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Structural Variations in the Oyster Genome and Their Role in Environmental Adaptation

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Abstract Oysters play a key role in the ecosystem and are also an important breeding shellfish, but their living environment faces multiple pressures such as salinity and temperature. Research in recent years has found that structural variants (SVs) are widely present in the oyster genome, including deletion, insertion, inversion, translocation and replication of large fragments. These structural variations not only increase the genetic diversity of oyster populations, but also play an important role in the environmental adaptive evolution of oysters by affecting gene dose and gene regulation. Based on the review of the characteristics of oyster genomes, this study focuses on discussing the types of genome structural variants, detection technology and their distribution characteristics in the oyster genome. Combined with environmental stress cases such as high salt, low oxygen and high temperature, it explains how structural variants affect gene expression and physiological phenotypes, thereby promoting the adaptation of oysters to environmental changes. Finally, the application prospects of oyster genome structural variation research in aquatic breeding, environmental monitoring and gene editing are prospected.

Keywords Oysters; Genomic structural mutation; Environmental adaptation; High salt stress; High temperature stress

1 Introduction

Oysters are an important part of the nearshore marine ecosystem. They have ecological functions such as filtering water quality and building habitats. They are also an important aquaculture shellfish in the world and occupy an important position in the coastal economy. Varieties such as Pacific oysters and Omi oysters are widely cultivated in China and around the world, with huge output and economic value. However, environmental stresses caused by climate change and human activities (such as sudden salinity changes, hypoxia and seawater warming, etc.) pose challenges to the survival and biodiversity of oyster populations (Li et al., 2021).

For organisms to adapt to environmental changes in a short period of time, they depend not only on existing genetic variations but also on phenotypic plasticity. Oysters live in areas with severe environmental fluctuations such as the intertidal zone, and their high genetic diversity and phenotypic plasticity are considered key factors for their successful environmental adaptation (Guo et al., 2018). Structural variation refers to a sequence rearrangement or copy number change in the genome that is larger in length, which can directly affect the coding sequence or change the gene regulatory network, thereby producing phenotypic effects. For adaptive evolution under drastic changes in the environment, SV provides a large amount of genetic material, and its importance in the evolution of stress resistance and survival strategies of animals and plants is becoming increasingly prominent (Wang et al., 2023).

Based on the above background, this study reviews the overall characteristics of the oyster genome and its comparison with other shellfish, introduces the types of SVs and advanced detection methods, analyzes the distribution and characteristics of SVs in the oyster genome, and focuses on discussing the influence mechanism of SV on gene function and environmental adaptability. Finally, it is expected that the prospect of applying SV research to oyster genetic improvement and ecological protection.

2 Overall Characteristics of Oyster Genome

2.1 Progress in sequencing and assembly of oyster genomes

With the development of high coverage long read and long sequencing and advanced assistive technologies, the quality of oyster genome assembly has been significantly improved. Using the third generation of PacBio sequencing ($>200\times$ depth) combined with Hi-C technology, researchers successfully constructed the chromosomal-level genome of Pacific oysters. Based on this chromosomal reference, researchers further resequencing 495 wild Pacific oyster individuals whole genome, constructed the first comprehensive oyster variation map, identified about 4.8 million high-quality SNPs, 600 000 small indexes, and 49 000 copy number variants (CNVs), revealing that there are variation differences in about 21% of genomic regions between individuals (Qi et al., 2021). In addition to Pacific oysters, genome sequencing of other oyster species has also made progress. For example, the genomes of American oysters and Portuguese oysters were assembled and announced successively, while oysters used nanopore sequencing to obtain a highly continuity genome of 613.9 Mb, of which 99.6% of the sequences were localized to 10 chromosomes (Li et al., 2023).

2.2 Genomic size, chromosomal structure and genetic diversity

The genome size of most oyster species is about 0.5 Gb~0.7 Gb, and the number of chromosomes is generally 10 pairs. Although Pacific oysters and oysters belong to different lineages, their genome sizes are similar and the number of chromosomes is the same. Collinear analysis shows that the sequence consistency between the two is more than 95% (Qi et al., 2022). This shows that the oyster species are more conservative in the macroscopic structure of the genome.

The oyster genome has a high degree of polymorphism and heterozygity. It is reported that there are more than 10 polymorphic loci per kilobase in the genome of Pacific oysters, with a much higher level of genetic diversity than most vertebrates. This is considered a genetic strategy for oysters to adapt to frequent environmental fluctuations: high variation provides rich material for natural selection. In addition to SNP, structural variations such as copy number variations further increase the breadth of genetic variation within the population. Studies have shown that there are a large number of gene duplication differences among individuals in eastern oysters (*Crassostrea virginica*), and some chromosomal regions are enriched with high-density duplication fragments (Modak et al., 2021). These structural variations allow populations to have greater genetic response space when facing different environments, which are believed to contribute to the evolutionary success of oysters.

2.3 Comparison with genomes of other bivalve species

Compared with other bivalve shellfish, such as scallops and mussels, the oyster genome exhibits some unique features and similar patterns. On the one hand, multiple shellfish genomes are rich in repeat sequences and transposable elements, which may be an important basis for shellfish to adapt to complex environments (Takeuchi et al., 2016; McElroy et al., 2024). On the other hand, some of the gene families associated with environmental stress in the oyster genome have undergone significant expansion, which has also been reported in other bivalves, but the degree of oysters is particularly prominent. The *HSP70* heat shock protein gene amplifies to dozens of copies in oysters, while the family is smaller in many mollusc species. For example, the solute carrier (*SLC*) gene family, research has found that it has expanded on a large scale in Oripe oysters and American oysters that adapt to low salinity estuaries (Figure 1), but it is not obvious in Pacific oysters living in open and open waters of high salinity. This phenomenon of gene amplification is considered a "convergent evolution" strategy carried out by different species for their respective habitats, suggesting that gene replication is crucial in shellfish stress adaptation. In addition, there are also differences in ploidy and genomic structures of different shellfish. Some clams are polyploid or highly heterogeneous heterogeneous genomes, while oysters are mainly diploid, with occasional reports of natural triploid individuals.

3 Types and Detection Technology of Genomic Structural Variants

3.1 The main types of structural mutations

Genome structural variation generally refers to sequence changes of more than 50 bp relative to the reference

genome, mainly including two major categories: equilibrium variation and non-equilibrium variation. Equilibrium SVs such as inversion and translocation refer to the inversion or exchange of chromosomal fragments, but the total copy number of genomes has not changed; non-equilibrium SVs include deletion, insertion, and duplication, which can cause changes in gene dosage. A deletion of a sequence may cause several genes to be lost, and insertion may add exogenous or repeat sequences, while duplications (including tandem and dispersed repeats) may lead to an increase in copy number of genes or regulatory elements. In addition, large-scale copy number variation (CNV) is sometimes listed alone, usually referring to an increase or decrease in the number of fragments relative to the reference genome, which can be regarded as a general term for deletion and amplification (Pettersson, 2019). The distribution of structural variations in the genome is not uniform, and their size can range from 50 bp to millions of bp, and their effects on genes also vary according to their location. The SV that occurs in the coding region may interrupt the open reading frame or alter the coding sequence, thereby directly altering protein function.

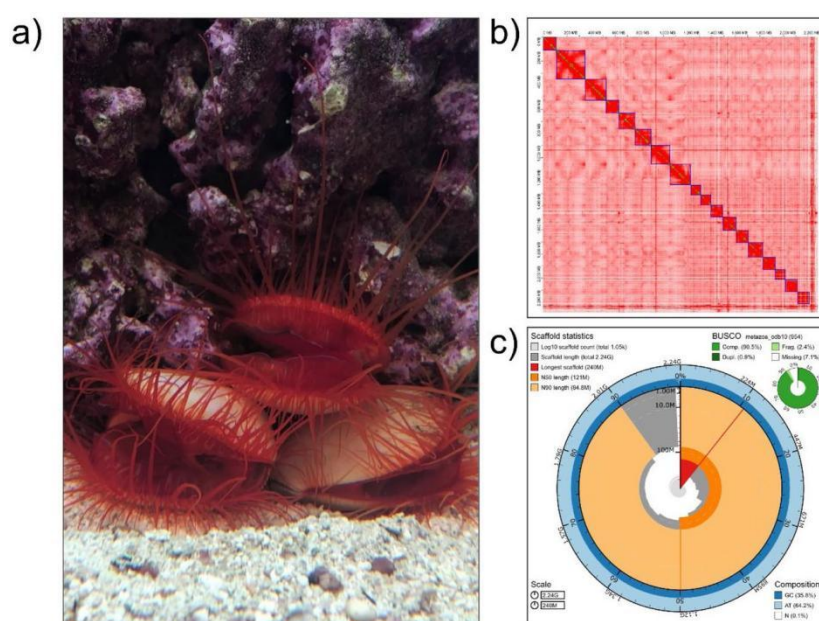


Figure 1 *Ctenoides ales* and summary of its genome assembly (Adopted from McElroy et al., 2024)

Image caption: (A) Adult *Ctenoides ales* in aquarium setting, flashing light display visible in middle individual. Image credit: Jeanne M Serb. (B) Hi-C contact map for *C. ales*, highlighting the 18 chromosomes recovered from the genome assembly. Darker red indicates higher density of contact, blue and green boxes denote chromosome and contigs, respectively. (C) Snail plot summarizing key assembly statistics for final *C. ales* assembly with BUSCO results (Adopted from McElroy et al., 2024)

3.2 Application of high-throughput sequencing and long-reading technology in SV detection

Since structural variations usually involve large fragment sequence changes, it is difficult for traditional molecular markers and PCR methods to detect them globally. The development of high-throughput sequencing technology provides a revolutionary means for SV detection. Based on the data of second-generation sequencing short read lengths, genomic structural variation can be predicted through strategies such as paired-end mapping, read length alignment spacing abnormalities and sequencing depth analysis. However, the limitation of short read length makes it less effective when resolving large SVs in complex or repetitive areas (Romagnoli et al., 2023). With the advent of third-generation sequencing, long read length sequencing (such as PacBio and Oxford Nanopore technologies) can generate ultra-long read lengths of tens of thousands to millions of bases. These read lengths cover many repeating sequence areas where short read lengths cannot be uniquely aligned, greatly improving the sensitivity to detection of large or complex structural variations. It is reported that a single mammalian genome can detect more than 20 000 to 30 000 SVs using long-read-length technology, which is 3 to 6 times that of short-read-length detection. In oyster research, the application of long-read long-read technology has also achieved remarkable results. Yildiz et al. (2022) integrated a variety of alignment and variation detection tools to

conduct long-read-length SV detection on two oyster reference genomes, identifying about 190 000 to 220 000 SVs, covering 31%~35% of the genome, far exceeding the detection capabilities of previous short-read-length methods (Yildiz et al., 2022).

3.3 Prospects of multiomics method combined with SV research

Although a single genomic assay can locate SV, it is difficult to directly explain its functional consequences. By introducing data such as transcriptome, epigenetic group, proteome, etc., the mechanism by which SV affects biological traits can be revealed from a functional level. This idea has begun to emerge in the study of oyster adaptability (Jiao et al., 2021). Some studies have integrated genomic variation, acetylation modification and phenotypic data of oysters, and found that under the action of environmental selection, oyster populations have genetic differentiated on a subtle geographical scale, and high phenotypic plasticity is consistent with the adaptation direction. They also found that some genes associated with energy metabolism and antioxidant exhibited co-differentiation of genomic structural variation and gene expression during adaptation, suggesting that SV may participate in adaptive evolution through regulatory metabolic pathways (Figure 2) (Bai et al., 2023; Lu et al., 2024). Some studies compared the genomic differences between the intertidal and subtidal oysters and found that there was no significant difference in structural variation between the two, but there was heritable differentiation in the genomic methylation pattern, indicating the role of epigenetics in environmental "memory".

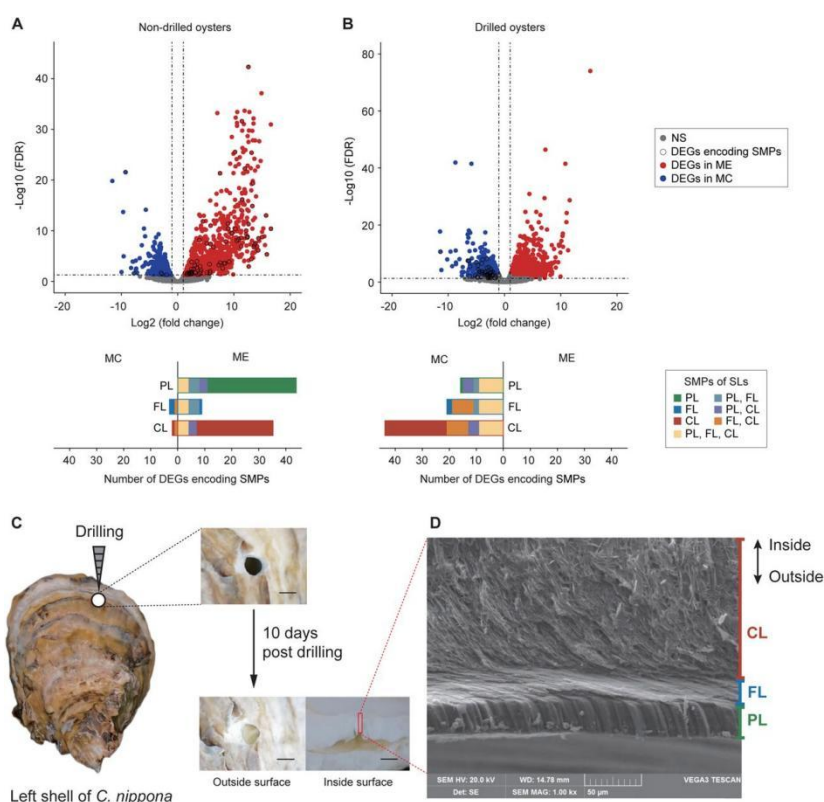


Figure 2 Rapid reconstruction of the *Crassostrea nippona* shell. Abbreviations as in figure 2, and DEGs, differentially expressed genes; ME, mantle edge; MC, mantle center; NS, Non-significant expression; SLs, shell layers (Adopted from Bai et al., 2023)
Image caption: (A) Differential gene expression and number of DEGs encoding SMPs in mantle tissues of non-drilled *C. nippona* and (B) drilled oysters. (C) Schematic illustration of shell-drilling experiment and observation of shell regeneration process of *C. nippona*. Scale bar, 5 mm. (D) Ultrastructure of cross section of the whole repaired shell (Adopted from Bai et al., 2023)

4 Structural Variant Distribution and Characteristics in Oyster Genome

4.1 SV distribution patterns in different chromosomal regions

Genome structural variations are not randomly distributed in the oyster genome. Studies have shown that some chromosomes or regions are enriched with high density of variation, while others are relatively conservative. In the study of the eastern oyster genome, Modak et al. used high-quality reference sequence alignment to find that

SV is distributed in almost all 10 chromosomes, but there are differences in the frequency of SV on different chromosomes. Among them, individual chromosomes carry significantly more repeated amplification regions than average, presenting SV "hot spot" regions. At the same time, SVs vary greatly between individuals, with some regions having repeated or deletion variations in different individuals, while others remain stable in most individuals (Quan et al., 2021). The population variation map of Pacific oysters also provides similar information: about 21% of genomic regions have CNV differences between individuals, indicating that the sequence copy number of these regions is frequently changed (Jiao et al., 2021). Typically, these highly variable regions tend to be rich in repeat sequences or multigene families.

4.2 Structural variations associated with repeat sequences and transposons

There is a lot of evidence that repeat sequences and transposable moving elements in the genome are often one of the sources of structural variation. The oyster genome contains a high proportion of scattered repeats and various types of transposons. The replication and insertion of these elements within the genome will directly form new structural mutations. For example, the insertion of retrotransposons can be considered as a special insertion-like SV; non-allergic recombination of multiple homologous transposons can lead to the deletion or repetition of large fragments (Wang et al., 2019). The study found that the SINE-like transposon activity in the oyster genome contributes a large number of structural polymorphic sites. For oysters, stresses such as high salt and heavy metals may induce some transposon activation, resulting in genomic rearrangements and enhance the phenotypic plasticity of oysters to adversity. Although more experimental evidence is needed to support this aspect, similar speculations have been made in the resilient adaptation of other shellfish such as mussels. Repeat sequences are also prone to induce non-allelic homologous recombination (NAHR), resulting in duplication or deletion of large fragments (Tunjić-Cvitanić et al., 2024). There are many tandem repeat gene clusters and intraspecific repeats in the oyster genome, and these regions often experience NAHR and form CNV. For example, oyster immune-related genes are often distributed in clusters, and if unequal exchange occurs, it is possible to amplify the number of genes in that cluster in one individual, while some genes are missing in the other (Modak et al., 2021). Therefore, at the population level, such regions exhibit rich structural variation.

4.3 Population differences in structural variation

Oyster populations live in different geographical and ecological environments, and their genomic structural variation spectrum may also vary. Population genetics studies have confirmed that there is differentiation in allelic frequencies of oyster populations from different origins, including conventional mutations and structural variations. Research on eastern oysters shows that structural variation forms an important part of population genetic variation. They found that in different geographical groups of oysters in the eastern region, the distribution frequency of repeated segments is different. Some repeated segments are found in almost every group, but rarely in another group. This means that these SVs may be affected by habitat environmental selection pressures. In addition, there are also SV differences between different breeding lines. Artificial targeted breeding may inadvertently fix some structural variations that are beneficial to the target traits, while losing some variations in natural populations. The study found that the genetic diversity of artificially bred Oyster population is lower than that of wild populations, which may include loss of some structural variation, suggesting that attention should be paid to the problem of decreased genetic diversity caused by long-term breeding (Biet et al., 2023).

5 The Relationship Between Structural Variation and Environmental Adaptability

5.1 The effect of structural variation on gene expression and regulation

Genome structural mutations can affect gene expression levels and regulatory methods through various mechanisms, thus physiologically affecting the organism's ability to respond to the environment. First, structural variation changes the dosage and structure of the gene. Gene deletion will directly lead to a lack of relevant gene products, reducing biological tolerance in harmful environments. Modak et al. (2021) pointed out that a considerable proportion of repeat region fragments in the eastern oyster genome are located in the gene or contain exons, which means that a large number of SVs directly affect the structure and copy number of the gene (Modak et al., 2021).

Secondly, SV can change the regulatory elements and chromatin structure of genes. Some insertion mutations will introduce new promoter or enhancer elements to activate originally silent gene expression; inversion and translocation will change the relative position of genes and regulatory elements, which may cause genes that were originally regulated to be deregulated or obtain new regulation. Studies have shown that changes in the position of cis regulatory elements caused by SV can change the three-dimensional chromatin topology between regulatory elements and target genes, thereby affecting gene transcription. In oysters, there are examples that structural variation leads to differences in gene expression: for example, a repeat sequence deletion in a heat shock gene promoter region was detected in a high-temperature-resistant oyster strain, which caused the gene to be expressed less frequently but was upregulated more significantly during heat stress, which is considered an adaptive regulatory variant (Jiao et al., 2021).

5.2 Correlation with adaptation mechanisms of environmental stress

Oyster populations in nature are under the test of various environmental stresses such as salinity, high and low temperatures, and low oxygen. Structural variation, as an important form of genetic variation, is often associated with adaptive traits under these stress conditions. In terms of high salt stress, oysters need to maintain the balance of osmotic pressure in and out of cells, and structural variations in some gene amplification have been proven to be beneficial to this function. Recent studies have found that solute carrier transporter (*SLC*) gene family has significantly expanded in oyster species living in low-salt estuary environments (Li et al., 2021). The expanded *SLC* gene helps enhance transmembrane transport of ion and organic osmotics, thereby improving the ability of oysters to regulate cell osmotic pressure at different salinity. In the Jinjiang oyster population in China, some copy number variations in the *SLC* gene vary in frequency between populations in high-salt and low-salt environments, suggesting that these SVs are selected by the environment and are involved in salinity adaptation (Zhang et al., 2022).

In terms of hypoxia stress, benthic shellfish such as oysters often encounter an oxygen-deficient environment during low tides in the intertidal zone. Although structural variations in oyster hypoxia adaptation are rare, some have been found in fish and other studies: For example, a snailfish is fixed inverted chromosomes during freshwater settlement, including multiple genes related to hypoxia tolerance.

In terms of temperature stress, structural variation is particularly closely related to the heat resistance of oysters. Large-scale amplification of the heat shock protein gene is one of the important molecular basis for oysters to withstand high temperature. In addition, genetic analysis of temperature adaptation in oyster populations showed that there were selected sites of structural variation among different populations.

5.3 Coupling of genomic structural variation and phenotypic diversity

Genome structural variation is one of the important genetic basis for oyster phenotype diversity. There are significant variations in oysters in morphology, physiology and stress resistance, such as shell shape, color, high temperature and low salt resistance, etc., and there are often obvious differences between different populations and strains. Behind these phenotypic differences, the role of structural variation is often implicit. Gene dose changes directly caused by structural variation can lead to continuous phenotypic differences. For example, shell shape and growth traits are controlled by multiple genes. Studies have analyzed oyster breeding populations, which show that some gene regions related to growth have enriched copy number variations, and individuals with higher copy number have larger shell shapes (Jiao et al., 2021).

Secondly, regulatory changes caused by structural variation can produce an on/off phenotypic transformation. Also in oysters, certain resistant phenotypes were also observed to be inherited in the form of presence/absence variants: some families either had a repeat amplification of a group of disease-resistant related genes, showing high resistance, or were completely lacking, showing susceptibility. In oyster breeding, the introduction of SV detection is expected to improve the accuracy of genetic assessment of yield and stress-resistant traits (Sun and Mai, 2025).

6 Case Analysis: The Adaptation Mechanism of Oysters to High-salt Environment

6.1 Phenotype response and physiological changes under high salt stress

Salinity is one of the key environmental factors that affect the survival and distribution of marine shellfish. Oysters are broad-salt animals and can adapt to salinity fluctuations through physiological regulation within a certain range. However, when salinity rises or drops sharply beyond the tolerance range, its metabolism and survival will be seriously affected. Under high salt (high osmotic pressure) stress, oysters initiate a series of stress response mechanisms to maintain intracellular osmotic pressure and ionic equilibrium. Oysters can reduce the contact between body fluids and external high saline water bodies by closing the shell cover and reducing water filtering, so as to buffer osmotic shock in the short term (Chen et al., 2021). At the same time, at the molecular level, oysters accumulate organic osmotic protectors (such as free amino acids such as taurine and glycine) and regulate inorganic ions discharge to balance the intra- and extracellular osmotic pressure gradients. In addition, high-salt environments are often accompanied by an increase in oxidative stress, and the oyster body will increase the activity of antioxidant enzymes (such as SOD, catalase) and the expression of protective molecules such as heat shock proteins to prevent cell damage. In terms of energy metabolism, high salt can increase the basal metabolic rate of oysters (She et al., 2022) to cover the energy cost of osmotic regulation, but excessive energy consumption may lead to growth stagnation or even death.

6.2 The relationship between genome structural variation and osmotic regulation genes

Genomic structural mutation plays a key role in the genetic basis of oysters adapting to a high-salt environment. Especially for genes related to osmotic pressure regulation, their copy number variation and regulatory region variation will directly affect the salt tolerance of oysters. Ao Li et al.'s study on the Omi oyster genome found that the *SLC* gene family of this species showed significant expansion, with a total of hundreds of members, significantly more than the Pacific oysters. These genes encode multiple ion and solute transporters and are believed to play an important role in both low-salt and high-salt environments. Population genetic analysis showed that copy numbers of some genes in the *SLC* gene family differed between oyster populations in different salinity habitats, suggesting that natural selection prefers structural variant copies that favor extreme salinity tolerance (Figure 3). In addition to the *SLC* family, other genes related to osmotic regulation may also enhance adaptability through structural variation (Qiu et al., 2024). Some studies have compared the two related species of oysters that Pacific oysters, which are more sensitive to salinity, may have a condition that the regulatory efficiency of taurine synthesis pathway is not as good as that of oysters. It is speculated that there are variants in the promoter of the key enzyme gene involved. In molecular breeding practice, people have also begun to pay attention to variation in osmotic regulatory genes (Wang and Mai, 2025). For example, through genome-wide selection and association analysis, some genetic markers related to salinity tolerance were screened, including several CNV sites.

6.3 Case implications: the key role of structural variation in ecological adaptation

The case of oyster adaptation to high-salt environments highlights the importance of genomic structural variation. (1) Structural variation enriches the sources of adaptive genetic variation: Compared with the gradient effect produced by point mutations, the genomic rearrangement or replication of large fragments can change the performance of multiple genes at the same time, allowing organisms to achieve significant improvement in adaptability in extreme environments. Oyster amplification of *SLC* and *HSP* genes, etc., belong to this category, and a multigene synergistic anti-response effect is generated through a genomic event (Li et al., 2021; Zhang et al., 2022). (2) Structural variations often become targets of natural selection: environmental pressures will select favorable structural variations to carry individuals to proliferate in the population. From the comparison of Omi oysters and Pacific oysters, it can be inferred that populations living in low-salt estuary environments accumulate more osmotic regulatory gene amplification variants, which allow them to survive in low-salt or even freshwater environments, whereas Pacific oysters lack these amplifications and are limited in growth under low-salt. (3) The relationship between structural variation and phenotype can be used to guide breeding and protection: The genetic mechanism of high-salt adaptation tells us that certain beneficial structural variations can be used as molecular markers to assist in the breeding of high-salt-resistant oyster varieties. In terms of environmental protection,

structural variation analysis can also be used to evaluate the adaptability of populations to salinity changes. For example, by comparing the genomes of historical and current populations, it is possible to determine whether they already have a recessive variation basis for adapting to higher salinity. This is of reference value for predicting the impact of increased salinity along the coast on oyster populations under global climate change.

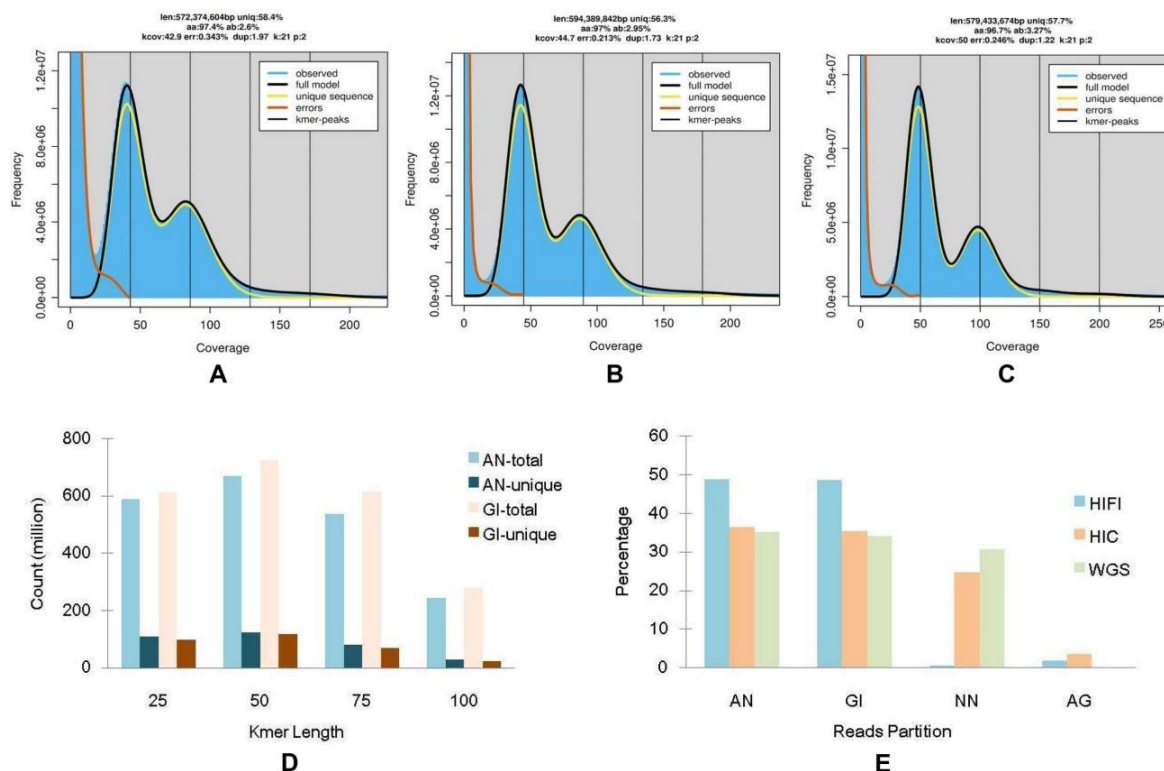


Figure 3 Genome feature survey and trio sequencing reads partition based on k-mer analysis (Adopted from Qiu et al., 2024)

Image caption: (A–C) GenomeScope analysis for male *C. angulata* (A), female *C. gigas* (B), and the hybrid offspring (C), respectively. x-axis: the sequencing reads coverage. y-axis: the 21-mer frequency. (D) The distributions of 25-, 50-, 75-, and 100-mers in the AN (*C. angulata*) and GI (*C. gigas*) short sequencing reads. x-axis: k-mer length. y-axis: k-mer count. (E) The offspring reads partition by unique k-mers. x-axis: reads partition types. y-axis: the percentage of the reads. AN: reads that only contain *C. angulata* unique k-mers. GI: reads that only contain *C. gigas* unique k-mers. NN: reads that do not contain *C. angulata* or *C. gigas* unique kmers. AG: reads that contain *C. angulata* and *C. gigas* unique k-mers (Adopted from Qiu et al., 2024)

7 Case Analysis: Adaptation Mechanism of Oysters to High Temperature Stress

7.1 Effect of high temperature stress on oyster survival rate and metabolic pathway

High summer temperatures often trigger large-scale deaths of oysters and are considered one of the greatest environmental stresses on the oyster industry and populations in the context of global warming. When the ambient temperature exceeds the oyster tolerance range (usually $>30^{\circ}\text{C}$), the steady state in the oyster body will be severely disrupted. High temperatures can destroy the immune balance of oysters. Studies have shown that under continuous stress at 30°C , the total hemolymphological antioxidant capacity (T-AOC) of Pacific oysters and Kumamoto oysters and their hybrid offspring decreased significantly, and the activity of several key immunoselectrons was also significantly reduced (Jiang et al., 2022). This means that high temperatures lead to increased oxidative stress in oysters and impaired immune system functions, which is one of the causes of oysters susceptible pathogens or direct death. Secondly, high temperatures will affect the metabolism and energy expenditure of oysters. To combat heat stress, oysters need to synthesize large amounts of molecular chaperone proteins (such as HSPs) and antioxidants, which consume a lot of energy. At the same time, high temperatures accelerate the metabolism of organisms and increase oxygen consumption. In the intertidal zone with limited dissolved oxygen, high temperatures often occur at the same time as hypoxia, which makes oysters face a "double blow": on the one hand, more oxygen is needed to support the stress response, and on the other hand, the environmental oxygen supply is reduced, leading to an energy crisis. Studies have found that oysters mobilize

energy reserves under high temperature stress and accelerate anaerobic glycolysis pathways to provide ATP in the short term, but in the long term it will cause energy overdraft (Zhang et al., 2022).

7.2 Structural variation and expression regulation of heat shock protein (HSP)-related genes

Heat shock protein is one of the main forces of organisms to resist high temperature stress. The structural variation and expression regulation of its genes in the oyster genome play a key role in heat resistance adaptation. The biggest feature of the Oyster *HSP* gene family is its extremely rich membership. Taking the *HSP70* family as an example, about 88 *HSP70* genes were identified in the Pacific oyster genome, several times that of model organisms such as mammals. Most of these *HSP70* genes are distributed in clusters on chromosomes through tandem repetition. The number of *HSP70* genes in *Ostrea denselamellosa* is significantly smaller than that of other oysters, which may explain its sensitivity to high temperatures. This once again confirms the close relationship between structural variation (gene replication or contraction) and heat-resistant phenotype. In addition to differences in gene copy number, high temperature adaptation also depends on the effectiveness of *HSP* gene regulation. Structural variation also participates in this regulation and improvement. Some studies have found that different oyster lines or subspecies have slight insertion/deletion variants in the promoter region of the *HSP* gene, which can affect the transcription factor binding site and thus change the initiation efficiency of *HSP* genes under thermal stimulation (Liu et al., 2020; Wang et al., 2023).

7.3 Case implications: the role of structural variation in temperature adaptation and climate change response

The high-temperature adaptation cases further highlight the core role of genomic structural variation in the environmental adaptation of oysters, and adaptive structural variation is the "buffer" for species survival in the context of climate change. As global warming, extreme events in seawater temperature will be more frequent. Populations with rich structural variation have greater genetic diversity to deal with these changes. Repeated evolution utilizes structural variations to adapt to different environments is a common pathway for organisms to adapt to different environments (Modak et al., 2021). As shown in the study of Stickleback fish, prickly insects and other organisms, when different populations or species adapt to similar environments, similar types of structural mutations often appear in parallel. Structural variation research can serve the protection and breeding of oysters. Using genomic means to screen wild oyster populations and identify structural variation sites related to key traits such as heat tolerance, helps to determine which populations have higher adaptability potential and should be given priority. At the same time, these key structural variants can also be used for the breeding of oyster stress-resistant strains. For example, individuals enriched with amplified variants of heat-resistant genes for breeding can shorten the cycle of nurturing new high-temperature resistant varieties (Ding et al., 2020).

8 Application Prospects of Research on Genome Structural Variation of Oysters

8.1 Potential applications in aquatic breeding

Research results on genomic structural variation are expected to play an important role in oyster genetic breeding. Using SV as a new molecular marker for assisted breeding selection is a promising direction. Currently, oyster breeding is mainly based on phenotypic selection and a small number of SNP markers, while structural variant markers may capture some sources of trait variants that SNP cannot cover. Through genome-wide association analysis (GWAS), we can lock in these SV sites associated with the target trait and design specific primers for breeding population screening. Secondly, structural variation research can reveal hidden adverse variants and help improve germplasm. Long-term artificial breeding may cause certain harmful structural mutations to accumulate in breeding populations, which may reduce population resilience. Monitoring SVs in breeding populations by genome sequencing allows us to timely detect and eliminate these potentially adverse variants to maintain genetic health. Structural variation research can also be used to optimize hybrid breeding strategies. Oyster hybridization is often used to introduce trait hybrid advantages, such as Kumamoto oyster x long oyster hybridization performs well in stress resistance and growth. Genomic analysis found that these hybrid progeny may carry different combinations of structural variants of parents at the same time, such as inheriting *HSP* amplification from one parent and carrying metabolic gene regulatory variants from another parent, thereby achieving complementary advantages.

8.2 Genomics tools in environmental monitoring and protection

Analytical methods based on genomic structural variation can be used for environmental adaptability monitoring and conservation management of oyster populations. In terms of environmental monitoring, the structural variation spectrum carried by oyster populations in different sea areas can be used as "natural biosensors" to reflect the history and intensity of local environmental pressure. For example, by comparing the genome of an oyster population in a region before and after industrialization, if the frequency of structural variations related to pollution resistance or high temperature is found to increase significantly, it means that oysters in this region are responding to environmental stress. For the restoration of oyster reef ecosystems, structural variation analysis can also provide guidance: individuals with high structural variation diversity can be selected for artificial proliferation and release to improve the reconstructed population adaptability. In terms of species conservation, it is crucial to focus on the preservation of key adaptive structural variations of oysters. In the context of climate change, if an oyster population in a certain region lacks high-temperature-resistant HSP amplification variation, then the population may be more vulnerable when extreme heat waves hit. Protectors can take measures accordingly, such as introducing individuals with relevant variants from heat-resistant populations to enhance genetic diversity, or providing shelter for populations in the region to survive the high temperature period.

8.3 Promote the application of gene editing and synthetic biology in shellfish research

The in-depth research on genomic structural variation also provides targets and inspiration for future improvement of oyster stress-resistant traits through gene editing. In recent years, gene editing technologies such as CRISPR/Cas9 have been successfully applied to basic research on marine shellfish such as oysters. In 2019, Chinese researchers developed a method based on the direct injection of fertilized eggs based on the ribonucleoprotein complex, achieving efficient gene site-directed knockout in Pacific oysters. They chose genes such as muscle growth inhibitor (MSTN) and *Twist* for knockout, and successfully obtained oyster larvae with deletion mutations. This proves that oyster genome editing is feasible. Going forward, we can consider simulating or introducing favorable structural variations to improve oyster traits. Gene editing means are used to target the amplification of the copy number of certain stress-resistant genes, or insert enhanced regulatory elements at artificially designed positions, thereby improving the heat and salt resistance of oysters. This is actually accelerating the structural variation that may take thousands of years to accumulate in natural evolution, through synthetic biology.

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Conflict of Interest Disclosure

The authors confirm that the study was conducted without any commercial or financial relationships and could be interpreted as a potential conflict of interest.

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