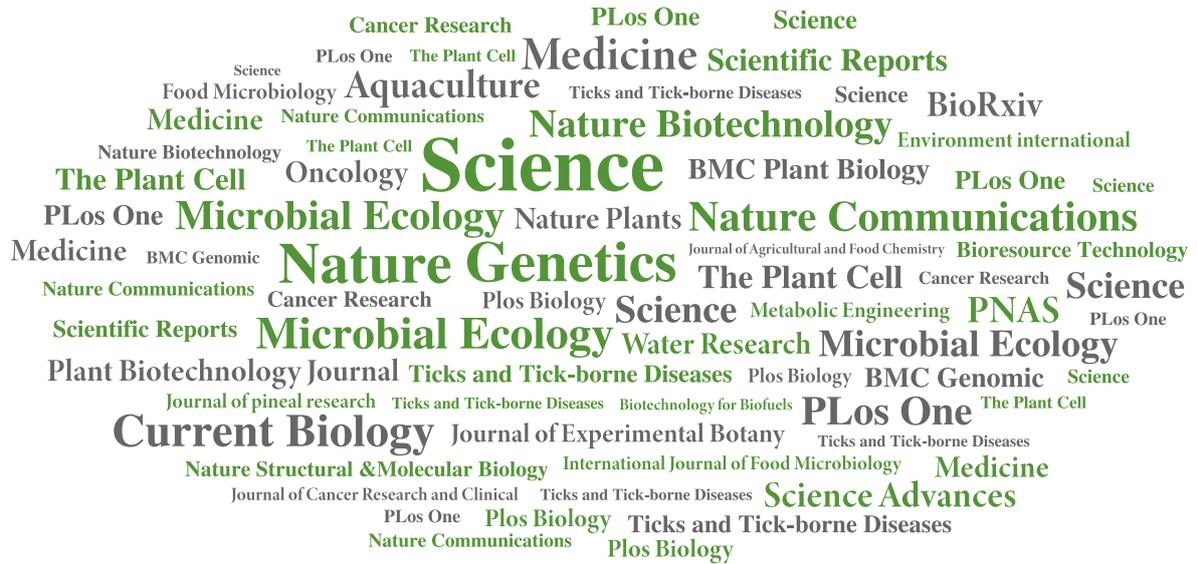


Novogene Research Collection



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Additional Publications



The *Apostasia* genome and the evolution of orchids

Species: Orchids

Journal: Nature

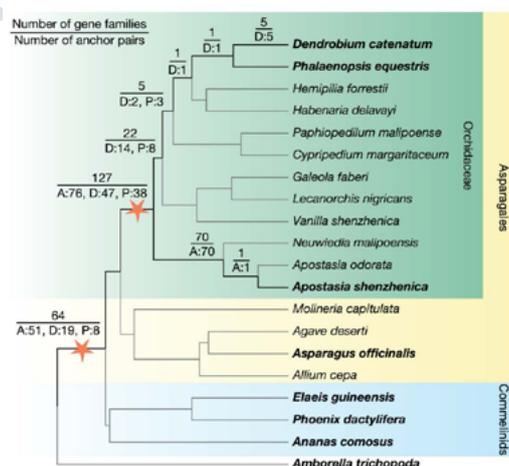
Impact factor: 40.137

Customer coauthor: The National Orchid Conservation Center of China, The Orchid Conservation and Research Center of Shenzhen

Publication time: September 2017

Abstract

Constituting approximately 10% of flowering plant species, orchids (Orchidaceae) display unique flower morphologies, possess an extraordinary diversity in lifestyle, and have successfully colonized almost every habitat on Earth. Here we report the draft genome sequence of *Apostasia shenzhenica*, a representative of one of two genera that form a sister lineage to the rest of the Orchidaceae, providing a reference for inferring the genome content and structure of the most recent common ancestor of all extant orchids and improving our understanding of their origins and evolution. In addition, we present transcriptome data for representatives of Vanilloideae, Cypripedioideae and Orchidoideae, and novel third generation genome data for two species of Epidendroideae, covering all five orchid subfamilies. *A. shenzhenica* shows clear evidence of a whole-genome duplication, which is shared by all orchids and occurred shortly before their divergence. Comparisons between *A. shenzhenica* and other orchids and angiosperms also permitted the reconstruction of an ancestral orchid gene toolkit. We identify new gene families, gene family expansions and contractions, and changes within MADS-box gene classes, which control a diverse suite of developmental processes, during orchid evolution. This study sheds new light on the genetic mechanisms underpinning key orchid innovations, including the development of the labellum and gynostemium, pollinia, and seeds without endosperm, as well as the evolution of epiphytism; reveals relationships between the Orchidaceae subfamilies; and helps clarify the evolutionary history of orchids within the angiosperms.



Phylogenomic analysis of orchid WGD events

Reference

G. Q. Zhang, et al., The *Apostasia* genome and the evolution of orchids. Nature doi:10.1038/nature23897 (2017).

Scallop genome reveals molecular adaptations to semi-sessile life and neurotoxins

Species: Scallop

Journal: Nature Communications

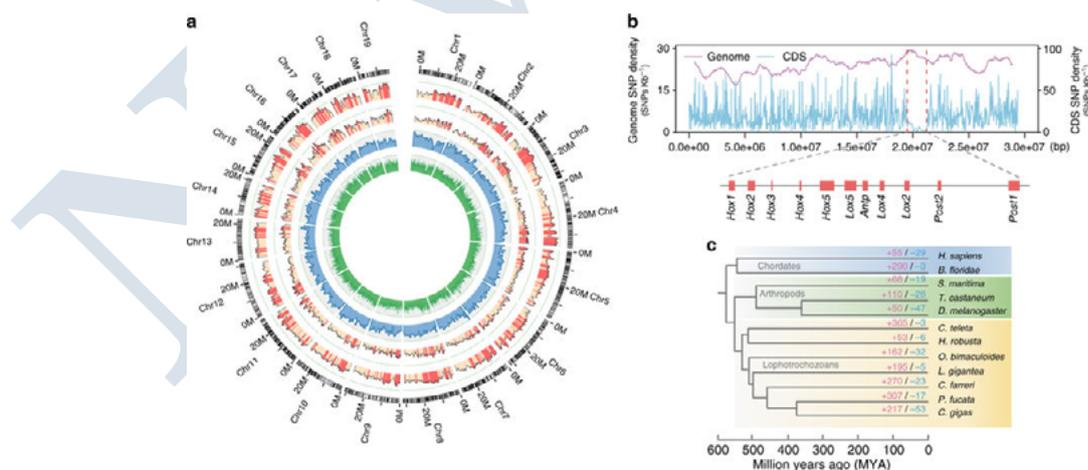
Impact factor: 12.124

Customer coauthor: Ocean University of China, Rutgers University

Publication time: November 2017

Abstract

Bivalve molluscs are descendants of an early-Cambrian lineage superbly adapted to benthic filter feeding. Adaptations in form and behavior are well recognized, but the underlying molecular mechanisms are largely unknown. Here, we investigate the genome, various transcriptomes, and proteomes of the scallop *Chlamys farreri*, a semi-sessile bivalve with well-developed adductor muscle, sophisticated eyes, and remarkable neurotoxin resistance. The scallop's large striated muscle is energy-dynamic but not fully differentiated from smooth muscle. Its eyes are supported by highly diverse, intronless opsins expanded by retroposition for broadened spectral sensitivity. Rapid byssal secretion is enabled by a specialized foot and multiple proteins including expanded tyrosinases. The scallop uses hepatopancreas to accumulate neurotoxins and kidney to transform to high-toxicity forms through expanded sulfotransferases, probably as deterrence against predation, while it achieves neurotoxin resistance through point mutations in sodium channels. These findings suggest that expansion and mutation of those genes may have profound effects on scallop's phenotype and adaptation.



Genome landscape and polymorphism analysis of the scallop *C. farreri*

Reference

Y. Li, et al., Scallop genome reveals molecular adaptations to semi-sessile life and neurotoxins. Nature Communications 3, 946 (2017).

The *Aegilops tauschii* genome reveals multiple impacts of transposons

Species: Wheat

Journal: Nature Plants

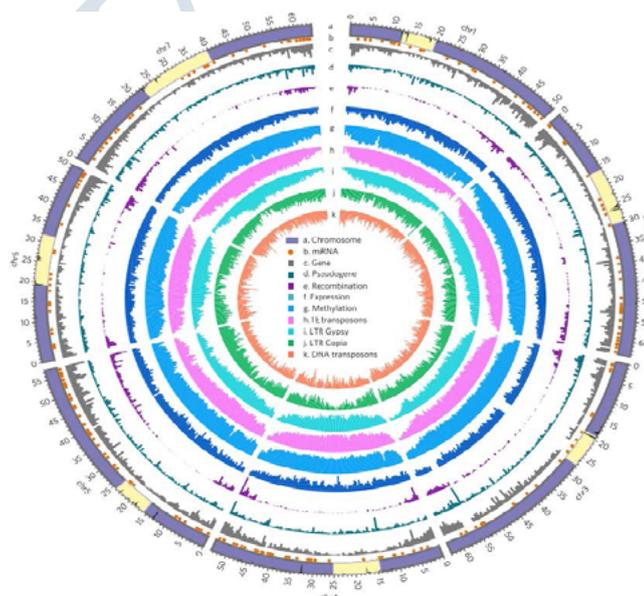
Impact factor: 10.3

Customer coauthor: Chinese Academy of Agricultural Sciences, Chinese Academy of Sciences

Publication time: November 2017

Abstract

Wheat is an important global crop with an extremely large and complex genome that contains more transposable elements (TEs) than any other known crop species. Here, we generated a chromosome-scale, high-quality reference genome of *Aegilops tauschii*, the donor of the wheat D genome, in which 92.5% sequences have been anchored to chromosomes. Using this assembly, we accurately characterized genic loci, gene expression, pseudogenes, methylation, recombination ratios, microRNAs and especially TEs on chromosomes. In addition to the discovery of a wave of very recent gene duplications, we detected that TEs occurred in about half of the genes, and found that such genes are expressed at lower levels than those without TEs, presumably because of their elevated methylation levels. We mapped all wheat molecular markers and constructed a high-resolution integrated genetic map corresponding to genome sequences, thereby placing previously detected agronomically important genes/quantitative trait loci (QTLs) on the *Ae. tauschii* genome for the first time.



Distribution of genomic features in the *Aegilops tauschii* genome

Reference

G. Zhou, et al., The *Aegilops tauschii* genome reveals multiple impacts of transposons. *Nature Plants* 3, 946 (2017).

Comprehensive variation discovery and recovery of missing sequence in the pig genome using multiple *de novo* assemblies

Species: Pig

Journal: Genome Research

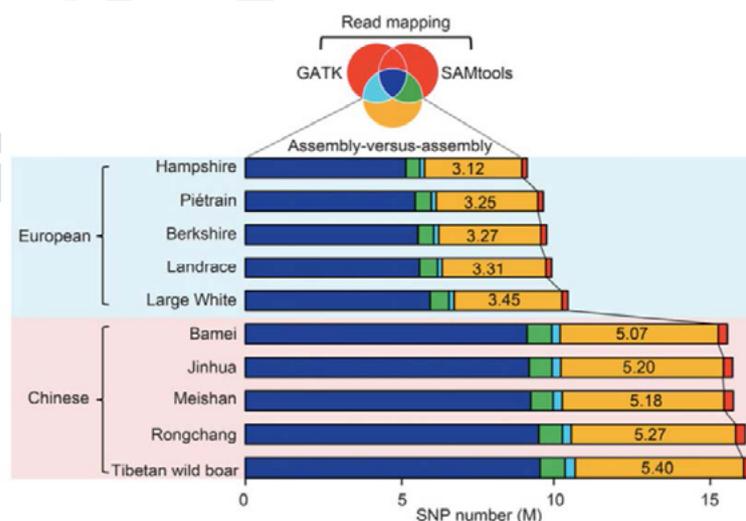
Impact factor: 11.351

Customer coauthor: Sichuan Agricultural University, Harvard Medical School

Publication time: May 2017

Abstract

Uncovering genetic variation through resequencing is limited by the fact that only sequences with similarity to the reference genome are examined. Reference genomes are often incomplete and cannot represent the full range of genetic diversity as a result of geographical divergence and independent demographic events. To more comprehensively characterize genetic variation of pigs (*Sus scrofa*), we generated *de novo* assemblies of nine geographically and phenotypically representative pigs from Eurasia. By comparing them to the reference pig assembly, we uncovered a substantial number of novel SNPs, structural variations, as well as 137.02 Mb sequences harboring 1,737 protein coding genes that were absent in the reference assembly, revealing variants left by selection. Our results illustrate the power of whole-genome *de novo* sequencing relative to resequencing, and provide valuable genetic resources that enable effective use of pigs in both agricultural production and biomedical research.



Comparison of SNP calling between assembly-versus-assembly method and resequencing approaches based on read mapping

Reference

M. Li, et al., Comprehensive variation discovery and recovery of missing sequence in the pig genome using multiple *de novo* assemblies. *Genome Research* 27, 865 (2017).

Scallop genome provides insights into evolution of bilaterian karyotype and development

Species: Scallop

Journal: Nature Ecology & Evolution

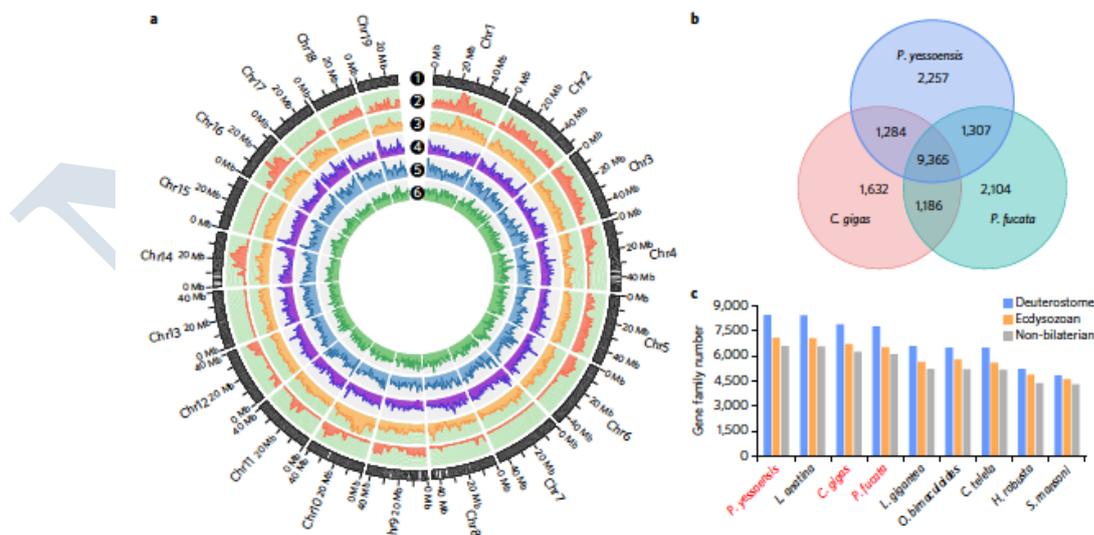
Impact factor: N/A

Customer coauthor: Ocean University of China, Rutgers University

Publication time: April 2017

Abstract

Reconstructing the genomes of bilaterian ancestors is central to our understanding of animal evolution, where knowledge from ancient and/or slow-evolving bilaterian lineages is critical. Here we report a high-quality, chromosome-anchored reference genome for the scallop *Patinopecten yessoensis*, a bivalve mollusc that has a slow-evolving genome with many ancestral features. Chromosome-based macrosynteny analysis reveals a striking correspondence between the 19 scallop chromosomes and the 17 presumed ancestral bilaterian linkage groups at a level of conservation previously unseen, suggesting that the scallop may have a karyotype close to that of the bilaterian ancestor. Scallop Hox gene expression follows a new mode of subcluster temporal colinearity that is possibly ancestral and may provide great potential in supporting diverse bilaterian body plans. Transcriptome analysis of scallop mantle eyes finds unexpected diversity in phototransduction cascades and a potentially ancient Pax2/5/8-dependent pathway for noncephalic eyes. The outstanding preservation of ancestral karyotype and developmental control makes the scallop genome a valuable resource for understanding evolution and biology.



The genome landscape and gene family analysis of the scallop *P. yessoensis*

Reference

S. Wang, et al., Scallop genome provides insights into evolution of bilaterian karyotype and development. Nature Ecology & Evolution 1, 0120 (2017).

Sequencing of allotetraploid cotton (*Gossypium hirsutum* L. acc. TM-1) provides a resource for fiber improvement

Species: Allotetraploid cotton

Journal: Nature Biotechnology

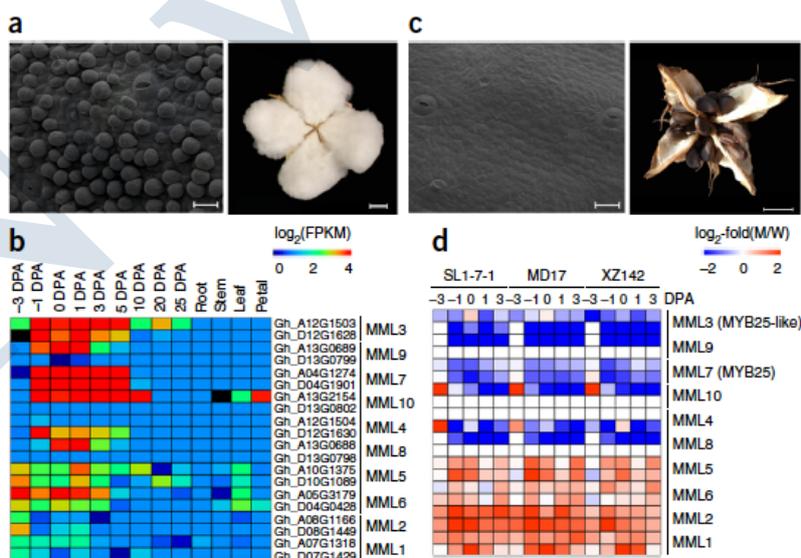
Impact factor: 43.113

Customer coauthor: Nanjing Agricultural University, University of Texas at Austin

Publication time: April 2015

Abstract

Upland cotton is a model for polyploid crop domestication and transgenic improvement. Here we sequenced the allotetraploid *Gossypium hirsutum* L. acc. TM-1 genome by integrating whole-genome shotgun reads, bacterial artificial chromosome (BAC)-end sequences and genotype-by-sequencing genetic maps. We assembled and annotated 32,032 A-subgenome genes and 34,402 Dsubgenome genes. Structural rearrangements, gene loss, disrupted genes and sequence divergence were more common in the A subgenome than in the D subgenome, suggesting asymmetric evolution. However, no genome-wide expression dominance was found between the subgenomes. Genomic signatures of selection and domestication are associated with positively selected genes (PSGs) for fiber improvement in the A subgenome and for stress tolerance in the D subgenome. This draft genome sequence provides a resource for engineering superior cotton lines.



Expression pattern of the MYBMIXTA- like gene family in wild type cotton and fiberless

Reference

T. Zhang, et al., Sequencing of allotetraploid cotton (*Gossypium hirsutum* L. acc. TM-1) provides a resource for fiber improvement. *Nature Biotechnology* 33, 531 (2015).

Whole-genome sequencing of the snub-nosed monkey provides insights into folivory and evolutionary history

Species: Snub-nosed monkey

Journal: Nature Genetics

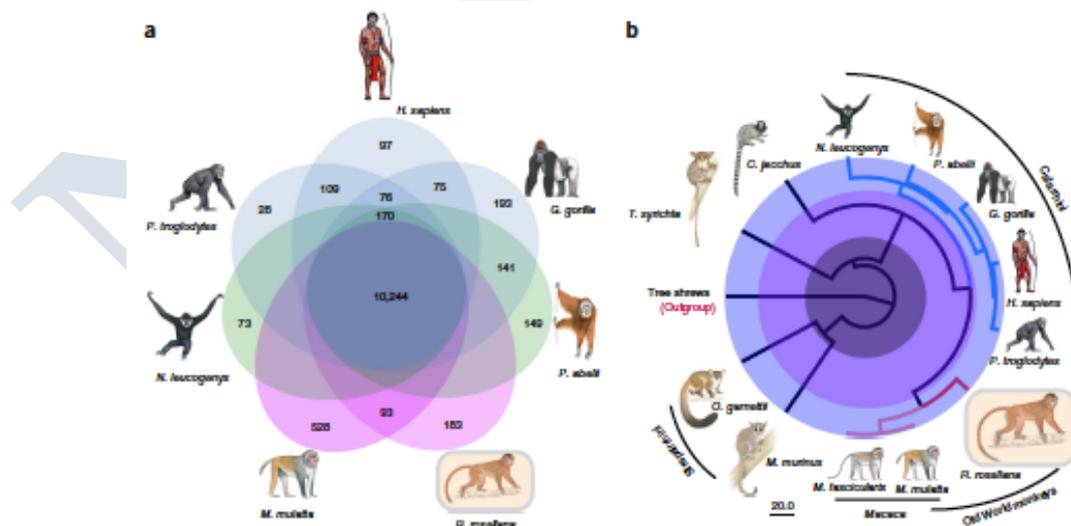
Impact factor: 29.352

Customer coauthor: Institute of Zoology, Chinese Academy of Sciences

Publication time: November 2014

Abstract

Colobines are a unique group of Old World monkeys that principally eat leaves and seeds rather than fruits and insects. We report the sequencing at 146× coverage, de novo assembly and analyses of the genome of a male golden snub-nosed monkey (*Rhinopithecus roxellana*) and resequencing at 30× coverage of three related species (*Rhinopithecus bieti*, *Rhinopithecus brelichi* and *Rhinopithecus strykeri*). Comparative analyses showed that Asian colobines have an enhanced ability to derive energy from fatty acids and to degrade xenobiotics. We found evidence for functional evolution in the colobine RNASE1 gene, encoding a key secretory RNase that digests the high concentrations of bacterial RNA derived from symbiotic microflora. Demographic reconstructions indicated that the profile of ancient effective population sizes for *R. roxellana* more closely resembles that of giant panda rather than its congeners. These findings offer new insights into the dietary adaptations and evolutionary history of colobine primates.



Orthologous gene families and phylogenetic tree of primates

Reference

X. Zhou, et al., Whole-genome sequencing of the snub-nosed monkey provides insights into folivory and evolutionary history. Nature Genetics 46, 1303 (2014).

Genomic analyses identify distinct patterns of selection in domesticated pigs and Tibetan wild boars

Species: Tibetan wild boars

Journal: Nature Genetics

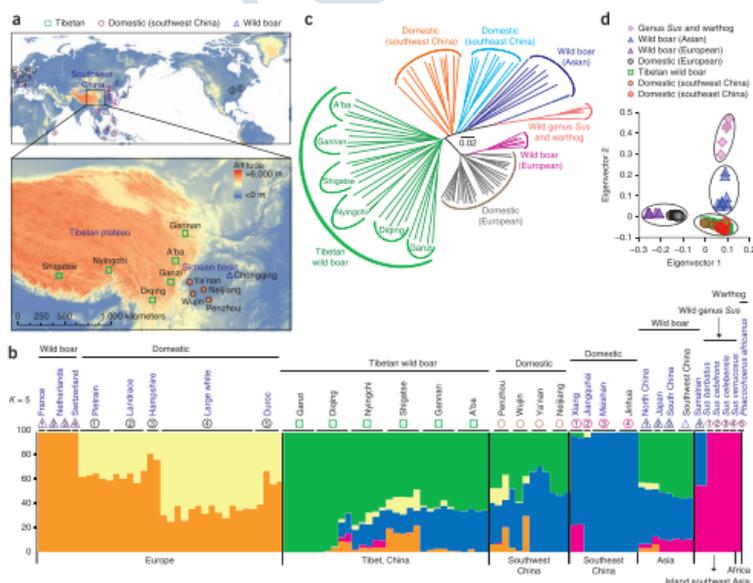
Impact factor: 29.352

Customer coauthor: Sichuan Agricultural University

Publication time: October 2013

Abstract

We report the sequencing at 131× coverage, *de novo* assembly and analyses of the genome of a female Tibetan wild boar. We also resequenced the whole genomes of 30 Tibetan wild boars from six major distributed locations and 18 geographically related pigs in China. We characterized genetic diversity, population structure and patterns of evolution. We searched for genomic regions under selection, which includes genes that are involved in hypoxia, olfaction, energy metabolism and drug response. Comparing the genome of Tibetan wild boar with those of neighboring Chinese domestic pigs further showed the impact of thousands of years of artificial selection and different signatures of selection in wild boar and domestic pig. We also report genetic adaptations in Tibetan wild boar that are associated with high altitudes and characterize the genetic basis of increased salivation in domestic pig.



Population genetics and demographic history

Reference

M. Li, et al., Genomic analyses identify distinct patterns of selection in domesticated pigs and Tibetan wild boars. *Nature Genetics* 45, 1431 (2013).

Genetic alterations in esophageal tissues from squamous dysplasia to carcinoma

Species: Human

Journal: Gastroenterology

Impact factor: 18.39

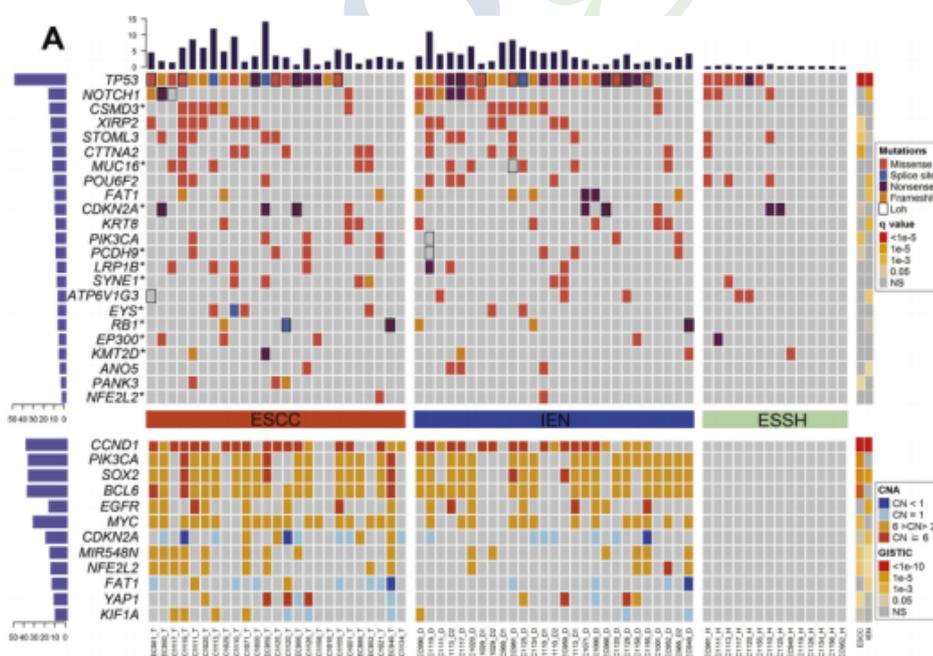
Customer coauthor: Shantou University Medical College

Publication time: July 2017

Abstract

BACKGROUND & AIMS: Esophageal squamous cell carcinoma(ESCC) is the most common subtype of esophageal cancer. Little is known about the genetic changes that occur in esophageal cells during the development of ESCC. We performed next generation sequence analyses of esophageal nontumor, intraepithelial neoplasia (IEN), and ESCC tissues from the same patients to track genetic changes during tumor development

CONCLUSIONS: We analyzed mutations and gene copy number changes in nontumor, IEN, and ESCC samples, collected from 70 patients. IEN and ESCCs each had similar mutations and markers of genomic instability, including apolipoprotein B messenger RNA editing enzyme, catalytic polypeptide-like. Genomic changes observed in precancerous lesions might be used to identify patients at risk for ESCC.



The variation landscape of ESCC, IEN, and ESSH

Reference

X. Liu, et al., Genetic alterations in esophageal tissues from squamous dysplasia to carcinoma. *Gastroenterology* 153, 166 (2017).

Probing meiotic recombination and aneuploidy of single sperm cells by whole-genome sequencing

Species: Human, sperm cells

Journal: Science

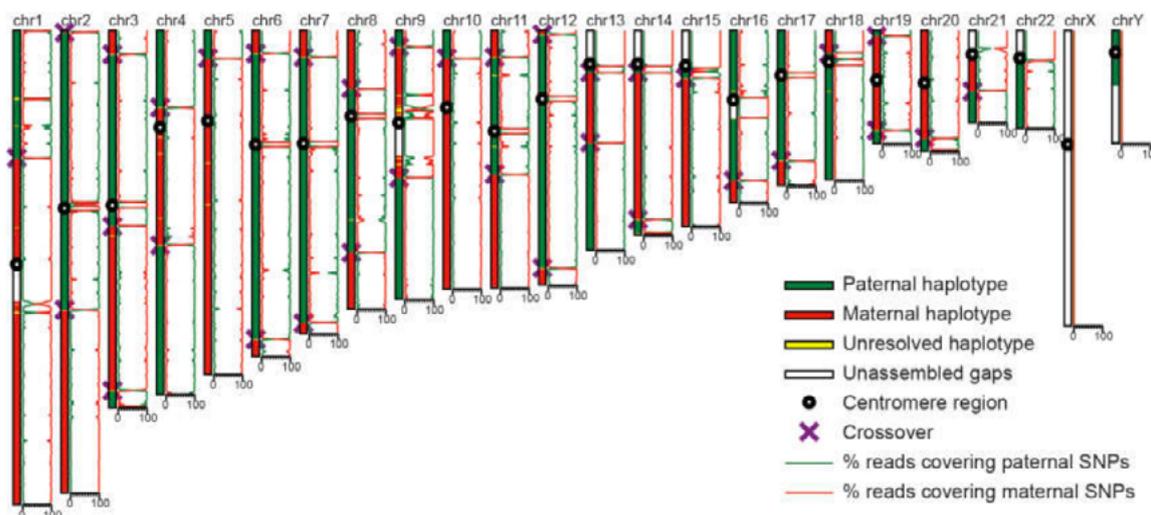
Impact factor: 35.26

Customer coauthor: Harvard University, Peking University

Publication time: December 2012

Abstract

Meiotic recombination creates genetic diversity and ensures segregation of homologous chromosomes. Previous population analyses yielded results averaged among individuals and impacted by evolutionary pressures. Here we sequenced 99 sperm from an Asian male using the newly developed amplification method—Multiple Annealing and Looping-Based Amplification Cycles (MALBAC)—to phase the personal genome and map at high resolution recombination events, which are non-uniformly distributed across the genome in the absence of selection pressure. The paucity of recombination near transcription start sites observed in individual sperm indicates such a phenomenon is intrinsic to the molecular mechanism of meiosis. Interestingly, a decreased crossover frequency in companion with an increase of autosomal aneuploidy is observable on a global per-sperm basis.



Genetic map of single sperm

Reference

S. Lu, et al., Probing meiotic recombination and aneuploidy of single sperm cells by whole-genome sequencing. *Science* 338, 1627 (2012).

Simultaneous evolutionary expansion and constraint of genomic heterogeneity in multifocal lung cancer

Species: Human, lung cancer cells

Journal: Nature Communications

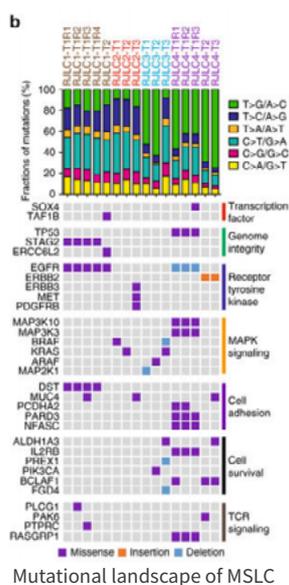
Impact factor: 12.124

Customer coauthor: Shanghai Jiao Tong University, University of California, San Francisco

Publication time: October 2017

Abstract

Recent genomic analyses have revealed substantial tumor heterogeneity across various cancers. However, it remains unclear whether and how genomic heterogeneity is constrained during tumor evolution. Here, we sequence a unique cohort of multiple synchronous lung cancers (MSLCs) to determine the relative diversity and uniformity of genetic drivers upon identical germline and environmental background. We find that each multicentric primary tumor harbors distinct oncogenic alterations, including novel mutations that are experimentally demonstrated to be functional and therapeutically targetable. However, functional studies show a strikingly constrained tumorigenic pathway underlying heterogeneous genetic variants. These results suggest that although the mutation-specific routes that cells take during oncogenesis are stochastic, genetic trajectories may be constrained by selection for functional convergence on key signaling pathways. Our findings highlight the robust evolutionary pressures that simultaneously shape the expansion and constraint of genomic diversity, a principle that holds important implications for understanding tumor evolution and optimizing therapeutic strategies.



Reference

P. Ma, et al., Simultaneous evolutionary expansion and constraint of genomic heterogeneity in multifocal lung cancer. Nature Communications 8, 823 (2017).

Single-cell exome sequencing identifies mutations in KCP, LOC440040, and LOC440563 as drivers in renal cell carcinoma stem cells

Species: Human, renal cell carcinoma stem cells

Journal: Cell Research

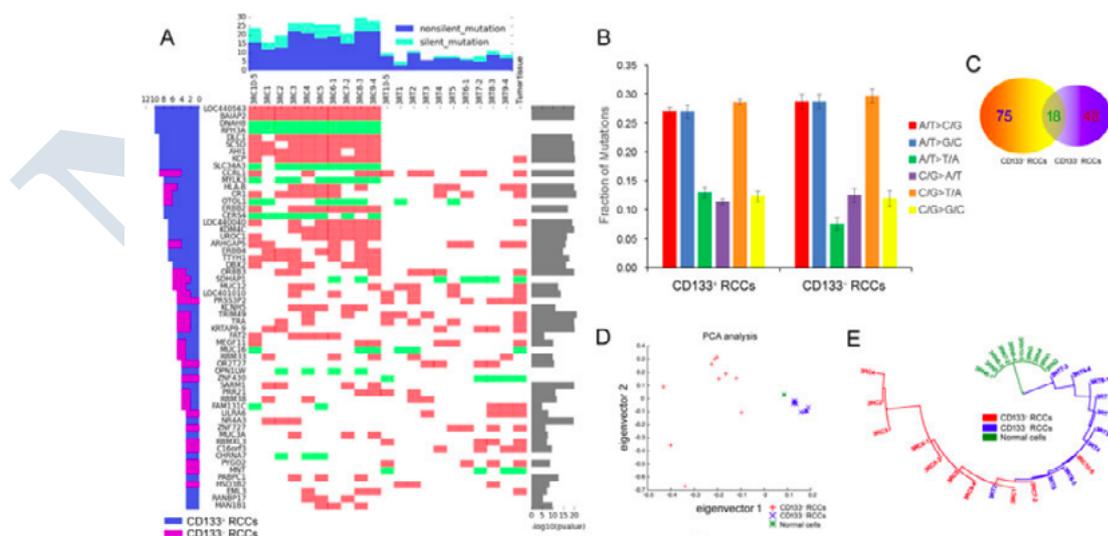
Impact factor: 14.812

Customer coauthor: Chinese Academy of Sciences

Publication time: April 20177

Abstract

In summary, using single-cell exome sequencing, we discovered that CD133+ RCC cells have CSC properties and likely originate from cancer cells instead of from normal renal cells. KCP, LOC440040, and LOC440563 mutations are novel renal cancer stem cell drivers. LOC440563 encodes an RNA-binding protein, which belongs to the subfamily of heterogeneous nuclear ribonucleoproteins (hnRNPs). It influences pre-mRNA processing, metabolism and transport bib88, bib99. LOC440563 is significantly mutated in colon cancer; however, the mutations are different from what we identified in RCC CSCs bib1010. Considering the contribution of the hnRNP family to DNA damage repair bib1111, it is possible that the LOC440563 mutation may drive CSC stemness via impairing the DNA repair process. LOC440040 is a GRM5 (glutamate receptor, metabotropic 5) pseudogene. GRM5 belongs to the mGluR family, and dysregulated glutamatergic signaling is involved in many cancer types, such as glioma and melanoma bib1212. However, the relationship between LOC440040 and cancer is currently unknown (from the last paragraph of the paper).



Identification of driver genes in renal cell carcinoma stem cells via single-cell exome sequencing

Reference

C. Li, et al., Single-cell exome sequencing identifies mutations in KCP, LOC440040, and LOC440563 as drivers in renal cell carcinoma stem cells. Cell Research 27, 590 (2017).

Signatures of adaptation in the weedy rice genome

Species: Weedy rice

Journal: Nature Genetics

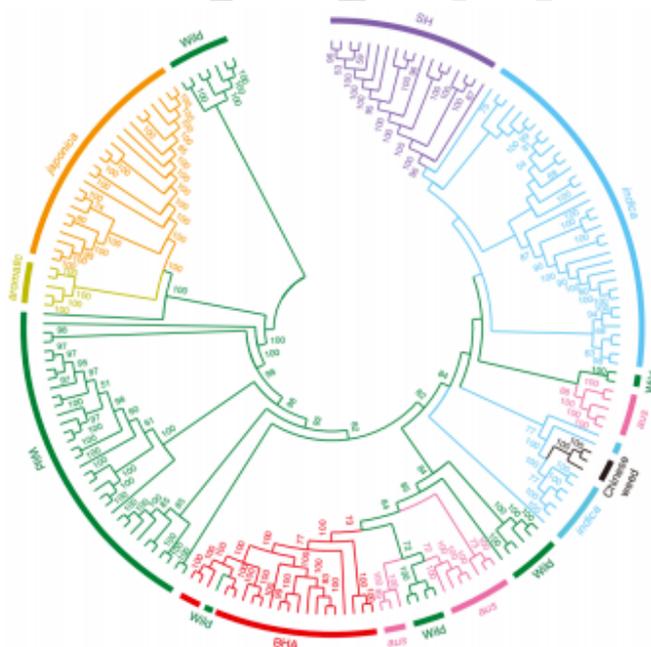
Impact factor: 29.6

Customer coauthor: Chinese Academy of Sciences, Washington University in St. Louis

Publication time: April 2017

Abstract

Crop domestication provided the calories that fueled the rise of civilization. For many crop species, domestication was accompanied by the evolution of weedy crop relatives, which aggressively outcompete crops and reduce harvests. Understanding the genetic mechanisms that underlie the evolution of weedy crop relatives is critical for agricultural weed management and food security. Here we use whole-genome sequences to examine the origin and adaptation of the two major strains of weedy rice found in the United States. We find that de-domestication from cultivated ancestors has had a major role in their evolution, with relatively few genetic changes required for the emergence of weediness traits. Weed strains likely evolved both early and late in the history of rice cultivation and represent an under-recognized component of the domestication process. Genomic regions identified here that show evidence of selection can be considered candidates for future genetic and functional analyses for rice improvement.



Neighbor-joining tree of the 183 wild, cultivated, and weedy rice accessions

Reference

L. F. Li, et al., Signatures of adaptation in the weedy rice genome. *Nature Genetics* 49, 811 (2017).

Single-cell 5-formylcytosine landscapes of mammalian early embryos and ESCs at single-base resolution

Species: Mice

Journal: Cell Stem Cell

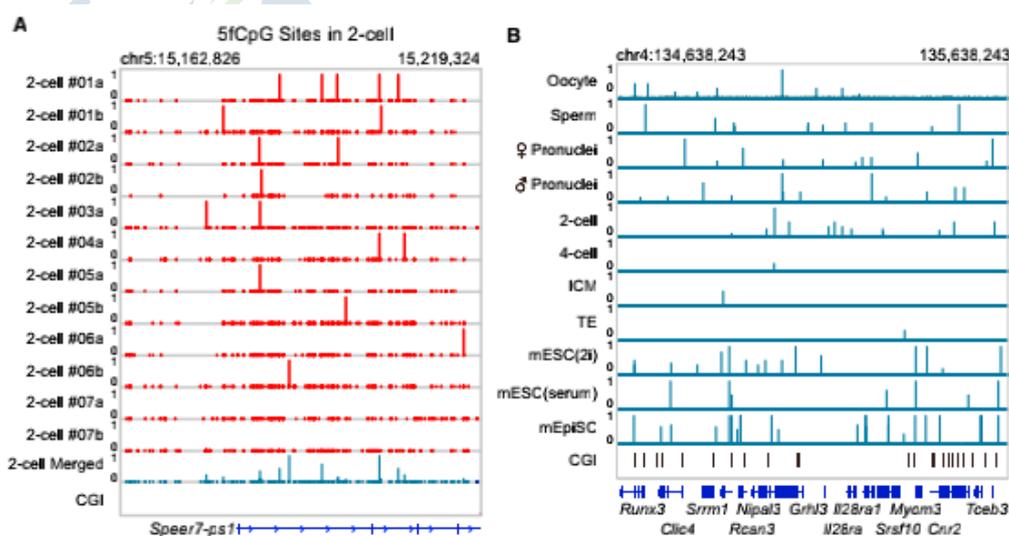
Impact factor: 22.387

Customer coauthor: Chinese Academy of Sciences, Harvard Medical School

Publication time: March 2017

Abstract

Active DNA demethylation in mammals involves ten-eleven translocation (TET) family protein-mediated oxidation of 5 methylcytosine (5mC). However, base-resolution landscapes of 5-formylcytosine (5fC) (an oxidized derivative of 5mC) at the singlecell level remain unexplored. Here, we present “CLEVER-seq” (chemical-labeling-enabled C-to-T conversion sequencing), which is a single-cell, single-base resolution 5fC-sequencing technology, based on biocompatible, selective chemical labeling of 5fC and subsequent C-to-T conversion during amplification and sequencing. CLEVER-seq shows intrinsic 5fC heterogeneity in mouse early embryos, Epi stem cells (EpiSCs), and embryonic stem cells (ESCs). CLEVER-seq of mouse early embryos also reveals the highly patterned genomic distribution and parental-specific dynamics of 5fC during mouse early pre-implantation development. Integrated analysis demonstrates that promoter 5fC production precedes the expression up-regulation of a clear set of developmentally and metabolically critical genes. Collectively, our work reveals the dynamics of active DNA demethylation during mouse pre-implantation development and provides an important resource for further functional studies of epigenetic reprogramming in single cells.



The landscape of DNA formylation in mouse pluripotent stem cells and early embryos

Reference

C. Zhu, et al., Single-cell 5-formylcytosine landscapes of mammalian early embryos and ESCs at single-base resolution. Cell Stem Cell 20, 720 (2017)

Population genomics reveals low genetic diversity and adaptation to hypoxia in snub-nosed monkeys

Species: Snub-nosed monkey

Journal: Molecular Biology and Evolution

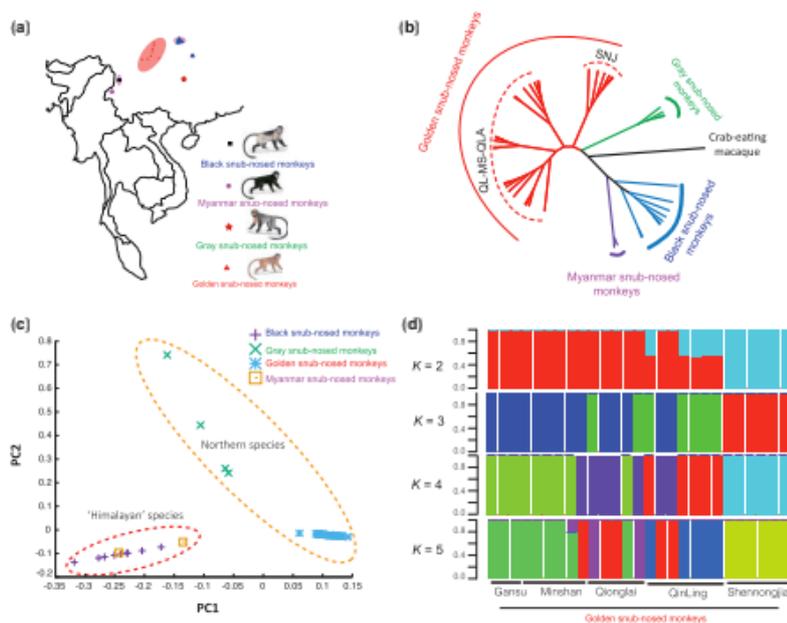
Impact factor: 13.649

Customer coauthor: Chinese Academy of Sciences, Harvard Medical School

Publication time: August 2016

Abstract

Snub-nosed monkeys (genus *Rhinopithecus*) are a group of endangered colobines endemic to South Asia. Here, we re-sequenced the whole genomes of 38 snub-nosed monkeys representing four species within this genus. By conducting population genomic analyses, we observed a similar load of deleterious variation in snub-nosed monkeys living in both smaller and larger populations and found that genomic diversity was lower than that reported in other primates. Reconstruction of *Rhinopithecus* evolutionary history suggested that episodes of climatic variation over the past 2 million years, associated with glacial advances and retreats and population isolation, have shaped snub-nosed monkey demography and evolution. We further identified several hypoxia-related genes under selection in *R. bieti* (black snub-nosed monkey), a species that exploits habitats higher than any other nonhuman primate. These results provide the first detailed and comprehensive genomic insights into genetic diversity, demography, genetic burden and adaptation in this radiation of endangered primates.



Geographic distribution, phylogenetics, and population structure of snub-nosed monkeys

Reference

X. Zhou, et al., Population genomics reveals low genetic diversity and adaptation to hypoxia in snub-nosed monkeys. *Molecular Biology & Evolution* 33, 2670 (2016).

Whole-genome sequencing of native sheep provides insights into rapid adaptations to extreme environments

Species: Sheep

Journal: Molecular Biology and Evolution

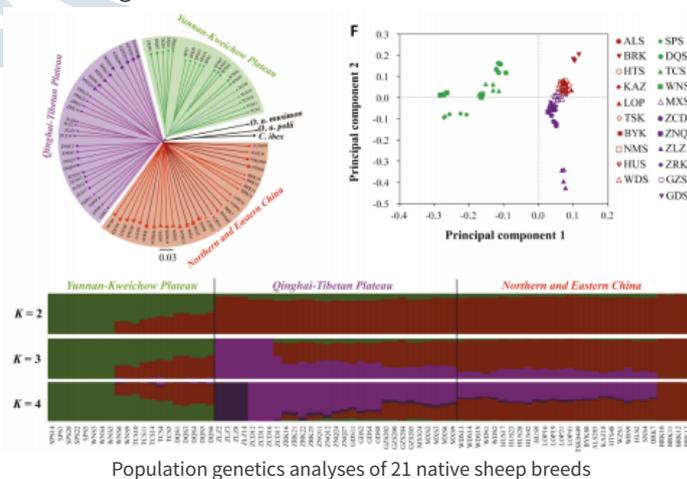
Impact factor: 13.649

Customer coauthor: Chinese Academy of Sciences

Publication time: July 2016

Abstract

Global climate change has a significant effect on extreme environments and a profound influence on species survival. However, little is known of the genome-wide pattern of livestock adaptations to extreme environments over a short time frame following domestication. Sheep (*Ovis aries*) have become well adapted to a diverse range of agroecological zones, including certain extreme environments (e.g., plateaus and deserts), during their post-domestication (approximately 8–9 kya) migration and differentiation. Here, we generated whole-genome sequences from 77 native sheep, with an average effective sequencing depth of $\sim 5\times$ for 75 samples and $\sim 42\times$ for two samples. Comparative genomic analyses among sheep in contrasting environments, i.e., plateau ($> 4,000$ m above sea level) versus lowland (< 100 m), high-altitude region ($> 1,500$ m) versus low-altitude region ($< 1,300$ m), desert (< 10 mm average annual precipitation) versus highly humid region (> 600 mm), and arid zone (< 400 mm) versus humid zone (> 400 mm), detected a novel set of candidate genes as well as pathways and GO categories that are putatively associated with hypoxia responses at high altitudes and water reabsorption in arid environments. Additionally, candidate genes and GO terms functionally related to energy metabolism and body size variations were identified. This study offers novel insights into rapid genomic adaptations to extreme environments in sheep and other animals, and provides a valuable resource for future research on livestock breeding in response to climate change.



Population genetics analyses of 21 native sheep breeds

Reference

J. Yang, et al., Whole-genome sequencing of native sheep provides insights into rapid adaptations to extreme environments. *Molecular Biology & Evolution* 33, 2576 (2016).

Genomic analyses reveal demographic history and temperate adaptation of the newly discovered honey bee subspecies *Apis mellifera sinisxinyuan* n. ssp.

Species: Honey bee

Journal: Molecular Biology and Evolution

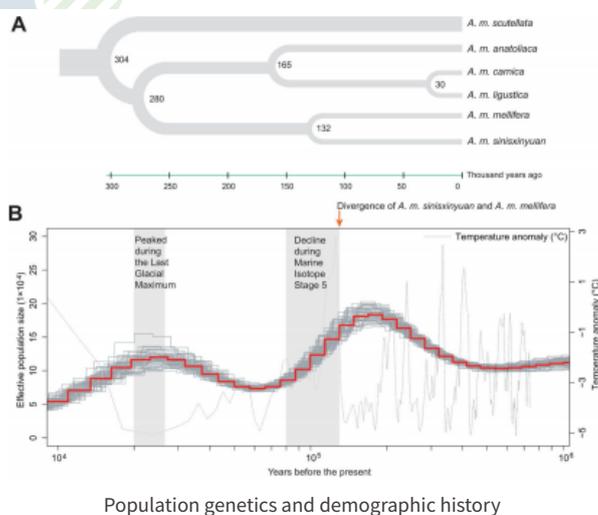
Impact factor: 13.649

Customer coauthor: Chinese Academy of Agricultural Sciences

Publication time: January 2016

Abstract

Studying the genetic signatures of climate-driven selection can produce insights into local adaptation and the potential impacts of climate change on populations. The honey bee (*Apis mellifera*) is an interesting species to study local adaptation because it originated in tropical/subtropical climatic regions and subsequently spread into temperate regions. However, little is known about the genetic basis of its adaptation to temperate climates. Here, we resequenced the whole genomes of ten individual bees from a newly discovered population in temperate China and downloaded resequenced data from 35 individuals from other populations. We found that the new population is an undescribed subspecies in the M-lineage of *A. mellifera* (*Apis mellifera sinisxinyuan*). Analyses of population history show that long-term global temperature has strongly influenced the demographic history of *A. m. sinisxinyuan* and its divergence from other subspecies. Further analyses comparing temperate and tropical populations identified several candidate genes related to fat body and the Hippo signaling pathway that are potentially involved in adaptation to temperate climates. Our results provide insights into the demographic history of the newly discovered *A. m. sinisxinyuan*, as well as the genetic basis of adaptation of *A. mellifera* to temperate climates at the genomic level. These findings will facilitate the selective breeding of *A. mellifera* to improve the survival of overwintering colonies.



Reference

C. Chen, et al., Genomic analyses reveal demographic history and temperate adaptation of the newly discovered honey bee subspecies *Apis mellifera sinisxinyuan* n. ssp. *Molecular Biology & Evolution* 33, 1337 (2016).

The draft genome of watermelon (*Citrullus lanatus*) and resequencing of 20 diverse accessions

Species: Watermelon

Journal: Nature Genetics

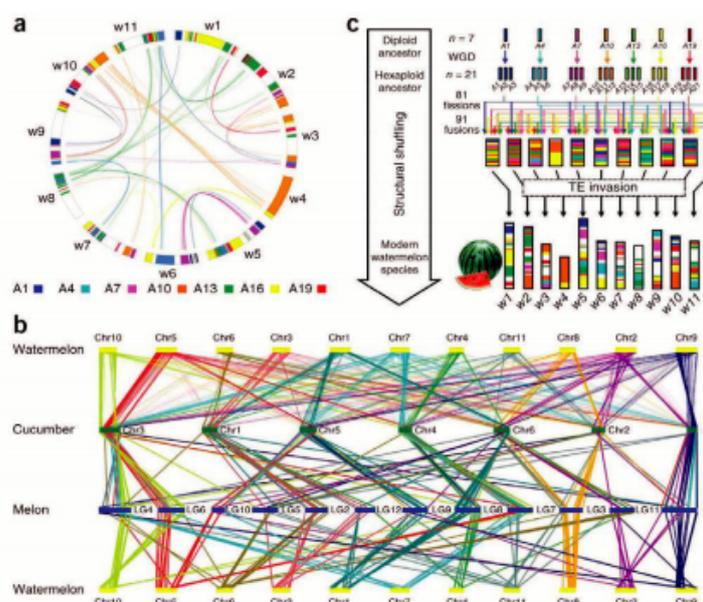
Impact factor: 29.352

Customer coauthor: Beijing Academy of Agriculture and Forestry Sciences, Cornell University, University of California, Davis

Publication time: November 2012

Abstract

Watermelon, *Citrullus lanatus*, is an important cucurbit crop grown throughout the world. Here we report a high-quality draft genome sequence of the east Asia watermelon cultivar 97103 ($2n = 2 \times = 22$) containing 23,440 predicted protein-coding genes. Comparative genomics analysis provided an evolutionary scenario for the origin of the 11 watermelon chromosomes derived from a 7-chromosome paleohexaploid eudicot ancestor. Resequencing of 20 watermelon accessions representing three different *C. lanatus* subspecies produced numerous haplotypes and identified the extent of genetic diversity and population structure of watermelon germplasm. Genomic regions that were preferentially selected during domestication were identified. Many disease-resistance genes were also found to be lost during domestication. In addition, integrative genomic and transcriptomic analyses yielded important insights into aspects of phloem-based vascular signaling in common between watermelon and cucumber and identified genes crucial to valuable fruit-quality traits, including sugar accumulation and citrulline metabolism.



Genome synteny, duplication patterns and evolutionary history of watermelon, cucumber and melon

Reference

S. Guo, et al., The draft genome of watermelon (*Citrullus lanatus*) and resequencing of 20 diverse accessions. *Nature Genetics* 45, 5 (2012).

Single-cell RNA-seq analysis maps development of human germline cells and gonadal niche interactions

Species: Human

Journal: Cell Stem Cell

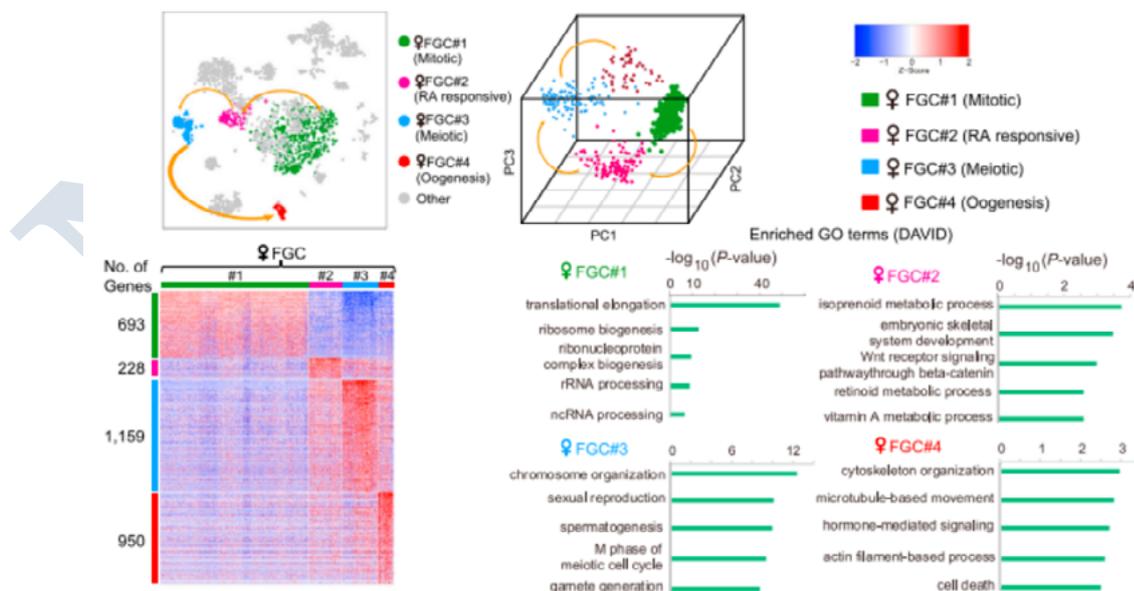
Impact factor: 22.2

Customer coauthor: Peking University

Publication time: June 2017

Abstract

Human fetal germ cells (FGCs) are precursors to sperm and eggs and are crucial for maintenance of the species. However, the developmental trajectories and heterogeneity of human FGCs remain largely unknown. Here we performed single-cell RNA-seq analysis of over 2,000 FGCs and their gonadal niche cells in female and male human embryos spanning several developmental stages. We found that female FGCs undergo four distinct sequential phases characterized by mitosis, retinoic acid signaling, meiotic prophase, and oogenesis. Male FGCs develop through stages of migration, mitosis, and cell-cycle arrest. Individual embryos of both sexes simultaneously contain several subpopulations, highlighting the asynchronous and heterogeneous nature of FGC development. Moreover, we observed reciprocal signaling interactions between FGCs and their gonadal niche cells, including activation of the bone morphogenic protein (BMP) and Notch signaling pathways. Our work provides key insights into the crucial features of human FGCs during their highly ordered mitotic, meiotic, and gametogenetic processes in vivo.



Dynamic gene Expression Patterns of Human Female FGCs

Reference

L. Li, et al., Single-cell RNA-seq analysis maps development of human germline cells and gonadal niche interactions. Cell Stem Cell 20, 858 (2017).

Identification and functional characterization of hypoxia-induced endoplasmic reticulum stress regulating lncRNA (HypERlnc) in pericytes

Species: Human

Journal: Circulation Research

Impact factor: 11.1

Customer coauthor: Beijing Neurosurgical Institute, University of California, San Diego

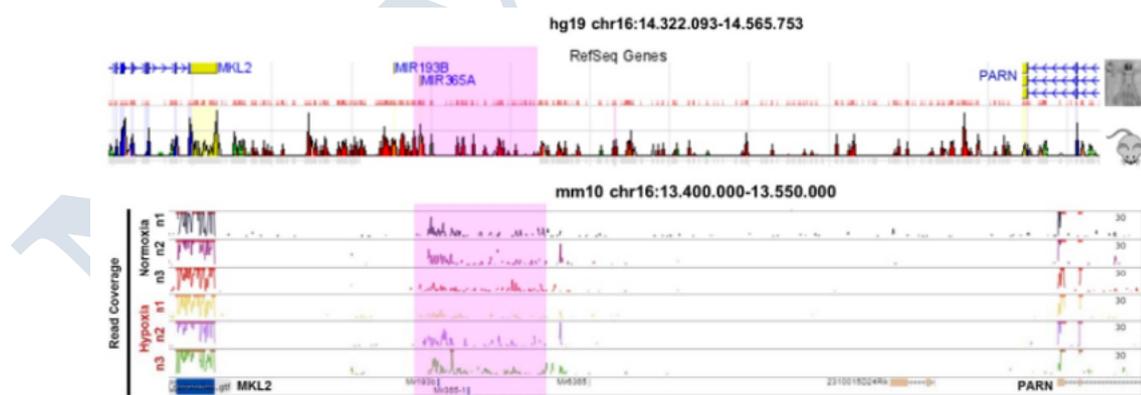
Publication time: June 2017

Abstract

Rationale: Pericytes are essential for vessel maturation and endothelial barrier function. Long non-coding RNAs (lncRNAs) regulate many cellular functions, but their role in pericyte biology remains unexplored.

Objective: Here we investigate the effect of Hypoxia-Induced Endoplasmic Reticulum Stress Regulating lncRNA (HypERlnc, also known as ENSG00000262454) on pericyte function in vitro and its regulation in human heart failure and idiopathic pulmonary arterial hypertension.

Conclusions: Here we show that HypERlnc regulates human pericyte function and the endoplasmic reticulum stress response. In addition, RNA sequencing analyses in conjunction with reduced expression of HypERlnc in heart failure and correlation with pericyte markers in idiopathic pulmonary arterial hypertension indicate a role of HypERlnc in human cardiopulmonary disease.



RNA-seq in primary mouse pericytes demonstrates high read coverage of the possible mHypERlnc orthologue (in purple)

Reference

F.C. Bischoff, et al., Identification and functional characterization of hypoxia-induced endoplasmic reticulum stress regulating lncRNA (HypERlnc) in pericytes. Circulation Research 121, 368 (2017).

RNA-seq of 272 gliomas revealed a novel, recurrent PTPRZ1-MET fusion transcript in secondary glioblastomas

Species: Human

Journal: Genome Research

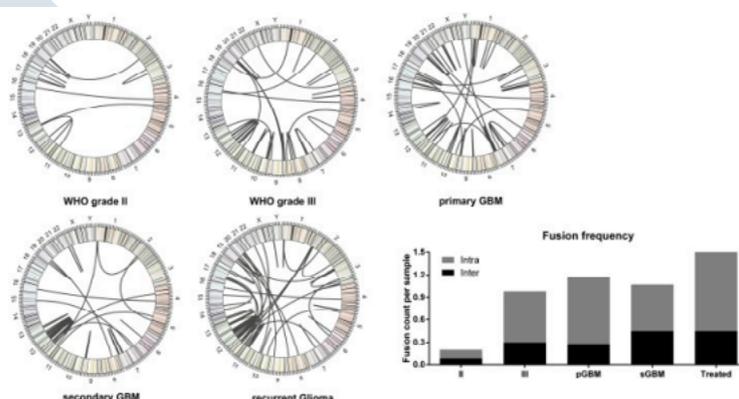
Impact factor: 11.351

Customer coauthor: Beijing Neurosurgical Institute, University of California, San Diego

Publication time: August 2014

Abstract

Studies of gene rearrangements and the consequent oncogenic fusion proteins have laid the foundation for targeted cancer therapy. To identify oncogenic fusions associated with glioma progression, we catalogued fusion transcripts by RNA-seq of 272 gliomas. Fusion transcripts were more frequently found in high-grade gliomas, in the classical subtype of gliomas, and in gliomas treated with radiation/temozolomide. Sixty-seven in-frame fusion transcripts were identified, including three recurrent fusion transcripts: FGFR3-TACC3, RNF213-SLC26A11, and PTPRZ1-MET(ZM). Interestingly, the ZM fusion was found only in grade III as astrocytomas (1/13; 7.7%) or secondary GBMs (sGBMs, 3/20; 15.0%). In an independent cohort of sGBMs, the ZM fusion was found in three of 20 (15%) specimens. Genomic analysis revealed that the fusion arose from translocation events involving introns 3 or 8 of PTPRZ and intron 1 of MET. ZM fusion transcripts were found in GBMs irrespective of isocitrate dehydrogenase 1 (IDH1) mutation status. sGBMs harboring ZM fusion showed higher expression of genes required for PIK3CA signaling and lowered expression of genes that suppressed RB1 or TP53 function. Expression of the ZM fusion was mutually exclusive with EGFR overexpression in sGBMs. Exogenous expression of the ZM fusion in the U87MG glioblastoma line enhanced cell migration and invasion. Clinically, patients afflicted with ZM fusion harboring glioblastomas survived poorly relative to those afflicted with non-ZM-harboring sGBMs ($P < 0.001$). Our study profiles the shifting RNA landscape of gliomas during progression and revealed ZM as a novel, recurrent fusion transcript in sGBMs.



Distribution of fusion transcripts

Reference

Z. S. Bao, et al., RNA-seq of 272 gliomas revealed a novel, recurrent PTPRZ1-MET fusion transcript in secondary glioblastomas. *Genome Research* 24, 1765 (2014).

Single-cell RNA-seq profiling of human preimplantation embryos and embryonic stem cells

Species: Human embryo

Journal: Nature Structural & Molecular Biology

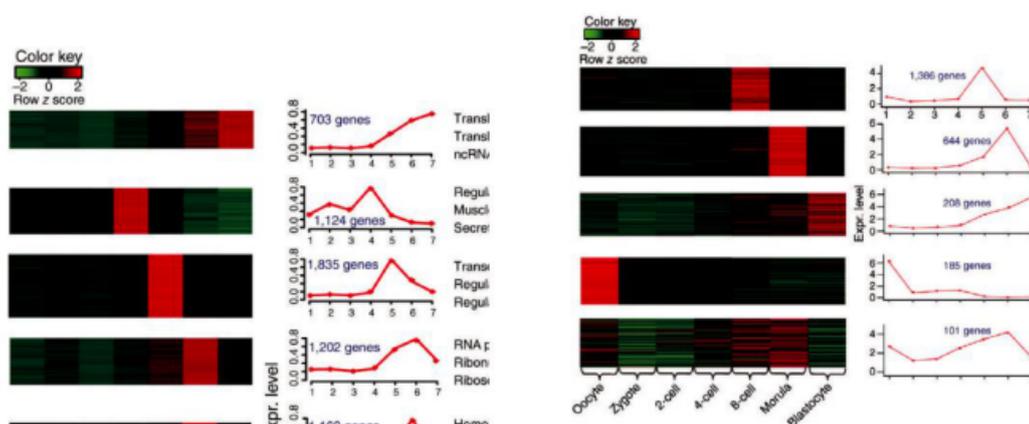
Impact factor: 11.681

Customer coauthor: Peking University

Publication time: September 2013

Abstract

Measuring gene expression in individual cells is crucial for understanding the gene regulatory network controlling human embryonic development. Here we apply single-cell RNA sequencing (RNA-Seq) analysis to 124 individual cells from human preimplantation embryos and human embryonic stem cells (hESCs) at different passages. The number of maternally expressed genes detected in our data set is 22,687, including 8,701 long noncoding RNAs (lncRNAs), which represents a significant increase from 9,735 maternal genes detected previously by cDNA microarray. We discovered 2,733 novel lncRNAs, many of which are expressed in specific developmental stages. To address the long-standing question whether gene expression signatures of human epiblast (EPI) and in vitro hESCs are the same, we found that EPI cells and primary hESC outgrowth have dramatically different transcriptomes, with 1,498 genes showing differential expression between them. This work provides a comprehensive framework of the transcriptome landscapes of human early embryos and hESCs.



Clusters of genes showing representative expression patterns during human preimplantation development and clusters of lncRNAs showing representative expression patterns during human preimplantation development

Reference

L. Yan, et al., Single-cell RNA-seq profiling of human preimplantation embryos and embryonic stem cells. Nature Structural & Molecular Biology 20, 1131 (2013).

JNK1 negatively controls antifungal innate immunity by suppressing CD23 expression

Species: Mice

Journal: Nature Medicine

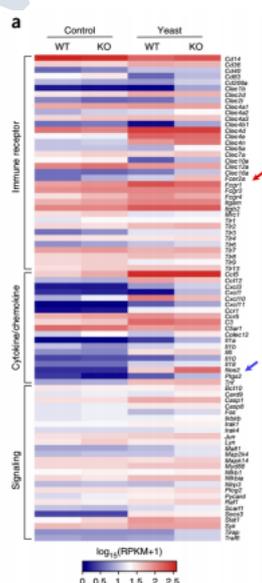
Impact factor: 29.886

Customer coauthor: Tsinghua University School of Medicine, The University of Texas MD Anderson Cancer Center

Publication time: January 2017

Abstract

Opportunistic fungal infections are a leading cause of death among immune-compromised patients, and there is a pressing need to develop new antifungal therapeutic agents because of toxicity and resistance to the antifungal drugs currently in use. Although C-type lectin receptor- and Toll-like receptor-induced signaling pathways are key activators of host antifungal immunity, little is known about the mechanisms that negatively regulate host immune responses to a fungal infection. Here we found that JNK1 activation suppresses antifungal immunity in mice. We showed that JNK1-deficient mice had a significantly higher survival rate than wild-type control mice in response to *Candida albicans* infection, and the expression of JNK1 in hematopoietic innate immune cells was critical for this effect. JNK1 deficiency leads to significantly higher induction of CD23, a novel C-type lectin receptor, through NFATc1-mediated regulation of the CD23 gene promoter. Blocking either CD23 upregulation or CD23-dependent nitric oxide production eliminated the enhanced antifungal response found in JNK1-deficient mice. Notably, JNK inhibitors exerted potent antifungal therapeutic effects in both mouse and human cells infected with *C. albicans*, indicating that JNK1 may be a therapeutic target for treating fungal infection.



WT and JNK1 KO BMDMs were stimulated with yeast-form *C. albicans* for 24h or medium as a control

Reference

X. Zhao, et al., JNK1 negatively controls antifungal innate immunity by suppressing CD23 expression. Nature Medicine 23, 337 (2017).

Tracing haematopoietic stem cell formation at single-cell resolution

Species: Mice

Journal: Nature

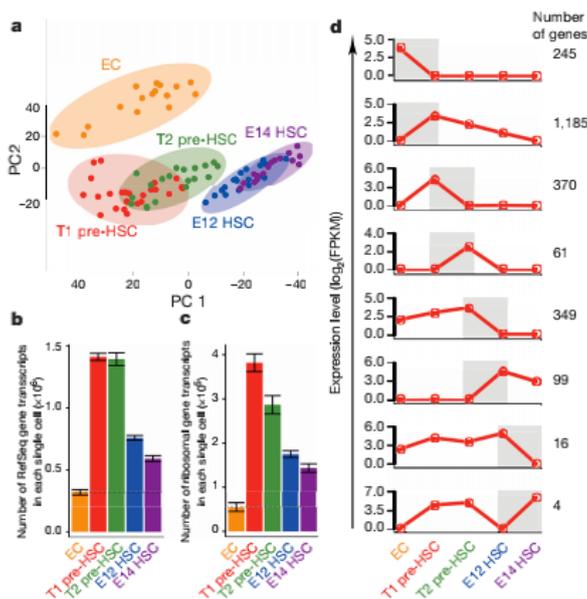
Impact factor: 42.351

Customer coauthor: Affiliated Hospital, Academy of Military Medical Sciences

Publication time: May 2016

Abstract

Haematopoietic stem cells (HSCs) are derived early from embryonic precursors, such as haemogenic endothelial cells and prehaematopoietic stem cells (pre-HSCs), the molecular identity of which still remains elusive. Here we use potent surface markers to capture the nascent pre-HSCs at high purity, as rigorously validated by single-cell-initiated serial transplantation. Then we apply singlecell RNA sequencing to analyse endothelial cells, CD45⁻ and CD45⁺ pre-HSCs in the aorta–gonad–mesonephros region, and HSCs in fetal liver. Pre-HSCs show unique features in transcriptional machinery, arterial signature, metabolism state, signalling pathway, and transcription factor network. Functionally, activation of mechanistic targets of rapamycin (mTOR) is shown to be indispensable for the emergence of HSCs but not haematopoietic progenitors. Transcriptome data-based functional analysis reveals remarkable heterogeneity in cell-cycle status of pre-HSCs. Finally, the core molecular signature of pre-HSCs is identified. Collectively, our work paves the way for dissection of complex molecular mechanisms regulating stepwise generation of HSCs in vivo, informing future efforts to engineer HSCs for clinical applications.



Global gene expression dynamics during HSC formation

Reference

F. Zhou, et al., Tracing haematopoietic stem cell formation at single-cell resolution. Nature 533, 487 (2016).

Integration of Hippo signalling and the unfolded protein response to restrain liver overgrowth and tumorigenesis

Species: Mouse

Journal: Nature Communications

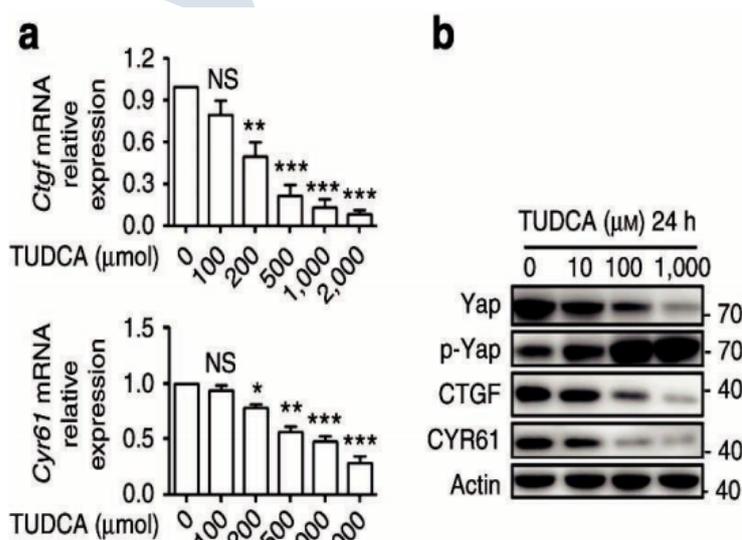
Impact factor: 11.47

Customer coauthor: Xiamen University, University of Texas, M.D. Anderson Cancer Center

Publication time: February 2015

Abstract

The role of the unfolded protein response (UPR) in tissue homeostasis remains largely unknown. Here we find that loss of Mst1/2, the mammalian Hippo orthologues, or their regulator WW45, leads to a remarkably enlarged endoplasmic reticulum (ER) size-associated UPR. Intriguingly, attenuation of the UPR by tauroursodeoxycholic acid (TUDCA) diminishes Mst1/2 mutant-driven liver overgrowth and tumorigenesis by promoting nuclear exit and degradation of Hippo downstream effector Yap. Yap is required for UPR activity and ER expansion to alleviate ER stress. During the adaptive stage of the UPR, PERK kinase-eIF2a axis activates Yap, while prolonged ER stress-induced Hippo signalling triggers assembly of the GADD34/PP1 complex in a negative feedback loop to inhibit Yap and promote apoptosis. Significantly, the deregulation of UPR signals associated with Yap activation is found in a substantial fraction of human hepatocellular carcinoma (HCC). Thus, we conclude Yap integrates Hippo and UPR signalling to control liver size and tumorigenesis.



Quantitative PCR analysis

Reference

H. Wu, et al., Integration of Hippo signalling and the unfolded protein response to restrain liver overgrowth and tumorigenesis. Nature Communications 6, 6239 (2015).

mRNA and small RNA transcriptomes reveal insights into dynamic homoeolog regulation of allopolyploid heterosis in nascent hexaploid wheat

Species: Hexaploid wheat

Journal: The Plant Cell

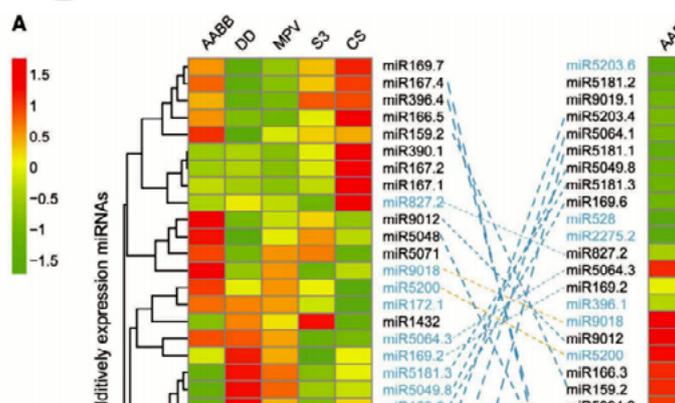
Impact factor: 10.529

Customer coauthor: China Agricultural University

Publication time: May 2014

Abstract

Nascent allohexaploid wheat may represent the initial genetic state of common wheat (*Triticum aestivum*), which arose as a hybrid between *Triticum turgidum* (AABB) and *Aegilops tauschii* (DD) and by chromosome doubling and outcompeted its parents in growth vigor and adaptability. To better understand the molecular basis for this success, we performed mRNA and small RNA transcriptome analyses in nascent allohexaploid wheat and its following generations, their progenitors, and the natural allohexaploid cultivar Chinese Spring, with the assistance of recently published A and D genome sequences. We found that nonadditively expressed protein-coding genes were rare but relevant to growth vigor. Moreover, a high proportion of protein-coding genes exhibited parental expression level dominance, with genes for which the total homoeolog expression level in the progeny was similar to that in *T. turgidum* potentially participating in development and those with similar expression to that in *Ae. tauschii* involved in adaptation. In addition, a high proportion of microRNAs showed nonadditive expression upon polyploidization, potentially leading to differential expression of important target genes. Furthermore, increased small interfering RNA density was observed for transposable element-associated D homoeologs in the allohexaploid progeny, which may account for biased repression of D homoeologs. Together, our data provide insights into small RNA-mediated dynamic homoeolog regulation mechanisms that may contribute to heterosis in nascent hexaploid wheat.



Hierarchical clustering of miRNAs displaying nonadditive expression and hierarchical clustering analysis of miRNAs displaying parental ELD in young spikes

Reference

A. Li, et al., mRNA and Small RNA Transcriptomes Reveal Insights into Dynamic Homoeolog Regulation of Allopolyploid Heterosis in Nascent Hexaploid Wheat. *The Plant Cell* 26, 1878 (2014).

Lineage-specific functions of TET1 in the postimplantation mouse embryo

Species: Mouse

Journal: Nature Genetics

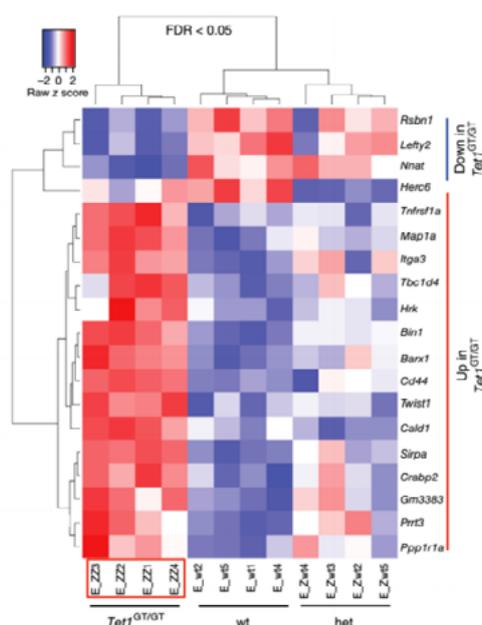
Impact factor: 27.959

Customer coauthor: Stem Cell Institute Leuven, La Jolla Institute for Allergy and Immunology

Publication time: May 2017

Abstract

The mammalian TET enzymes catalyze DNA demethylation. While they have been intensely studied as major epigenetic regulators, little is known about their physiological roles and the extent of functional redundancy following embryo implantation. Here we define non-redundant roles for TET1 at an early postimplantation stage of the mouse embryo, when its paralogs Tet2 and Tet3 are not detectably expressed. TET1 regulates numerous genes defining differentiation programs in the epiblast and extraembryonic ectoderm. In epiblast cells, TET1 demethylates gene promoters via hydroxymethylation and maintains telomere stability. Surprisingly, TET1 represses a majority of epiblast target genes independently of methylation changes, in part through regulation of the gene encoding the transcriptional repressor JMJD8. Dysregulated gene expression in the absence of TET1 causes embryonic defects, which are partially penetrant in an inbred strain but fully lethal in non-inbred mice. Collectively, our study highlights an interplay between the catalytic and non-catalytic activities of TET1 that is essential for normal development.



Heat map cluster of the differentially expressed genes that are regulated by TET1 in the epiblast

Reference

R. Khoeiry, et al., Lineage-specific functions of TET1 in the postimplantation mouse embryo. *Nature Genetics* 49, 1061 (2017).

Whole-genome analysis of 5-hydroxymethylcytosine and 5-methylcytosine at base resolution in the human brain

Species: Human

Journal: Genome Biology

Impact factor: 11.313

Customer coauthor: Peking University, The University of Chicago

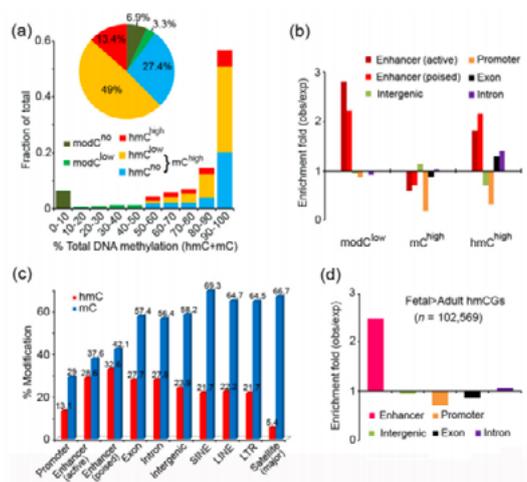
Publication time: May 2014

Abstract

Background: 5-methylcytosine (mC) can be oxidized by the tet methylcytosine dioxygenase (Tet) family of enzymes to 5-hydroxymethylcytosine (hmC), which is an intermediate of mC demethylation and may also be a stable epigenetic modification that influences chromatin structure. hmC is particularly abundant in mammalian brains but its function is currently unknown. A high resolution hydroxymethylome map is required to fully understand the function of hmC in the human brain.

Results: We present genome-wide and single-base resolution maps of hmC and mC in the human brain by combined application of Tet-assisted bisulfite sequencing and bisulfite sequencing. We demonstrate that hmCs increase markedly from the fetal to the adult stage, and in the adult brain, 13% of all CpGs are highly hydroxymethylated with strong enrichment at genic regions and distal regulatory elements. Notably, hmC peaks are identified at the 5' splicing sites at the exon-intron boundary, suggesting a mechanistic link between hmC and splicing. We report a surprising transcription-correlated hmC bias toward the sense strand and an mC bias toward the antisense strand of gene bodies. Furthermore, hmC is negatively correlated with H3K27me3-marked and H3K9me3-marked repressive genomic regions, and is more enriched at poised enhancers than active enhancers.

Conclusions: We provide single-base resolution hmC and mC maps in the human brain and our data imply novel roles of hmC in regulating splicing and gene expression. Hydroxymethylation is the main modification status for a large portion of CpGs situated at poised enhancers and actively transcribed regions, suggesting its roles in epigenetic tuning at these regions.



Features of hydroxymethylome in the human brain

Reference

L. Wen, et al., Whole-genome analysis of 5-hydroxymethylcytosine and 5-methylcytosine at base resolution in the human brain. *Genome Biology* 15, R49 (2014).

Cohesin loss eliminates all loop domains

Species: Human, colon cancer cell

Journal: Cell

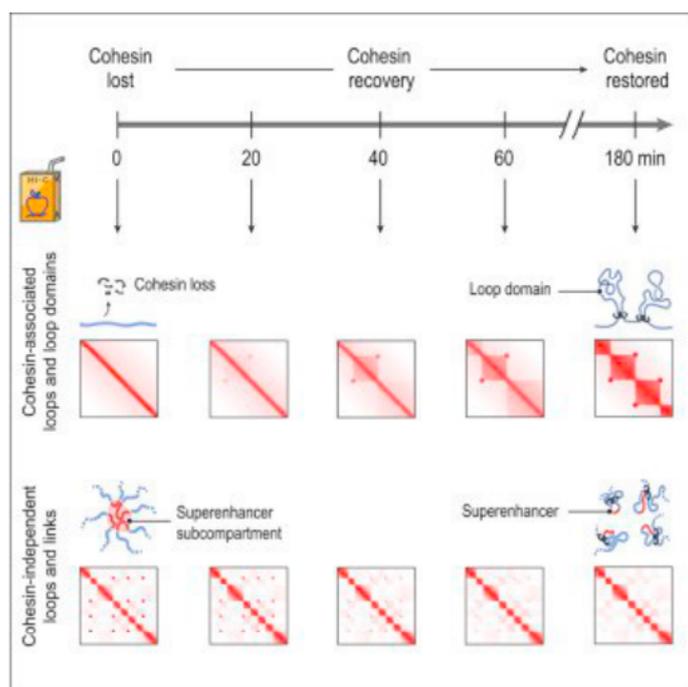
Impact factor: 30.410

Customer coauthor: Baylor College of Medicine, Stanford University, Rice University,

Publication time: October 2017

Abstract

The human genome folds to create thousands of intervals, called “contact domains,” that exhibit enhanced contact frequency within themselves. “Loop domains” form because of tethering between two loci—almost always bound by CTCF and cohesin—lying on the same chromosome. “Compartment domains” form when genomic intervals with similar histone marks co-segregate. Here, we explore the effects of degrading cohesin. All loop domains are eliminated, but neither compartment domains nor histone marks are affected. Loss of loop domains does not lead to widespread ectopic gene activation but does affect a significant minority of active genes. In particular, cohesin loss causes superenhancers to co-localize, forming hundreds of links within and across chromosomes and affecting the regulation of nearby genes. We then restore cohesin and monitor the re-formation of each loop. Although re-formation rates vary greatly, many megabase-sized loops recovered in under an hour, consistent with a model where loop extrusion is rapid.



Cohesin degradation eliminates loop domains, while compartment domains remain unaffected

Reference

S.S.P. Rao, et al., Cohesin loss eliminates all loop domains. Cell 171, 305 (2017).

The microbiota maintain homeostasis of liver-resident $\gamma\delta$ T-17 cells in a lipid antigen/CD1d-dependent manner

Species: $\gamma\delta$ T cells

Journal: Nature Communications

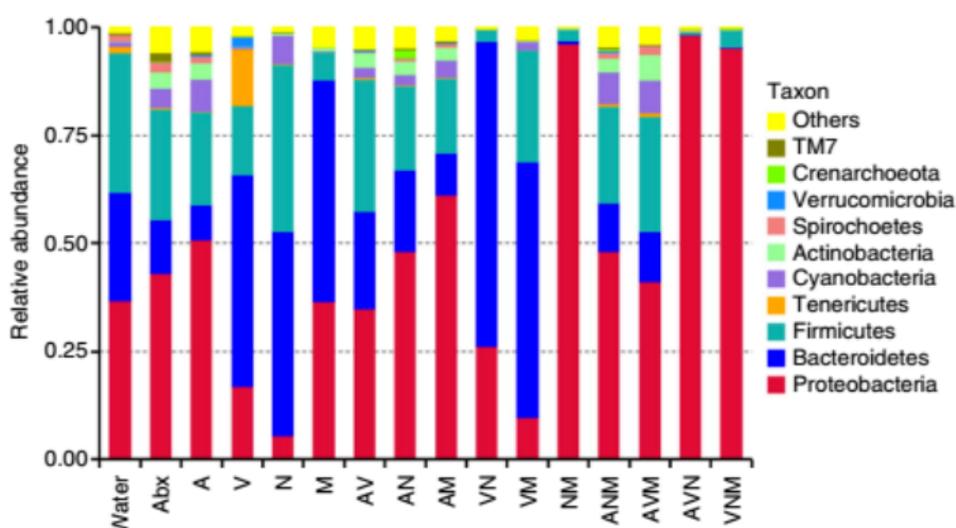
Impact factor: 10.7

Customer coauthor: University of Science and Technology of China

Publication time: January 2017

Abstract

The microbiota control regional immunity using mechanisms such as inducing IL-17A-producing $\gamma\delta$ T ($\gamma\delta$ T-17) cells in various tissues. However, little is known regarding hepatic $\gamma\delta$ T cells that are constantly stimulated by gut commensal microbes. Here we show hepatic $\gamma\delta$ T cells are liver-resident cells and predominant producers of IL-17A. The microbiota sustain hepatic $\gamma\delta$ T-17 cell homeostasis, including activation, survival and proliferation. The global commensal quantity affects the number of liver-resident $\gamma\delta$ T-17 cells; indeed, *E. coli* alone can generate $\gamma\delta$ T-17 cells in a dose-dependent manner. Liver-resident $\gamma\delta$ T-17 cell homeostasis depends on hepatocyte-expressed CD1d, that present lipid antigen, but not Toll-like receptors or IL-1/IL-23 receptor signalling. Supplementing mice in vivo or loading hepatocytes in vitro with exogenous commensal lipid antigens augments the hepatic $\gamma\delta$ T-17 cell number. Moreover, the microbiota accelerate nonalcoholic fatty liver disease through hepatic $\gamma\delta$ T-17 cells. Thus, our work describes a unique liver-resident $\gamma\delta$ T-17 cell subset maintained by gut commensal microbes through CD1d/lipid antigens.



16S rDNA sequencing reveals that commensal microbe load positively correlates with hepatic $\gamma\delta$ T-17 cell numbers

Reference

F. Li, et al., The microbiota maintain homeostasis of liver-resident $\gamma\delta$ T-17 cells in a lipid antigen/CD1d-dependent manner. Nature Communication 8, 13839 (2017).

Cryptophyte farming by symbiotic ciliate host detected in situ

Species: Soil microbial communities

Journal: Proceedings of the National Academy of Sciences of the United States of America

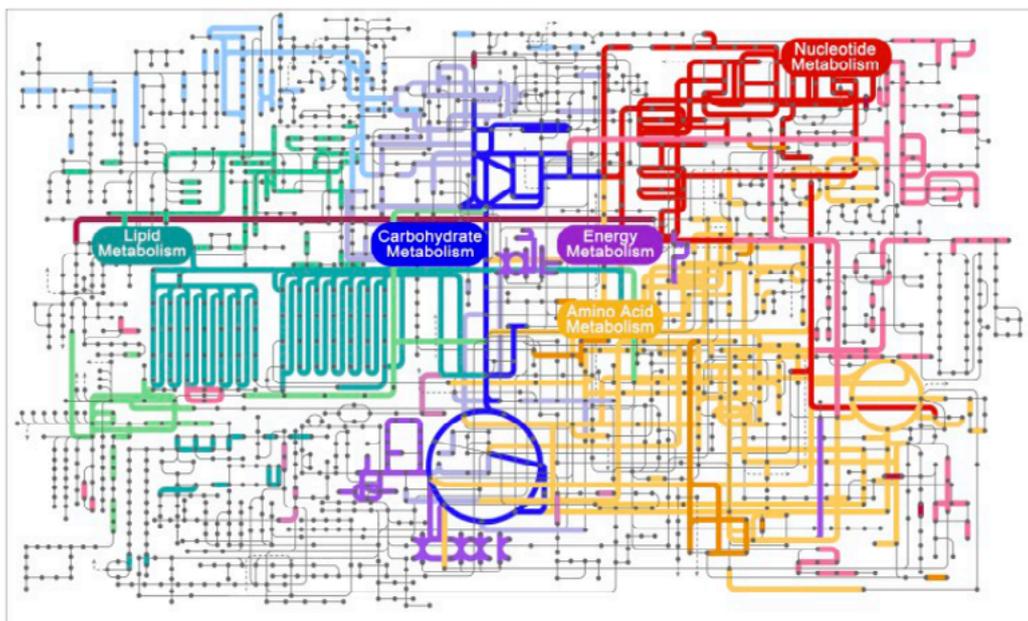
Impact factor: 9.423

Customer coauthor: Chinese Academy of Sciences, University of Connecticut

Publication time: October 2016

Abstract

Protist-alga symbiosis is widespread in the ocean, but its characteristics and function in situ remain largely unexplored. Here we report the symbiosis of the ciliate *Mesodinium rubrum* with cryptophyte cells during a red-tide bloom in Long Island Sound. In contrast to the current notion that *Mesodinium* retains cryptophyte chloroplasts or organelles, our multiapproach analyses reveal that in this bloom the endosymbiotic *Teleaulax amphioxeia* cells were intact and expressing genes of membrane transporters, nucleus-to-cytoplasm RNA transporters, and all major metabolic pathways. Among the most highly expressed were ammonium transporters in both organisms, indicating cooperative acquisition of ammonium as a major N nutrient, and genes for photosynthesis and cell division in the cryptophyte, showing active population proliferation of the endosymbiont. We posit this as a "Mesodinium-farming-Teleaulax" relationship, a model of protist-alga symbiosis worth further investigation by metatranscriptomic technology.



Metabolic circuit map constructed from the cryptophyte subset of the metatranscriptome.

Reference

D. Qiu, et al., Cryptophyte farming by symbiotic ciliate host detected in situ. Proceedings of the National Academy of Sciences of the United States of America 113, 12208 (2016).

Comparative genomics identifies the *Magnaporthe oryzae* avirulence effector AvrPi9 that triggers Pi9-mediated blast resistance in rice

Species: *Magnaporthe oryzae*

Journal: New Phytologist

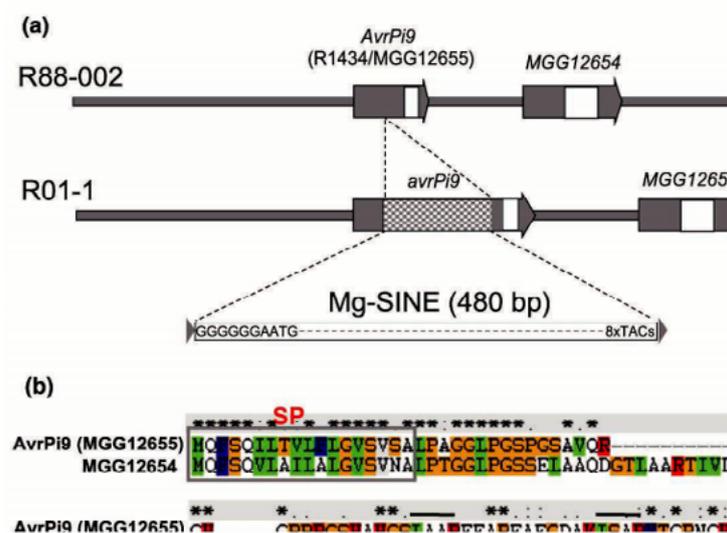
Impact factor: 7.21

Customer coauthor: Central South University, International Rice Research Institute

Publication time: June 2015

Abstract

We identified the *Magnaporthe oryzae* avirulence effector AvrPi9 cognate to rice blast resistance gene Pi9 by comparative genomics of requisite strains derived from a sequential planting method. AvrPi9 encodes a small secreted protein that appears to localize in the biotrophic interfacial complex and is translocated to the host cell during rice infection. AvrPi9 forms a tandem gene array with its paralogue proximal to centromeric region of chromosome 7. AvrPi9 is expressed highly at early stages during initiation of blast disease. Virulent isolate strains contain Mg-SINE within the AvrPi9 coding sequence. Loss of AvrPi9 did not lead to any discernible defects during growth or pathogenesis in *M. oryzae*. This study reiterates the role of diverse transposable elements as off-switch agents in acquisition of gain-of-virulence in the rice blast fungus. The prevalence of AvrPi9 correlates well with the avirulence pathotype in diverse blast isolates from the Philippines and China, thus supporting the broad-spectrum resistance conferred by Pi9 in different rice growing areas. Our results revealed that Pi9 and Piz-t at the Pi2/9 locus activate race specific resistance by recognizing sequence-unrelated AvrPi9 and AvrPiz-t genes, respectively.



Genomic structure of the AvrPi9 locus in *Magnaporthe oryzae*

Reference

J. Wu, et al., Comparative genomics identifies the *Magnaporthe oryzae* avirulence effector AvrPi9 that triggers Pi9-mediated blast resistance in rice. *New Phytologist* 206, 1463 (2015).

Microbiota modulate tumoral immune surveillance in Lung through $\gamma\delta$ T17 immune cell dependent mechanism

Species: Commensal bacteria in mouse

Journal: Cancer Research

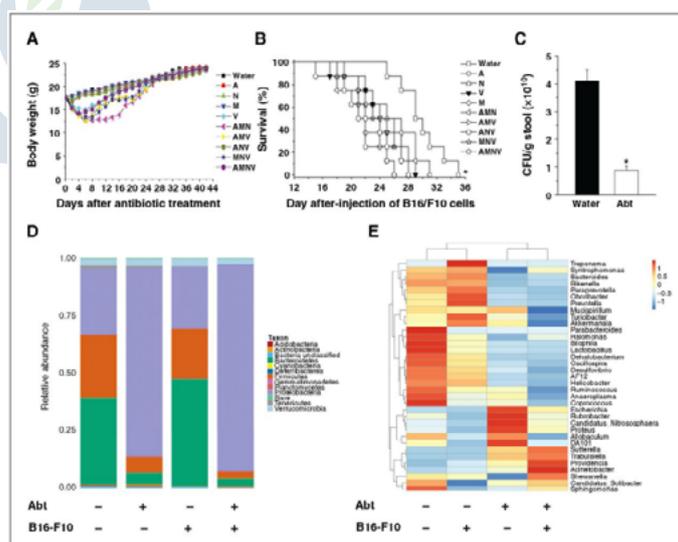
Impact factor: 9.329

Customer coauthor: Anhui Province Hospital Affiliated Anhui Medical University

Publication time: June 2014

Abstract

Commensal bacteria are crucial to maintain immune homeostasis in mucosal tissues and disturbances in their ecology can affect disease susceptibility. Here, we report evidence that commensal bacteria shape the efficiency of immune surveillance in mucosal tissues. Antibiotic-treated (Abt) mice were more susceptible to development of engrafted B16/F10 melanoma and Lewis lung carcinoma, exhibiting a shortened mean survival time with more numerous and larger tumor foci in the lungs. The defective antitumor response of Abt mice was independent of dehydration caused by antibiotics. Host defenses relied upon intact commensal bacteria with no class specificity. Mechanistic investigations revealed a defective induction of the $\gamma\delta$ T17 cell response in lungs of Abt mice; here, more aggressive tumor development was observed, possibly related to a reduction in IL6 and IL23 expression there. Adding normal $\gamma\delta$ T cells or supplementing IL17 restored the impaired immune surveillance phenotype in Abt mice. Overall, our results demonstrated the importance of commensal bacteria in supporting the host immune response against cancer, defined an important role for $\gamma\delta$ T17 responses in the mechanism, and suggested deleterious effects of antibiotic treatment on cancer susceptibility and progression.



Microbiota variations after different antibiotic treatments

Reference

M. Cheng, et al., Microbiota modulate tumoral immune surveillance in lung through a $\gamma\delta$ T17 immune cell-dependent mechanism. *Cancer Research* 74, 4030 (2014).

Additional Publications:

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Tianjin Sequencing Center & Clinical Lab

Tianjin Novogene Bioinformatic Technology Co., Ltd.

Tianjin Novogene Med LAB Co., Ltd.

Tianjin Novogene Technology Co., Ltd.

Nanjing Sequencing Center

Nanjing Novogene Bio Technology Co., Ltd.

Hong Kong Subsidiary

Novogene (HK) Company Limited

U.S. Subsidiary & UC Davis Sequencing Center

Novogene Corporation Inc.

U.K. Subsidiary & UK Sequencing Center

Novogene (UK) Company Limited

Netherlands Subsidiary

Novogene Netherlands B.V.

Novogene (NL) International Holding B.V.

Singapore Joint Venture & Sequencing Center NovogeneAIT

Genomics Singapore Pte. Ltd.

Novogene International Pte. Ltd.

Japan Subsidiary

Novogene Japan K.K.