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September 2017 • VOLUME 7 • ISSUE 9 • www.g3journal.org

GENOME REPORTS

- 2883–2889 **Whole Genome Sequence of the Heterozygous Clinical Isolate *Candida krusei* 81-B-5**
Christina A. Cuomo, Terrance Shea, Bo Yang, Reeta Rao, and Anja Forche
Candida krusei is an important fungal pathogen in immunocompromised patients and is innately resistant to the antifungal drug fluconazole. Cuomo *et al.* generated a high quality genome assembly of a clinical *C. krusei* isolate using PacBio sequencing technology. They report high levels of heterozygosity across most of the genome and a unique profile of transporters that could impact the species' drug sensitivity and adaptation to different environments. This genome will serve as a reference for further genetic study of this pathogen.
- 2891–2898 **The Nuclear and Mitochondrial Genomes of the Facultatively Eusocial Orchid Bee *Euglossa dilemma***
Philipp Brand, Nicholas Saleh, Hailin Pan, Cai Li, Karen M. Kapheim, and Santiago R. Ramirez
Bees provide indispensable pollination services and have become important models for the study of learning and memory, plant–insect interactions, and social behavior. Here, Brand *et al.* describe the nuclear and mitochondrial genomes of the facultatively eusocial orchid bee *Euglossa dilemma*. The *E. dilemma* genome has high conservation of gene synteny when compared to the honey bee, despite genome size difference and evolutionary divergence. This study provides valuable genomic resources for genetic analyses on the ecology, evolution, and conservation of orchid bees and the evolution of sociality in bees.
- 2899–2906 **Genome-Wide Analysis of the First Sequenced *Mycoplasma capricolum* subsp. *capripneumoniae* Strain M1601**
Shengli Chen, Huafang Hao, Ping Zhao, François Thiaucourt, Ying He, Pengcheng Gao, Han Guo, Wenheng Ji, Zhanhui Wang, Zhongxin Lu, Yuefeng Chu, and Yongsheng Liu
Mycoplasma capricolum subsp. *capripneumoniae* (Mccp) is a common goat pathogen that causes contagious caprine pleuropneumonia. Chen *et al.* closed the gap in the Mccp M1601 draft genome and corrected the rRNA operon sequences to yield complete genomic sequences. Comprehensive genomic analysis identified twenty-six potential virulence genes, and Chen *et al.* also performed comparative and phylogenetic analyses. Further understanding the virulence genes, genome features, and genetics of Mccp will help determine its pathogenic mechanisms and genetics.

MUTANT SCREEN REPORT

- 2907–2917 **Genome-Wide Screen for Genes Involved in *Caenorhabditis elegans* Developmentally Timed Sleep**
Huiyan Huang, Chen-Tseh Zhu, Lukas L. Skuja, Dustin J. Hayden, and Anne C. Hart
Huang *et al.* describe the first genome-wide, classic genetic screen focused on identifying genes required for developmentally timed sleep in *C. elegans*. In the screen, they identified causal genes for two mutant lines with decreased sleep: *goa-1* and *gpb-2*. To understand the role of GPB-2, they examined previously described regulators of G protein signaling (RGS) proteins and determined which proteins contribute to developmentally timed sleep. The work presented here highlights the importance of G protein signaling in sleep regulatory pathways.

INVESTIGATIONS

- 2919–2929 **Habitat Predicts Levels of Genetic Admixture in *Saccharomyces cerevisiae***
Viranga Tilakaratna and Doua Bensasson
Natural crosses between domesticated plants or animals and their wild relatives have played an important role in adaptation to local environments. Here, Tilakaratna and Bensasson show that wine yeast in vineyards cross naturally with nearby wild woodland yeast of the same species and find that, despite this interplay, woodland yeast from different parts of the eastern USA are genetically isolated from each other. They also identify a North African strain that is closely related to wine yeast and which could prove useful in understanding how these yeast were domesticated.
- 2931–2943 **ASPsiRNA: A Resource of ASP-siRNAs Having Therapeutic Potential for Human Genetic Disorders and Algorithm for Prediction of Their Inhibitory Efficacy**
Isha Monga, Abid Qureshi, Nishant Thakur, Amit Kumar Gupta, and Manoj Kumar
Allele-specific siRNAs holds therapeutic potential because of they selectively inhibit disease causing alleles while sparing expression of their wild-type counterparts. Here, Monga *et al.* describe the ASPsiRNA resource (<http://crdd.osdd.net/servers/aspsirna/>), which is composed of a database, a prediction algorithm, and important analysis tools. This dedicated bioinformatics platform will aid in tackling currently intractable gain-of-function disorder and is expected to accelerate research in the field of RNAi-based therapeutics for human genetic diseases.
- 2945–2956 **Functional Profiling of Transcription Factor Genes in *Neurospora crassa***
Alexander J. Carrillo, Patrick Schacht, Iva E. Cabrera, Johnathon Blahut, Loren Prudhomme, Sarah Dietrich, Thomas Bekman, Jennifer Mei, Cristian Carrera, Vivian Chen, Isaiah Clark, Gerardo Fierro, Logan Ganzen, Jose Orellana, Shelby Wise, Kevin Yang, Hui Zhong, and Katherine A. Borkovich
Few eukaryotes have a complete catalogue of transcription factor genes and functions, despite their critical importance to basic biology. In this study, Carrillo *et al.* present annotation for 312 transcription genes and phenotypes for 242 mutants in the model filamentous fungus *Neurospora crassa*. They show that the majority of mutants possess one or more growth or developmental phenotypes and, using available mRNA expression data, implicate roles in sexual development for co-transcribed groups of transcription factors.
- 2957–2968 **Reduced Protein Expression in a Virus Attenuated by Codon Deoptimization**
Benjamin R. Jack, Daniel R. Boutz, Matthew L. Paff, Bartram L. Smith, James J. Bull, and Claus O. Wilke
Viral attenuation involves extensive recoding of synonymous codons in the viral genome, but the mechanistic underpinnings of this approach remain unclear. Using quantitative proteomics and RNA sequencing, Jack *et al.* explore the molecular basis of attenuation in a strain of bacteriophage T7 whose capsid gene was designed with 182 suboptimal codons. While transcription is unaffected, translation is halved for this recoded capsid gene and is also diminished for several downstream genes, suggesting that reduced translation of an essential polycistronic transcript and diminished virion assembly form the basis of attenuation in this phage.
- 2969–2977 **The *Caenorhabditis elegans* Female-Like State: Decoupling the Transcriptomic Effects of Aging and Sperm Status**
David Angeles-Albores, Daniel H. W. Leighton, Tiffany Tsou, Tiffany H. Khaw, Igor Antoshechkin, and Paul W. Sternberg
C. elegans enters adulthood as a hermaphrodite with a finite sperm supply. Over the first three days of adulthood, it lays 300 eggs and becomes self-sterile. Angeles-Albores *et al.* measured the effect of ageing as *C. elegans* goes from a first day adult to a 6th day adult and showed that the expression levels of a quarter of the genes in the *C. elegans* genome are impacted. However, not all transcriptome changes are due to ageing; spermlessness partially phenocopies the ageing process, so they postulate that sperm status mediates entry into an undescribed life state they call the ‘female state’.
- 2979–2989 **The SEK-1 p38 MAP Kinase Pathway Modulates Gq Signaling in *Caenorhabditis elegans***
Jill M. Hoyt, Samuel K. Wilson, Madhuri Kasa, Jeremy S. Rise, Irini Topalidou, and Michael Ailion
To understand how the heterotrimeric G protein Gq regulates neuronal activity, Hoyt *et al.* performed a forward genetic screen in *C. elegans* for suppressors of an activated Gq mutant. Here, they identify one of these suppressors as a mutation in *sek-1*, a component of a p38 MAP kinase pathway. The p38 pathway has been best characterized for its role in responding to a variety of cellular stresses. Their results suggest that the *sek-1* p38 pathway may also regulate neuronal activity by modulating the output of Gq signaling.

- 2991–2998 **Two Types of Etiological Mutation in the Limb-Specific Enhancer of *Shh***
Takanori Amano, Tomoko Sagai, Ryohei Seki, and Toshihiko Shiroishi
- Mutations in the *Shh* limb enhancer cause an anterior ectopic expression of *Shh* in the developing limb, resulting in polydactyly in human and mouse. Amano *et al.* found that two different types of regulatory mutations have the same outcome: misexpression of *Shh*. One type abolishes an existing TF-binding motif relevant to negative regulation, consequently resulting in the ectopic *Shh* expression. Another type gives rise to a new binding motif for positive regulation, as a gain-of-activation type mutation. These findings provide an insight into the regulation of *Shh* in limb buds.
- 2999–3017 **Gene Expression Networks in the Murine Pulmonary Myocardium Provide Insight into the Pathobiology of Atrial Fibrillation**
Jordan K. Boutilier, Rhonda L. Taylor, Tracy Mann, Elyshia McNamara, Gary J. Hoffman, Jacob Kenny, Rodney J. Dilley, Peter Henry, Grant Morahan, Nigel G. Laing, and Kristen J. Nowak
- The pulmonary myocardium is a muscular coat surrounding the pulmonary veins that may be involved in atrial fibrillation. Boutilier *et al.* analyzed a whole lung transcriptome dataset from the BXD recombinant inbred mouse resource. They report a pulmonary cardiomyocyte gene network of 24 transcripts, coordinately regulated by loci on chromosomes 1 and 2. Promoter enrichment analysis, gene ontology, interrogation of publicly available ChIP-seq data and immunohistochemical analysis of lung sections lead them to propose that perturbed regulation of this gene network might lead to altered calcium handling, myocyte growth, and contractile force, thus contributing to the aberrant electrophysiological properties observed in atrial fibrillation.
- 3019–3029 **Genome-Wide Sequence and Expression Analysis of the NAC Transcription Factor Family in Polyploid Wheat**
Philippa Borrill, Sophie A. Harrington, and Cristobal Uauy
- Transcription factors are vital in plants to regulate gene expression in response to environmental stimuli and to control developmental processes. In this study, Borrill, Harrington, and Uauy annotated and classified transcription factors in polyploid bread wheat into gene families and explored the NAC family in detail. They combined phylogenetic analysis and transcriptome analysis, using publicly available RNA-seq data, to characterize the NAC gene family and provide hypotheses for putative functions of many NAC transcription factors. This study lays the groundwork for future studies on transcription factors in wheat which may be of great agronomic relevance.
- 3031–3045 **RNA-seq of Rice Yellow Stem Borer *Scirpophaga incertulas* Reveals Molecular Insights During Four Larval Developmental Stages**
Pichili Renuka, Maganti S. Madhav, Ayyagari Phani Padmakumari, Kalyani M. Barbadikar, Satendra K. Mangrauthia, Kola Vijaya Sudhakara Rao, Soma S. Marla, and Vemuri Ravindra Babu
- To design novel pest control strategies and to understand the biology of development of rice Yellow stem borer (YSB), an important insect pest of rice, Renuka *et al.* performed RNA seq at four larval stages. About 229 Mbp data was generated and *de novo* assembled into 24, 775 transcripts. The data reflected the transcripts involved in key metabolic processes *viz.*, detoxification mechanism, chemoreception and hormonal regulators which provided insights into transcript expression patterns. Data also provided strong evidence about the presence of distinct RNAi machinery in YSB. Identification of strong specific visual recognition coupled chemosensory mechanisms evidenced the possible monophagous feeding behavior of YSB. Several differentially expressed novel transcripts were identified which can be deployed for pest control strategies.
- 3047–3058 **Annotated Draft Genome Assemblies for the Northern Bobwhite (*Colinus virginianus*) and the Scaled Quail (*Callipepla squamata*) Reveal Disparate Estimates of Modern Genome Diversity and Historic Effective Population Size**
David L. Oldeschulte, Yvette A. Halley, Miranda L. Wilson, Eric K. Bhattarai, Wesley Brashear, Joshua Hill, Richard P. Metz, Charles D. Johnson, Dale Rollins, Markus J. Peterson, Derek M. Bickhart, Jared E. Decker, John F. Sewell, and Christopher M. Seabury
- Oldeschulte *et al.* assembled and annotated a first-generation draft genome for the scaled quail and a second-generation draft genome for the bobwhite. Analyses using conserved set of nuclear orthologs to assess genome completeness indicated that both quail draft genomes are comparative in their completeness to other more established avian genomes (*i.e.*, chicken, turkey, zebra finch). Modern estimates of genome diversity for the bobwhite were > 1.5 times higher than those predicted for the scaled quail, which resulted in the estimation of a larger historic effective population size for the bobwhite, and both species were predicted to experience declines approximately 15–20 kya.

- 3059–3071 **Whole-Genome Sequencing and Concordance Between Antimicrobial Susceptibility Genotypes and Phenotypes of Bacterial Isolates Associated with Bovine Respiratory Disease**
Joseph R. Owen, Noelle Noyes, Amy E. Young, Daniel J. Prince, Patricia C. Blanchard, Terry W. Lehenbauer, Sharif S. Aly, Jessica H. Davis, Sean M. O'Rourke, Zaid Abdo, Keith Belk, Michael R. Miller, Paul Morley, and Alison L. Van Eenennaam
- Owen *et al.* used whole-genome sequencing to perform *de novo* genome assembly of bacterial pathogens associated with bovine respiratory disease (BRD), the leading cause of U.S. cattle deaths. Available genomic sequences for four bacterial species, *Histophilus somni*, *Mycoplasma bovis*, *Mannheimia haemolytica*, and *Pasteurella multocida*, increased two fold. *In silico* gene prediction methods identified antimicrobial resistance genes which showed an overall concordance rate of 72.7% with phenotypic susceptibility testing. This suggests care should be exercised in basing treatment decisions solely on genomic data. More data are needed to better predict the most effective BRD treatment regime based on specific “gene-bacterium-host” combinations.
- 3073–3082 **Genome-Wide Transcriptional Dynamics in the Companion Bacterial Symbionts of the Glassy-Winged Sharpshooter (Cicadellidae: *Homalodisca vitripennis*) Reveal Differential Gene Expression in Bacteria Occupying Multiple Host Organs**
Gordon M. Bennett and Rebecca A. Chong
- Many insects harbor bacterial symbionts for essential nutrition, and symbionts experience extensive genomic degradation. Bennett and Chong examined patterns of gene expression in the dual-bacterial symbionts of the glassy-winged sharpshooter to determine how companion symbiont gene expression patterns are affected by the symbiotic condition and whether symbionts infecting multiple tissues exhibit distinct cellular functions. Symbionts exhibit similar profiles of expressed genes essential to the symbioses, highlighting common evolutionary adaptations to the symbiotic condition. The younger symbiont retains the capability to differentially express essential nutrition pathways in different host tissues. This result is unusual since symbiotic bacteria lose these abilities as their genomes degrade.
- 3083–3090 **Regulation of Small Mitochondrial DNA Replicative Advantage by Ribonucleotide Reductase in *Saccharomyces cerevisiae***
Elliot Bradshaw, Minoru Yoshida, and Feng Ling
- Mitochondrial DNA (mtDNA) deletion mutations can disrupt mitochondrial function and are associated with pathological symptoms in several organisms, yet regulatory mechanisms governing their replicative advantage over wild-type molecules are not fully understood. Ribonucleotide reductase (RNR) catalyzes the rate-limiting step of cellular dNTP synthesis. Using yeast, Bradshaw, Yoshida, and Ling identify RNR as a major regulator of the replicative advantage of small mtDNA molecules over full-length mtDNA. Genetic manipulations that increased dNTP synthesis by RNR were able to partially rescue full-length mtDNA replication in the presence of small mtDNA, raising the possibility that insufficient RNR activity may cause pathological mtDNA expansion in higher organisms.
- 3091–3102 **3'-Terminated Overhangs Regulate DNA Double-Strand Break Processing in *Escherichia coli***
Edyta Đermić, Davor Zahradka, Dušica Vujaklija, Siniša Ivanković, and Damir Đermić
- The essential process of DNA double-strand break (DSB) repair is performed chiefly by homologous recombination, during which two 3'-terminated tails are produced from a DSB by helicase/nuclease activity and then covered by recombinase protein. Đermić *et al.* induced DSBs in *Escherichia coli* by gamma rays and report that the crucial factor in controlling DSB processing is 3'-overhangs. They limit DSB processing when long and stable, which is achieved by: i) RecA recombinase polymerization onto them, ii) inactivation of nucleases that trim them, and iii) their excessive length. Their results suggest that 3' overhangs regulate DSB processing by inhibiting helicase reloading onto DSBs.
- 3103–3113 **Application of Response Surface Methods To Determine Conditions for Optimal Genomic Prediction**
Řeka Howard, Alicia L. Carriquiry, and William D. Beavis
- The performance of genomic prediction methods is influenced by many factors including the number of segregating progeny, number of markers, number of QTL, the proportion of genotypic variation explained by epistasis, and heritability. Here, Howard, Carriquiry, and Beavis employ Response Surface Methodology to explore these factors and find factor combinations that produce the most accurate predictions without evaluating all possible factor combinations. They compare the performance of BLUP and Support Vector Machine techniques in terms of accuracy of prediction and demonstrate the benefit of Response Surface Methodology for model comparison.

- 3115–3121 **A Large Deletion in the *NSDHL* Gene in Labrador Retrievers with a Congenital Cornification Disorder**
Anina Bauer, Michela De Lucia, Vidhya Jagannathan, Giorgia Mezzalana, Margret L. Casal, Monika M. Welle, and Tosso Leeb
- Bauer *et al.* provide strong evidence that a large genomic deletion harboring the last three exons of the *NSDHL* gene causes an X-linked genodermatosis in dogs that shows some similarities to the human CHILD syndrome. Their study contains an initial clinical and histopathological description of the diseases, as well as the genetic analysis.
- 3123–3131 **Sequence-Based Mapping and Genome Editing Reveal Mutations in Stickleback *Hps5* Cause Oculocutaneous Albinism and the *casper* Phenotype**
James C. Hart and Craig T. Miller
- Hart and Miller discovered a spontaneous, recessive, viable mutation called *casper* that results in oculocutaneous albinism in threespine stickleback fish. They used a next-generation sequencing approach to map *casper* to a genomic region containing the Hermansky-Pudlak Syndrome 5 (*Hps5*) gene. *casper* mutants contain a one base pair insertion in *Hps5* and CRISPR/Cas9-induced mutations in *Hps5* phenocopy *casper*. Injecting a pair of *Hps5* guide RNAs induced more efficient deletions than single guides alone. They found that *casper* facilitated visualizing fluorescent reporter gene patterns in older juvenile fish. This work provides a locus to study pigmentation, genome editing, and transgene expression in sticklebacks.
- 3133–3144 **Ankyrin-1 Gene Exhibits Allelic Heterogeneity in Conferring Protection Against Malaria**
Hong Ming Huang, Denis C. Bauer, Patrick M. Lelliott, Matthew W. A. Dixon, Leann Tilley, Brendan J. McMorran, Simon J. Foote, and Gaetan Burgio
- In malaria endemic regions, many individuals developed natural resistance against the disease by having certain genetic mutations that affect the ability of malarial parasites to survive. However, it is often observed that different mutations within the same gene could give rise to different degree of malaria protection. Huang *et al.* describe a novel direct observation of this phenomenon on ankyrin-1 gene and propose that this phenomenon could explain why people living in malaria endemic regions have wide variation in their natural malaria protection and that this phenomenon might be more common than expected.
- 3145–3155 **Evolutionary Dynamics of Male Reproductive Genes in the *Drosophila virilis* Subgroup**
Yasir H. Ahmed-Braimah, Robert L. Unckless, and Andrew G. Clark
- Fertilization success is a central component of fitness, and postcopulatory sexual selection plays a key role in shaping the molecular traits that maximize that success. It is also an important component of fitness in many animal taxa where the opportunity for gametic competition is present, such as in females that have prolonged sperm storage and/or mate multiply. However, the genetic basis of these processes are not well understood. Here, Ahmed-Braimah, Unckless, and Clark analyze classes of genes that control the molecular interactions at the postcopulatory level in a group of species that significantly diverged in gametic phenotypes.
- 3157–3167 **The Douglas-Fir Genome Sequence Reveals Specialization of the Photosynthetic Apparatus in Pinaceae**
David B. Neale, Patrick E. McGuire, Nicholas C. Wheeler, Kristian A. Stevens, Marc W. Crepeau, Charis Cardeno, Aleksey V. Zimin, Daniela Puiu, Geo M. Pertea, U. Uzay Sezen, Claudio Casola, Tomasz E. Koralewski, Robin Paul, Daniel Gonzalez-Ibeas, Sumaira Zaman, Richard Cronn, Mark Yandell, Carson Holt, Charles H. Langley, James A. Yorke, Steven L. Salzberg, and Jill L. Wegrzyn
- A reference genome sequence for *Pseudotsuga menziesii* var. *menziesii* (Douglas-fir) is reported, providing a reference sequence for a third genus of the family Pinaceae with a contiguity and quality of genome assembly far exceeding that of other conifers (contig N50 = 44,136 bp and scaffold N50 = 340,704 bp). Comparative genome annotation with angiosperm species reveals gene-family expansion and contraction in Douglas-fir and other conifers. Neale *et al.* provide an important resource for Douglas-fir breeders and geneticists and shed light on the evolutionary processes that have led to the divergence of angiosperms from gymnosperms.

- 3169–3176 **Genome-Wide SNP Discovery and Analysis of Genetic Diversity in Farmed Sika Deer (*Cervus nippon*) in Northeast China Using Double-Digest Restriction Site-Associated DNA Sequencing**
Hengxing Ba, Boyin Jia, Guiwu Wang, Yifeng Yang, Gilead Kedem, and Chunyi Li
 Ba *et al.* generated over 1.45 billion high-quality paired-end reads (288 GB) across 42 unrelated individuals using double-digest restriction-site associated DNA sequencing (ddRAD-seq) and identified a total of 96,188 (29.63%) putative bi-allelic SNP loci with an average sequencing depth of 23x. Based on the analysis, they found that majority of the loci had a deficit of heterozygotes ($F_{IS} > 0$) and low values of H_{obs} , which could be due to inbreeding and Wahlund effects. They also developed a collection of high-quality SNP probes that would likely be useful in a variety of applications in genotyping for cervid species in the future.
- 3177–3184 **The Stress-Inducible Peroxidase TSA2 Underlies a Conditionally Beneficial Chromosomal Duplication in *Saccharomyces cerevisiae***
Robert A. Linder, John P. Greco, Fabian Seidl, Takeshi Matsui, and Ian M. Ehrenreich
 Aneuploidization is typically deleterious but can sometimes enable cells to tolerate specific mutations and environmental stresses. The genetic and molecular mechanisms underlying these conditionally beneficial effects are not fully understood. In this paper, Linder *et al.* identify and genetically characterize a chromosomal duplication that makes haploid yeast more tolerant to oxidative stress. They determine that duplication of a single stress-inducible peroxidase is mostly responsible for the effect of the aneuploidy on oxidative stress tolerance. Their results support the idea that some aneuploidies are conditionally beneficial because of dosage changes at a small number of contextually important genes.
- 3185–3193 **Ras/MAPK Modifier Loci Revealed by eQTL in *Caenorhabditis elegans***
Mark G. Sterken, Linda van Bemmelen van der Plaats, Joost A. G. Riksen, Miriam Rodriguez, Tobias Schmid, Alex Hajnal, Jan E. Kammenga, and Basten L. Snoek
 Although it has long been known that mutations can lead to different phenotypes in different individuals, identifying causal loci is difficult. Here, Sterken *et al.* measure gene expression to determine how a Ras/MAPK *let-60* gain-of-function (gf) mutation is affected by variation in the genetic background in a *Caenorhabditis elegans* RIL panel. They found that the *let-60(gf)* mutation specifically results in novel *trans*-eQTL, mostly clustered in six eQTL hotspots. For the chromosome I hotspot they identified allelic variation in *amx-2* as explanatory of the *trans*-eQTL. Yet, network analysis and the known molecular function of *amx-2* make it likely that it indirectly affects these transcripts.
- 3195–3202 **The Integrated Genomic Architecture and Evolution of Dental Divergence in East African Cichlid Fishes (*Haplochromis chilotes* x *H. nyererei*)**
C. Darrin Hulsey, Gonzalo Machado-Schiaffino, Lara Keicher, Diego Ellis-Soto, Frederico Henning, and Axel Meyer
 Using a hybrid mapping cross of two Lake Victoria cichlid species, Hulsey *et al.* examined genomic regions associated with their dental diversity. A similar genomic region was found to be associated with the most variation in oral jaw tooth numbers in cichlids from both Lake Malawi and Lake Victoria. This same genomic region was also associated with variation in pharyngeal jaw tooth number. Highly similar correlations in tooth numbers on the two jaws in both the Victoria hybrid population and across the phylogenetic diversity of Malawi cichlids suggests teeth in haplochromine cichlids might generally coevolve according to their genetic correlations.
- 3203–3215 **A Functional Link Between Bir1 and the *Saccharomyces cerevisiae* Ctf19 Kinetochores Complex Revealed Through Quantitative Fitness Analysis**
Vasso Makrantonis, Adam Ciesiolka, Conor Lawless, Josefin Fernius, Adele Marston, David Lydall, and Michael J. R. Stark
BIR1 encodes a component of the *Saccharomyces cerevisiae* chromosome passenger complex (CPC), which includes the protein kinase *Ipl1* and promotes correct attachment of chromosomes to microtubules during mitosis. Through a genome-wide screen using Quantitative Fitness Analysis, Makrantonis *et al.* show that the Ctf19 kinetochores protein complex becomes essential in cells with a defective *bir1* allele (*bir1-17*). While the core components of the Ctf19 complex are also essential in an *ipl1* mutant, the more peripheral components are only required in *bir1-17* cells. Their findings indicate a novel functional connection between Bir1 and a specific subset of proteins within the Ctf19 kinetochores complex.

- 3217–3227 **Trans-ancestry Fine Mapping and Molecular Assays Identify Regulatory Variants at the *ANGPTL8* HDL-C GWAS Locus**
Maren E. Cannon, Qing Duan, Ying Wu, Monica Zeynalzadeh, Zheng Xu, Antti J. Kangas, Pasi Soininen, Mika Ala-Korpela, Mete Civelek, Aldons J. Lusis, Johanna Kuusisto, Francis S. Collins, Michael Boehnke, Hua Tang, Markku Laakso, Yun Li, and Karen L. Mohlke
- Cannon *et al.* perform statistical fine-mapping analyses at an HDL cholesterol locus and examine the function of candidate causal variants. They show that the variants are associated with *ANGPTL8* expression level in adipose tissue samples and that *ANGPTL8* expression level is itself associated with HDL cholesterol levels. *ANGPTL8* is a nearby gene with known roles in cholesterol metabolism. They identify drivers of *ANGPTL8* tissue specificity and variants that may contribute to the mechanism of the HDL cholesterol association. These studies are important for understanding how regulatory variants can alter gene expression and lead to changes in phenotype.
- 3229–3236 **Accelerating Wright–Fisher Forward Simulations on the Graphics Processing Unit**
David S. Lawrie
- GO Fish is a massively parallel implementation of the single-locus Wright-Fisher forward simulation, which can be accelerated by over two orders of magnitude on a computer's Graphics Processing Unit relative to a serial Wright-Fisher algorithm running on the Central Processing Unit. GO Fish is also highly flexible in the evolutionary scenarios it can model and this combined speed and flexibility allows for more powerful population genetics inferences to be made faster. The widely applicable parallel programming techniques underlying GO Fish serve as an exciting template for future research into accelerating computation in evolution. Website and manual available at: <http://dl42.github.io/ParallelPopGen/>.