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INVESTIGATIONS

- 1363–1372 **Insight Into Genomic Changes Accompanying Divergence: Genetic Linkage Maps and Synteny of *Lucania goodei* and *L. parva* Reveal a Robertsonian Fusion**
Emma L. Berdan, Genevieve M. Kozak, Ray Ming, A. Lane Rayburn, Ryan Kiehart, and Rebecca C. Fuller
 Linkage maps are fundamental tools in evolutionary genetics. Here, the authors created linkage maps for two closely related killifish species, *Lucania goodei* and *L. parva*. Synteny comparisons between closely related species can illuminate changes in genomic architecture that accompany divergence. Comparison of synteny between the species maps revealed that a chromosomal fusion has likely occurred in the *L. parva* lineage. These maps will be critical in determining the role of chromosomal fusion in this speciation event and for future QTL mapping studies in *Lucania* and related species.
- 1373–1384 **Essential Domains of *Schizosaccharomyces pombe* Rad8 Required for DNA Damage Response**
Lin Ding and Susan L. Forsburg
Schizosaccharomyces pombe Rad8 is homologous to *S. cerevisiae* and human Rad5. Among its three conserved domains, the E3 ligase and HIRAN domains are required for proper DNA damage response, but unexpectedly, the authors observed no phenotype with mutations in the helicase domain. They examined a panel of non-essential helicase mutants and found they clustered into five phenotypic groups. The rad8 helicase mutation shows synthetic interactions with a subset of recombination mutants. Their data suggest that the Rad8 ubiquitin ligase activity is primarily important for damage response, while the helicase domain plays only minor role during specific forms of replication stress.
- 1385–1394 **Validation of Six Genetic Determinants of Susceptibility to Estrogen-Induced Mammary Cancer in the Rat and Assessment of Their Relevance to Breast Cancer Risk in Humans**
John A. Colletti II, Kristin M. Leland-Wavrin, Scott G. Kurz, Maureen Peters Hickman, Nicole L. Seiler, Nyssa Becker Samanas, Quincy A. Eckert, Kirsten L. Dennison, Lina Ding, Beverly S. Schaffer, and James D. Shull
 Congenic rat strains were generated and characterized to confirm the existence of six genetic loci that determine susceptibility to 17 β -estradiol-induced mammary cancer in the rat. The relevance of these loci to breast cancer risk in humans is discussed.
- 1395–1405 **Fluorescence *In Situ* Hybridization and Optical Mapping to Correct Scaffold Arrangement in the Tomato Genome**
Lindsay A. Shearer, Lorinda K. Anderson, Hans de Jong, Sandra Smit, José Luis Goicoechea, Bruce A. Roe, Axin Hua, James J. Giovannoni, and Stephen M. Stack
 Sequenced scaffolds in the tomato genome were recently assembled into pseudomolecules based on the order of markers in a high density linkage map. Here the authors use two independent physical methods, fluorescence *in situ* hybridization (FISH) and optical mapping, to evaluate this assembly and find that scaffolds representing a third of the sequenced genome and several thousand genes were incorrectly ordered and/or oriented. These scaffolds were largely, but not exclusively, in pericentric heterochromatin where crossing over is suppressed, suggesting that other large genomes that have been assembled using linkage maps alone may have similar assembly problems.

- 1407–1416 **Population Dynamics and Evolutionary History of the Weedy Vine *Ipomoea hederacea* in North America**
Brandon E. Campitelli and John. R. Stinchcombe
 This study explores nuclear DNA sequences in the highly selfing, weedy vine *Ipomoea hederacea*—whose geographic origin is unknown, but previous evidence reveals strong adaptive signals—to establish hypotheses of the evolutionary processes that may have shaped its patterns of genetic variation. Results revealed ubiquitously and remarkably low levels of genetic diversity, and significant population structure; however, genetic structuring is patchy and cannot reconcile the documented patterns of adaptation. The authors discuss hypotheses for the population dynamics that may influence the patterns they observe, and the challenge of detecting selection in the face evolutionary forces that should mask adaptive signals.
- 1417–1427 **Genetic Interactions Between P Elements Involved in piRNA-Mediated Repression of Hybrid Dysgenesis in *Drosophila melanogaster***
Michael J. Simmons, Marshall W. Meeks, Erik Jessen, Jordan R. Becker, Jared T. Buschette, and Michael W. Thorp
 Transposons are regulated by small RNAs that interact with the Piwi class of proteins—the so-called piRNAs. For the P transposons of *Drosophila melanogaster*, this regulation is anchored in elements situated within repeated DNA at a telomere of the X chromosome. This regulation is markedly enhanced when two telomeric P elements are present. A maternal effect, called presetting, contributes to this synergism. Regulation is also strengthened by genetic interactions between telomeric and non-telomeric P elements, possibly because their piRNAs and mRNAs feed a cycle that amplifies the overall piRNA pool.
- 1429–1444 **Genomic Profiling of Collaborative Cross Founder Mice Infected with Respiratory Viruses Reveals Novel Transcripts and Infection-Related Strain-Specific Gene and Isoform Expression**
Hao Xiong, Juliet Morrison, Martin T. Ferris, Lisa E. Gralinski, Alan C. Whitmore, Richard Green, Matthew J. Thomas, Jennifer Tisoncik-Go, Gary P. Schroth, Fernando Pardo-Manuel de Villena, Ralph S. Baric, Mark T. Heise, Xinxia Peng, and Michael G. Katze
 The reference mouse annotation is heavily based on one mouse strain and may not accurately reflect the transcriptional complexity of mouse transcriptomes. Therefore to compare the transcriptomes of genetically diverse mice, the authors infected eight mouse strains with flu and SARS viruses and sequenced 124 lung samples. They found 221,870 instances of putative novel transcripts not recorded in the reference annotation. Many of the new transcripts were differentially expressed, pointing to potential functional roles in the host response. Differential isoform expression were inferred from 4287 instance of alternative splicing junction differential expression and 59 genes showed *cis*-regulated isoform differential expression.
- 1445–1453 ***BZcon1*, a SANT/Myb-Type Gene Involved in the Conidiation of *Cochliobolus carbonum***
Jun-xiang Zhang, Yi-xin Wu, Honhing Ho, Hao Zhang, Peng-fei He, and Yue-qiu He
 Asexual spores play a major role in the epidemics of some phytopathogenic fungi, and so deciphering the molecular mechanisms involved in conidiation development is a prerequisite to provide novel strategies for disease management. The authors report a novel gene, *BZcon1*, is essential for asexual spore formation in *C. carbonum*. Interestingly, they also found of *BZcon1* homologs in *Aspergillus nidulans*, *Neurospora crassa* and *Candida albicans*. Thus, these findings suggest that *C. carbonum* should also be a candidate model fungus with great potentials to provide new insights into the molecular mechanisms in the conidiation of fungi.
- 1455–1464 **Construction of a Microsatellites-Based Linkage Map for the White Grouper (*Epinephelus aeneus*)**
Lior Dor, Andrey Shirak, Sergei Gorshkov, Mark R. Band, Abraham Korol, Yefim Ronin, Arie Curzon, Gideon Hulata, Eyal Seroussi, and Micha Ron
 The white grouper (*Epinephelus aeneus*) is a promising candidate for domestication and aquaculture due to its fast growth, excellent taste and high market price. 222 microsatellites markers were developed based on deep-sequencing data. A first generation linkage map was constructed with all markers assigned to 24 linkage groups in accordance with the 24 chromosomal pairs. The male map is compressed in comparison to the female map. Comparative mapping showed high synteny relationships among the white grouper, kelp grouper (*E. bruneus*) and orange-spotted grouper (*E. coioides*) thus indicating the potential of integration of markers into a comprehensive consensus map of groupers.

- 1465–1478 **Association Mapping of Germination Traits in *Arabidopsis thaliana* Under Light and Nutrient Treatments: Searching for G×E Effects**
Ginnie D. Morrison and C. Randal Linder
 The authors feel that there is a general need to examine complex traits under different environmental conditions. While complex traits have been extensively studied in the past, a continuing challenge is identifying natural variation for such traits and further, the genetic basis for these complex traits in different environments. To help address this challenge, they used genome-wide association mapping to look for genes potentially influencing germination under different light and nutrient conditions.
- 1479–1489 **Interplay of Interlocus Gene Conversion and Crossover in Segmental Duplications Under a Neutral Scenario**
Diego A. Hartasánchez, Oriol Vallès-Codina, Marina Brasó-Vives, and Arcadi Navarro
 This study represents an important new step towards the understanding of patterns of variation and linkage disequilibrium in segmental duplications by exploring the complex interplay between interlocus gene conversion and crossover. In order to do so, the authors have created a tool that can now be used to gain knowledge on the molecular evolution of duplicated genomic regions in a broad range of scenarios.
- 1491–1501 **Linking Genetics to Structural Biology: Complex Heterozygosity Screening with Actin Alanine Scan Alleles Identifies Functionally Related Surfaces on Yeast Actin**
Stephanie DiPrima, Brian Haarer, Susan Viggiano, Carles Pons, Chad L. Myers, and David C. Amberg
 Many genetic disorders arise due to the interactions between alleles of multiple genes and it can be difficult to identify the contributing genes. Yeast genetics was used to construct diploid, complex heterozygotes between 32 actin site-directed mutants and null alleles of 238 genes known to interact genetically with actin. The actin alleles were then grouped by similarity of their genetic interactions and those groups were mapped onto the structure of the actin protein. These groups appear to identify regions of the surface that have functional commonality e.g. binding sites. This is the first structurally correlated genetic interaction network.
- 1503–1514 **Pattern of Mutation Rates in the Germline of *Drosophila melanogaster* Males from a Large-Scale Mutation Screening Experiment**
Jian-Jun Gao, Xue-Rong Pan, Jing Hu, Li Ma, Jian-Min Wu, Ye-Lin Shao, Shi-Meng Ai, Shu-Qun Liu, Sara A. Barton, Ronny C. Woodruff, Ya-Ping Zhang, and Yun-Xin Fu
 The authors report the data of a large scale mutation screening experiment and its analysis. They show that the recessive lethal or nearly lethal mutation rate at first cell division is in general even higher when compared with those previously reported; the second division rate drops rapidly but it is still appreciably higher than the rest of the cleavage stages. However, no evidence of different mutation rates are found among the five cell divisions of spermatogenesis. Examination of the dynamics of the germline population shows that there is modestly biased sampling leading to slightly more primordial germ cells.
- 1515–1527 **Differentiation State-Specific Mitochondrial Dynamic Regulatory Networks Are Revealed by Global Transcriptional Analysis of the Developing Chicken Lens**
Daniel Chauss, Subhasree Basu, Suren Rajakaruna, Zhiwei Ma, Victoria Gau, Sara Anastas, Lisa A. Brennan, J. Fielding Hejtmancik, A. Sue Menko, and Marc Kantorow
 The eye lens is a useful model to elucidate mitochondrial dynamic pathways since mitochondria are required by the lens epithelium for homeostasis while mitochondria must be eliminated from differentiating lens fiber cells for transparency. Chauss *et al.* used a high-throughput RNA sequencing and bioinformatics approach to elucidate the entire range and spectrum of transcripts expressed by differentiating regions of the lens and identified those specific for mitochondrial regulation and degradation. The work establishes those pathways that operate to maintain mitochondria in lens epithelial cells and degrade mitochondria in differentiating lens fiber cells.

- 1529–1538 **Histone H2B Ubiquitination Promotes the Function of the Anaphase-Promoting Complex/Cyclosome in *Schizosaccharomyces pombe***
Zachary C. Elmore, Janel R. Beckley, Jun-Song Chen, and Kathleen L. Gould
- Ubiquitination and deubiquitination of proteins are reciprocal events involved in many cellular processes, including the cell cycle. During mitosis, the metaphase to anaphase transition is regulated by the ubiquitin ligase activity of the anaphase-promoting complex/cyclosome (APC/C). However, it is not clear if deubiquitinating proteases (DUBs) play a role in reversing APC/C substrate ubiquitination. Here, the authors report a role for the SAGA complex DUB, Ubp8, in antagonizing the function of the APC/C through the modulation of histone H2B ubiquitination status rather than reversing substrate ubiquitination. This work identifies a new link between chromatin state and cell cycle progression mediated by DUBs.
- 1539–1553 **Harnessing Natural Sequence Variation to Dissect Posttranscriptional Regulatory Networks in Yeast**
Mina Fazlollahi, Eunjee Lee, Ivor Muroff, Xiang-Jun Lu, Pilar Gomez-Alcala, Helen C. Causton, and Harmen J. Bussemaker
- Dynamic control of messenger RNA half-life is an under-appreciated mechanism of gene expression regulation. In this study, the authors investigated to what extent such post-transcriptional control can explain differences in genomewide expression between yeast strains. To this end, using a biophysical network modeling approach, we carefully defined the sequence specificity of a panel of RNA binding proteins, and then searched for genetic polymorphisms that modulated their regulatory activity. The analysis uncovered distinct genetic modulators for the post-transcriptional metabolism regulators Puf3p and Puf4p, and more generally suggests a significant role for post-transcriptional networks as drivers of genetic variation in gene expression.
- 1555–1564 **Proteomic Analysis Reveals CACN-1 Is a Component of the Spliceosome in *Caenorhabditis elegans***
Michael F. Doherty, Guillaume Adelmant, Alyssa D. Cecchetelli, Jarrod A. Marto, and Erin J. Cram
- CACN-1 is a well conserved protein of unknown function that regulates cell migration and other developmental processes. This proteomic study reveals that CACN-1 associates with a tight network of spliceosomal proteins, many of which also regulate developmental cell migration.
- 1565 **CORRIGENDUM**