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COMMENTARY

- 1451–1452 **Functional Genetics in the Post-genomics Era: Building a Better Roadmap in *Drosophila***
Rob J. Kulathinal

In this commentary, Rob Kulathinal discusses two papers from the Perrimon lab that describe new online resources to assist geneticists in the design of their RNAi experiments. Hu *et al.*'s "UP-TORR: online tool for accurate and up-to-date annotation of RNAi reagents" and "FlyPrimerBank: An Online Database for *Drosophila melanogaster* Gene Expression Analysis and Knockdown Evaluation of RNAi Reagents", are published, respectively, in this month's issue of *GENETICS* and the upcoming issue of *G3*.

INVESTIGATIONS AND AUTHOR SUMMARIES

- 1453–1465 **Mutation Rates, Spectra, and Genome-Wide Distribution of Spontaneous Mutations in Mismatch Repair Deficient Yeast**

Gregory I. Lang, Lance Parsons, and Alison E. Gammie

Lynch Syndrome, a leading cause of inherited cancer mortality in the United States, is a consequence of defects in mismatch repair. Cells lacking DNA mismatch repair accumulate mutations at a high rate, but how these mutations are distributed across the genome and how local sequence context affects the rate of mutation remains unknown. These authors used passaged yeast mismatch repair defective cell lines combined with whole-genome sequencing approaches to address questions surrounding mutation rates, mutation accumulation context, and mutation spectra. Their findings provide mechanistic insight into the mutagenic processes in mismatch repair deficient cells.

- 1467–1479 **Sequence Diversity in Coding Regions of Candidate Genes in the Glycoalkaloid Biosynthetic Pathway of Wild Potato Species**

Norma C. Manrique-Carpintero, James G. Tokuhsa, Idit Ginzberg, Jason A. Holliday, and Richard E. Veilleux

Variation among and within tuber-bearing potatoes for genes that contribute to accumulation and quality of steroidal glycoalkaloids (SGAs) in the plant may affect their defense against insects and the flavor and toxicity of the tubers. The authors examined sequence diversity in amplified regions of five genes—three in primary and two in secondary metabolism—along the biochemical pathway leading to SGA production in six wild and one cultivated potato species. Single nucleotide polymorphisms within the amplicons were analyzed for possible effect on SGAs measured in the leaves. The authors discovered that some common allelic differences were associated with SGA production. They found more variation within intronic vs. exonic regions and in the genes of secondary vs. primary metabolism.

- 1481–1492 **Large Scale Full-Length cDNA Sequencing Reveals a Unique Genomic Landscape in a Lepidopteran Model Insect, *Bombyx mori***
Yoshitaka Suetsugu, Ryo Futahashi, Hiroyuki Kanamori, Keiko Kadono-Okuda, Shun-ichi Sasanuma, Junko Narukawa, Masahiro Ajimura, Akiya Jouraku, Nobukazu Namiki, Michihiko Shimomura, Hideki Sezutsu, Mizuko Osanai-Futahashi, Masataka G Suzuki, Takaaki Daimon, Tetsuro Shinoda, Kiyoko Taniai, Kiyoshi Asaoka, Ryusuke Niwa, Shinpei Kawaoka, Susumu Katsuma, Toshiaki Tamura, Hiroaki Noda, Masahiro Kasahara, Sumio Sugano, Yutaka Suzuki, Haruhiko Fujiwara, Hiroshi Kataoka, Kallare P. Arunkumar, Archana Tomar, Javaregowda Nagaraju, Marian R. Goldsmith, Qili Feng, Qingyou Xia, Kimiko Yamamoto, Toru Shimada, and Kazuei Mita
- These authors embarked on a large-scale full-length cDNA collection containing 11,104 full-length cDNAs to perform a complete genome annotation of the domesticated silkworm. The large average intron size was 1904bp, resulting from a high accumulation of transposons. Orthology analysis of 153 species, including 11 insects, revealed the 403 silkworm-specific genes. The authors also discovered distinctive features of sexual dimorphism in their analysis of testis-/ovary-specific genes. Over 40% of genes expressed in specific tissues mapped in tissue-specific chromosomal clusters. The newly-obtained FL-cDNA sequences enabled the authors to annotate the genome more accurately. These new sequences will also enhance genomic and functional studies of Lepidoptera and comparative analyses with other insect orders.
- 1493–1509 **The Developmental Transcriptome of the Mosquito *Aedes aegypti*, an Invasive Species and Major Arbovirus Vector**
Omar S. Akbari, Igor Antoshechkin, Henry Amrhein, Brian Williams, Race Diloreto, Jeremy Sandler, and Bruce A. Hay
- Mosquitoes are vectors of a number of important human and animal diseases. The creation of novel vector control strategies requires a thorough understanding of mosquito biology. To facilitate this process, the authors used RNA-seq to identify novel genes. Here they provide the first high-resolution view of the transcriptome throughout development and in response to blood feeding in a mosquito vector of human disease, *Aedes aegypti*, the primary vector for Dengue and yellow fever.
- 1511–1523 **Fast Genomic Predictions via Bayesian G-BLUP and Multilocus Models of Threshold Traits Including Censored Gaussian Data**
Hanni P. Kärkkäinen and Mikko J. Sillanpää
- The availability of genome-wide sets of molecular markers along with cost-effective genotyping has made genomic estimated breeding values an essential resource in plant and animal breeding. The increased data sets are also placing heavy demands on the estimation methods. While there are numerous fast Bayesian estimation methods available for Gaussian traits, there is a shortage of corresponding models of discrete or censored phenotypes. In this article the authors consider a threshold approach of binary, ordinal, and censored Gaussian observations for Bayesian multilocus association models and Bayesian G-BLUP. They present a high-speed generalized expectation maximization algorithm for parameter estimation under these models.
- 1525–1530 **Genetic Determinants of Cell Size at Birth and Their Impact on Cell Cycle Progression in *Saccharomyces cerevisiae***
Sandra K. Truong, Ryan F. McCormick, and Michael Polymenis
- Cells of the same genetic background maintain their size during successive rounds of cell division. However, it is not clear how cells regulate their size. Here the authors describe a genome-wide survey of genes that determine size at birth. Different groups of genes contribute to a small or large size at birth. Interestingly, mutants that are born large will likely stay large, and they do not divide faster. Cells that are born small are more likely to divide slower. This work will pave the way for a better understanding of cell size control.

- 1531–1538 **Combinatorial Effects of Transposable Elements on Gene Expression and Phenotypic Robustness in *Drosophila melanogaster* Development**
Alexa W. Clemmons and Steven A. Wasserman
- Mutations are genetic perturbations that can disrupt embryonic development, but they usually do so in an invariant manner. These authors were therefore intrigued by a set of alleles for a *Drosophila melanogaster* gene called *tube* that causes hypervariable defects in dorsoventral patterning. They identified a transposon near the *tube* gene in these alleles and found that it reduces mean *tube* expression in a context-specific manner. Here they show that additional transposon insertions interact with the primary insertion to synergistically disrupt *tube* expression. These hypervariable alleles provide a readout of stochastic processes in the cell and help demonstrate the impact transposons can have on gene expression and development.
- 1539–1543 **The Development of a Monoclonal Antibody Recognizing the *Drosophila melanogaster* Phosphorylated Histone H2A Variant (γ -H2AV)**
Cathleen M. Lake, Julie Korda Holsclaw, Stephanie P. Bellendir, Jeff Sekelsky, and R. Scott Hawley
- These authors have developed a monoclonal antibody to the phospho-specific form of histone H2A variant in *Drosophila melanogaster*. Using a variety of techniques, they characterized the specificity of this antibody in the recognition of double strand breaks in meiotic tissue, cell culture, and whole tissue. This antibody will be widely used in the *Drosophila* community for the study of many processes including DNA repair, meiotic recombination, DNA damage response and post-translational processing of histones.
- 1545–1552 **Mitochondrial DNA with a Large-Scale Deletion Causes Two Distinct Mitochondrial Disease Phenotypes in Mice**
Shun Katada, Takayuki Mito, Emi Ogasawara, Jun-Ichi Hayashi, and Kazuto Nakada
- Patient studies have suggested that the clinical phenotypes of some mitochondrial diseases might transit from one disease to another (Pearson syndrome [PS] to Kearns-Sayre syndrome [KSS]) in single individuals carrying mitochondrial (mt) DNA with a deletion (Δ mtDNA). However, the precise mechanism by which Δ mtDNA induces different disease phenotypes is unclear. By using a mouse model in which genetic variation was restricted to the load of Δ mtDNA, the authors succeeded in demonstrating that a Δ mtDNA has the pathogenic potential to cause PS-like and KSS-like phenotypes at different ages. They also observed the transition of the two phenotypes in single mice carrying Δ mtDNA.
- 1553–1571 **Identification of Pedigree Relationship from Genome Sharing**
William G. Hill and Ian M. S. White
- Assessing the degree of pedigree relationship between individuals with unknown pedigree is important in studies of human, natural, and agricultural populations. Dense marker data provide the opportunity to utilize all information on relationship from the numbers and distribution of shared genome segments, computed by simulation, to discriminate between alternative relationships. Although one can distinguish with some power between different degrees of relationship and also between those of the same degree but different pedigree (e.g. uncle-nephew and half sibs), discrimination is poor unless the degree of relationship is quite high.
- 1573–1576 **Maternal Loss of miRNAs Leads to Increased Variance in Primordial Germ Cell Numbers in *Drosophila melanogaster***
Jan-Michael Kugler, Ya-Wen Chen, Ruifen Weng, and Stephen M. Cohen
- microRNAs (miRNAs) are important post-transcriptional regulators of gene expression. Because miRNAs have been shown to be able to fine-tune target transcript levels, it has been suggested that miRNAs may confer robustness to developmental processes. However, there is little quantitative evidence supporting this hypothesis thus far. In this study, the authors identified two *Drosophila melanogaster* miRNAs that are maternally required to stabilize a quantitative phenotypic trait: primordial germ cell numbers in the embryo. This observation is consistent with the idea that these miRNAs confer robustness to this developmental process.

- 1577–1585 **Effects of Body-Color Mutations on Vitality: An Attempt to Establish Easy-to-Breed See-Through Medaka Strains by Outcrossing**
Ayaka Ohshima, Noriko Morimura, Chizuru Matsumoto, Ami Hiraga, Ritsuko Komine, Tetsuaki Kimura, Kiyoshi Naruse, and Shoji Fukamachi
- The see-through medaka is a unique tool for researches, but it is difficult to breed. Anticipating that heterosis should increase its vitality, the authors outcrossed two see-through strains to a genetically divergent wild-type strain. The F₂s with the see-through phenotypes were restored. Although genome-wide genotyping elucidated that the hybrid strains actually have the mixed genomic background, neither viability nor fecundity was improved. The results also indicated that four of the five see-through mutations additively reduce vitality. Given that the outcrosses could not overwhelm the effects from the mutations, more complex methods seem to be required to establish easy-to-breed see-through strains.
- 1587–1595 **The *ben1-1* Brassinosteroid-Catabolism Mutation Is Unstable Due to Epigenetic Modifications of the Intronic T-DNA Insertion**
Kulbir Singh Sandhu, Pushpa Sharma Koirala, and Michael M. Neff
- T-DNA insertion mutants are heavily used in the plant research community. This article highlights certain undesirable aspects of T-DNA-intronic insertion mutants. When present in the same genetic background, multiple T-DNAs can interact in a complex manner, including transgene silencing and enhanced intron splicing. The authors show that these interaction effects can also be inherited epigenetically in the following generations. This complicates the genetic analysis for which the T-DNA insertion mutants are commonly used. The authors further suggest that DNA methylation contributes to the molecular mechanism resulting in this complex genetic interaction among T-DNAs.
- 1597–1605 **Transcriptome Profiling of *Nasonia vitripennis* Testis Reveals Novel Transcripts Expressed from the Selfish B Chromosome, Paternal Sex Ratio**
Omar S. Akbari, Igor Antoshechkin, Bruce A. Hay, and Patrick M. Ferree
- The Paternal Sex Ratio (PSR) chromosome is a non-essential, paternally-transmitted centric fragment that segregates in natural populations of the jewel wasp, *Nasonia vitripennis*. To begin to understand this system at the mechanistic level, these authors carried out transcriptional profiling of testis from wild type and PSR-carrying males. They were able to identify a number of transcripts that are differentially expressed between these conditions.
- 1607–1616 **FlyPrimerBank: An Online Database for *Drosophila melanogaster* Gene Expression Analysis and Knockdown Evaluation of RNAi Reagents**
Yanhui Hu, Richelle Sopko, Marianna Foes, Colleen Kelley, Ian Flockhart, Noemie Ammeux, Xiaowei Wang, Elizabeth Perkins, Norbert Perrimon, and Stephanie E. Mohr
- Evaluating the levels of RNA transcripts is important to a wide range of studies. Quantitative real-time PCR (qPCR) is a common approach for evaluating RNA levels, used either on its own or as a follow-up to high-throughput approaches such as microarray or RNA-seq. Designing high-quality qPCR primers is not trivial. We have developed and experimentally validated a genome-wide qPCR primer resource for *Drosophila*, FlyPrimerBank, and made the resource available online. FlyPrimerBank allows researchers to identify and view primer sets, evaluation data, etc. as well as to submit their own validated primers and data to further improve the resource
- 1617 **CORRIGENDUM**