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INVESTIGATIONS

- 235–244 **Comparative Phylogenomics of Pathogenic and Nonpathogenic Species**
Emily Whiston and John W. Taylor
- The Ascomycete Onygenales order embraces a diverse group of non-pathogens and mammalian pathogens, including the potentially fatal human pathogen *Coccidioides* spp. The authors of this study have sequenced four non-pathogenic species more closely related to *Coccidioides* spp. than any other known Onygenales species. In addition to gene family expansion/contraction analyses and evidence of positive selection, they confidently identified nearly 800 genes unique to the pathogenic *Coccidioides* species. These unique *Coccidioides* genes have few known protein domains, and their transcription is elevated in the pathogenic phase as compared to the environmental phase. These genes likely include those that make these fungi such exceptional pathogens.
- 245–254 **An RNAi-Based Candidate Screen for Modifiers of the CHD1 Chromatin Remodeler and Assembly Factor in *Drosophila melanogaster***
Sharon Kim, Lakshmi Bugga, Eugenie S. Hong, Rebecca Zabinsky, Rebecca G. Edwards, Parimal A. Deodhar, and Jennifer A. Armstrong
- While necessary for DNA compaction and organization, chromatin presents a problem in that nucleosomes can impede the progress of RNA polymerases. The conserved CHD1 protein participates in histone turnover and recycling during transcription, but it is unclear how CHD1 is recruited to genes and whether it partners with other proteins. The authors of this work created a novel genetic assay in the fruit fly to evaluate interactions between CHD1 and other factors. Their results indicate that CHD1 may act in opposition to other chromatin remodeling factors, including INO80, and that the localization of CHD1 to active genes is dependent upon RTF1.
- 255–262 **A RAB3GAP1 SINE Insertion in Alaskan Huskies with Polyneuropathy, Ocular Abnormalities, and Neuronal Vacuolation (POANV) Resembling Human Warburg Micro Syndrome 1 (WARBM1)**
Michaela Wiedmer, Anna Oevermann, Stephanie E. Borer-Germann, Daniela Gorgas, G. Diane Shelton, Michaela Drögemüller, Vidhya Jagannathan, Diana Henke, and Tosso Leeb
- This paper provides a comprehensive clinical and pathological description of the POANV phenotype in Alaskan Huskies. Similar phenotypes were previously described in other dog breeds, most notably in Rottweilers and Brazilian Terriers. The authors additionally present strong evidence that an insertion of a SINE element into the coding sequence of the RAB3GAP1 gene causes this disease.

- 263–279 **The Mouse Universal Genotyping Array: From Substrains to Subspecies**
Andrew P. Morgan, Chen-Ping Fu, Chia-Yu Kao, Catherine E. Welsh, John P. Didion, Liran Yadgary, Leeanna Hyacinth, Martin T. Ferris, Timothy A. Bell, Darla R. Miller, Paola Giusti-Rodriguez, Randal J. Nonneman, Kevin D. Cook, Jason K. Whitmire, Lisa E. Gralinski, Mark Keller, Alan D. Attie, Gary A. Churchill, Petko Petkov, Patrick F. Sullivan, Jennifer R. Brennan, Leonard McMillan, and Fernando Pardo-Manuel de Villena
 Genotyping microarrays (“SNP chips”) are a valuable tool in laboratory and population genetics. Here the authors present the most recent version of the Mouse Universal Genotyping Array, GigaMUGA, a 143,259-marker Illumina Infinium array for the house mouse (*Mus musculus*). GigaMUGA is informative across the spectrum of relatedness, from closely related laboratory strains and substrains to other *Mus* species.
- 281–286 **argyle: An R Package for Analysis of Illumina Genotyping Arrays**
Andrew P. Morgan
 Genotyping microarrays (“SNP chips”) are an important tool in basic and applied genetics research. In this work, the author presents argyle, a software package for the R statistical computing environment, designed to allow researchers to perform quality control and exploratory analysis of genotyping array data.
- 287–298 **SAGA DUB-Ubp8 Deubiquitylates Centromeric Histone Variant Cse4**
Claudia Canzonetta, Stefano Vernarecci, Michele Iuliani, Cristina Marracino, Claudia Belloni, Paola Ballario, and Patrizia Filetici
 Unbalanced segregation of chromosomes during cell division induces a state called aneuploidy that is recurrent in many tumors and the cause of birth defects and hereditary diseases. The centromeres are selectively marked by specialized histone variants such as the CEN-H3 Cse4/CENPA to avoid a tight control of chromosome segregation. Psh1 Polyubiquitylation of Cse4 regulates its proteolysis and deposition. This study shows an epistatic link between Psh1 and DUB-Ubp8 and a novel role for Ubp8 in the deubiquitylation and Ub-mediated proteolysis of Cse4. These findings highlight the importance of SAGA complex in the control of ubiquitylation of Cse4, its localization and centromere behavior.
- 299–310 **The wavy Mutation Maps to the Inositol 1,4,5-Trisphosphate 3-Kinase 2 (IP3K2) Gene of Drosophila and Interacts with IP3R to Affect Wing Development**
Derek M. Dean, Luana S. Maroja, Sarah Cottrill, Brent E. Bomkamp, Kathleen A. Westervelt, and David L. Deitcher
 Mutations in *wavy*, a classic, previously unmapped locus of *Drosophila melanogaster*, cause specific defects in wing morphology. Dean *et al.* mapped *wavy* mutations to the *IP₃ 3-kinase 2 (IP3K2)* gene and showed that *IP3K2* function was required in the wing disk during early pupal life. They also uncovered genetic interactions between *IP3K2* and the *IP₃ receptor* locus and, in light of these findings, proposed models for how the underlying *IP₃* signaling network affects wing development.
- 311–319 **Quantitative Trait Locus and Genetical Genomics Analysis Identifies Putatively Causal Genes for Fecundity and Brooding in the Chicken**
Martin Johnsson, Kenneth B. Jonsson, Leif Andersson, Per Jensen, and Dominic Wright
 In this paper, Johnsson *et al.* have mapped candidate quantitative trait genes for egg fecundity in an intercross of wild and domestic chickens. They combined quantitative trait locus mapping with gene expression to search for candidate genes underlying the QTL. In total, they found 12 loci for different aspects of egg fecundity. They then combined the genomic confidence intervals of these loci with expression quantitative trait loci from bone and hypothalamus in the same intercross. Thus, the authors suggest new candidate genes for these life history traits in the chicken.
- 321–335 **The Extent of mRNA Editing Is Limited in Chicken Liver and Adipose, but Impacted by Tissular Context, Genotype, Age, and Feeding as Exemplified with a Conserved Edited Site in COG3**
Pierre-François Roux, Laure Frésard, Morgane Boutin, Sophie Leroux, Christophe Klopp, Anis Djari, Diane Esquerré, Pascal GP Martin, Tatiana Zerjal, David Gourichon, Frédérique Pitel, and Sandrine Lagarrigue
 Since 2009, roughly 30 studies have been carried out to depict mRNA editomes in vertebrates, all focusing on mammals, and they have raised contradictory conclusions regarding the extent of this phenomenon. This study, which further points to the requirement of rigorous bio-informatics pipelines to limit false positives when dealing with current high-throughput technologies, is an answer to the lack of editome characterizations on non-mammalian vertebrates. The authors provide evidence that mRNA editing is a rare phenomenon in chicken and give new insights on the role of mRNA editing in vertebrates by highlighting effects of different genetic and environmental factors on mRNA editing level.

- 337–349 **An Amphiphysin-Like Domain in Fus2p Is Required for Rvs161p Interaction and Cortical Localization**
Richard A. Stein, Jean A. Smith, and Mark D. Rose
 Cell fusion is ubiquitous among eukaryotes. Fus2p is a key regulator of cell fusion in budding yeast. For fusion to occur, Fus2p must bind to an amphiphysin known as Rvs161p. Amphiphysins are a broad class of dimeric proteins involved in a wide variety of membrane-associated processes. Here the authors found that Fus2p contains an amphiphysin-like domain, which is responsible for the binding to Rvs161p. Localization of Fus2p to the cortical membrane is dependent on Rvs161p and a novel carboxy-terminal domain.
- 351–356 **Chromoanasythetic Genomic Rearrangement Identified in a *N*-Ethyl-*N*-Nitrosourea (ENU) Mutagenesis Screen in *Caenorhabditis elegans***
Omar A. Itani, Stephane Flibotte, Kathleen J. Dumas, Donald G. Moerman, and Patrick J. Hu
 Chromoanasythesis is a newly discovered process that generates complex genomic rearrangements (CGRs) in response to catastrophic chromosomal damage. How these CGRs are induced and how prevalent such CGRs are in animal species are not known. Here Itani *et al.* describe a CGR that emerged from an ENU mutagenesis screen. Structural and sequence analysis revealed that this CGR is likely a product of chromoanasythesis. Their findings suggest that point mutations may suffice to induce CGRs. The relatively subtle phenotype of animals harboring this CGR suggests that the prevalence of CGRs in the genomes of mutant and/or phenotypically unremarkable animals may be grossly underestimated.
- 357–363 **Effects of DNA Methylation and Chromatin State on Rates of Molecular Evolution in Insects**
Karl M. Glastad, Michael A. D. Goodisman, Soojin V. Yi, and Brendan G. Hunt
 Epigenetic information is an important mediator of the genotype-phenotype relationship. However, the influence of epigenetics on the evolution of genes remains poorly understood. The authors studied epigenetic contributions to gene evolution, demonstrating that DNA methylation strongly influences synonymous substitutions. However, a comparison of gene evolution in ants that exhibit DNA methylation to flies that lack DNA methylation revealed that observed variation in substitution rates was explained by underlying chromatin structure, rather than the mutational effect of DNA methylation itself. Thus, chromatin structure is the primary epigenetic driver of gene evolution in insects.
- 365–376 **Dynamics of Dark-Fly Genome Under Environmental Selections**
Minako Izutsu, Atsushi Toyoda, Asao Fujiyama, Kiyokazu Agata, and Naoyuki Fuse
 In this work, Izutsu *et al.* addressed the genetic basis of environmental adaptation using in Dark-fly, an unusual *Drosophila melanogaster* line that has been maintained in constant dark conditions for 60 years. The authors previously determined the whole genome sequence of Dark-fly but did not clarify which genes are really involved in Dark-fly's adaptation. Here, they performed a re-selection experiment with large mixed populations of Dark-fly and the wild-type fly, using light and dark conditions, and analyzed the population genomes across time-course trajectories. They successfully observed condition-dependent selections towards some genomic regions and identified some candidate genes involved in the fitness of Dark-fly.
- 377–390 **Genetic Mapping of Resistance to *Meloidogyne arenaria* in *Arachis stenosperma*: A New Source of Nematode Resistance for Peanut**
Soraya C. M. Leal-Bertioli, Márcio C. Moretzsohn, Philip A. Roberts, Carolina Ballén-Taborda, Tereza C. O. Borba, Paula A. Valdisser, Rosana P. Vianello, Ana Cláudia G Araiújo, Patricia M. Guimarães, and David J. Bertioli
 Root-knot nematodes are a very damaging pest of peanuts. Chemical treatments are expensive and hazardous; the best solution is the use of resistant varieties. Currently, only a single source of resistance is available. There are serious concerns that this resistance could be broken. Here the authors investigated a new source of resistance, the wild species *Arachis stenosperma*. They located resistance genes on three chromosomes and developed DNA markers, which will be used in breeding programs to aid the development of peanut cultivars with this new source of resistance.
- 391–396 **Genetic Determinants of RNA Editing Levels of ADAR Targets in *Drosophila melanogaster***
Yerbol Z. Kurmangaliyev, Sammi Ali, and Sergey V. Nuzhdin
 Analysis of genetic variation is a powerful approach to study the regulatory mechanisms underlying various phenotypic traits. Population-level RNA-Seq data allows us to study the genetic variation in different transcriptomic traits. Previously, analysis of individual transcriptomes has revealed widespread natural variation in gene expression and splicing profiles. Here the authors uncovered a novel type of functional genetic variation affecting the editing of individual ADAR target sites. Their discovery raises a provocative question about the contribution of this variation to diseases and other phenotypes of interest.

- 397–422 **Diversity and Divergence of Dinoflagellate Histone Proteins**
Georgi K. Marinov and Michael Lynch
 Unique among eukaryotes, dinoflagellates have lost nucleosomes as a major constituent of chromatin, yet they have retained histone genes. The authors used sequence data from multiple species to characterize the diversity of histones in dinoflagellates, with a focus on the conservation and divergence of the histone code, and analyzed the set of histone chaperones, chromatin mark readers, writers, and remodelers. The histone code appears to have diverged significantly in some of its components, yet others are conserved. Most importantly, the authors' results strongly suggest that transcription through nucleosomal arrays happens in dinoflagellates. Finally, they discuss the plausible roles of histones in dinoflagellate nuclei.
- 423–433 **MicroRNA Maturation and MicroRNA Target Gene Expression Regulation Are Severely Disrupted in Soybean *dicer-like1* Double Mutants**
Shaun J. Curtin, Jean-Michel Michno, Benjamin W. Campbell, Javier Gil-Humanes, Sandra M. Mathioni, Reza Hammond, Juan J. Gutierrez-Gonzalez, Ryan C. Donohue, Michael B. Kantar, Andrew L. Eamens, Blake C. Meyers, Daniel F. Voytas, and Robert M. Stupar
 Curtin *et al.* used a ZFN reagent to mutate both Dcl1 (Dcl1a and Dcl1b) copies in soybean and show defective miRNA precursor transcript processing efficiency and deregulated miRNA target gene expression in the double *dcl1* mutant soybean plants.
- 435–446 **Tying Down Loose Ends in the *Chlamydomonas* Genome: Functional Significance of Abundant Upstream Open Reading Frames**
Frederick R. Cross
 Genome sequences are only useful when annotated. The *Chlamydomonas* annotation has a very high frequency of upstream ORFs proposed to exist in mRNAs, which could interfere with effective translation. This paper develops and applies methods to “proofread” the annotation with respect to the critical choice of initiator ATG.
- 447–452 **FAST^mC: A Suite of Predictive Models for Nonreference-Based Estimations of DNA Methylation**
Adam J. Bewick, Brigitte T. Hofmeister, Kevin Lee, Xiaoyu Zhang, David W. Hall, and Robert J. Schmitz
 The authors of this work have developed a fully non-referenced method, coined FAST^mC, for accurate estimations of genome-wide DNA methylation. The models they developed are accurate and sensitive to changes in DNA methylation caused by mutations in key proteins, cell-type differences within a species, and changes associated with development. Thus, their models make practical previously intractable studies (e.g., high-resolution time course, developmental, and large diversity panels), regardless of species, genome size and availability of a reference genome. Furthermore, these models could greatly contribute to high-resolution screening of either developmental- or environmental-induced epigenomic reprogramming events.
- 453–462 **Formation of Extrachromosomal Circular DNA from Long Terminal Repeats of Retrotransposons in *Saccharomyces cerevisiae***
Henrik D. Møller, Camilla E. Larsen, Lance Parsons, Anders Johannes Hansen, Birgitte Regenber, and Tobias Mourier
 Circular DNAs are generated from all across the baker's yeast genome. A large proportion of the circular DNAs are derived from transposable elements. It is, however, unknown whether these circles are the product of circularization of episomal double-stranded DNA that is part of the elements' life cycle or whether they are generated through intra-chromosomal recombination events. The presented analysis strongly suggests that circular DNAs containing transposable elements are predominantly derived from chromosomal recombination between the long terminal repeats flanking the transposable elements. This opens the possibility of transposable elements moving around in the genome through circularization events.
- 463–474 **Genome-Wide Analysis of the TORC1 and Osmotic Stress Signaling Network in *Saccharomyces cerevisiae***
Jeremy Worley, Arron Sullivan, Xiangxia Luo, Matthew E. Kaplan, and Andrew P. Capaldi
 Worley *et al.* developed a novel automated pipeline and used it to measure the expression of a TORC1 dependent ribosome biogenesis gene (NSR1) during osmotic stress in 4700 *Saccharomyces cerevisiae* strains from the yeast knock-out collection. This led to the identification of 440 strains with significant and reproducible defects in NSR1 repression. The cell growth control and stress response proteins deleted in these strains form a highly connected network, including 56 proteins involved in vesicle trafficking and vacuolar function, 53 proteins that act downstream of TORC1, over 100 proteins involved in signaling and metabolism, and 17 proteins that directly interact with TORC1.

- 475–484 **Back to Acid Soil Fields: The Citrate Transporter SbMATE Is a Major Asset for Sustainable Grain Yield for Sorghum Cultivated on Acid Soils**
Geraldo Carvalho Jr, Robert Eugene Schaffert, Marcos Malosetti, Joao Herbert Moreira Viana, Cicero Bezerra Menezes, Lidianne Assis Silva, Claudia Teixeira Guimaraes, Antonio Marcos Coelho, Leon V. Kochian, Fred A. van Eeuwijk, and Jurandir Vieira Magalhaes

Abiotic stress tolerance genes have been cloned in crops, but their usefulness for breeding is frequently unknown. Aluminum toxicity limits agriculture on acid soils, which comprise half of the world's lands. The SbMATE gene confers aluminum tolerance in sorghum. To determine SbMATE's real world impact, multi-trait analysis revealed a QTL colocalized with SbMATE that increased grain yield by 0.6 ton ha⁻¹ without yield reduction in the absence of toxicity. An allele effect of 0.5 ton ha⁻¹ shows that SbMATE also functions in hybrids. SbMATE is thus indispensable for food security on acid soils, which are common in developing countries.

MUTANT SCREEN REPORT

- 485–494 **A Genome-Wide Screen with Nicotinamide to Identify Sirtuin-Dependent Pathways in *Saccharomyces cerevisiae***
John S. Choy, Bayan Qadri, Leah Henry, Kunal Shroff, Olatomiwa Bifarin, and Munira A. Basrai

Sirtuins are a class of enzymes called lysine deacetylases, which serve important roles in packaging DNA and in longevity extension in yeast and animals. To gain greater insight into sirtuin function, Choy *et al.* performed a genome-wide screen for yeast mutants that are sensitive to the sirtuin inhibitor, nicotinamide (NAM). This approach allowed the authors to determine nearly all processes that depend on sirtuin activity. Their results reveal a set of novel genes that interact with sirtuins and point to a variety of processes that sirtuins influence that impact genome stability. This work provides an important resource for future studies of sirtuin biology.

495 **CORRIGENDUM**

497 **CORRIGENDUM**