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INVESTIGATIONS

- 499–507 **Partial Dominance, Overdominance, Epistasis and QTL by Environment Interactions Contribute to Heterosis in Two Upland Cotton Hybrids**
Lianguang Shang, Yumei Wang, Shihu Cai, Xiaocui Wang, Yuhua Li, Abdugheni Abduweli, and Jinping Hua
- Heterosis is widely exploited in crop breeding; however, its genetic basis has not been elucidated. This is the first time the authors have studied heterosis in two Upland cotton hybrids by testing a recombinant inbred line and their backcross population. This article reveals that (1) partial dominance and overdominance effects at the single-locus level, (2) epistasis at the two-locus level and (3) QTL-by-environment interactions elucidated the genetic basis of heterosis in Upland cotton.
- 509–519 **Exploring a Nonmodel Teleost Genome Through RAD Sequencing—Linkage Mapping in Common Pandora, *Pagellus erythrinus* and Comparative Genomic Analysis**
Tereza Manousaki, Alexandros Tsakogiannis, John B. Taggart, Christos Palaiokostas, Dimitris Tsaparis, Jacques Lagnel, Dimitrios Chatziplis, Antonios Magoulas, Nikos Papandroulakis, Constantinos C. Mylonas, and Costas S. Tsigenopoulos
- Common pandora (*Pagellus erythrinus*) is a marine fish belonging to the teleost family Sparidae. Through ddRAD methodology, the authors genotyped a full-sib family and constructed a genetic linkage map based on 917 polymorphic markers. The map comprises 24 linkage groups corresponding to the species karyotype. Comparative genomic analyses revealed conserved synteny with model teleosts suggesting a conserved evolution for the genome of common pandora. Finally, the results indicate a phylogenetically close relationship of Sparidae to stickleback and a high sequence similarity to European seabass; this is expected to have a promising impact in genomic research for important species in European aquaculture.
- 521–527 **Whole-Genome Sequencing of a Canine Family Trio Reveals a *FAM83G* Variant Associated with Hereditary Footpad Hyperkeratosis**
Shumaila Sayyab, Agnese Viluma, Kerstin Bergvall, Emma Brunberg, Vidhya Jagannathan, Tosso Leeb, Göran Andersson, and Tomas F. Bergström
- This is the first study in which whole-genome sequencing (WGS) of a canine family trio (a single affected offspring and its two healthy parents) has been successfully applied for the identification of a disease-causing allele of a canine disorder. It will serve as a proof of principle that this is a powerful method for identifying causative genetic variants for Mendelian disorders in dogs, and the authors predict that the results will have a major impact on the future of canine genetic research.

529–540 **Performance of Seven Tree Breeding Strategies Under Conditions of Inbreeding Depression**

Harry X. Wu, Henrik R. Hallingbäck, and Leopoldo Sánchez

Most tree breeding programs in the world were initiated in the 1950s with plus tree selection and progeny testing, and many of them have now entered into the second, third or even fourth generation. Recurrent selection has been the principal method for improvement of quantitative traits in tree species. In order to increase short- and long-term genetic gains and to manage inbreeding and diversity, several advanced tree breeding strategies were proposed, including single population, multiple populations, sublimes, nucleus breeding, and inbreeding and crossbreeding. However, there have been no genetic bases presented so far to quantify the advantages and disadvantages of these proposed strategies. In this paper, the authors set up a gene-based model to compare these breeding strategies under additive and nonadditive modes of inheritance. A finite locus genomic model was simulated to examine relevant population parameters, the genetic gain in breeding and production populations, fixation of unfavourable or recessive alleles, and accumulation of inbreeding. They also assessed whether certain systematic inbreeding methods could be suitable to overcome inbreeding depression by purging of ID and unfavourable alleles given a certain range of conditions.

Measured by genetic gain of production population, the nucleus breeding and the single breeding population with mass selection strategies were equal or superior to subline and single breeding population with within-family selection strategies. Inbreeding and crossbreeding effectively decreased inbreeding depression and could in some scenarios produce genetic gains during the first few generations. However, in all scenarios considerable fixation of unfavorable alleles rendered the purging performance of selfing and crossbreeding strategies ineffective and resulted in substantial inferiority in comparison to the other strategies in the long term.

541–549 **Aberrant Activation of p38 MAP Kinase-Dependent Innate Immune Responses Is Toxic to *Caenorhabditis elegans***

Hilary K. Cheesman, Rhonda L. Feinbaum, Jose Thekkiniath, Robert H. Downen, Annie L. Conery, and Read Pukkila-Worley

Homeostatic regulation of innate immune defenses is important for many organisms. Here the authors investigated the physiological consequences of immune hyperactivation in *Caenorhabditis elegans*. They found that aberrant stimulation of the conserved p38 MAPK PMK-1 innate immune pathway, either exogenously by the administration of an anti-infective xenobiotic or endogenously through a gain-of-function mutation, drives immune responses that are protective during infection but are toxic to nematodes under normal growth conditions. These data highlight the deleterious effects of inappropriate immune activation and suggest that there are ancient, physiological mechanisms to regulate the extent of p38 MAPK pathway activation in *C. elegans*.

551–558 **Isolation of a Hypomorphic *skn-1* Allele That Does Not Require a Balancer for Maintenance**

Lanlan Tang, William Dodd, and Keith Choe

The nematode *Caenorhabditis elegans* is an important model organism for understanding how specific genes influence longevity. A *C. elegans* gene named *skn-1* is under intense study because it promotes life span and resistance to environmental damage and has the same functions as a human gene named *nrf2*. In a large genetic screen, the authors identified a new allele of *skn-1* that reduces its function. This new allele overcomes some limitations with current alleles that are lethal, and the authors expect that it will enhance genetic analysis of this important aging and longevity gene.

559–571 **Novel Heterotypic Rox Sites for Combinatorial Dre Recombination Strategies**

Katherine Chuang, Eileen Nguyen, Yuri Sergeev, and Tudor C. Badea

Site-specific recombinases such as Cre, Flp and Dre are used in genetic approaches for cell labeling and manipulation, either separately or in combination. The authors of this study previously described an intersectional strategy combining Dre and Cre and now report a mutagenesis screen aimed at identifying roxP base pairs critical for self-recognition. They describe several roxP variants that are incompatible with roxP but efficiently recombine with themselves in purified system or in bacterial and eukaryotic tissue culture. These rox sites are not recognized by Cre, thus enabling combinatorial strategies involving Cre and Dre.

- 573–578 **A Novel Recombinant DNA System for High Efficiency Affinity Purification of Proteins in *Saccharomyces cerevisiae***
Brian H. Carrick, Linxuan Hao, Philip J. Smaldino, and David R. Engelke
 Isolation of rare or unstable protein complexes in their physiologically relevant form from *Saccharomyces cerevisiae* would greatly benefit from tagging chromosomal genes with affinity tools that allow rapid, inexpensive and gentle purification. This work documents a recombinant DNA construct encoding a highly effective affinity tag with an adjoining selection marker for insertion of DNA fragments encoding a cellulose-binding protein domain at the C-termini of chromosomal open reading frames. Single-step affinity purification from cell extracts is accomplished by binding to cellulose and elution with TEV protease. An optional C-myc affinity tag can also be used for detection or additional purification.
- 579–588 **Genetic Architecture of Conspicuous Red Ornaments in Female Threespine Stickleback**
Lengxob Yong, Catherine L. Peichel, and Jeffrey S. McKinnon
 While conspicuous ornaments are commonly thought to be male attributes resulting from sexual selection, females of many species frequently exhibit similar elaborate traits. To understand the causes for female ornament evolution, the genetic architecture of red throat (a classic male-typical trait) and spine ornaments was investigated in a threespine stickleback population in which both males and females express the traits. Both ornaments are found to have some degree of a shared genetic basis between the sexes, implicating the role of a genetic correlation and/or pleiotropy in mediating the evolution of red ornaments in a stickleback population.
- 589–597 **FW: An R Package for Finlay–Wilkinson Regression that Incorporates Genomic/Pedigree Information and Covariance Structures Between Environments**
Lian Lian and Gustavo de los Campos
 Plant breeders use the Finlay–Wilkinson Regression to assess how the performance of a genotype varies as a function of the environmental effects. The standard implementation uses environment means as environment effects and regresses the performance of each genotype on the environmental means. In this article, the authors described a Bayesian method that performs better than the standard method by estimating the genotype and environment parameters jointly. The authors also extended the model to include genomic/pedigree information and environment covariance and presented an R package that implements both the standard method and the Bayesian method.
- 599–607 **Genetic Correlates of Individual Differences in Sleep Behavior of Free-Living Great Tits (*Parus major*)**
Erica F. Stuber, Christine Baumgartner, Niels J. Dingemans, Bart Kempenaers, and Jakob C. Mueller
 Even within single populations, a wide variety of sleeping patterns in birds in the wild can be observed. Some individuals display consistent patterns in sleep that are different from others. The authors of this study investigated whether naturally occurring variation in candidate genes that are related to sleep behaviors in other animals might underlie differences in sleep behavior in the wild. Genes related to the biological clock and the melanocortin system are related to patterns of sleep behaviors displayed in the wild.
- 609–622 **The Effects of Both Recent and Long-Term Selection and Genetic Drift Are Readily Evident in North American Barley Breeding Populations**
Ana M. Poets, Mohsen Mohammadi, Kiran Seth, Hongyun Wang, Thomas J. Y. Kono, Zhou Fang, Gary J. Muehlbauer, Kevin P. Smith, and Peter L. Morrell
 Barley was introduced to North America ~400 years ago, but its adaptation to modern production environments is more recent. Here Poets *et al.* present a population genetic study of a comprehensive sample representing barley production in North America. They identified genomic regions involved in adaptation and improvement. Their results highlight the large role of drift and linked selection acting on breeding programs, and the authors identified genetic variants putatively involved in both recent and long-term selection. Finally, they were able to identify recent bouts of gene flow between breeding populations that could point to the sharing of agronomically adaptive variation.

- 623–629** **Suppression of F1 Male-Specific Lethality in *Caenorhabditis* Hybrids by *cbr-him-8***
Vaishnavi Ragavapuram, Emily Elaine Hill, and Scott Everet Baird
- cbr-him-8* has been identified as a maternal-effect suppressor of F1 male-specific lethality in crosses of *Caenorhabditis nigoni* males to *Caenorhabditis briggsae* sperm-depleted hermaphrodites. *C. briggsae* X-bearing F1 males obtained from these crosses were fertile. Viable F2 and B2 male and hermaphrodite progeny were obtained from crosses of these F1 males to F1 females and *C. briggsae* hermaphrodites, respectively. In crosses of F1 males to *C. nigoni* females, all progeny died during embryogenesis. X chromosomes in *C. briggsae cbr-him-8* mutant hermaphrodites likely are unpaired, which implicates meiotic silencing of X-linked gene expression as a possible mechanism of suppression.
- 631–639** **Genome-Based Selection and Characterization of *Fusarium circinatum*-Specific Sequences**
Mkhululi N. Maphosa, Emma T. Steenkamp, and Brenda D. Wingfield
- Robust and accurate diagnostics are an important aspect of the control and management of all pathogens. However, suitable markers that are taxon specific and that will avoid recording false positives or negatives are typically difficult to identify. Here the authors used a comparative genomics approach, combined with PCR and hybridization-based assays, to identify genes unique to an important forestry pathogen. These genes could thus represent good candidates for the development of a rapid, in-the-field diagnostic assay for the pathogen. Their study demonstrates how genome sequence information can be mined for the identification of new diagnostic markers for the detection of pathogens.
- 641–652** **Vesicular Trafficking Systems Impact TORC1-Controlled Transcriptional Programs in *Saccharomyces cerevisiae***
Joanne M. Kingsbury and Maria E. Cardenas
- The Target of Rapamycin Complex I (TORC1) pathway orchestrates a global transcriptional reprogramming in response to environmental signals, which is influenced by the endomembrane network. The authors surveyed the impact of Golgi-to-endosome trafficking on TORC1-orchestrated transcriptional programs in yeast. Perturbation of Golgi-to-endosome trafficking led to reduced expression of nitrogen catabolite-responsive, phosphate-responsive, and ribosomal biogenesis genes and induced sulfur-containing amino acid metabolism genes, following a shift from optimal to TORC1-inhibitory low-quality nitrogen medium, but not upon rapamycin treatment. Given the conservation of TORC1 and endomembrane networks, these findings have potential implications for TORC1-mediated responses to nutritional cues in mammals.
- 653–667** **Combinatorial *Cis*-regulation in *Saccharomyces* Species**
Aaron T. Spivak and Gary D. Stormo
- Gene regulation often involves multiple transcription factors (TFs) working cooperatively, but which combinations of TFs interact is largely unknown. The authors of this study developed a method to identify significantly co-occurring TFs across multiple species. Previous experimental data support most of these combinations, and the authors also experimentally verified some of the novel predictions. They also show that these combinations can explain regulatory rewiring, where the same set of TFs can control different sets of genes in different species.
- 669–682** **A Computational Approach to Estimating Nondisjunction Frequency in *Saccharomyces cerevisiae***
Daniel B. Chu and Sean M. Burgess
- Errors segregating homologous chromosomes during meiosis results in aneuploidy, a leading cause of birth defects in humans. *Saccharomyces cerevisiae* has long served as a model organism for studying the gene network supporting normal chromosome segregation. Estimating nondisjunction frequencies for individually marked chromosomes, however, is labor intensive and can require dissecting thousands of tetrads. Here, the authors have developed a computational analysis tool (TetFit) to estimate the contributions of nondisjunction and random spore death to spore inviability based observed live:dead tetrad distributions. Importantly, TetFit does not require any special strain construction and can be applied to as few as 200 tetrads.

- 683–694 **Diverse Hormone Response Networks in 41 Independent *Drosophila* Cell Lines**
Marcus Stoiber, Susan Celniker, Lucy Cherbas, Ben Brown, and Peter Cherbas
- This study represents the first genome-wide study of hormone response in more than a select few cell states. This extensive range of initial cell states allows for the first well-founded predictive models of cell type-specific response. The authors observe that the global level of transcriptional response is dependent upon Ecdysone Receptor (EcR) titer and that relevant gene responses are EcR isoform dependent. They also present evidence of local genomic response. This study demonstrates the importance of assessing many initial cell states for a range of biological questions as the results can vary tremendously and provide novel biological insight.
- 695–708 **Major Improvements to the *Heliconius melpomene* Genome Assembly Used to Confirm 10 Chromosome Fusion Events in 6 Million Years of Butterfly Evolution**
John W. Davey, Mathieu Chouteau, Sarah L. Barker, Luana Maroja, Simon W. Baxter, Fraser Simpson, Richard M. Merrill, Mathieu Joron, James Mallet, Kanchon K. Dasmahapatra, and Chris D. Jiggins
- This article presents a new version of the *Heliconius melpomene* genome, considerably increasing the contiguity of the genome and enabling analysis of *Heliconius* chromosomes. Davey *et al.* show that 10 of the *Heliconius* chromosomes are fusions of 20 chromosomes in a sister genus *Eueides*, which implies that these fusions happened relatively rapidly over 6 million years, with the chromosome number within *Heliconius* and *Eueides* being mostly static. This is a peculiar result that may have implications for the rapid speciation of the *Heliconius* butterflies.
- 709–720 **The E2F-DP1 Transcription Factor Complex Regulates Centriole Duplication in *Caenorhabditis elegans***
Jacqueline G. Miller, Yan Liu, Christopher W. Williams, Harold E. Smith, and Kevin F. O’Connell
- The precise duplication of centrioles is critical for the processes of cell division, cell signaling and cell motility. Here the authors show that the transcription regulator E2F-DP1 both positively and negatively regulates this process in the *Caenorhabditis elegans* embryo. They envision that this regulatory pathway serves as a homeostatic control mechanism for centriole assembly.
- 721–729 **Identification and Characterization of Wor4, a New Transcriptional Regulator of White-Opaque Switching**
Matthew B. Lohse and Alexander D. Johnson
- The human fungal pathogen *Candida albicans* can switch between two cell types, “white” and “opaque,” each with distinctive single cell and colony morphologies and each heritable for many generations. Six transcriptional regulators, which form a highly interconnected circuit, have previously been shown to regulate this switch. Here, the authors identify a seventh key regulator of white-opaque switching (Wor4) whose deletion and overexpression does not phenocopy those of the other regulators of white-opaque switching. The identification of Wor4 and its characteristics indicates that the heritable white-opaque switch is considerably more complex than those controlling non-heritable gene expression.
- 731–741 **Differential Expression of Genes Involved in Host Recognition, Attachment, and Degradation in the Mycoparasite *Tolypocladium ophioglossoides***
C. Alisha Quandt, Yanming Di, Justin Elser, Pankaj Jaiswal, and Joseph W. Spatafora
- Within *Tolypocladium*, there has been an inter-kingdom host jump from insect pathogenesis to mycoparasitism of truffles. Previous genome sequencing studies revealed similarities in gene content between truffle parasite, *Tolypocladium ophioglossoides*, and insect pathogen, *Tolypocladium inflatum*. To examine the role that differential expression may be playing in the ability of *T. ophioglossoides* to parasitize truffles, Quandt *et al.* grew the fungus under four experimental conditions, including media amended with two parts of truffle tissue, insect cuticle (representing the ancestral host), and a rich culture medium. RNA-Seq revealed many differentially expressed genes, and the authors discuss several, including G-protein coupled receptors, chitinases, adhesins, and secondary metabolism.

- 743–753 **Implementation of the Realized Genomic Relationship Matrix to Open-Pollinated White Spruce Family Testing for Disentangling Additive from Nonadditive Genetic Effects**
Omnia Gamal El-Dien, Blaise Ratcliffe, Jaroslav Klápště, Ilga Porth, Charles Chen, and Yousry A. El-Kassaby

The authors of this study utilized DNA data to construct the genomic pairwise relationship among members of 214 white spruce open-pollinated families grown on one site and compared the obtained genetic parameters to those derived from classical pedigree. The DNA data permitted genetic variance decomposition and the disentanglement of additive from all non-additive factors. The DNA data permitted the generation of genetic parameters (i.e., dominance and epistasis) that can only be generated from sophisticated interconnected mating designs that included half- and full-sib families coupled with vegetative replication of individuals. The utilized DNA data allowed better accounting of environmental factors and heritability and genetic ranking.

- 755–765 **Genome-Wide Investigation of MicroRNAs and Their Targets in Response to Freezing Stress in *Medicago sativa* L., Based on High-Throughput Sequencing**
Yongjun Shu, Ying Liu, Wei Li, Lili Song, Jun Zhang, and Changhong Guo

In alfalfa, freezing tolerance is a complex trait determined by interactions among many genes, which is a major limitation of its exploitation. Understanding the complex regulation mechanisms of freezing tolerance is imperative for alfalfa genetic breeding. The authors identified and characterized the important roles of the miRNAs and their targets in the cold and/or freezing stress response by small RNA sequencing and degradome sequencing. The results provide valuable information for determining molecular mechanisms of freezing tolerance, which will aid future efforts to improve freezing tolerance in alfalfa.

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