. A.; Goddard, M. E.; Visscher, P. M. and Price, A. L. (2014). Advantages and pitfalls in the application of mixed-model association methods. *Nature Genetics*, 46(2), 100–106.

16. Zeng, Z.-B. (1994). Precision mapping of quantitative trait loci. *Genetics*, 136(4), 1457–1468.
17. Kang, H. M.; Zaitlen, N. A.; Wade, C. M.; Kirby, A.; Heckerman, D.; Daly, M. J. and Eskin, E. (2008). Efficient control of population structure in model organism association mapping. *Genetics*, 178(3), 1709–1723.
18. Stephens, M. and Balding, D. J. (2009). Bayesian statistical methods for genetic association studies. *Nature Reviews Genetics*, 10(10), 681–690.
19. Ogutu, J. O.; Schulz-Streeck, T. and Piepho, H.-P. (2012). Genomic selection using regularized linear regression models: Ridge regression, lasso, elastic net, and extensions. *BMC Genomics*, 13(Suppl 1), S1.
20. McCarthy, M. I.; Abecasis, G. R.; Cardon, L. R.; Goldstein, D. B.; Little, J.; Ioannidis, J. P. and Hirschhorn, J. N. (2008). Genome-wide association studies for complex traits: Consensus, uncertainty and challenges. *Nature Reviews Genetics*, 9(5), 356–369.
21. Martin, A. R.; Kanai, M.; Kamatani, Y.; Okada, Y.; Neale, B. M. and Daly, M. J. (2019). Clinical use of current polygenic risk scores may exacerbate health disparities. *Nature Genetics*, 51(4), 584–591.
22. Wray, N. R.; Goddard, M. E. and Visscher, P. M. (2007). Prediction of individual genetic risk to disease from genome-wide association studies. *Genome Research*, 17(10), 1520–1528.
23. Flint, J. and Munafò, M. R. (2014). The endophenotype concept in psychiatric genetics. *Psychological Medicine*, 44(5), 871–876.
24. Barnett, I. J.; Lee, S. and Lin, X. (2013). Detecting rare variant effects using extreme phenotype sampling in sequencing association studies. *Genetic Epidemiology*, 37(2), 142–151.
25. **Abecasis**, G. R.; Cherny, S. S.; Cookson, W. O. and Cardon, L. R. (2002). Merlin—rapid analysis of dense genetic maps using sparse gene flow trees. *Nature Genetics*, 30(1), 97–101.
26. Chanock, S. J.; Manolio, T.; Boehnke, M.; Boerwinkle, E.; Hunter, D. J.; Thomas, G.; *et al*. (2007). Replicating genotype–phenotype associations. *Nature*, 447(7145), 655–660.
27. Evangelou, E. and Ioannidis, J. P. (2013). Meta-analysis methods for genome-wide association studies and beyond. *Nature Reviews Genetics*, 14(6), 379–389.
28. Benjamini, Y. and Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society: Series B (Methodological)*, 57(1), 289–300.
29. Devlin, B. and Roeder, K. (1999). Genomic control for association studies. *Biometrics*, 55(4), 997–1004.
30. Silventoinen, K.; Sammalisto, S.; Perola, M.; Boomsma, D. I.; Cornes, B. K.; Davis, C.; *et al*. (2003). Heritability of adult body height: a comparative study of twin cohorts in eight countries. Twin Research and Human Genetics, 6(5), 399-408.
31. Thompson, P. M.; Stein, J. L.; Medland, S. E.; Hibar, D. P.; Vasquez, A. A.; Renteria, M. E., *et al*. (2014). The ENIGMA Consortium: large-scale collaborative analyses of neuroimaging and genetic data. Brain imaging and behavior, 8, 153-182.
32. Rockman, M. V. and Kruglyak, L. (2008). Breeding designs for recombinant inbred advanced intercross lines. *Genetics*, 179(2), 1069–1078.
33. Lobell, D. B.; Schlenker, W. and Costa-Roberts, J. (2015). Climate trends and global crop production since 1980. *Science*, 333(6042), 616–620.
34. Hayes, B. J.; Pryce, J.; Chamberlain, A. J.; Bowman, P. J. and Goddard, M. E. (2010). Genetic architecture of complex traits and accuracy of genomic prediction: Coat colour, milk-fat percentage, and type in Holstein cattle as contrasting model traits. *PLoS Genetics*, 6(9), e1001139.
35. Rowland, R. R. R.; Lunney, J. and Dekkers, J. (2012). Control of porcine reproductive and respiratory syndrome (PRRS) through genetic improvements in disease resistance and tolerance. *Frontiers in Genetics*, 3, 260.
36. Bouwman, A. C.; Daetwyler, H. D.; Chamberlain, A. J.; Ponce, C. H.; Sargolzaei, M.; Schenkel, F. S.; *et al*. (2018). Meta-analysis of genome-wide association studies for cattle stature identifies common genes that regulate body size in mammals. *Nature Genetics*, 50(3), 362–367.
37. Xiao, J.; Li, J.; Grandillo, S.; Ahn, S. N.; Yuan, L.; Tanksley, S. D. and McCouch, S. R. (1996). Genes from wild rice improve yield. *Nature*, 384(6606), 223–224.

38. Andersson, L. (2001). Genetic dissection of phenotypic diversity in farm animals. *Nature Reviews Genetics*, 2(2), 130–138.
39. Lamont, S. J.; Lakshmanan, N. and Plotsky, Y. (2003). Genetic markers for disease resistance in poultry. *Poultry Science*, 82(6), 870–876.
40. Rothschild, M. F. and Soller, M. (1997). Candidate gene analysis to detect genes controlling traits of economic importance in domestic livestock. *Probe*, 8(1), 13–20.
41. Meuwissen, T. H. E.; Hayes, B. J. and Goddard, M. E. (2001). Prediction of total genetic value using genome-wide dense marker maps. *Genetics*, 157(4), 1819–1829.
42. Huang, X.; Han, B. and Tian, F. (2018). Genomic selection and its application in maize breeding. *Theoretical and Applied Genetics*, 131(12), 2553–2564.
43. Garnett, T.; Appleby, M. C.; Balmford, A.; Bateman, I. J.; Benton, T. G.; Bloomer, P.; *et al*. (2013). Sustainable intensification in agriculture: Premises and policies. *Science*, 341(6141), 33–34.
44. Grisart, B.; Coppieters, W.; Farnir, F.; Karim, L.; Ford, C.; Berzi, P., *et al*. (2002). Positional candidate cloning of a QTL in dairy cattle: Identification of a missense mutation in the bovine DGAT1 gene with major effect on milk yield and composition. *Genome Research*, 12(2), 222–231.